ISSN 2587-9596 (Online) 16+

ACTA BIOMEDICA SCIENTIFICA

Vol. 8
N 5
2023

ISSN 2587-9556 (Online) 16+

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Address of publisher and editorial board: SC FHHRP. 16 Timiryazev str., Irkutsk, Russia, 664003
Tel. (3952) 20-90-48.
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Acta Biomedica Scientifica is registered in Federal Service of Supervision in communication sphere, information technologies and mass media (ROSKOMNADZOR). Certificate of Mass Media Registration – PI No FS 77-69383 from 06 April 2017.

Previous title changed after April 2017 – "Bulletin of Eastern-Siberian Scientific Center of Siberian Branch of the Russian Academy of Medical Sciences".

Acta Biomedica Scientifica has been founded in 1993.
Co-founders – Scientific Centre for Family Health and Human Reproduction Problems (16 Timiryazev str., Irkutsk, Russia, 664003), Irkutsk Scientific Centre of Surgery and Traumatology (1 Bortsov Revolyutsii str., Irkutsk, Russia, 664003), S. Fyodorov Eye Microsurgery Federal State Institution (59A Beskudnikovskiy blvd, Moscow, 127486).
Acta Biomedica Scientifica is in Abstract Journal and Data base of All-Russian Institute of Scientific and Technical Information. Information about our journal is published in Ulrich's Periodicals Directory. The journal is indexed in Russian Science Citation Index (Russian platform), Scopus, DOAJ, etc.
Acta Biomedica Scientifica is included in «List of Russian reviewed scientific periodicals where main scientific results of dissertations for a degree of Candidate and Doctor of Science should be published».

Subscription index is 24347 in Russia. Open price.

ISSN 2541–9420 (Print)
ISSN (Online) 2587-9596
Key title: Acta Biomedica Scientifica

ISSN 2587-9556 (Online)

16+

ACTA BIOMEDICA SCIENTIFICA

Том 8
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Тел.: (3952) 20-90-48.
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Журнал «Acta Biomedica Scientifica» зарегистрирован в Федеральной службе по надзору в сфере связи, информационных технологий и массовых коммуникаций (РОСКОМНАДЗОР). Свидетельство о регистрации СМИ – ПИ № ФС 77–69383 от 06 апреля 2017 г.

До апреля 2017 г. журнал имел название «Бюллетень Восточно-Сибирского научного центра Сибирского отделения Российской Академии медицинских наук» (Бюллетень ВСНЦ СО РАМН). Основан в 1993 году.

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Журнал «Acta Biomedica Scientifica» входит в «Перечень ведущих рецензируемых научных журналов и изданий, выпускаемых в Российской Федерации, в которых должны быть опубликованы основные научные результаты диссертаций на соискание учёной степени кандидата и доктора наук».

Подписной индекс 243447. Свободная цена.

ISSN 2541–9420 (Print)
ISSN 2587–9596 (Online)
Ключевое название: Acta Biomedica Scientifica

DEPUTY EDITOR-IN-CHIEF'S PREFACE

DEPUTY EDITOR-IN-CHIEF'S PREFACE TO ISSUE 5, 2023

Vladimir A. Sorokovikov

Dr. Sc. (Med.), Professor

Dear readers!

Here is the latest issue of the Acta Biomedica Scientifica, which includes works on topical issues of Russian medical science and practical healthcare.

The leading article in this issue, in my opinion, is the article by V.A. Koryak et al. (Irkutsk) "Assessing socio-economic damage caused by coxarthrosis in the population" which examines an important problem – assessing the value and structure of economic damage in connection with the provision of medical and social care to the patients with coxarthrosis at the state level of the Russian Federation. Using the example of the Irkutsk region, the authors showed that the average annual socio-economic damage from coxarthrosis reaches 0.1 % of the gross regional product. At the same time, the most of the damage (64.4 %) consists of indirect costs due to disability. The results of the study confirm the economic feasibility of surgical treatment of coxarthrosis, especially in patients of working age.

The largest section of the journal is devoted to the problems of traumatology and orthopedics. Among these articles, the work by D.V. Menshova et al. (Irkutsk) "Assessment of the effectiveness of surgical treatment of patients with massive tears of the rotator cuff tendons using arthroscopically assisted transposition of the latissimus dorsi tendon" is of great interest. It demonstrates an original method of treatment of this severe pathology. World experience in treatment of massive rotator cuff tears is summarized in the articles of D.V. Menshova (Irkutsk) and E.N. Slaikovskiy et al. (Irkutsk).

Traditionally, our journal publishes scientific reviews. In this issue, we should highlight a review concerning the rehabilitation of patients with unstable injuries of the pelvic ring by A.A. Melkostupov et al. (Irkutsk). The possibilities of verticalization of patients and using axial load on the lower extremities in the postoperative period are considered as the main rehabilitation measures. It is noted that when resolving the issue of axial load in case of unstable pelvic ring injury, the value of the load and the timing of its start should be determined individually, depending on the physical condition of the patient, the characteristics of the injury and the presence of concomitant injuries.

N.A. Sholokhova et al. (Moscow) in their article "The current state of the issue of using cone beam computed tomography in the diagnosis of musculoskeletal diseases" showed that cone-beam computed tomography is a modern and promising technique which can contribute to the assessing the shape and contour of the bone, the solution of continuity of the bone and the position of bone fragments, the structure of bone tissue and the pathological processes in it (destruction, osteoporosis, osteosclerosis), joint congruence and changes in articular surfaces surrounding soft tissues. The authors believe that this technique will find wide application in traumatology and orthopedics.

M.L. Lebed et al. (Irkutsk) in the article "Acute kidney injury after primary total hip replacement" established that acute kidney injury was detected in 7.3 % of patients who after primary total hip replacement. Low initial blood hemoglobin concentrations have been identified as risk factors for the development of this complication, which may indicate a prerenal mechanism for the pathogenesis of this condition.

In the article by A.I. Plakhov et al. (Irkutsk) "Microcirculation parameters of the damaged segment of the lower extremity after treatment of diaphyseal fractures using a locked intramedullary nail", the authors studied microcirculation parameters of injured leg bones during fragments fixation with locked intramedullary nail in the early postoperative period. A disorder in local circulation of the ischemic type with compensation due to the anastomoses inclusion was revealed.

V.E. Potapov et al. (Irkutsk) in their article raise the problem of treating dysfunction of the dynamic stabilization system in the lumbar spine. The study shows that in a number of patients, discectomy and dynamic stabilization of the spine with the Coflex system are followed by failure and heterotypic ossification of the implant, and development of neoarthrosis. Implantation of a lumbar peek cage while maintaining the Coflex device allows for the formation of a rigid interbody fusion, that is, it is a sufficient and well-grounded surgical technology for treating the failure of the dynamic stabilization structure.

V.G. Fedorov and I.V. Kuzin (Izhevsk) in the article "The results of treatment of femoral diaphysis fractures using locked intramedullary osteosynthesis and extramedullary osteosynthesis (results for 10 years)" showed the undeniable advantage of using locked intramedullary osteosynthesis compared to external osteosynthesis in the treatment of femoral fractures.

V.M. Prokhorenko and Yu.A. Afanasiev (Novosibirsk) in their article present surgical treatment of intra-articular fractures of the proximal humerus using autoplasty with a non-free osteomuscular graft from the coracoid process and demonstrate its effectiveness.

Among the articles describing clinical cases, we can highlight an article by L.K. Skuratova et al. (Novosibirsk) "The possibility of a favourable outcome and reversibility of severe ankle joint damage on the example of a clinical observation" which demonstrated the possibility of early diagnosis of aseptic necrosis of the talus and regression of pathological changes.

The article by A.E. Medvedchikov et al. (Novosibirsk) presents a clinical example of using a new technique of reinsertion with two cortical buttons in complete rupture of distal biceps.

An interesting case of successful stepwise treatment of a rare foot pathology – bilateral brachymetatarsia with shortening of the third and fourth metatarsal bones in combination with valgus deviation of the first toe – is presented in the article of I.V. Usoltsev et al. (Irkutsk).

The work of K.B. Lelyavin et al. (Irkutsk) from the "Oncology" section is devoted to demonstrating clinical observation of a case of testicular diffuse large B-cell lymphoma.

The section "Neurology and Neurosurgery" is represented by an article by V.A. Sorokovikov et al. (Irkutsk) "Experience of unilateral and bilateral transpedicular fixation in degenerative diseases of the lumbar spine", which demonstrates that unilateral decompressive and stabilizing interventions in patients with posterolateral and foraminal hernias of the lumbar spine can reduce the duration of the surgery and the severity of pain in the postoperative period due to adequate decompression of the neurovascular formations of the spinal canal and stabilization of the spinal motion segment, which prevents relapse of the disease and ensures early rehabilitation of patients.

The "Surgery" section opens with an article by A.G. Muradov et al. (Krasnoyarsk) "Short-term and long-term results of bimammary bypass surgery in patients with multivessel coronary disease and type 2 diabetes mellitus after propensity score matching" which proved that bimammary bypass surgery in patients with type 2 diabetes mellitus is a safe and effective method of surgical treatment for coronary heart disease both in the short and long term and can be the operation of choice in patients with multi-vessel disease.

The article by E.A. Ilyicheva et al. "Quality of life of patients with single and multigland parathyroid disease in sporadic primary hyperparathyroidism before and after surgical treatment" has proved that surgical tactics aimed at reducing the frequency of persistence of hyperparathyroidism can achieve an improvement in the quality of life in most patients with multigland parathyroid disease in case of primary hyperparathyroidism. The second work of these authors is also devoted to the problem of morphological diagnosis of hyperparathyroidism, and it was established that multigland parathyroid disease in any clinical variant of hyperparathyroidism is characterized by a predominance of hyperplasia: 80 % in primary and 100 % in secondary and tertiary hyperparathyroidism.

The article by E.A. Anastasieva et al. (Novosibirsk) "Restoration of X-ray bone density when replacing cortical plate defects with a tissue-engineered construct in the experiment" is undoubtedly of great interest to readers; it was experimentally proven that the use of a tissue-engineered construct based on deproteinized cancellous bone with a stromal-vascular fraction of adipose tissue to fill perforation defects in the cortical plate of the rabbit femur results in to early restoration of X-ray bone density in the defect area.

Readers can also be interested in scientific reviews by A.V. Nevezhina and T.V. Fadeeva (Irkutsk), dedicated to the study of the antimicrobial potential of iodine-containing substances and materials, and N.N. Dremina et al. (Irkutsk), considering the use of natural components as the structure of hydrogels for cell therapy and tissue engineering.

Here's another issue for you!

For citation: Sorokovikov V.A. Deputy Editor-in-Chief's preface to Issue 5, 2023. *Acta biomedica scientifica.* 2023; 8(5): 5-10. doi: 10.29413/ABS.2023-8.5.1

ПРЕДИСЛОВИЕ ЗАМЕСТИТЕЛЯ ГЛАВНОГО РЕДАКТОРА К № 5 (2023)

Сороковиков Владимир Алексеевич

доктор медицинских наук, профессор

Уважаемые читатели!

Перед Вами свежий номер журнала «Acta Biomedica Scientifica», в котором опубликованы работы по актуальным вопросам российской медицинской науки и практического здравоохранения.

Передовой статьёй данного номера, на мой взгляд, является статья В.А. Корьяк и соавт. (Иркутск) «Опыт оценки социально-экономического ущерба, обусловленного заболеваемостью населения коксартрозом», в которой рассматривается важная проблема – оценка величины и структуры экономического ущерба в связи с оказанием медицинской и социальной помощи пациентам с коксартрозом на уровне субъекта Российской Федерации. На примере Иркутской области показано, что среднегодовой социально-экономический ущерб от коксартроза достигает 0,1 % от валового регионального продукта. При этом основную часть ущерба (64,4 %) составляют непрямые затраты в связи с инвалидностью. Результаты исследования подтверждают экономическую целесообразность хирургического лечения коксартроза, особенно у пациентов трудоспособного возраста.

Самый большой раздел журнала посвящён проблемам травматологии и ортопедии. В этом разделе большой интерес представляет статья Д.В. Меньшовой и соавт. (Иркутск) «Оценка эффективности хирургического лечения пациентов с массивными разрывами сухожилий вращательной манжеты плеча с использованием артроскопически-ассистированной транспозиции сухожилия широчайшей мышцы спины», в которой продемонстрирована оригинальная методика лечения пациентов с этой тяжёлой патологией. Мировой опыт лечения пациентов с массивными разрывами вращательной манжеты плеча обобщён в работах Д.В. Меньшовой (Иркутск) и Е.Н. Слайковского и соавт. (Иркутск).

Традиционно журнал публикует научные обзоры. В данном номере журнала следует выделить обзор, касающийся вопросов реабилитации пациентов с нестабильными повреждениями тазового кольца, представленный А.А. Мелкоступовым и соавт. (Иркутск). В качестве основных реабилитационных мероприятий рассматриваются возможности вертикализации пациентов и применения осевой нагрузки на нижние конечности в послеоперационном периоде. Отмечено, что в случае решения вопроса осевой нагрузки при нестабильном повреждении тазового кольца величина такой нагрузки и сроки начала её применения должны определяться индивидуально, в зависимости от физического состояния пациента, особенностей травмы и наличия сопутствующих повреждений.

Н.А. Шолохова и соавт. (Москва) в статье «Современное состояние вопроса использования конусно-лучевой компьютерной томографии в диагностике заболеваний опорно-двигательного аппарата» показали, что конусно-лучевая компьютерная томография – современная и перспективная методика, с помощью которой можно оценить форму и контур кости, наличие нарушения целостности кости и положение костных отломков, структуру костной ткани и протекающие в ней патологические процессы (деструкция, остеопороз, остеосклероз), конгруэнтность сустава и изменения суставных поверхностей, окружающие мягкие ткани. Авторы полагают, что данная методика найдёт широкое применение в травматологии и ортопедии.

М.Л. Лебедь и соавт. (Иркутск) в статье «Острое повреждение почек после первичного тотального эндопротезирования тазобедренного сустава» установили, что острое повреждение почек выявлено у 7,3 % пациентов, перенёсших первичное тотальное эндопротезирование тазобедренного сустава. В качестве факторов риска развития данного осложнения установлены низкие показатели исходной концентрации гемоглобина крови, что мо-

жет свидетельствовать в пользу преренального механизма патогенеза данного состояния.

В статье А.И. Плахова и соавт. (Иркутск) «Параметры микроциркуляции повреждённого сегмента нижних конечностей после лечения диафизарных переломов с помощью блокируемого интрамедуллярного гвоздя» в раннем послеоперационном периоде изучены показатели микроциркуляции травмированных костей голени при фиксации фрагментов блокируемым интрамедуллярным гвоздём. Выявлено нарушение местного кровообращения по ишемическому типу с компенсацией за счёт включения анастамозов.

В.Э. Потапов и соавт. (Иркутск) в своей статье поднимают проблему лечения дисфункции системы динамической стабилизации поясничного отдела позвоночника. Проведённое исследование свидетельствует о том, что у ряда пациентов после дискэктомии и динамической стабилизации позвоночника системой Coflex развиваются несостоятельность и гетеротипическая оссификация импланта, формируется неоартроз. Имплантация поясничного peek-кейджа при сохранении устройства Coflex позволяет сформировать ригидный межтеловой спондилодез, то есть является достаточной и обоснованной хирургической технологией лечения несостоятельности конструкции динамической стабилизации.

В.Г. Федоров и И.В. Кузин (Ижевск) в статье «Результаты лечения переломов диафиза бедренной кости блокируемым интрамедуллярным и накостным остеосинтезом (итоги за 10 лет)» показали неоспоримое преимущество применения блокируемого интрамедуллярного остеосинтеза по сравнению с накостным остеосинтезом при лечении переломов бедренной кости.

В.М. Прохоренко и Ю.А. Афанасьев (Новосибирск) представляют хирургическое лечение внутрисуставных переломов проксимального отдела плечевой кости методом аутопластики несвободным костно-мышечным трансплантатом из клювовидного отростка лопатки, демонстрируя его эффективность.

Среди статей, описывающих клинические случаи лечения заболеваний, представлена статья Л.К. Скуратовой и соавт. (Новосибирск) «Возможность хорошего исхода и обратимость тяжёлого поражения голеностопного сустава на примере клинического наблюдения», в которой продемонстрирована возможность ранней диагностики асептического некроза таранной кости, регресса патологических изменений.

В статье А.Е. Медведчикова и соавт. (Новосибирск) на клиническом примере показана новая техника реинсерции двумя кортикальными пуговицами при полнослойном повреждении дистального сухожилия двуглавой мышцы плеча.

Интересный случай успешного этапного лечения редкой патологии стопы – двусторонней брахиметатарзии с укорочением III и IV плюсневых костей в сочетании с вальгусным отклонением первого пальца – представлен в работе И.В. Усольцева и соавт. (Иркутск).

Демонстрации клинического наблюдения также посвящена работа К.Б. Лелявина и соавт. (Иркутск), описывающая случай диффузной крупноклеточной В-клеточной лимфомы яичка и представленная в разделе «Онкология».

Раздел «Неврология и нейрохирургия» представлен статьёй В.А. Сороковикова и соавт. (Иркутск) «Опыт одно- и двухсторонней транспедикулярной фиксации при дегенеративных заболеваниях поясничного отдела позвоночника», в которой продемонстрировано, что односторонние декомпрессивно-стабилизирующие вмешательства у пациентов с заднебоковыми и фораминальными грыжами поясничного отдела позвоночника позволяют уменьшить продолжительность операции, выраженность болевого синдрома в послеоперационном периоде за счёт адекватной декомпрессии нервно-сосудистых образований позвоночного канала и стабилизации позвоночно-двигательного сегмента, что предотвращает рецидив заболевания и обеспечивает раннюю реабилитацию пациентов.

Блок работ, посвящённых хирургии, открывает статья А.Г. Мурадова и соавт. (Красноярск) «Ближайшие и отдалённые результаты бимаммарного шунтирования у пациентов с многососудистым коронарным поражением и сахарным диабетом 2-го типа после псевдорандомизации», в которой доказано, что бимаммарное шунтирование у пациентов с сахарным диабетом 2-го типа является безопасным и эффективным методом хирургического лечения ишемической болезни сердца как в ближайшем, так и в отдалённом периоде и может быть операцией выбора у пациентов с многососудистым поражением.

В статье Е.А. Ильичевой и соавт. «Качество жизни пациентов с солитарным и множественным поражением околощитовидных желёз при спорадическом первичном гиперпаратиреозе до и после хирургического лечения» доказано, что хирургическая тактика, направленная на снижение частоты персистенции гиперпаратиреоза, позволяет добиться улучшения качества жизни у большинства пациентов с множественным поражением околощитовидных желёз при первичном гиперпаратиреозе. Проблеме морфологической диагностики гиперпаратиреоза посвящена и вторая работа этих авторов, в которой установлено, что множественное поражение околощитовидных желёз при любом клиническом варианте гиперпаратиреоза характеризуется преобладанием гиперплазии: 80 % при первичном и 100 % при вторичном и третичном гиперпаратиреозе.

Большой интерес для читателей, несомненно, представляет статья Е.А. Анастасиевой и соавт. (Новосибирск) «Восстановление рентгеновской плотности кости при замещении дефектов кортикальной пластины тканеинженерной конструкцией в эксперименте», в которой экспериментально доказано, что применение тканеинженерной конструкции на основе депротеинизированной губчатой кости со стромально-васкулярной фракцией жировой ткани для заполнения перфорационных дефектов кортикальной пластины бедренной кости кролика приводит к раннему восстановлению рентгеновской плотности костной ткани в зоне дефекта.

Интересны читателям будут и научные обзоры А.В. Невежиной и Т.В. Фадеевой (Иркутск), посвящённый изучению антимикробного потенциала йодсодержащих веществ и материалов, и Н.Н. Дреминой и соавт. (Иркутск), рассматривающий применение природных компонентов в качестве структуры гидрогелей для клеточной терапии и тканевой инженерии.

Итак, очередной выпуск перед Вами!

Для цитирования: Сороковиков В.А. Предисловие заместителя главного редактора к № 5 (2023). *Acta biomedica scientifica.* 2023; 8(5): 5-10. doi: 10.29413/ABS.2023-8.5.1

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DISCUSSION PAPERS, LECTURES, NEW TRENDS IN MEDICAL SCIENCE

ASSESSING SOCIO-ECONOMIC DAMAGE CAUSED BY COXARTHROSIS IN THE POPULATION

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ABSTRACT

Background. *About 40 % of patients diagnosed with coxarthrosis annually seek medical help and receive social support due to this disease. Increased use of an expensive surgery for treatment of coxarthrosis and projected growth of its prevalence in the population determine the relevance of socio-economic analysis.*
The aim of the study. *To assess the value and structure of economic damage caused by the delivering health and social care to patients with coxarthrosis at the state level of the Russian Federation.*
Methods. *To assess economic damage, we used the average annual number of various categories of patients and disabled people with coxarthrosis in the Irkutsk region for 2008–2017. Three main categories were identified: patients who visited the outpatients' clinic; patients with total hip replacement; disabled people due to coxarthrosis. For each category, we calculated weighted average damage per 1 conventional patient, taking into account direct and indirect costs and subsequent multiplication by the average annual number of individual categories of patients. Calculations were performed in 2017 prices.*
Results. *The average annual socio-economic damage from coxarthrosis amounted to 1.39 (1.34÷1.43) billion rubles or 0.1 % of the gross regional product. The most of the damage (64.4 %) were indirect costs associated with disability due to coxarthrosis, 22.2 % of the total amount were the costs of hip replacement surgery, 13.4 % were the costs of outpatient visits. Indirect economic losses due to disability in patients of working age were 4.2 times higher than losses due to disability of old-age pensioners.*
Conclusion. *The results of the study confirm the economic feasibility of surgical treatment of coxarthrosis, especially in patients of working age.*

Key words: *coxarthrosis, outpatient and inpatient treatment, endoprosthesis replacement, disability, socio-economic damage*

Received: 21.12.2022
Accepted: 01.08.2023
Published: 05.12.2023

For citation: Koryak V.A., Botvinkin A.D., Sorokovikov V.A., Chernikova O.M. Assessing socio-economic damage caused by coxarthrosis in the population. *Acta biomedica scientifica*. 2023; 8(5): 14-22. doi: 10.29413/ABS.2023-8.5.2

ОПЫТ ОЦЕНКИ СОЦИАЛЬНО-ЭКОНОМИЧЕСКОГО УЩЕРБА, ОБУСЛОВЛЕННОГО ЗАБОЛЕВАЕМОСТЬЮ НАСЕЛЕНИЯ КОКСАРТРОЗОМ

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РЕЗЮМЕ

Обоснование. *Около 40 % пациентов с установленным диагнозом «коксартроз» ежегодно обращаются за медицинской помощью и получают социальную поддержку в связи с этим заболеванием. Всё более широкое применение дорогостоящей операции для лечения и прогнозируемый рост распространённости этой патологии в популяции определяют актуальность проведения социально-экономического анализа.*

Цель исследования. *Оценка величины и структуры экономического ущерба в связи с оказанием медицинской и социальной помощи пациентам с коксартрозом на уровне субъекта Российской Федерации.*

Методы. *Для оценки экономического ущерба использовали среднегодовую численность различных категорий пациентов и инвалидов с коксартрозом в Иркутской области за 2008–2017 гг. Выделены три основных категории: пациенты, посетившие поликлинику; пациенты с тотальным эндопротезированием тазобедренного сустава; инвалиды по коксартрозу. Для каждой из категорий рассчитан средневзвешенный ущерб на 1 условного пациента с учётом прямых и непрямых затрат и последующим умножением на среднегодовую численность отдельных категорий пациентов. Расчёты выполнены в ценах 2017 г.*

Результаты. *Среднегодовой социально-экономический ущерб от коксартроза составил 1,39 (1,34÷1,43) млрд руб. или 0,1 % от валового регионального продукта. Основную часть ущерба (64,4 %) составляли непрямые затраты в связи с инвалидностью по коксартрозу, 22,2 % от общей суммы – затраты на эндопротезирование тазобедренного сустава, 13,4 % – затраты на поликлинический приём пациентов. Непрямые экономические потери из-за инвалидности в трудоспособном возрасте в 4,2 раза превышали потери из-за инвалидности пенсионеров по старости.*

Заключение. *Результаты исследования подтверждают экономическую целесообразность хирургического лечения коксартроза, особенно у пациентов трудоспособного возраста.*

Ключевые слова: *коксартроз, амбулаторное и стационарное лечение, эндопротезирование, инвалидность, социально-экономический ущерб*

Статья поступила: 21.12.2022
Статья принята: 01.08.2023
Статья опубликована: 05.12.2023

Для цитирования: Корьяк В.А., Ботвинкин А.Д., Сороковиков В.А., Черникова О.М. Опыт оценки социально-экономического ущерба, обусловленного заболеваемостью населения коксартрозом. *Acta biomedica scientifica*. 2023; 8(5): 14-22. doi: 10.29413/ABS.2023-8.5.2

INTRODUCTION

Assessment of socio-economic efficiency of high-tech medical care is an urgent scientific task. Coxarthrosis is among the chronic diseases with a low mortality rate, a high probability of disability and a significant reduction in quality of life. Hip replacement surgery is an expensive procedure, so many countries undertake a cost assessment of this treatment method. The results of studies confirm not only the clinical but also the cost-effectiveness of the treatment [1, 2]. Economic damage from coxarthrosis is increasing as a result of the increasing prevalence of the disease with the growing number of older age groups and obese people in the population of many countries around the world [3]. Recently, there has been a trend towards the development of the disease in younger individuals as a result of traumatic joint damage due to the increasing popularity of injury-prone sports [4]. Environmental problems of the modern world are also among the risk factors for this pathology [5–7]. Obviously, the medical community should be prepared for a significant increase in the demand for medical services for hip osteoarthritis treatment.

The majority of studies involving cost estimation caused by coxarthrosis have been published by foreign researchers. The dependence of treatment costs on the age of patients, the cost of prostheses, and a variety of other factors has been noted [8–10]. An experience of extrapolating the results of sample studies to the whole population of the country is also available [11].

Similar studies in the Russian Federation are very limited and focus not only on coxarthrosis, but on osteoarthritis in general [12–14]. Methods for assessing disease damage and cost-effectiveness of treatment can vary significantly depending on the specifics of the pathology under study, as well as among different authors, which makes it difficult to use the results in practical healthcare [15, 16]. This defines the relevance of continuing research to assess the socio-economic significance of osteoarthritis, taking into account the peculiarities of the organization of domestic health care.

Previously, we evaluated the average annual number of patients who received various types of medical care and social benefits in connection with the treatment of coxarthrosis by using the materials of the Irkutsk Region [17]. As a result, it was therefore possible to use the data obtained to calculate the damage from this disease to the economy of the region.

THE AIM OF THE STUDY

To assess the value and structure of economic costs of delivering health and social care to patients with coxarthrosis at the regional level.

MATERIALS AND METHODS

A retrospective epidemiological study was undertaken based on the materials of the Irkutsk region, including the data of the specialized trauma clinic of the Irkutsk Scientific Centre of Surgery and Traumatology. To assess the economic damage, the average annual number of different categories of patients and disabled people with coxarthrosis in the Irkutsk region for the period 2008–2017, determined in an earlier study [17], was used. Three main categories were identified: patients who visited the outpatient clinic; patients with total hip replacement (THR) surgery; and those disabled by coxarthrosis. The ratio of different categories of patients was further clarified using continuous samples from one of the polyclinics of the regional center ($n = 1237$) and the specialized clinic of the Irkutsk Scientific Center of Surgery and Traumatology for 2017 ($n = 782$). Calculations were performed in 2017 prices.

Direct and indirect socio-economic damage was assessed using methods previously tested in domestic healthcare [4, 12, 16, 18–20]. The weighted average damage per conditional case of coxarthrosis in different categories of patients was measured during the first stage. The obtained values were used to calculate the total regional costs through multiplying them by the average annual number of individual categories of patients with coxarthrosis. Confidence intervals with a significance level of 95 % (95% CI) for the amounts obtained were calculated by proportion based on previously determined 95% CIs for the number of patients in different categories [17].

Direct costs for outpatients included the cost of visits to various specialists at the primary care without taking into account the cost of medicines purchased at the patients' expense. The attendance cost was calculated based on the funding included in the territorial programme of compulsory health insurance, considering the coefficient of differentiation and increase in the cost of medical services across the Irkutsk region in accordance with the Appendix to the Federal Law dated December 19, 2016 No. 418-FZ "On the budget of the Federal Compulsory Health Insurance Fund for 2017 and for the planning period of 2018 and 2019" [21]. The weighted average attendance cost of different specialists was calculated using a continuous sample of outpatients who applied for coxarthrosis for the first time or repeatedly during the year ($n = 1237$) in one of Irkutsk primary care in 2017. Direct expenses in connection with THR are accepted according to the calculations of the accounting department of the specialized clinic of the Irkutsk Scientific Center of Surgery and Traumatology, made in accordance with the Resolution of the Government of the Russian Federation dated December 19, 2016 No. 1403 "On the program of state guarantees of free medical care for citizens for 2017 and for the planning period of 2018 and 2019". According to these data, the average cost of surgical treatment and hospitalization of a patient with one-stage and two-stage, unilateral and bilateral surgery and revision intervention amounted to 185,930 rubles.

The indirect costs of temporary disability (TD) benefit, lost gross regional product (GRP) and income tax due to sickness absence were differentiated according to the duration of TD and the proportion of working patients who received sick leave. These parameters were determined for outpatients using the continuous sample mentioned above (n = 1237). The proportion of employed among patients with THR surgery and the duration of hospital treatment for different types of surgery were also determined from a continuous sample of case histories (n = 782). The duration of TD during the rehabilitation period after hospital discharge was included in the calculations. Indirect damages for coxarthrosis disability and permanent disability (PD) included monthly pension payments, as well as GRP and income tax losses due to termination of employment prior to old-age retirement.

Information about the population employed in the economy, GRP per capita (2005.5 RUB per day), TD benefit (1813.6 RUB per day), PD benefit (15643.3, 17861.6 and 20893.8 RUB per month, depending on the disability group) and average personal income tax (PIT) (231.8 RUB) were obtained from the website of the Territorial Body of the Federal State Statistics Service for the Irkutsk Oblast over the course of the year 2017 [22].

RESULTS

Estimation of costs associated with outpatient clinic visits and outpatient treatment

The structure of direct costs for outpatients with coxarthrosis is presented in Table 1. The attendance costs of different specialists did not differ significantly, and the weighted average costs did not differ much from the arithmetic mean of the attendance costs (188 RUB). Consequently, at this stage there is an opportunity to simplify the calculation algorithm. A random sample of patients who visited the outpatient clinic for coxarthrosis was found to be 1.5 % of patients who received a sick leave for outpatient treatment, with a mean duration of TD lasting 30 days. Considering the duration of TD, the indirect loss per 1 patient with outpatient conservative treatment, including TD benefits and losses of GRP and taxes, amounted to 121,527 RUB (1813.6 + 2005.5 + 231.8 = 4050.1 RUB × 30 days). The obtained value of weighted average costs was used in the final calculation of losses caused by coxarthrosis (Table 5).

Estimation of costs associated with the total hip replacement surgery

The weighted average direct costs per 1 operated patient (185,930 RUB), as noted above, are calculated in the medical organization that performed prosthetics. This also made it much easier to estimate total costs. Indirect costs depended on the duration of treatment for different types of medical care and the proportion of working patients, which was 27.2 % (n = 213) of the total number of operated patients (Table 2). The obtained value of weighted average costs was used in the final calculation of losses from coxarthrosis (Table 5).

Assessment of damages due to coxarthrosis disability

Direct costs related to the provision of medical care to persons with disabilities are accounted for together with other categories of patients. The indirect damage was partially dependent on the proportion of group III disabled persons who continued to be employed but, due to THR, received TD benefits and did not participate in the creation of GRP during this period. These economic losses are accounted for in Table 2 and, accordingly, an adjustment is made in the final Ta-

TABLE 1

CALCULATION OF WEIGHTED AVERAGE DIRECT COSTS FOR OUTPATIENT ATTENDANCE OF PATIENTS WITH COXARTHROSIS ACCORDING TO THE POLYCLINIC DATA OVER THE YEAR 2017

Specialist attendance	Number of visits (n = 1,237)	The cost of 1 attendance, RUB	Amount of costs, RUB*
Therapist (initial attendance)	366	195.8	71663
Therapist (follow-up visit)	450	150.9	67905
Surgeon (initial attendance)	16	194.7	3115
Surgeon (follow-up visit)	3	165.2	496
Rheumatologist (initial attendance)	243	249.0	60507
Rheumatologist (follow-up visit)	159	172.7	27459
Total cost amount			231145
Weighted average cost of 1 patient visit			**187**

Note. * – rounded to integers.

ble 5 for the amount of indirect economic loss in the "able-bodied disabled" category. The correction was calculated on the basis of sample data, according to which the proportion of working disabled persons of group III accounted for 13.6 % of the number of patients who underwent surgery. After extrapolating these data to the average annual population of THR patients, it turned out that among them 84 disabled people were employed. The amount of indirect damage for this small group of disabled persons, taking into account the timing of TD as a result of THR surgery, amounted to 46,432,428 RUB per year (552,767 RUB × 84).

A more significant part of the damage is associated with payments of disability pensions depending on the disability group (Table 3).

Most of the damage was determined by the loss of GRP due to the onset of PD at working age. The number of working years and days lost by disabled individuals was determined using the retirement age for men and women in 2017 and the number of working days per year (247). As previously found, the proportion of coxarthrosis disabled persons who became disabled one year or more before old-age retirement was 54 % of their total number (n = 1,033). Damage amounts were calculated separately for men and women (Table 4).

As a result, the weighted average indirect damage associated with the payment of pensions to disabled persons, loss of GRP and taxes caused by the PD amounted to 747,702 RUB per year per 1 disabled person of work-

TABLE 2

CALCULATION OF THE WEIGHTED AVERAGE INDIRECT LOSS DUE TO THR SURGERY FOR EMPLOYED PATIENTS WITH COXARTHROSIS BASED ON 2017 DATA FROM A SPECIALIZED MEDICAL CLINIC

Type of medical care	Number of patients (n = 213)	Duration of 1 patient's treatment, days	Total number of days of TD	Amounts of damage, RUB			
				TD benefits	GRP losses	personal income tax losses	total*
Unilateral one-stage surgery	197	16	3152	5,716,467	6,321,336.0	730,633.6	12,768,437
Bilateral one-stage surgery	5	22	110	199,496	220,605.0	25,498.0	445,599
Unilateral two-stage surgery	2	27	54	97,934	108,297.0	12,517.2	218,749
Revision surgery	9	21	189	342,770	379,039.5	43,810.2	765,620
Outpatient postoperative follow-up treatment	213	120	25,560	46,355,616	51,260,580.0	5,924,808.0	103,541,004
Total cost amount							117,739,409
Weighted average costs per 1 employed patient							**552,767**

Note. * – rounded to integer values.

TABLE 3

CALCULATION OF WEIGHTED AVERAGE INDIRECT DAMAGES FOR COXARTHROSIS DISABILITY PENSION PAYMENTS (NUMBER OF DISABLED PEOPLE BASED ON AVERAGE DATA FOR 2008–2017)

Disability groups	Number of persons with disabilities (n = 1,908)	Amounts of damage, RUB		
		pension amount per month	annual pension amount	benefit amount per year*
Group I	36	20,893.8	250,725.6	9,026,122
Group II	443	17,861.6	214,339.2	94,952,266
Group III	1429	15,643.3	187,719.6	268,251,308
Total				372,229,696
Weighted average damage per 1 disabled person (RUB)				195,089

Note. * – rounded to integer values.

ing age (195,089 + 552,613 RUB). For disabled persons of old-age pension age, the weighted average loss is conditioned only by the payment of pensions and corresponded to the value shown in Table 3.

Assessment of damage to the regional economy

At the final stage, the weighted average costs for different categories of patients with confirmed coxarthrosis were used to calculate the total costs for the year for in-

TABLE 4

CALCULATION OF THE ANNUAL INDIRECT DAMAGE DUE TO THE LOSS OF GROSS REGIONAL PRODUCT AND PERSONAL INCOME TAX AS A RESULT OF A PERMANENT LOSS OF WORKING CAPACITY DUE TO COXARTHROSIS BEFORE RETIREMENT DUE TO OLD AGE (THE NUMBER OF DISABLED PEOPLE BASED ON AVERAGE DATA FOR 2008–2017)

Groups	Number of persons with disabilities a year or more before old-age pension age (*n* = 1,033)	The number of lost working days per year	The amount of lost working days	GRP damage + tax for 1 day, RUB	Amounts of damage, RUB*
Women	596	247	147,212	2237.3	329,357,408
Men	437	247	107,939	2237.3	241,491,925
Total					570,849,333
Weighted average damage per 1 disabled person of working age					552,613

Note. * – rounded to integer values.

TABLE 5

RETROSPECTIVE ASSESSMENT OF THE AVERAGE ANNUAL SOCIO-ECONOMIC DAMAGE ASSOCIATED WITH THE PROVISION OF MEDICAL AND SOCIAL CARE TO PATIENTS WITH COXARTHROSIS IN THE IRKUTSK REGION (IN 2017 PRICES)

Patient groups		Average annual number of patients*	Amount of damage (RUB)				Share in the amount of damage (%)
			direct costs per 1 patient	indirect costs per 1 patient	sum of direct and indirect costs per 1 patient	amount of damage in terms of number of patients (95% CI)*	
Patients of outpatient clinics	employed	1,497	187	121,527	121,714	182,205,858	**13.4**
	unemployed	28,209	187	0	187	5,275,083	
	total	29,706* (29,379÷30,018)			**187,480,941** (185,417,174÷189,450,040)		
Patients with THR surgery	employed	350	185,930	552,767	738,697	258,543,950	**22.2**
	unemployed	271	185,930	0	185,930	50,387,030	
	total	621* (564÷671)			**308,930,980** (280,574,996÷333,804,650)		
Disabled people	able to work	1033	**	747,702	747,702	725,943,738***	**64.4**
	unable to work	875	**	195,089	195,089	170,702,875	
	total	1,908* (1,876÷1,932)			**896,646,613** (881,608,515÷907,925,187)		
Total					**1,393,058,534** (1,347,600,685÷1,431,176,877)		**100**

Note. * – average annual number of patients with coxarthrosis during 2008–2017 according to [17]; ** – counted together with other patients of polyclinics and hospital; *** – adjusted (reduced by 46,432,428 RUB, explanations in the text).

dividual areas and for the region as a whole (Table 5). The main component of the total amount represents damages caused by PD. A comparison of total direct and indirect costs for the three main cohorts of patients with coxarthrosis shows that more than 60 % of the damage is associated with disability. Total economic losses associated with prosthetics were 1.7 times greater compared to outpatients, whose numbers were nearly 30 times greater.

The damage associated with the provision of medical care to working patients is significantly higher than that for patients who are not employed at work. This is determined by the higher number of employed patients among those seeking medical care and the indirect costs as a result of TD. The non-medical disability damage amounts were higher in the group of patients disabled before old-age retirement and were largely determined by the PD. Indirect economic losses due to disability in patients of working age were 4.2 times higher than losses due to disability of old-age pensioners.

The amount of direct costs for patients who underwent THR surgery for the year amounted to 115,462,530 RUB, which is about 20 times more than the direct costs for primary care patients (5,555,022 RUB). In total, all direct costs of medical organizations for the admission and treatment of patients accounted for only 8.7 % of the total coxarthrosis damage for the region during the year.

DISCUSSION

The study found that in a region with a population of about 2.5 million people, the economic damage from coxarthrosis exceeded 1.3 billion RUB per year (in 2017 prices), which amounted to about 0.1 % of GRP. Meanwhile, the prevalence of coxarthrosis in the population was previously estimated by us at 77.8 thousand people or 4.1 % of the total population [17]. Only 40.1 % (31,200) of them applied for medical care and received social benefits during the year.

Characterizing the cost structure appears to be a more important output of the work than determining the total amount of damage. Most of the damage is associated with early onset permanent disability and loss of working ability. As a result of the increase in the retirement age during the pension reform in 2019, the economic significance of this component of the damage increases significantly. Indirect costs prevailed in the damage structure as a whole (more than 64.4 %). It should be highlighted that the direct costs of implementing THR to medical organizations were about half as much as the social payments to the employed patients who underwent surgery. In 2008–2017, the vast majority of prosthetics were performed at the expense of the Compulsory Medical Insurance Fund, and only in a few cases the costs were paid by patients.

Thus, the cost structure confirms the economic feasibility of surgical treatment of coxarthrosis. We could not find any domestic publications devoted to the assessment of the socio-economic significance of coxarthrosis in the literature available to us. But the results we obtained are in general agreement with the data related to osteoarthritis of different localisation. For instance, it was found that indirect costs associated with the treatment of osteoarthritis prevailed and amounted to 70.4 % for an employed patient as a consequence of unproduced output at the onset of TD, and 91.4 % of the total amount of losses caused by the disease for a non-working disabled patient. In this case, the losses of personal income tax have not been considered [14]. A number of foreign studies have revealed that hip arthroplasty is much more favorable than conservative treatment, even for patients over 80 years of age [8, 23].

A simplified system of calculations was used, as the weighted average values of direct costs of inpatient and outpatient clinics were pre-calculated by the economists of medical organisations based on federal regulatory and methodological documents. Consequently, we have differentiated the costs of different surgery scenarios only in terms of indirect costs. The main complications are related to estimating the prevalence of coxarthrosis in the population and determining the number of population categories with a relatively homogeneous cost structure, which has been discussed by us previously [17], as well as by other studies [8, 16]. Precisely at this stage of the study, errors that can significantly distort estimates of economic damage are possible.

Other possible uncertainties and limitations of the study should be considered. Obviously, the estimate we obtained is underestimated, as it does not include costs from patients' and their families' funds, such as the purchase of medicines and orthopaedic equipment, transport costs and others. It has previously been shown that the economic burden is imposed not only onto the health care system, but also to the patient, whose ability to self-care is dramatically reduced, as well as to his or her family, which has to allocate financial, moral and physical resources to care for the disabled person [14, 24, 25]. According to some authors, the risks of complications associated with comorbid pathology, common among patients with reduced physical activity, should be included in the costs [11]. However, these costs are highly individualized as well as being difficult to account for.

This study is retrospective in nature, so absolute values of monetary estimates cannot be currently used as a consequence of changes in pricing policy, inflation and variability in the rate of people seeking medical care in the course of follow-up control. However, estimating the cost ratio of individual areas can be useful in making management decisions. The algorithm for estimating costs and damage to the economy that has been tested out is available for reproduction and is recommended for justification of further development of high-tech medical care for patients with coxarthrosis at the regional level.

CONCLUSIONS

In summary, the study revealed that the average annual socio-economic damage from coxarthrosis, associated with patients seeking medical care, payment of social benefits and losses of the region's economy due to perma-

nent disability, amounted to 1.39 (1.34÷1.43) billion RUB or 0.1 % of the gross regional product (in 2017 prices). The most of the damages (64.4 %) were indirect costs associated with disability caused by coxarthrosis, 22.2 % of the total amount was determined by the costs of hip replacement and 13.4 % by the costs of outpatient clinic services. The results of the study confirm the economic feasibility of coxarthrosis surgical treatment, especially in patients of working age.

Conflict of interest

The authors of this article declare no conflicts of interest.

Acknowledgements

The authors would like to express their gratitude to the administration and specialists of the accounting and statistical departments of the Irkutsk Scientific Centre of Surgery and Traumatology, Main Bureau of Medical and Social Expertise in the Irkutsk Region, Irkutsk City Clinical Hospital No. 1 (Polyclinic No. 1) for their assistance in conducting the study at the stage of primary data collection.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

BIOLOGY AND MEDICAL BIOLOGY

NATURAL COMPONENTS AS THE STRUCTURE OF HYDROGELS FOR CELLULAR THERAPY AND TISSUE ENGINEERING

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ABSTRACT

Hydrogels are a class of dimensional hydrophylic polymer networks capable of absorbing and retaining large amounts of water. Natural and synthetic components can serve as a material for the hydrogel production. Hydrogels have unique physico-chemical properties, which are determined by the material composition and concentration, its density, crosslinking methods, and production approaches. This review article describes natural materials used for the production of hydrogels having different properties.

The natural components of hydrogels are collagen, elastin, gelatin, chitosan, dextran, hyaluronic acid, alginate, silk fibroin and glycosaminoglycans. These components are considered biodegradable and biocompatible, since they do not have a toxic effect on tissues. Natural materials provide good cell adhesion, the spread of bioactive signals as well as they affect the behavior of cells in vitro and in vivo. To obtain hydrogels, physical and chemical methods of crosslinking are used, which determine the properties of the final product. Also, hydrogels can be further modified by various active molecules, growth factors that increase their biological functionality. To date, hydrogels made of natural materials are widely used in ophthalmology, neurosurgery, in the treatment of skin wounds, in various cardiovascular pathologies, in restoring the volume of circulating blood, some cartilage defects, targeted delivery of pharmacological drugs, active molecules, etc. Thus, hydrogels produced from natural components are an extremely promising material for cellular technologies and tissue engineering.

Key words: *hydrogel, natural materials, cellular technologies, tissue engineering*

Received: 29.11.2022
Accepted: 25.09.2023
Published: 05.12.2023

For citation: Dremina N.N., Trukhan I.S., Shurygina I.A. Natural components as the structure of hydrogels for cellular therapy and tissue engineering. *Acta biomedica scientifica*. 2023; 8(5): 23-35. doi: 10.29413/ABS.2023-8.5.3

ПРИРОДНЫЕ КОМПОНЕНТЫ КАК СТРУКТУРА ГИДРОГЕЛЕЙ ДЛЯ КЛЕТОЧНОЙ ТЕРАПИИ И ТКАНЕВОЙ ИНЖЕНЕРИИ

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РЕЗЮМЕ

Гидрогели – объёмные сетевые структуры, материалом для изготовления которых являются как природные, так и синтетические компоненты. Это гидрофильные полимеры, способные поглощать и удерживать значительное количество воды. Благодаря уникальным физико-химическим свойствам, программируемым в зависимости от цели дальнейшего применения, гидрогели широко используются в биомедицинской сфере. Данная обзорная статья посвящена природным материалам для создания гидрогелей с различными характеристиками.

К природным материалам для изготовления гидрогелей относятся коллаген, эластин, желатин, хитозан, декстран, гиалуроновая кислота, альгинат, фиброин шёлка, гликозаминогликаны. Являясь компонентами внеклеточного матрикса, натуральные материалы считаются наиболее физиологическими или биосовместимыми и не оказывают токсического воздействия на организм. Другим не менее важным параметром считается биодеградируемость, которую необходимо учитывать при выборе компонентов для изготовления гидрогелей. Природные материалы обеспечивают хорошую клеточную адгезию, распространение биоактивных сигналов, а также способны влиять на поведение клеток in vitro и in vivo. Для синтезирования гидрогелей используют физические и химические методы сшивания, с помощью которых задаются определённые свойства гидрогелей. Кроме того, гидрогели могут быть дополнительно модифицированы различными активными молекулами, факторами роста, повышающими их биофункциональность. На сегодняшний день гидрогели из природных материалов широко используются в офтальмологии, нейрохирургии, при лечении кожных ран, при различных сердечно-сосудистых патологиях, в восстановлении объёма циркулирующей крови, некоторых хрящевых дефектов, целенаправленной доставке фармакологических препаратов, активных молекул и во многом другом. Таким образом, гидрогели из природных компонентов являются крайне перспективным материалом в клеточных технологиях и тканевой инженерии.

Ключевые слова: *гидрогель, природные материалы, клеточные технологии, тканевая инженерия*

Статья поступила: 29.11.2022
Статья принята: 25.09.2023
Статья опубликована: 05.12.2023

Для цитирования: Дремина Н.Н., Трухан И.С., Шурыгина И.А. Природные компоненты как структура гидрогелей для клеточной терапии и тканевой инженерии. *Acta biomedica scientifica*. 2023; 8(5): 23-35. doi: 10.29413/ABS.2023-8.5.3

INTRODUCTION

Hydrogels are three-dimensional networks consisting of hydrophilic polymers crosslinked through covalent bonds or held together by physical intramolecular and intermolecular interactions, with water as the dispersion medium. They can be characterized by such physical parameters as size, modulus of elasticity and viscosity, swelling and degradation rate. For this reason, hydrogels are unique viscoelastic materials.

Hydrogels have the ability to absorb up to 90 % of water and are considered superabsorbent materials [1]. As a result of their ability to absorb water, hydrogels have a wide range of applications in various fields, among which medicine is one of the leading ones. The high hydrophilicity of hydrogels is explained by the presence of hydrophilic particles such as carboxyl, amide, amino and hydroxyl groups distributed along the backbone of the polymer chains. Water uptake by the hydrogel occurs until there is a balance between the osmotic forces that stimulate water into the hydrogel matrix and the cohesive forces of polymer bonds within the hydrogel that prevent excessive water uptake. In other words, the higher the degree of crosslinking of a particular hydrogel, the lower the degree of swelling [2].

Due to their unique properties, hydrogels are given close attention, numerous scientific studies are being conducted by researchers around the world, and practical applications of biohydrogels are carried out. As a result, hydrogels from natural components are extremely promising materials in the cellular technologies and tissue engineering.

This article objectives are to provide an analytical review of natural components for the manufacture of hydrogels and to identify their advantages and disadvantages.

Classification of hydrogels. Hydrogels can be categorized into natural, synthetic and semi-synthetic based on their origin. Natural hydrogels include collagen, silk fibroin, dextran, hyaluronic acid and derivatives of natural materials such as chitosan, alginate and other hydrogels derived from decellularized tissues [3]. Hydrogels from natural materials are considered to be the most physiological because they are components of the extracellular matrix. However, their final microstructure and properties are difficult to control. Mechanical properties and dependence on polymerisation or gelation conditions are often poorly understood by manufacturers, and, because of their natural origin (bovine fibrinogen, collagen from rat tail), composition from one batch to another can vary considerably. As a result of the above reasons, hydrogels from natural materials are often combined with synthetic materials to create composite polymers, which are currently under active research. Depending on the stability characteristics in physiological environment, hydrogels can be non-biodegradable and biodegradable.

Biocompatibility and biodegradability are two important parameters that require special attention when selecting a polymer. [4]. We should also note that biocompatible materials are not always biodegradable and vice versa, which once again emphasises the importance of proper material selection.

Biocompatibility is a specific material property, which consists in the absence of toxic or other harmful effects against biological tissues and systems, whereas biologically incompatible materials are capable of causing tissue reactions that include necrosis, dystrophic calcification, significant fibrosis, and foreign body reaction.

Biodegradation, i. e. the alteration of the physical, chemical and biochemical properties of a material under the influence of the biological environment, generally involves two steps:

1. Water penetrates into the polymer matrix, interacts with chemicals by hydrolysis, shortening the polymer chain length, as a result leading to molecular weight reduction, fragment metabolism and volume erosion.

2. Polymer surface erosion occurs when the rate at which water molecules penetrate the matrix is slower than the rate at which the polymer transforms into water-soluble materials.

A polymeric material biodegradation may take place either in the surface layer accessible to the liquid environment, when the material properties do not change before the surface layer is destroyed, or in the volume of the polymeric product, where the rate of the liquid biological environment exceeds the rate of polymer degradation [5]. An advantage of biodegradable polymers is the ability of most of them to allow good cell adhesion and proliferation *in vivo*, to persist for a certain time due to their tunable properties (permeability, elasticity, stiffness and chemical reactivity) and then degrade without harmful effects on the body [6].

A vital role in the formation and degradation of hydrogel structure belongs to cross-linkages, due to which polymer stabilisation (cross-linking) takes place, which in turn leads to multidimensional expansion of polymer chains, thereby resulting in the formation of stable network structures. Based on the types of cross-links, hydrogels can be divided into two groups: chemically cross-linked and physically cross-linked [7].

Chemical crosslinking of hydrophilic polymers, which includes free-radical polymerisation, polyaddition and polycondensation, and radiation polymerisation, is one of the main methods for hydrogel production. Chemical crosslinking involves the interaction of a hydrophilic polymer solution with a bifunctional crosslinking agent. Both natural and synthetic hydrophilic polymers are considered suitable for the preparation of hydrogels using this method. For example, albumin and gelatin-based hydrogels have been developed using dialdehyde or formaldehyde as crosslinking agents. High water content hydrogels based on cross-linking of functionalized polyethylene glycol and lysine-containing polypeptide have also been developed by this method [2].

Free radical polymerisation is used to obtain hydrogels from natural materials, provided that these polymers have suitable functional groups or are function-

alised with radical polymerisable groups. For example, this method has been used to develop various chitosan-based hydrogels [8]. The essence of the method is that radicals react with monomers, turning them into active forms that interact with a large number of other monomers, resulting in the formation of polymer matrices. This method can be used for both in-solution and bulk preparation. Solution polymerization is preferential for the synthesis of large quantities of hydrogels, in which case water is the most commonly used solvent. Bulk polymerisation proceeds faster than solution polymerisation with no need for solvent removal, which is time-consuming in many cases.

Physical cross-linking techniques include ionic interaction, hydrogen bonding and hydrophobic association.

During ionic interaction, polyelectrolyte attachment to polivalent ions of opposite charge is performed to form polyelectrolyte complexes in which bonds are formed between pairs of charged sites along the polymer chains. In this manner, for example, polymerization of alginate, which consists of glucuronic and mannuronic acids residues that are cross-linked with calcium ions, occurs [9].

A hydrogen bond between the polymer chains may also participate in the formation of a hydrogel, such as carboxymethylcellulose, with hydrogen bonds formed during dispersion in hydrochloric acid. The mechanism involves replacing sodium with hydrogen in an acidic solution to stimulate the creation of hydrogen bonds. Reducing the pH of the aqueous polymer solution is a prerequisite. Factors such as polymer concentration, polymer molar ratio, solvent type, solution temperature and the degree of connection between polymer functionalities also play an important role.

A hydrophobic association based on hydrophobic interactions is another way to produce hydrogels [10]. Both polymers and copolymers form structures which are separated by hydrophobic microdomains that act as associated cross-linking points throughout the polymer structure and are surrounded by hydrophilic water-absorbing regions. Nevertheless, this method is hardly used despite its low cost mainly as a result of poor interfacial adhesion.

Ionizing radiation techniques are also effective methods for the synthesis of hydrogels. Ionizing radiations, such as electron beams and γ-rays, are high energy and can ionize simple molecules in both air and water. In the process of irradiation of the polymer solution, reactive regions are formed along the polymer filaments, which eventually lead to the formation of a large number of cross-links [11]. The advantages of this method are simplicity, high speed, absence of catalysts to start the polymerization reaction and the possibility to control the process by varying the irradiation dose [12]. However, this method shall not be applied if the polymers decompose under ionising irradiation.

Meanwhile, hydrogels physically obtained are not homogeneous since the clusters formed by intermolecular or hydrophobic/ionic-bonded areas create inhomogeneities in the structure, the destruction of which can occur when conditions change, such as ionic strength, pH, temperature, directional force, addition of dissolved substances.

Material property also appears to depend on its supramolecular structure. This term can be defined as "the way macromolecules are packed in the space of distinguished elements, the size and shape of such elements and their mutual arrangement in space". Porous hydrogels comprise a dispersed system consisting of cell-pores interconnected through a polymer framework phase, promoting cell migration and improving the available surface area for cell-cell interaction with surrounding tissues. Some other parameters such as pore volume, pore size distribution, pore opening size, pore wall roughness, surface functionality, polymer structure and porous interconnectivity are also important [2].

As a function of pore size, pores can be divided into micropores (less than 2 nm), mesapores (2–50 nm) and macropores (greater than 50 nm). Therefore, the experiments have determined that the optimal pore size for angiogenesis and osteogenesis is 50–100 μm [13], 100–200 μm is necessary for cartilage regeneration [14] and 200–300 μm for regeneration of damaged skin [15].

Hydrogels of natural origin can be classified into three groups: **protein-based** materials (collagen, fibrin, elastin, gelatin, silk fibroin), **polysaccharides** (alginate, chitosan, glycosaminoglycans) and **decellularised tissue materials**. Natural gels are typically formed from proteins and extracellular matrix components, which makes them biocompatible, bioactive and promising materials for biomedical applications. Animal extracts, collagen from pig tissue or rat tails, while fibroin is extracted from insects, serves as the source of proteins.

Collagen. Collagen is generally an insoluble fibrillar protein with an elongated filamentous shape of molecules that forms the basis of connective tissue, provides its strength and elasticity, and plays an important role in cell signaling and modulation of cell behavior. A variety of collagen types are now widely available from tendons, skin, intestines, corneas and blood vessels of some mammalian animals as well as marine organisms and fish [16]. Biologically, collagen has low antigenicity and inflammatory response, yet high biocompatibility and biodegradability. Over 29 forms of collagen are available in mammalian tissues, of which only collagens types I, II, and III are considered true fibrillar proteins. Type I collagen is the most abundant fibrillar protein, accounting for 90 % of the collagen in the body. Collagen comprises a complex hierarchical four-level structure in which the primary structure is an amino acid triplet sequence Gly-X-Y, where Gly is represented by glycine, forming up to 30 % of the total amino acid content of collagen, and X-Y are proline and hydroxyproline, respectively. Its secondary structure comprises repeats of a given amino acid triplet chain, which are then assembled into a triple helix to form a tertiary level of organisation, where each chain contains about 1000 amino acids. Collagen fibres themselves constitute the quaternary structure of collagen and are formed by self-assembled fibres

[17]. It is also worth noting that the structural and mechanical properties of collagen fibrils are related to Ca^{2+} concentrations, which is associated with chelation between collagen molecules and Ca^{2+}. While the mechanical properties of collagen are ideal in native tissues, in collagen I-based biomaterials, mechanical strength is insufficient due to the lack of covalent (disulfide) bonds present in collagen types III, IV, VI, VII, and XVI. As a result, crosslinking by physical, chemical and biological methods is basically used to increase the mechanical properties of the material. Alternatively, the different collagen molecular forms in the body are able to form complexes that can also improve mechanical properties through transmembrane receptors, the main ones being the α1β1 and α2β1 integrins, which provide interactions between cells and the extracellular matrix. These integrins have been identified on activated T-cells, platelets, vascular, epithelial cells and fibroblasts [18]. Signaling through α1 contributes to the regulation of extracellular matrix composition, proliferation. Concurrently, a survival signal, considered unique among collagen-binding integrins, passes through α1 [19]. Integrin α2β1 has the ability to mediate cell adhesion, spreading on fibrillar sheath I and is the only collagen-binding integrin in platelets, and recognises type IV, VI and XII collagens [20]. To date, however, the exact mechanism of collagen recognition by integrins is currently not fully identified.

The collagen hydrogel properties are both affected by the collagen source (rat tail tendon, cattle skin, pig skin, etc.) and the extraction method. Nowadays, collagen hydrogels are generally synthesised by extraction at low pH values using acetic acid. The acid-dissolved collagen is then neutralized with concentrated (10×) phosphate-buffered saline (PBS), Hanks' balanced salt solution, or cell culture medium, followed by the addition of neutralizing agents (NaOH, HEPES) and other reagents (water, 1 × medium, 1 × PBS) to initiate fibril self-assembly at a temperature close to physiological pH and polymerization of 37 °C. An increase in pH around the isoelectric point at low ionic strength, however, can improve linear viscoelastic properties and transparency [21]. Notwithstanding, for physiological encapsulation, the pH of hydrogels is limited between 7.4 and 8.4 to maintain cell viability. The collagen obtained in this way largely retains the telopeptide regions that are sites for cross-linking, and in fact this extraction co-isolates a small number of multimers with intact cross-linking sites [22].

A combination of salt precipitation with enzymatic extraction exists along with acid extraction of collagen. In this case, digestion with pepsin results in completely cleaved terminal non-helical regions that contain intermolecular cross-links, and collagen acquires a soluble form [17].

The orientation of collagen fibrils plays an important role for some tissues. For instance, for nerve tissue [23] and cornea [24], the fibrils need to be previously aligned, for which microstructuring techniques have been developed using magnetic nanoparticles that, under the influence of an external magnetic field, promote correct fibrillar orientation.

Collagen hydrogels have found wide application in cell technology and regenerative medicine owing to their high bioeffectiveness. However, the biggest advantage of collagen hydrogel is that cells and bioactive components can be incorporated directly into it already during the manufacturing process [16]. At the same time, lowering the gelation temperature promotes the formation of a smaller number but longer and thicker collagen fibrils, while fibrils polymerized at higher temperatures form a smaller number of bundles that are furthermore less ordered, which affects the mechanical and structural properties of the hydrogel.

Collagen-based hydrogels with good optical characteristics and mechanical properties were obtained by ionic leaching method by adding NaCl. The hydrogel obtained in this way has found wide application in tissue engineering of the eye cornea [25].

Although type I collagen is the most abundant protein in the body, tissues such as articular cartilage and vitreous fluid contain predominantly type II collagen, which exhibits poor mechanical properties without cross-linking and is difficult to make structurally strong. In order to improve mechanical properties, type I and type II collagens are copolymerised to produce gels with a lower void content and high elastic modulus, which have potential as a framework for articular cartilage engineering [26].

A limitation in the use of collagen as a biomaterial is that when the vascular endothelium is damaged, the collagen located in the vascular wall under the endotheliocytes activates platelets, promoting their adhesion on the damaged surface. Afterwards, through the system of interrelationship of blood coagulation factors and formation of active complexes, a fibrin clot is formed [27]. Moreover, the high cost of pure collagen limits its availability as a cost-effective approach for large-scale biomaterial utilisation [28]. However, despite the drawbacks, hydrogels that include collagen have found worthy applications in regenerative medicine.

Elastin. The key fibrillar protein of the extracellular matrix is elastin, which is synthesized by fibroblasts, endotheliocytes and contains glycine, alanine, valine, and leucine in its composition. Due to the alternation of hydrophobic and hydrophilic domains within the structure, this protein is important for the elasticity and stability of many vertebrate tissues, including large arteries, lungs, ligaments, tendons, skin and elastic cartilage [29]. The elastin precursor, tropoelastin, in combination with microfibrils, contributes to tissue structural integrity and biomechanics through constant flexibility, which allows for repetitive cycles of stretching and relaxation dependent on a hydrated environment. It should be noted that the elastin monomer is capable of increasing in length by a factor of eight. A large number of hydrophobic radicals prevent the creation of a stable globule; as a result, elastin polypeptide chains do not form regular secondary and tertiary structures, but have the property of self-assembly with stable cross-links under physiological conditions, forming a stable molecule [3].

Being a native extracellular matrix protein, elastin is non-immunogenic. As a result of their biological activity and physicochemical properties, elastin and related peptides are ideal candidates to be used as biomedical materials including scaffolds, hydrogels and drug delivery systems in tissue engineering [30]. For instance, good results were obtained by using elastin and elastin-like peptides in the healing of such wounds as trophic foot ulcers in diabetes mellitus, burn wounds, etc. [31]. Elastin dressings mimic the extracellular matrix, providing a natural environment that regulates cell proliferation, migration, differentiation and an adequate overall healing process.

The mechanical properties of elastin-based biomedical materials can be improved by combining the latter with natural or synthetic polymers. Thus, polymers that combine repeating sequences of silk and elastin units are described. Silk-elastin promotes the migration of fibroblasts and macrophages and induces collagen production by fibroblasts, accelerating the formation of granulation tissue more than 3-fold [32]. By varying the sequence ratio, the solubility and material strength of the silk-elastic polymer can be controlled, and its self-gel forming ability is convenient for wound coverage, promoting moisture retention.

Silk-elastin-like polymers, which are in liquid state at room temperature and form hydrogels after injection into the body, are considered to be good candidates as polymer matrices for gene delivery. The mechanism of DNA binding and release with polymers is based on ion exchange [33]. At pH = 7.4, the primary amines of lysine and arginine residues are protonated and interact with negatively charged DNA phosphates. An increase in the ionic strength of the buffer leads to a rise in the concentration of counterions and a weakening of the interaction between DNA phosphates and amino groups, resulting in the release of bound DNA.

Their self-assembly under physiological conditions and thermosetting behavior of these polymers along with their biodegradability, biocompatibility and well-defined composition as a result of their indivudual design make them also attractive for controlled drug delivery [34].

By adding elastin to a mixture of gelatin and cellulose acetate, the structure of the fibre is altered and the rate of degradation of the framework is reduced, supporting fibroblast attachment and proliferation *in vitro* [35]. Fibroblast and keratinocyte proliferation is also promoted by mixing elastin with collagen and polycaprolactone. Improved flexibility caused by elastin also promotes cell infiltration and earlier neovascularisation. And, skin substitutes such as Matriderm and Glyaderm have bovine elastin in their composition, which increases the biomechanical stability and elasticity of remodelled tissue in treated wounds [30].

Elastin-based biomaterials have also been applied to regenerate damaged myocardium, create heart valves, and biostents to restore normal heart function or minimise various injuries [36, 37].

Moreover, the biomaterial, which has elastin in its composition, has shown good mechanical properties in vascular transplantology, both for tearing and suture preservation, at the same time providing effective blood circulation as well as the formation of endothelial cell layer [38].

Elastin-based biomaterials can be easily stored and are relatively inexpensive to produce. However, although elastin is a natural component of the extracellular matrix and is biocompatible and appropriately biodegradable, it is not often used for hydrogel production due to its ability to calcify [39, 40].

Fibrin. Fibrin, one of the main proteins involved in hemostasis, is also actively involved in the natural process of repairing damaged tissues. Fibrin gels have been considered to be an alternative to collagen since the cells cultured in fibrin gel produce more collagen and elastin than cells cultured in collagen gel [41]. Fibrin gels offer advantages such as their outstanding biocompatibility and reconfigurable porosity, providing sufficient surface area and space for cell adhesion, proliferation and regeneration of the extracellular matrix.

At present, fibrin hydrogels are widely used in clinics as haemostatic sealants, biological glues, and various dressings [42].

A hydrogel based on fibrin, fibrinogen and autologous blood with thrombin are being used for biological lung volume reduction, a new method of endobronchial treatment for patients with severe emphysema aimed at reducing the volume of the target lung lobe [43].

Good results have been made possible by attaching synthetic materials to fibrin hydrogels. For instance, a composite of fibrin and polylactic-co-glycolic acid ensures slow drug release and, as a consequence, promotes spinal cord regeneration. By increasing the elastic modulus with the addition of polylactide, earlier regeneration of bone and cartilage tissue occurs [44].

Fibrin-based hydrogels are also used in cardiac tissue engineering. Specifically, a fibrin-based composite material consisting of aligned microfilaments uniformly distributed throughout the hydrogel has been developed [45]. Nevertheless, often the main obstacle for fibrin gels without the addition of other agents is in the low mechanical strength, but combining hydrogels with stable and solid materials significantly improves the physical properties, allowing these limitations to be overcome.

Gelatin. Gelatin is a natural and inexpensive polymer, being biodegradable and having minimal immunogenicity, which make it remain one of the best materials for tissue engineering. Gelatin is also used in the food and pharmaceutical industries, in the manufacture of cosmetics and photographic films as a stabiliser, thickener, emulsifier and film former, and their mechanical properties depend on the supramolecular structure. The polymer is manufactured from the skin and bones of cattle and some fish species [46] by hydration of collagen, with gelatin type A treated with acids (pH = 1–3), gelatin type B – with alkaline solutions. As compared to type B gelatin, type A gelatin has more carboxil groups present, making it more pre-

ferable for creating framework materials. As an example, the addition of type A gelatin to collagen films increased film viscosity, tensile strength and elongation at break, while type B gelatin does not possess such properties [47]. At the same time, the stability of gelatin at high temperatures and a wide pH range makes it convenient to attach synthetic and natural polymers to the gelatin base. Specifically, a gelatin-based hydrogel with the addition of methacrylate promotes prolonged cell survival during transplantation as a consequence of efficient cell proliferation, adhesion and migration in an ischaemic environment. As an experimental result, this hydrogel induced blood flow restoration and neovascularisation in a mouse hind limb ischaemia model [48]. Another group of scientists combined gelatin with nanographene oxide in order to improve mechanical and biomedical properties. The manufactured hydrogel demonstrated unique properties such as moderate roughness, suitable pore size, temperature-dependent viscoelasticity and controlled biodegradation. The hydrogel showed outstanding interactions with bone marrow mesenchymal stem cells and rat chondrocytes. Furthermore, an *in vivo* study showed better formation of healthy hyaline cartilage after microfracture [49].

Gelatin-based hydrogel with added polyurethane with customisable mechanical properties and degradation rate gives the ability to print a complex structure such as a nose-shaped design. The stability of the hydrogel structure was maintained by two-step formation via Ca^{2+}-chelating and thermal gelation at 37 °C without toxic cross-linking reagent. Mesenchymal stem cells incubated with gelatin-polyurethane hydrogel have demonstrated good viability, high motility and proliferation rate [50]. In addition, the hydrogel, which includes gelatin, also increases cell viability during cryopreservation [51].

Solutions of gelatin derivatives are also used for rapid replenishment of circulating blood volume as a result of their iso-oncotic properties. Such solutions are excreted through the excretory system unchanged. In addition, gelatin solutions, as opposed to other colloids, do not affect coagulation and are therefore considered safe in cases of haemorrhage and thrombocytopenia [52]. The gelatin addition to alginate hydrogel improves the mechanical characteristics of the latter, increasing gelation time, swelling ratio, degradation rate, and pore size uniformity [53].

The potential of gelatin as a vascular scaffolding material is being actively studied. As opposed to collagen fibres, gelatin hydrogels have higher tensile strength (8–12 MPa), which makes it convenient to use gels for vascular tissue regeneration [28].

Different conformations of gelatin molecules can be achieved by varying the temperature, solvent, and pH; new materials based on gelatin are still being developed.

Fibroin. Silk fibroin, a protein produced by silkworms, spiders and scorpions, is widely used as a frame material for tissue regeneration [54]. The resulting protein is treated with solvents such as lithium bromide, formic acid, ionic liquids and a triple solvent system $CaCl_2$ – ethanol – water to remove sericin, which glues silk fibers. Water-soluble silk I and insoluble silk II can be classified. By means of an annealing process, silk I transforms into crystalline silk II, in which Young's modulus and tensile strength are both increased [55].

As compared to biomaterials such as collagen, silk fibroin has exceptional mechanical strength, impact toughness and thermal stability [56]. It is also worth remembering that for many decades, silk fibroin has also been used as a suture material.

As a consequence of its good mechanical properties, low immune response, minimal thrombogenicity and appropriate biodegradability, silk fibroin has been used in vascular engineering [28, 57], skin regeneration [56], bone repair [58, 59], nerve, ligament and cartilage recovery [60].

Hydrogels combining the properties of silk and elastin have been used for the controlled release of molecules including vitamin B12 and cytochrome as well as DNA [61].

Silk fibroin is widely used in 3D bioprinting technology, where silk is applied as a backbone obtained by a methacrylation process using glycidyl methacrylate. The mechanical and rheological properties of the hydrogel were found to be unique in experimental studies and are modulated by varying the silk fibroin content. This material has enabled the creation of complex organ structures including heart, blood vessels, brain, trachea and ear with excellent structural stability and can be used for tissue and organ engineering depending on specific biological requirements.

Dextran. Among the natural materials there are also polysaccharides such as dextran, alginate, chitosan and hyaluronic acid. Dextran itself is a non-toxic hydrophilic homopolysaccharide consisting of linear residues (α-1,6-linked d-glucopyranose) with a low percentage of α-1,2-, α-1,3- and α-1,4-linked side chains. Alternately, as a bacterially derived biopolymer, dextran can be synthesised from sucrose of *Leuconostoc mesenteroides* with dextransucrase or from maltodextrins with dextrinase. This polymer chain of glucosyl links may also be synthesised using dextransucrase by transferring the D-glucosyl unit from sucrose to acceptor molecules [62].

Dextran types of different sizes and structures are synthesised depending on the dextransucrase produced by the strain, and their solubility depends on the structure of the branched bonds. As an example, dextrans with more than 40 % branching on α-1,3-linkages is considered insoluble in water, whereas the presence of 95 % linear linkages makes it water-soluble and suitable for biomedical and pharmaceutical applications. A dextran, however, is susceptible to enzymatic degradation by dextranase, which exists in mammalian tissues including humans [63].

As compared to other polysaccharides having functional groups, dextran contains only hydroxyl groups, and new derivatives may be generated by incorporating functionalities without compromising its basic properties. Degree of substitution of dextran derivatives refers to the number of substituted hydroxyl groups per unit

and generally affects the properties of its derivatives, hence dextran can be designed by chemical modification for various purposes. Specifically, this polysaccharide is used to reduce vascular thrombosis by binding to erythrocytes, platelets and vascular endothelium, increasing their electronegativity, reducing erythrocyte aggregation and platelet adhesiveness by decreasing clotting factor VIII. Dextran-coated platelets are more evenly distributed in the thrombus and bound by coarse fibrin, facilitating thrombolysis, in which, by inhibiting α2-antiplasmin, dextran activates plasminogen. At the same time, larger dextrans, remaining in the blood vessels, can act as powerful osmotic agents to eliminate hypovolaemia. Increased volume causes hemodilution, which improves blood flow and further increases the patency of microanastomoses [64]. In addition, dextran is also capable of inhibiting the adhesion of leukocytes to the endothelium by attenuating the IL-8 release without preventing the endotheliocyte activation. As a result, the anti-inflammatory effect is realized [65]. Dextran prevents ischaemic-reperfusion injury in organ transplantation by being able to capture reactive oxygen species and reduce excessive platelet activation [66]. Soluble dextran-haemoglobin complexes synthesised by dialdehyde and alkylation methods can be used to replenish the for circulating blood volume in emergency situations. Chemically modified dextran with altered hydrophilicity (hydrophobicity), sensitivity to temperature, pH and ionic strength is being widely used for drug delivery [67].

Hydrogels can comprise a variety of functionalities, protecting bioactive molecules from being modified. In order to obtain hydrogels with different physical and biological properties including swelling, degradation rate, mechanics, crosslinking density, and biocompatibility, the dextran was introduced with allyl isocyanate, chloroacetic acid ethylamine, and maleic anhydride. Polyethylene glycol diacrylate was introduced as cross-linking agent [68]. In order to improve cell encapsulation by cross-linking glycidyl methacrylate dextran (Dex-GMA) and dithiothreitol (DTT) derivatives in physiological conditions by means of thiol-Michael addition reaction, a hydrogel was prepared and its mechanical properties, gelation process and degree of swelling may be adjusted by changing the pH of phosphate buffer solution [69].

Chitosan. One of the most abundant natural polysaccharides in the world after cellulose is chitin derived from cell walls of the crustacean, insect and fungus exoskeletons, which is used for the chitosan manufacture by deacetylation. Chitosan is a bioactive polymer with a wide range of applications as a result of its functional properties such as antibacterial activity, nontoxicity, ease of modification and biodegradability [70]. One of the advantages of chitosan is the ability to form films, in the process of which formation chitosan powder is mixed with acid solution, poured into a container and dried at room temperature, thermostatically. Among the disadvantages of chitosan-based hydrogels are their limited solubility in some solvents, and poor mechanical properties, which are minimised by chemical or physical modification [71].

Chitosan has a wide range of applications in medical fields. Similar to dextran, it is used for a controlled drug delivery, in tissue engineering, as a blood anticoagulant, an antimicrobial agent and a biomaterial for bone regeneration [72].

For the delivery of drugs and other active molecules, chitosan has unique properties such as *in situ* gelation, mucoadhesion, hydrophilic nature and enhanced permeability. The process of controlled drug release is also known to be dependent on external parameters (temperature, pH). As a consequence of their good biocompatibility and similarity to the extracellular matrix, chitosan hydrogels may serve as promising candidates for targeted delivery of cells, providing them with protection from the immune response and promoting increased cell viability. Additionally, through the reversible bonds of hydrogels, the embedded cells can not only proliferate and migrate but also adjust their morphology.

By considering the temperature sensitivity, which depends on the concentration, molecular weight and degree of deacetylation of chitosan, when using chitosan/αβ-glycerophosphate hydrogel, it was found that the optimum molecular weight was 1360 kDa, gelation temperature was 37 °C, and the percentage of deacetylated chitosan was 75 %, while no gel formation occurred when these characteristics were changed [73].

Chitosan hydrogel modified with 3-(3,4-dihydroxyphenyl)-propionic acid and polyethylene glycol based on sebacic acid modified with p-hydroxybenzaldehyde were prepared as a hemostatic preparation. Along with antibacterial properties, cytocompatibility and sufficient extensibility, the synthesized hydrogel showed a rapid haemostatic effect, due to which the volume of blood loss from the liver in mice was reduced by almost 90 % compared to the control group [74].

Hyaluronic acid. Hyaluronic acid is a polyanionic natural polymer that is a linear polysaccharide composed of glucuronic acid and N-acetylglucosamine. It is the most versatile macromolecule present in the connective tissue of all vertebrates. As a consequence of their good physicochemical properties, hyaluronic acid preparations are used in osteoarthritis surgery, eye surgery, plastic surgery, tissue engineering and drug delivery [75]. When chemically modified, hyaluronic acid can be converted into many physical forms – viscoelastic solutions, hydrogels, fibers, macroporous and fibrillar sponges. The chemical modifications target three functional groups: glucuronic acid carboxylic acid, primary and secondary hydroxyl groups, and N-acetyl group. Carboxylates have been modified by carbodiimide-mediated reactions, esterification and amidation; hydroxyls were subjected to etherification, divinyl sulfone crosslinking, esterification and bis-epoxide crosslinking.

To produce hyaluronic acid-based hydrogels, radical polymerization is used, which includes the formation of a radical under the action of an initiation source (light, temperature, redox reaction) that reacts with a reactive group on the hyaluronic acid macromer to generate kinetic

chains. More often photoinitiated polymerisation is used, the advantage of which is temporal and spatial control [76].

Acrylates and methacrylates are the most common reactive groups for application in radical polymerisation, since they react rapidly with radicals. Among the simplest and most widely used hyaluronic acid modification reactions is the reaction of the acid with methacrylic anhydride to form methacrylated hyaluronic acid, which has been successfully applied to seal corneal tears [77]. As an alternate method of modifying hyaluronic acid, glycidyl methacrylate and hyaluronic acid are reacted to form conjugates, with methacrylation occurring over a long period of time at room temperature. Obtaining tightly cross-linked gels is provided by photocrosslinking, which may also be used to obtain a range of complex fluids from flowable to viscoelastic [78]. Such modifications yield stable and enzymatically degradable hydrogels. In some cases, however, biodegradation needs to be slowed down to limit cell migration and cell-to-cell contacts, or for a system with individualised temporal properties. To that end, hyaluronic acid macromers have been synthesised to form hydrogels that are both hydrolytically and enzymatically degradable by introducing hydrolytically degradable esters (lactic acid, caprolactone) between the hyaluronic acid backbone and the photoreactive groups [79].

Alginate. Alginates – salts of alginic acid – are considered to be no less promising natural materials. Alginic acid is a viscous rubber-like substance, a polysaccharide which is extracted from red, brown, green algae and bacterial source. Alginates are unbranched polysaccharides composed of 1-4-linked β-d-mannuronic acid and its C-5 epimer α-l-guluronic acid.

Alginate biosynthesis may be divided into four stages:

1. Synthesis of mannuronic acid precursor.
2. Cytoplasmic membrane transfer and polymerization into polymannuronic acid.
3. Periplasmic transfer and modification.
4. Export through the outer membrane.

Alginate modification, which can only be carried out in stage 3, depends on solubility, reactivity and characteristics. Alginates can be dissolved in aqueous, organic or mixed media, and the degree of solubility can influence the substitution pattern of the derivatives. The modification occurs at two eOH positions (C-2 and C-3) or at a single eCOOH position (C-6). The difference in reactivity can be easily applied to selectively modify either of these two types [80]. To improve the physicochemical properties, chemical modification is used to increase the ionic strength of the gel, enhance biodegradation, and introduce new properties. In this process, the alginate is being processed by acetylation, phosphorylation, sulfation, hydrophobic modification, attachment of cellular signalling molecules, covalent cross-linking and copolymerisation.

Alginates can be characterised by such biological activities as antimicrobial and haemostatic action, antitoxic and anti-radiation action, hypolipidemic effect, suppression of the activity of facultative flora, and slowing down the rate of glucose absorption from the small intestine. Alginates are an important polysaccharide family for producing hydrogels at moderate pH and temperature conditions which are suitable for sensitive biomolecules such as proteins, nucleic acids [80]. Additionally, complex monosaccharide compositions and the ability to create controlled sequences make alginates a promising material for a variety of applications. Currently, alginates are used as wound dressings [81], have a significant impact in the progression of cystic fibrosis, but more important is the use of alginate cross-linking in the manufacture of hydrogels for the encapsulation of cells and islets of Langerhans in the treatment of diabetes mellitus. Specifically, a thermosensitive sodium alginate/poloxamer 407 (hydrophilic nonionic surfactant of copolymer class)/ pluronic F-127/polyvinyl alcohol hydrogel with the addition of amikacin was developed for wound healing. This hydrogel had good tensile strength and mechanical properties while maintaining elasticity and flexibility due to sufficient cross-linking between hydrogel components. A microscopic investigation revealed a rough surface with sufficient pore size, the presence of which promoted wound oxygenation to accelerate the healing process, provided a moist environment to intensify re-epithelialisation and granulation tissue formation, as well as supported longer release of encapsulated drugs [82]. Similar results were obtained by other researchers who designed a sodium alginate/H_2S hydrogel with $CaCl_2$ as cross-linking agent.The pore size was approximately 50–90 μm, which was suitable for cell penetration and migration; the hydrogel mass increased by more than 120 %. Meanwhile, it has been observed that the release kinetics of the encapsulated substance depends on the pH of the surrounding solution, and release is faster in an acidic environment than in a neutral one [83].

As the majority of hydrogels based on natural materials, alginate gels are used for controlled drug delivery as they have great potential to create drug carriers with adaptive behavior and adjustable properties. To achieve this, the hydrogels were cross-linked by simultaneous photopolymerisation of vinyl groups and photodimerisation of anthracene with the addition of doxorubicin. The involvement of anthracene in the gel leads to reversible crosslinking control and transition between gel/sol states [84].

Alginate/polyacrylamide hydrogel is a potential candidate material for vascular remodelling, which has mechanical strength, resistance to enzymatic degradation and anti-calcification ability, and can inhibit platelet adhesion, aggregation and activation, promote endothelial cell adhesion and proliferation. Additionally, it is able to stimulate the secretion of NO and PGI2, which are important factors, involved in vascular remodelling and repair [85].

CONCLUSION

Currently, naturally occurring polymers are increasingly being used as raw materials for the preparation of hy-

drogels. These are mainly caused by the absence of negative impact on the environment, as well as by the biofunctionality of the derivative products. As a general rule, these polymers allow the production of hydrogels that have desirable properties such as biocompatibility, biodegradability, and non-cytotoxicity. Hydrogels made from natural components show decent results in such biomedical fields as aesthetic medicine, tissue engineering, drug screening, oncological pathology therapy, and others. As a result, natural materials in the basis of hydrogels occupy one of the key places and are promising components in the improvement of existing compositions and the development of new ones.

Conflict of interest

The authors of this article declare no conflicts of interest.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

MICROBIOLOGY AND VIROLOGY

ANTIMICROBIAL POTENTIAL OF IODINE-CONTAINING SUBSTANCES AND MATERIALS

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ABSTRACT

Despite the search and development of new antimicrobial drugs with antibiotic or antiseptic properties, the spread of multidrug-resistant strains of microorganisms remains a serious problem in the treatment and prevention of infectious diseases (wound, postoperative and burn infections, preoperative preparation of the surgical and injection fields, hygienic disinfection of the hands of surgeons, medical personnel, etc.). This review of modern domestic and foreign literature sources is devoted to the analysis of data on the prospects of using antiseptics with iodine and iodides as antimicrobial agents. In modern conditions, there is an increasing number of scientific works devoted to the study and development of various drugs, distinguished by their diversity and their specific application. Antimicrobial iodine-containing compounds can be applied to a wide range of materials such as textile, plastics, metals, ceramics to make them resistant to microbial and biofilm growth. The article summarized the literature data on the high antimicrobial activity of iodine both in neutral carriers and in synergy with substances already possessing similar properties. Such complex preparations lose their toxicity to a large extent, having prolonged action with the preservation of their properties. The main mechanisms of antimicrobial action of iodine and iodine compounds are determined by their strong oxidizing ability. Attention is drawn to the spectrum of activity of iodine preparations. Along with the antimicrobial effect, they can promote regeneration processes. In general, innovative iodine preparations with antibacterial and fungicidal properties are promising for medical and other purposes.

Key words: *iodine, iodine preparations, practical use, antimicrobial activity, opportunistic microorganisms*

Received: 02.06.2023
Accepted: 19.10.2023
Published: 05.12.2023

For citation: Nevezhina A.V., Fadeeva T.V. Antimicrobial potential of iodine-containing substances and materials. *Acta biomedica scientifica*. 2023; 8(5): 36-49. doi: 10.29413/ABS.2023-8.5.4

АНТИМИКРОБНЫЙ ПОТЕНЦИАЛ ЙОДСОДЕРЖАЩИХ ВЕЩЕСТВ И МАТЕРИАЛОВ

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РЕЗЮМЕ

Несмотря на поиск и разработку новых антимикробных препаратов с антибиотическими или антисептическими свойствами, распространение полирезистентных штаммов микроорганизмов по-прежнему остаётся серьёзной проблемой в лечении и профилактике инфекционных заболеваний (раневые, послеоперационные и ожоговые инфекции, предоперационная обработка операционного и инъекционного поля пациента, гигиеническая обработка рук хирургов, медицинского персонала и т. д.). Настоящий обзор современных отечественных и зарубежных литературных источников посвящён анализу данных о перспективах применения веществ и материалов с йодом и йодидами в качестве антимикробных агентов. В современных условиях возрастающее количество научных работ посвящены изучению и разработке различных препаратов, обладающих характеристиками, специфичными для их применения. Антимикробные соединения с йодом могут быть применены к широкому спектру материалов, таких как текстиль, пластик, металлы, керамика, что позволяет этим материалам быть устойчивыми к микробному росту и росту биоплёнок. Обобщены литературные данные по высокой антимикробной активности йода как в нейтральных носителях, так и в синергии с уже обладающими подобными свойствами веществами. Такие комплексные препараты в значительной мере теряют токсичность, действуя пролонгировано с сохранением своих свойств. Основные механизмы противомикробного воздействия йода и соединений с йодом предопределяет их сильная окислительная способность. Обращено внимание на спектр активности препаратов йода. Наряду с антимикробным эффектом, они могут способствовать процессам регенерации. В целом инновационные препараты с йодом с антибактериальными и фунгицидными свойствами перспективны для медицинских и других целей.

Ключевые слова: *йод, препараты йода, практическое использование, антимикробная активность, условно-патогенные микроорганизмы*

Статья поступила: 02.06.2023
Статья принята: 19.10.2023
Статья опубликована: 05.12.2023

Для цитирования: Невежина А.В., Фадеева Т.В. Антимикробный потенциал йодсодержащих веществ и материалов. *Acta biomedica scientifica*. 2023; 8(5): 36-49. doi: 10.29413/ABS.2023-8.5.4

INTRODUCTION

The treatment of diseases caused by infections is currently complicated by the diversity of strains and the emergence of microbial resistance to preparations such as antiseptics and antibiotics [1]. For instance, some microorganisms showed decreased sensitivity to chlorhexidine, triclosan, peracetic acid, benzalkonium chloride, mupirocin, tetracycline and others. [2–4]. The increase in antimicrobial resistance has currently led to fewer treatment options for patients and an associated increase in morbidity and mortality. According to the World Health Organization (WHO), antimicrobial resistance is a global threat to human health and development, and the overuse of these preparations is a major factor in the growth of drug-resistant strains [5].

Susceptibility and resistance to antiseptics and antibiotics are caused by natural adaptive mechanisms regulated by chromosomal DNA as well as by extra-chromosomal elements (plasmids, transposons, etc.) that can move within the genome throughout a single cell or be transmitted to other members of the community through horizontal gene transfer. Phenotypic and genetic mechanisms of antimicrobial resistance have been identified, with the main ones being restriction of drug transport through the cell wall, modification of the drug target, drug deactivation and active drug excretion by outflow systems, as well as the biofilm formation [6].

In about 80 % of chronic and recurrent bacterial infections in the human body are considered to be associated with the biofilm structures formed by infectious agents [7]. Biofilms represent microbial cells in an extracellular matrix produced by them, consisting of polysaccharides, extracellular DNA and other components. As compared to planktonic cells, cells in biofilm are much less sensitive to antimicrobials and this becomes a major cause of ineffective treatment. New technologies development in medicine leads to the expansion of the range of creation and application of various materials, including those with antimicrobial properties, antimicrobial agents of bactericidal and bacteriostatic action of local and systemic application. An important place among modern antiseptic agents, which are an integral part of medicine, is currently being occupied by iodine preparations.

Iodine is known to have antimicrobial activity against a wide range of microbial strains. Being widespread in nature, performing a variety of functions within the majority of living organisms, relatively low cost and environmental safety, iodine has a high potential for use as an antimicrobial agent. Microbial resistance to iodine has not been identified to date. It has recently been shown by the example of *Staphylococcus aureus* that even subinhibitory concentrations of povidone iodine do not lead to the emergence of iodine-resistant bacterial strains [8]. It is caused by the wide variety of microbial cell targets damaged by iodine. The effective disinfection time of bacterial cell populations has been revealed to be between 3 and 15 s at concentrations ranging from 6 to 13 ppm of available iodine, although spores were found to be more resistant to iodine compared to vegetative cells [9]. The elemental iodine, however, is toxic and volatile and can be destroyed by ultraviolet rays, making it difficult to use. Additionally, since iodine is an active oxidant, its partial inactivation by proteins is possible during *in vivo* contact with internal tissues. Consequently, safe materials and preparations containing iodine compounds with certain characteristics that favour the use of iodine regardless of environmental factors are still being developed. An opportunity to obtain stable forms with iodine expands its application as an antiseptic in various spheres, including medicine, veterinary medicine, food industry.

With reference to the above, the aim of the current review is to substantiate the efficacy of iodine, iodine compounds and iodine-containing complexes against infectious agents and to characterize their antimicrobial activity.

CHARACTERISTICS OF IODINE

Iodine, along with chlorine, is a halogen often used to kill microorganisms. The name had come from the Greek "iodes", which means "purple". Iodine is widely, albeit in very diverse concentrations, distributed in nature. It is mainly found in the marine environment. In nature, iodine is known to be involved in the metabolism of some microorganisms. Bacteria can both oxidize and methylate iodide and can also accumulate iodide [10]. Iodine in human biology regulates metabolism, affects the immune and antioxidant systems [11].

Halogens appear to be strong oxidizing agents since they have seven electrons on their outer shell; as oxidizing agents, halogens accept an electron, becoming a halide ion. The antimicrobial efficacy of halogens is a result of both their oxidative capacity and substitution reactions. Halenes, however, differ in their oxidizing potential and disinfecting ability. In particular, the halogen with the strongest oxidizing capacity is fluorine, followed by chlorine, bromine and iodine [12]. However, among these halogens, iodine is the more stable element in the environment.

Iodine is poorly soluble in water; it has been reported that the biological effects of this halogen are associated with its relative hydrophobicity [13]. Iodine has also been reported to be lipophilic and this favours its diffusion through the cell membrane of microorganisms [14]. The water solubility of iodine can be increased in the presence of iodide ions, where polyiodide formation occurs; in order to do this, potassium iodide is most often added to the solution [15]. Although iodine is much better soluble in alcohols, these solvents penetrate the tissues too quickly, causing an excess of iodine, which in turn leads to irritation and other undesirable side effects [16]. A number of studies are available examining the cytotoxicity of iodine and its complexes on fibroblasts, keratinocytes and other cell lines [17].

Some evidence exists demonstrating that compounds containing chlorine and iodine are equally effective in killing vegetative cells, but chlorine compounds are more effective in inactivating spores [9].

Many studies have repeatedly confirmed that elemental iodine I_2 is the most powerful antimicrobial agent compared to other forms of iodine. It is followed by hypoiodous acid (HIO) [18] and the iodine cation H_2OI^+; other forms of iodine dissolved in water have no bactericidal activity [19].

MECHANISMS OF IODINE ANTIMICROBIAL ACTIVITY

Being a small molecule, iodine is able to penetrate the cell wall of microorganisms and react with various cellular components such as proteins, nucleic acids and lipids. As a result, proteins are denatured, nucleic acids are oxidized and cell membranes are destroyed, ultimately leading to cell death. Aromatic hydrocarbons, sulfur-containing amino acids (cysteine, methionine) and unsaturated fatty acids appear to be the main targets [20]. Protein denaturation is achieved by oxidation of SH-groups in cysteine and methionine, and the formation of hydrogen bonds between the amino groups of arginine and histidine and the phenolic groups of tyrosine is also prevented. Iodine is capable of binding to fatty acids via carbon-carbon bonds and to some nucleotides (adenine, cytosine and guanine), thereby changing the structure of nucleic acids, causing DNA strand breaks and mutations in genetic material [21]. Iodine is also effective in inhibiting the activity of enzymes involved in the metabolic pathways of microbes. Eukaryotes are using the reactivity of some iodine species to counteract infections. In mammals, antimicrobial forms of iodine can be secreted as by-products of peroxidases [11]. It induces oxidative stress and eventually leads to microbial cell death. In summary, the antimicrobial mechanism of iodine involves several nonspecific pathways targeting different components of microbial cells, making it an effective and versatile antimicrobial agent.

IODINE PREPARATIONS ACTIVITY SPECTRUM

It is one of the few antimicrobial agents that had been found to be effective against bacteria, viruses, fungi and protozoa as a consequence of its oxidizing properties. *Candida* species are resistant to many antifungal agents. They are capable of producing biofilm, which is an important factor in the pathogenesis of candida infections [22]. It has been also demonstrated that iodine has strong antifungal activity against *Candida* species, including *Candida albicans*, and inhibits the growth and formation of their biofilms. Iodine preparations are known to induce oxidative stress in *Candida* cells. However, there are strains that are less susceptible to oxidative stress. Thus, a study by S. Cuellar-Rufino et al. have revealed mutant strains producing catalase and superoxide dismutases 1 and 2 among *Candida glabrata* strains, which appeared to be more resistant to iodine [23]. Iodine preparations also have fungicidal activity against other genera, including *Aspergillus* [24].

It is considered that the thicker the peptidoglycan layer, the more resistant bacteria are to surfactant antimicrobial preparations [25]. Obviously, iodine preparations have a different effect on the cell membrane of gram-positive and gram-negative bacteria as a result of their structure peculiarities. Gram-positive bacteria have no outer membrane, however, this is compensated for by the construction of a thicker cell wall with peptidoglycan [25]. Peptidoglycan consists of polymerized glycans that form linear chains cross-linked by short peptides. These glycan filaments consist of β-1,4-bound N-acetylglucosamine residues alternating with N-acetylmuramic acid residues [26]. Since iodine is a highly reactive oxidant, there is probably an ability to break chemical bonds in the peptidoglycan layer. Gram-negative bacteria are generally being more protected since their outer membrane, which acts as a permeability barrier for various substances, can probably make iodine penetration less efficient as well [27]. Iodine inactivation of outflow pumps is an important issue, since many multiple drug resistance strains have pumps to remove toxic compounds from the periplasm and cytoplasm [28]. Iodine has the potential to induce the production of reactive oxygen species [29], and in a study of the effects of singlet oxygen on gram-positive and gram-negative bacterial strains, it was revealed that the gram-negative *Escherichia coli* strain was less sensitive to oxidative stress due to the outer membrane compared to the gram-positive *Enterococcus faecium* strain [30].

ANTISEPTIC PREPARATIONS AND MATERIALS WITH IODINE

Since the anti-septic properties of iodine have been discovered, many different preparations with iodine as an active ingredient have been developed. I.V. Popov et al. differentiate the history of creation of these antiseptics into two stages: before the middle of the 20th century – simple; after the middle of the 20th century – complex iodine-containing antiseptics [31]. The authors emphasize in their review that both iodophores and iodine-containing antiseptics derived from enzyme systems and their modifications are currently available for use in practice.

Existing iodine preparations and remedies are diverse in form, including alcoholic 5 % iodine solution, iodized solutions, iodized films and dressings, ointments and creams containing iodine, as well as in properties and areas of application (medicine, veterinary medicine, ecology, food industry). Common combinations with iodine that may be contained in antiseptics include iodine and alcohol, aqueous iodine solution, iodine and polyvinylpyrrolidone, iodine and polyvinyl alcohol, iodine and formaldehyde, and others. Each of the iodine-based antiseptics available on the market today has its own features and recommendations for use.

Antiseptic preparations based on molecular iodine are called iodophores. They are applied in the prevention and in the treatment of infectious complications in medicine and veterinary medicine. The most widely used of the lat-

ter has been povidone iodine available for more than sixty years. This iodophor remains a highly effective agent for the treatment of acute and chronic wounds as a result of its rapid, potent antimicrobial action on both planktonic cells and biofilms [32]. Free iodine is slowly being released from the complex, thereby allowing the gradual release of small amounts of iodine that are not toxic to tissue cells. Forms of povidone iodine preparations are diverse, in various concentrations – from 9 to 12 % – it is available in the form of solution, spray, ointment, etc. [19]. Comparison of 5 % povidone iodine solution with 1 % *in vitro* revealed greater efficacy at lower concentration [33]. Native povidone iodine is hydrophilic, has a pH of about 4.0 and may have an irritant effect [33, 34]. Its antibacterial activity is observed in the pH range of 2.5–7.0 [21]. It has low cytotoxicity compared to many other antiseptics [35]. However, there is evidence that povidone iodine may have cytotoxic effects on human and animal tissue cells, negatively affecting wound healing in preclinical trials, especially in early stages [17]; an increased risk of sensitization has also been reported [36]. Therefore, the search for new iodophores is relevant, as evidenced by the analysis of the literature in recent years.

In addition to povidone iodine, there are many compounds with iodine. Complexation can contribute to controlled release (polymers can be designed for slow and stable release of iodine, which provides a stable antimicrobial effect without cytotoxic effect), increased stability (since iodine can be unstable and easily decompose, but when encapsulated in a matrix it can be protected from decomposition and maintain its antimicrobial activity for long periods time), improved adhesion (the ability to adhere to surfaces such as skin or a water purification filter), reduced toxicity (by minimizing contact of high concentrations with human cells and tissues). These complexes contain molecular iodine, iodide ions, and polymeric substances. Iodine complexes are usually produced hydrophobic as they interact more easily with the bacterial membrane, which consists of a double lipid layer. The hydrophobic material is also better at adsorbing proteins than the hydrophilic material [37]. A significant parameter for a drug has been its surface potential (zeta potential) as it affects its ability to attach to other surfaces as well as to cells.

Iodine carrier polymers may be both of natural (chitosan, chitin, albumin, starch, glycogen, silk, etc.) and synthetic origin (polyvinyl alcohol, polyvinylpyrrolidone, polyamides, etc.) [15]. Apart from that, there are binary compounds of iodine with metals that mutually enhance bactericidal properties of each other. The antibacterial and fungicidal activities of some substances and materials with iodine are summarized in Table 1.

Recently, cationic acrylate copolyvidone-iodine nanoparticles (CACPVI) have been obtained [38]. Being positively charged on its surface, CACPVI demonstrated excellent antibacterial effects on *E. coli*, since the phospholipid molecular layer on the cell membrane of gram-negative bacteria is negatively charged, and inhibited *S. aureus* at a slightly higher concentration. This antibacterial polymer material has a long-lasting effect and is capable of finding applications in the creation of coatings, dyes and inks to minimize bacterial infection.

Iodophor based on antimicrobial rubber nanocapsules of trans-polyisoprene (TPI) has been not only proven to have antimicrobial effects but also promotes wound healing [17]. It was found that this iodophore had the properties of amphiphilicity and biocompatibility, as well as the ability to stimulate cell proliferation. In the study, iodophor was compared with the clinical drug povidone-iodine and demonstrated better antibacterial activity on *E. coli*.

Z. Edis et al. obtained the triiodide complex $[Na(12\text{-crown-}4)_2]I_3$ [14]. Triiodide complex proved to be a broad-spectrum bactericidal agent against reference and clinical isolates of gram-positive *(Streptococcus pneumoniae*, *S. aureus*, *Enterococcus faecalis*, *Streptococcus pyogenes*, *Bacillus subtilis*), gram-negative bacteria *(Proteus mirabilis*, *Klebsiella pneumoniae*, *E. coli*, *Pseudomonas aeruginosa*) and *C. albicans*. Although the size and molecular weight prevent the passage of this compound through the membrane of a bacterial cell, $[Na(12\text{-crown-}4)_2]I_3$ is attracted to it through electrostatic interactions. This compound is hydrophobic and lipophilic, which presumably enhanced the antimicrobial activity. The strong halogen bond between the triiodide ions, however, prevented the release of free molecular iodine. As a result of this phenomenon, on the other hand, the compound $[Na(12\text{-crown-}4)_2]I_3$ remains stable for a long time.

L. Tonoyan et al. have announced the synthesis of a biocidal complex, which is formed following the reaction between ion-oxidisable salts iodide and thiocyanate in the presence of hydrogen peroxide as an oxidation source [39]. Iodine-thiocyanate complex (ITC) is able to incorporate more molecular iodine than povidone iodine. The sensitivity of *E. coli* ATCC 25922, *P. aeruginosa* NCIMB 10421, *S. aureus* DSM 15676 and *S. aureus* MRSA BH1CC strains, their single-species biofilms, as well as two-species biofilms of *S. aureus* DSM 15676 and *Streptococcus uberis* strains were tested to ITC. ITC demonstrated antimicrobial activity against all strains and biofilms tested. The minimum bactericidal concentrations and the minimum concentrations for the destruction of biofilm were in the range of 7.8–31.3 and 31.3–250 $\mu g \times mL^{-1}$, respectively. Against *P. aeruginosa* biofilm, ITC was considered by the authors as the least effective, as a concentration of 125 $\mu g \times mL^{-1}$ was not sufficient for complete killing, but a significant reduction in cell number was observed. The minimum eradication concentration of the mixed biofilm was 250 $\mu g \times mL^{-1}$. This complex can be applied as an antimicrobial agent and for surface disinfection. Further biocompatibility studies are needed.

The hemostatic macroporous polymer foams developed by J.G. Lundin et al. were found to be capable of smooth sustained iodine release as a result of high iodine loading, whereas low loading resulted in its abrupt release [40]. The kaolin contained in the complex served as a haemostatic agent and influenced iodine content and its release rate. In combination with iodine, these polymers are active against *E. coli, K. pneumoniae, P. aeruginosa* and *S. aureus*. This development can be used as a dressing material for wounds.

TABLE 1

IODINE-CONTAINING SUBSTANCES AND MATERIALS AND THEIR ANTIBACTERIAL AND FUNGICIDAL EFFECTS

Names of substances and materials with iodine/ iodides	The substance under study	Strains	Antibacterial and fungicidal effects	Reference
CACPVI	Nanoparticles of about 200 nm in size	*E. coli*, *S. aureus*	Completely inhibited the growth of *E. coli* at a concentration of 20.00 μg × mL^{-1}. Inhibited the growth of *S. aureus* at a concentration of 40.00 μg × mL^{-1}.	[38]
Trans-polyisoprene rubber nanocapsules doped with iodine for 9h (TPI NPs-I_2-9h) and 24h (TPI NPs-I_2-9h)	Spherical rubber nanoparticles with an average diameter of ≈ 120 nm	*E. coli*	Iodide concentration: TPI NPs-I_2-9h, 1.5 wt%; TPI NPs-I_2-24h, 2.5 wt%. MIC: TPI NPs-I_2-9h – 2.5 μg/mL; TPI NPs-I_2-24h – 1.25 μg/mL;	[17]
Triiodide complex [Na (12-crown-4)$_2$]I_3	Lipophilic complex in the form of triclinic crystals	Reference and clinical strains of *S. pneumoniae*, *S. aureus*, *S. pyogenes*, *E. faecalis*, *B. subtilis*, *P. aeruginosa*, *E. coli*, *K. pneumoniae*, *C. albicans* species	The complex at a concentration of 13.3 mg/mL showed ZOI: *S. aureus* – 43 mm, *S. pyogenes* – 34 mm, *E. faecalis* – 39 mm, *S. pneumoniae* – 28 mm. ZOI for *B. subtilis* is 15 mm. At a concentration of 10 mg/mL, the ZOI was: *E. coli* – 23 mm, *P. aeruginosa* – 20 mm, *K. pneumoniae* – 15 mm. ZOI of a clinical sample of *C. albicans* was 50 mm at a concentration of 13.3 mg/mL. ZOI for *C. albicans* WDCM 00054 – 40 mm at a concentration of 10 mg/mL.	[14]
Iodine-thiocyanate complex (ITC) (H_2O_2/KI/KSCN)	A solution of H_2O_2/ KI/KSCN in a ratio of 1:1:1 with a 1% final concentration of the components	*E. coli* ATCC 25922, *P. aeruginosa* NCIMB 10421, *S. aureus* DSM 15676, *S. aureus* BH1CC	MIC/MBC (μg × mL^{-1}): *E. coli* – 15.6/15.6; *P. aeruginosa* – 31.3/31.3; *S. aureus* – 7.8/7.8; *S. aureus* – 15.6/15.6	[39]
Hemostatic macroporous polymeric polyethylene glycol polymer foams enriched with iodine in the form of triiodides	Polymer foam with macroporous structure	*E. coli* ATCC 35695, *S. aureus* ATCC 11987, *K. pneumoniae* ATCC 13883, *P. aeruginosa* ATCC 27853	The ZOI for *E. coli* was 14 ± 1 and 22 ± 2.7 mm; for *K. pneumoniae* – 9.2 ± 0.3 and 19.33 ± 3.2 mm; for *S. aureus* – 12.8 ± 0.3 and 27.8 ± 2.5 mm with KFoam-0.1 and KFoam-1.0 respectively; for *P. aeruginosa* – 14.7 ± 2.1 with KFoam-1.0.	[40]

Note. CACPVI – cationic acrylate copolyvidone-iodine nanoparticles; TPI – trans-polyisoprene; MIC – minimum inhibitory concentration; [Na(12-crown-4)$_2$]I_3 – sandwich complex of two 12-crown-4 molecules surrounding one sodium ion; ZOI – inhibition zone; ITC – iodine-thiocyanate complex; H_2O_2/KSCN – hydrogen peroxide in combination with potassium thiocyanate; MBC –minimum bactericidal concentration; KFoam-0.1, KFoam-1.0 – samples of polymer foam with kaolin impregnated with iodine solutions in ethanol in 0.1 % and 1.0 % mass ratios, respectively.

An assessment of the antimicrobial activity of polyazolidinediammonium modified iodine hydrate ions (PAAG-M) has demonstrated antibiofilm activity against the type strain of *E. coli* ATCC 25922 and clinical *E. coli* FimH [41]. High-

er sensitivity was observed in *E. coli* carrying the virulence gene *FimH*. The complex was previously evaluated against reference strains and clinical isolates of bacteria, microscopic fungi, and RNA-containing viruses [42]. The preparation was found to have an efficient bactericidal effect against strains of gram-positive (*S. aureus* 209P, *Bacillus cereus* 8035) and gram-negative bacteria (*E. coli* 113 – 13, *P. aeruginosa* ATCC 27853), with gram-positive bacteria being more sensitive to this complex [43]. With these findings, PAAG-M should be recommended for use in the treatment of medical devices to prevent infections, including those associated with the presence of microbial biofilms.

As far back as in the last century, K.G. Kristinsson et al. assumed that iodine complex with biologically active polymer matrix, for example, with chitosan, has better biocompatibility with human skin tissues in comparison with iodine adducts with synthetic polymers [44]. Some iodine-containing substances and materials based on organic polymers are presented in Table 2. However, native chitosan membrane has revealed several problems such as low porosity, poor mechanical strength and instability over long time, and low hydrophilicity [45].

Y. Tang et al. successfully obtained a stable iodide complex with chitosan (CTS) [46]. Iodization results revealed

TABLE 2

IODINE-CONTAINING SUBSTANCES AND MATERIALS BASED ON ORGANIC POLYMERS AND THEIR ANTIBACTERIAL AND FUNGICIDAL EFFECT

Names of substances and materials with iodine/iodides	The substance under study	Strains	Antibacterial and fungicidal effects	Reference
Gellan nanocomposite film with polysilicic acid enriched with iodine	Film thickness 0.75 ± 0.02 mm	*E. coli* MTCC 1652, *S. aureus* MTCC 7443	ZOI is 15 ± 1 and 17.3 ± 1 mm for *E. coli* and *S. aureus* strains, respectively.	[48]
Nanocomposite based on starch-reduced graphene oxide and polyiodide (SRGO-PI)	Thin SRGO-PI sheets in several layers with slight creasing	*E. coli* KCTC 2571, *S. aureus* KCTC 3881	The values of half-maximal inhibitory concentration (IC50) were 0.45 and 0.41 mg/mL for *E. coli* and *S. aureus*, respectively. MIC and MBC were 2.5 and 5 mg/mL, respectively, for both *E. coli* and *S. aureus*.	[51]
Porous polymers based on triazine with iodine (I_2@NRPOP-1 and I_2@NRPOP-2)	Porous polymers NRPOP-1 and NRPOP-2 consist of agglomerated spheres having different sizes and different pore densities	*E. coli* (155065A), *P. aeruginosa* (155250A), *M. luteus* (155155A)	ZOI values: in contact with NRPOP-1: for *E. coli* – 0.9 ± 0.1 mm; for *P. aeruginosa* – 1.8 ± 0.1 mm; for *M. luteus* – 2.7 ± 0.2 mm. In contact with NRPOP-2: for *E. coli* – 0.9 ± 0.1 mm; for *P. aeruginosa* – 1.8 ± 0.1 mm; for *M. luteus* – 2.0 ± 0.1 mm.	[54]
Iodine-containing arabinogalactan composite	Nanoparticles ranging in size from 26 to 200 nm	*E. coli* ATCC 25922, *K. pneumoniae* ATCC 700603, *P. aeruginosa* ATCC 27853, *S. aureus* ATCC 25923, *E. faecalis* ATCC 29212, *C. albicans* ATCC	MIC/MBC and MFC values: for *E. coli* - 0.62/1.25 mg/mL; for *P. aeruginosa* - 5/5 mg/mL; for *K. pneumoniae* - 5/5 mg/mL; for *S. aureus* - 1.25/5 mg/mL; for *E. faecalis* - 2.5/5 mg/mL; for *C. albicans* - 1.25/1.25 mg/mL.	[55]

Note. ZOI – inhibition zone; SRGO-PI – a nanocomposite based on starch-reduced graphene oxide with polyiodide; IC50 – semi-maximal inhibitory concentration; MIC – minimum inhibitory concentration; MBC – minimum bactericidal concentration; NRPOP – porous organic polymer based on triazine; MFC – minimum fungicidal concentration.

that the CTS – CTS – I_2 complex exhibited strong antibacterial activity against two bacteria, *E. coli* and *S. aureus*. The results revealed that the complex could have potential applications in biomedical fields such as drug delivery and wound dressing.

Chitosan treatment of polyacrylonitrile fibre material modified with hydroxylamine and iodine (PAN-GA-I_2) was recently undertaken to improve the physical and mechanical properties and water absorption capacity of these materials. It has consequently led to an increase in the strength and hydrophilicity of the material [47].

A nanocomposite film consisting of polysilicic acid, gellan and iodine was prepared and assessed in terms of antibacterial properties by R. Sharma et al. [48]. Gellan gum is an extracellular linear anionic heteropolysaccharide which is obtained via fermentation by the *Sphingomonas paucimobilis* microorganism. Such a carrier is of interest as it is biocompatible, biodegradable and mucoadhesive in nature. This complex showed antibacterial activity to a greater extent for *S. aureus* than for *E. coli*. It is expected to have future applications in pharmaceuticals. *In vivo* model studies are expected to further studies concerning their transformation into a suitable dosage form.

S.G. Sharipova et al. have studied the possibility of stabilization of iodine complex with chitosan by adding gellan gum to it. Since the stability constant increased by an order of magnitude, the authors considered that the presence of gellan gum in the system contributes to the stabilization of the complex [49].

Graphene oxide has long been proven as a carrier for antibacterial agents. It represents an extra-large organic molecule containing a two-dimensional carbon mesh. Graphene oxide particles are highly hydrophilic. They form stable aqueous dispersions over a wide range of concentrations, as well as stable dispersions in a number of organic solvents. Graphene oxide thin films have high optical transparency [50]. A new nanocomposite based on starch reduced graphene oxide with polyiodide showed equally good bactericidal effect against pathogenic gram-negative *E. coli* and gram-positive *S. aureus* bacteria [51]. Such nanomaterial can be used for food packaging.

The effect of multi-walled carbon nanotubes (MWCNTs) functionalized with iodine (15, 10 and 5 wt%) on *E. coli* species and MCF-7 breast adenocarcinoma tumor cells was also studied. By modifying with 15 and 10 wt% iodine, the MWCNTs became significantly antimicrobial active and the survival rate of *E. coli* at concentrations of 0.1 and 0.01 g/L was less than 2 %, while the rate for MWCNTs without iodine was 7 and 30 %, respectively. Reducing the amount of iodine to 5 % slightly reduced the biocidal effect. By comparing the effects of iodine within MWCNTs and pure iodine, the cytotoxic effect of pure iodine was much higher than that of MWCNTs containing iodine in the same concentrations [52].

A.A. Zubenko et al. proposed activated carbon as an iodine carrier eliminating its toxic effect and studied the effect of this complex against *E. coli* and *S. aureus* species. The results revealed that this preparation with 14.5 % iodine content had bacteriostatic activity comparable to that of other preparations (Iodinol and potassium iodide) [53].

The development of porous materials that adsorb iodine has recently become a popular trend as they can provide both its storage and subsequent release. Triazines comprise a class of heterocyclic compounds. Triazine-based porous organic polymers (I_2@NRPOP) with iodine may be promising as antibacterial agents for environmental remediation and drug delivery system [54]. These polymers have the ability to trap iodine vapour back and adsorb it. Iodine loaded polymers demonstrated good antibacterial activity against *Micrococcus luteus*, *E. coli* and *P. aeruginosa* to the same extent.

A method for the preparation of a nanocomposite containing iodine in a natural polymer, arabinogalactan, at a concentration of 13.97 % was recently described [55]. The nanocomposite was most effective against *E. coli* strain ATCC 25922, and least effective against *P. aeruginosa* ATCC 27853 and the ESBL-producing test microorganism *K. pneumoniae* ATCC 700603. Assessment of the inhibitory and fungicidal effects of the nanocomposite revealed its antifungal activity against *C. albicans*. Along with known halogen-containing compounds traditionally used in medicine, this water-soluble composite material of increased stability also has a prospect of use in medical practice and in the development of innovative domestic antimicrobial drugs.

Another study used aqueous dispersions of iodine (18 %) included in a matrix of arabinogalactan at six concentrations (0.1, 0.01, 0.001, 0.0001, 0.00001 and 0.000001 g of starting substance in 1 mL of suspension) [56]. The antimicrobial effect of nanoparticles was studied using five *E. coli* cultures with different biochemical properties (*E. coli* with normal enzymatic activity (NFA) – 3 autostrains; *E. coli* with weak enzymatic activity (WFA) – 1 strain; *E. coli* with hemolytic activity – 1 strain). In a sensitivity assay to iodo-arabinogalactan nanoparticles, *E. coli* showed antibacterial activity against all strains tested only at a concentration of 0.1 g of starting substance in 1 mL of suspension and against two *E. coli* strains NFA and WFA at a concentration of 0.01 g/mL. The authors suggest that the size of the nanoparticles, incompatibility of the arabinogalactan matrix with iodine, or resistance of the strains tested may have contributed to the low efficacy of the complex in this study.

Pectin has the ability to act as a polymeric carrier as a result of its bioactivity and safety. Intermolecular interactions of iodine with low-methoxylated apple pectin modified with pharmacophores were studied. Stable iodine-containing complexes have been obtained on the basis of pharmacophore-containing low-methoxylated pectins with antibacterial activity and prolonged iodine release [57].

V.I. Kostin et al. reduced iodine toxicity via complexation with amaranth pectins. As a result, complexes of iodine, potassium iodide-iodide with amaranth pectin were obtained in a 1:6 ratio (one iodine molecule per six monosaccharide

moieties). In the course of this study, iodine was found to form several types of stable complexes with amaranth pectins. It was found that the obtained complexes of pectin with iodine are superior to iodinol and other iodine preparations in their effectiveness in terms of bacteriostatic action [58].

A.N. Sabitov et al. synthesized a new antimicrobial compound in the system tryptophan – iodine – sodium iodide – water. Cytotoxicity test on MDCK cell culture and determination of mutagenic activity of the complex on L5178Y cell line confirmed the safety of this compound. The complex demonstrated bactericidal activity against both sensitive and multi-drug resistant bacterial strains in the range of 125–250 μg/mL. The test was performed on *S. aureus* ATCC 6538-P; *S. aureus* ATCC BAA-39; *E. coli* ATCC 8739; *E. coli* ATCC BAA-196; *P. aeruginosa* ATCC 9027; *P. aeruginosa* TA2. This complex has the potential to be used as an antimicrobial agent since its low cytotoxicity and antimicrobial activity [59].

Studies in the area of antimicrobial activity of organometallic compounds have expanded in recent years. Some iodine-containing substances and metal-based materials and their antibacterial effects are summarized in Table 3. A.N. Au-Duong et al. developed iodine-enriched zeolite imidazolate framework-8 (ZIF-8), which proved to be an effective bactericide [60]. The result was observed at pH = 6.0 for 3 min, however no appreciable antimicrobial activity could be revealed at pH > 7.0. Gram-negative *E. coli* strain, gram-positive *Staphylococcus epidermidis* and *S. aureus* were killed at a concentration of 0.2 g/L. This is assumed to be a promising protective compound for coating surfaces to prevent bacterial biofilm formation.

TABLE 3

IODINE-CONTAINING SUBSTANCES AND MATERIALS BASED ON METALS AND THEIR ANTIBACTERIAL EFFECT

Names of substances and materials with iodine/iodides	The substance under study	Strains	Antibacterial effect	Reference
Copper iodide nanoparticles	Nanoparticles with an average size of 8 nm	*B. subtilis* ATCC 6633, *S. aureus* ATCC 29737, *E. coli* ATCC 10536, *Shigella dysenteriae* ATCC 12039, *E. coli* DH5α (K12), *E. coli* (EC 505970)	MIC/MBC values: for *E. coli* DH5α – 0.066/0.083 mg/mL; for *E. coli* – 0.1/0.11 mg/mL; for *S. aureus* – 0.1/0.15 mg/mL; for *E. coli.* (EC 505970) – 0.1/0.11 mg/mL; for *S. dysenteriae* – 0.1/0.11 mg/mL; for *B. subtilis* – 0.15/0.18 mg/mL.	[64]
Zeolite imidazolate framework-8, enriched with iodine (ZIF-8@I)	ZIF-8@I nanoparticles are about 530 ± 105 nm in size. ZIF-8 has the shape of a rhombic dodecahedron	*E. coli, S. aureus, K. pneumoniae* and *P. aeruginosa*	The tested strains were killed at a concentration of 0.2 g/L and pH = 6 for 3 min.	[60]
Microgranules of MOF composites passively releasing iodine	Composite MOF UiO-66 microgranules containing encapsulated gold nanorods coated with silica shells doped with iodine	*E. coli, S. aureus*	The concentration of iodine in AuNR@SiO_2@UiO-66 was 0.9 mg(I_2) × mg^{-1}. ZOI for *S. aureus* growth is 31–33 mm; for *E. coli* growth – 24–26 mm.	[16]
Calcium titanate and alloys of calcium titanate with iodine	Nanolayer consisting of calcium titanate and rutile, about 1 μm thick with 0.7–10.5 % iodine on the surface	*S. aureus* MRSA, *S. aureus* ATCC 6538P, *S. epidermidis* ATCC 49134, *E. coli* IFO 3972	Complexes that had been enriched with 8.6 % iodine showed antibacterial activity (reduction rate > 99 %) against all strains; a 97.3 % reduction in MRSA was observed after soaking in PBS for 6 months.	[61]

Note. MIC/MBC – minimum inhibitory concentration/minimum bactericidal concentration; ZIF-8@I – iodine-enriched zeolite imidazolate framework-8; MOFUiO-66 – zirconium-based organometallic framework (UiO – Universitetet of Oslo); ZOI – zone of inhibition; MRSA – methicillin-resistant *Staphylococcus aureus*; PBS – phosphate-buffered saline solution.

MOF UiO-66 microgranules containing encapsulated gold nanorods coated with a silica shell (AuNR@SiO_2@UiO-66) developed by X. Han et al., adsorb and accumulate iodine in very high concentrations and can release it in two ways: slowly and passively in low concentrations or – when exposed to near-infrared light – quickly and actively in high concentrations [16]. The iodine concentration in the microgranules was 0.9 mg(I_2) × mg^{-1}. The diameters of the growth inhibition zones were larger against *S. aureus* than against *E. coli*. The inhibition areas under irradiation had a larger diameter than in the absence of irradiation. Compared to povidone iodine, the inhibition of bacterial growth by this composite film was higher at similar iodine concentrations. The results reveal the promising potential of this composite material for preventing nosocomial and other microbial infections, including coatings for medical instruments or hospital surfaces.

Iodine has the potential to be used as an antimicrobial component in prosthetic materials. It has been recently outlined that calcium titanate and calcium titanate alloys were successfully loaded with iodine and slowly released iodine over a period of 90 days [61]. The sample with an 8.6 % iodine content was tested according to ISO 22196 and revealed high antibacterial activity against *S. aureus* (MRSA), *S. aureus*, *E. coli* and *S. epidermidis*, which persisted for several months. Iodine-containing Ti and its alloys are both expected to be particularly useful for orthopaedic and dental implants, however, *in vivo* studies are still required.

Iodine-supported implants are proving to be very promising in the prevention and treatment of infections, even in the presence of large bone defects. These findings have been disclosed in a review article by K. Ong et al. [62]. It provides some examples about successful demonstration of the antibacterial action of iodine-supported Ti implants in a rabbit femur study. Fewer signs of *S. aureus* and *E. coli* infection and signs of inflammation were observed with iodine-supported Ti implants. The efficacy of iodine-supported Ti implants in the treatment of patients with spinal osteomyelitis, malignant bone tumour or pyrogenic arthritis is also being outlined in this study. No signs of infection were observed in all cases at the time of their most recent follow-up.

Iodine is also capable at forming antimicrobial compounds with metals such as silver, copper and zinc along with polymers [63–65]. These compounds have enhanced antimicrobial activity compared to iodine or metal alone. A complex compound based on silver and iodine, for example, has been developed. Test cultures of the following microorganisms were used in the experiment: *E. coli* ATCC 25922, *Salmonella enterica* subsp. *enterica* ATCC BAA-2162, *S. pneumoniae* ATCC 49619, *S. aureus* ATCC 6538. As a result, the antibacterial activity of the complex compound at 50% concentration against all test bacterial cultures was revealed [66].

A particular feature of copper iodide nanoparticles developed by A. Pramanik et al. comprises their ability to produce reactive oxygen intermediates [64]. Among the tested bacteria, *E. coli* DH5a was more sensitive and *B. subtilis* was more resistant to CuI nanoparticles. Membrane damage is the main mechanism for the bactericidal activity of these nanoparticles. They could potentially be applied in antibiotic therapy.

The complex of zinc iodide with Schiff bases synthesized by M. Montazerozohori et al. has antimicrobial activity against *E. coli* ATCC 25922, *P. aeruginosa* ATCC 9027, *S. aureus* ATCC 6538, *B. subtilis* ATCC 6633, *C. albicans* and *Aspergillus niger* [65].

The "green" synthesis has been recently increasing in popularity, with the key factor being the reduction of toxic impact on the environment. "Green" synthesis involves the use of bacteria, fungi, yeasts, algae or plants that are able to modify the properties of nanoparticles as a result of their metabolic processes. Biosynthesized silver iodide nanoparticles by M. Kannan et al. revealed complete biofilm deactivation at a concentration of 50 mg/mL [63]. Nanoparticles with a mean diameter of 21 nm inhibited the growth of gram-negative bacteria such as *E. coli*, *Vibrio cholerae*, *Salmonella typhi*, and *P. aeruginosa* at nanoparticle concentrations of 75 mg/mL or higher. Study of the mechanisms revealed that free radicals and oxidative stress were responsible for the antibacterial activity.

Silicone is actively used for medical purposes. To the extent that microbial cells adhere to the surface of silicone materials and form biofilms, methods for imparting antimicrobial activity to silicone materials have become in high demand. A method for antibacterial treatment of silicone membranes by a two-step process of immersion in iodine and silver nitrate solutions has recently been developed [67]. Silver iodide particles ranging in size from a few nanometres to a few tens of nanometres were present on the surface of the silicone membrane. Antibacterial activity against *E. coli* NBRC 3301, *S. aureus* NBRC 13276 remained high even after 10-fold acid treatment (pH = 2).

CONCLUSION

Since the heyday of antibiotic therapy with modern antimicrobials, iodine-containing antiseptics have become less popular in light of their increased toxicity. In response to the problem of high antibiotic resistance that has developed over time, however, the approach to the use of preparations in which iodine and iodides are the active ingredients has been reconsidered. Numerous data indicate that many diverse compounds of safe iodide preparations with no pre-existing deficiencies have been developed and have the potential to be used as highly active antimicrobial agents.

Being efficient and non-resistant, iodine is ideal for treating many infectious agents, including those that form biofilms. Iodine-containing compounds are of great interest because of possessing specific parameters, antibacterial and antifungal activity, and low cytotoxicity in various applications.

The literature data studied in this review represent the prospects of using iodine complexes that contribute to the prevention and treatment of infectious complications and diseases in a wide range of medical specialties,

reduce the risk of infection transmission, and prevent microbial growth (treatment and prevention of wound infections and postoperative complications in surgery, traumatology, dentistry, dermatology, burns in combustiology; prevention of superinfection in nosocomial infections, disinfection of operating rooms and injection fields of patients in preparation for surgical interventions and invasive examinations (biopsies, punctures, injections); hygienic treatment of the hands of surgeons and medical personnel, etc.), increasing the strength and durability of materials.

Also promising potential is the use of iodine complexes in the development of new antimicrobial drugs and materials, which in the future may be applied to control microbial activity and prevent the development of infections.

Conflict of interest

The authors of this article declare no conflicts of interest.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

MORPHOLOGY, PHYSIOLOGY AND PATHOPHYSIOLOGY

MORPHOLOGICAL CRITERIA FOR SPORADIC MULTIPLE PARATHYROID GLAND DISEASE

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ABSTRACT

Background. *There are no specific morphological signs for sporadic multiglandular disease (MGD) in primary hyperparathyroidism (PHPT).*

The aim of the study. *To study the structure of the morphological substrate of primary, secondary and tertiary hyperparathyroidism and to assess the effectiveness of morphological criteria in the diagnosis of sporadic multiglandular disease in primary hyperparathyroidism.*

Methods. *The study included 69 patients; 18 patients with PHPT and sporadic multiglandular disease ($n_{preparation}$ = 31) formed the main group, 51 patients ($n_{preparations}$ = 104) – the comparison group. The comparison group was divided into 3 subgroups: 1) patients with PHPT and solitary parathyroid gland (PTG) lesions – 26 patients ($n_{preparations}$ = 26); 2) patients with secondary hyperparathyroidism (SHPT) – 15 patients ($n_{preparations}$ = 48); 3) patients with tertiary hyperparathyroidism (TGPT) – 10 patients ($n_{preparations}$ = 30).*

Results. *The morphological structure of the comparison groups is homogeneous: group 1 is represented by parathyroid adenoma (26 (100 %)), groups 2 and 3 – by hyperplasia (48 (100 %) and 30 (100 %), respectively). Most of the PTG specimens of the main group are represented by hyperplasia (25 (80 %)), and in 1/5 cases – by adenomas (6 (19.4 %)). Sporadic multiglandular disease in PHPT was characterized by a predominant frequency of detecting the absence of a capsule and a rim of unchanged tissue, as well as the presence of adipocytes ($p_{\chi 2} < 0.01$). Components of the PTG morphological structure make it possible to identify changes specific to the sporadic multiglandular disease in PHPT, with a diagnostic efficiency of 76.5–90.3 %.*

Conclusion. *Sporadic multiglandular disease in any clinical variant of hyperparathyroidism is characterized by a high prevalence of hyperplasia – 80 % in PHPT and 100 % in SHPT and TGPT. The following morphological criteria for sporadic multiglandular disease in PHPT have been established: the presence of adipocytes in the PTG parenchyma (diagnostic efficiency (DE) – 90 %)); absence of a capsule (DE = 78 %) and a rim of unchanged gland tissue (DE = 76 %).*

Key words: *pathological assessment, sporadic multiglandular disease, hyperparathyroidism*

Received: 22.06.2023
Accepted: 27.09.2023
Published: 05.12.2023

For citation: Ilyicheva E.A., Kanya O.V., Rozhanskaya E.V., Bersenev G.A. Morphological criteria for sporadic multiple parathyroid gland disease. *Acta biomedica scientifica*. 2023; 8(5): 50-59. doi: 10.29413/ABS.2023-8.5.5

МОРФОЛОГИЧЕСКИЕ КРИТЕРИИ МНОЖЕСТВЕННОГО ПОРАЖЕНИЯ ОКОЛОЩИТОВИДНЫХ ЖЕЛЕЗ ПРИ ПЕРВИЧНОМ ГИПЕРПАРАТИРЕОЗЕ

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РЕЗЮМЕ

Обоснование. *Специфических морфологических признаков множественного поражения околощитовидных желез (ОЩЖ) при первичном гиперпаратиреозе (ПГПТ) нет.*

Цель исследования. *Изучить структуру морфологического субстрата первичного, вторичного и третичного гиперпаратиреоза и оценить эффективность морфологических критериев в диагностике множественного поражения околощитовидных желез при первичном гиперпаратиреозе.*

Методы. *В исследование включены 69 пациентов, из которых основную группу составили 18 пациентов с ПГПТ и множественным поражением ОЩЖ ($n_{препаратов} = 31$), группу сравнения – 51 пациент ($n_{препаратов} = 104$). Группа сравнения была разделена на 3 подгруппы: 1) с ПГПТ и солитарным поражением ОЩЖ – 26 пациентов ($n_{препаратов} = 26$); 2) с вторичным гиперпаратиреозом (ВГПТ) – 15 пациентов ($n_{препаратов} = 48$); 3) с третичным гиперпаратиреозом (ТГПТ) – 10 пациентов ($n_{препаратов} = 30$).*

Результаты. *Морфологическая структура групп сравнения однородна: 1-я группа представлена аденомой ОЩЖ (26 (100 %)), 2-я и 3-я группы – гиперплазией (48 (100 %) и 30 (100 %) соответственно). Большинство препаратов ОЩЖ основной группы представлены гиперплазией (25 (80 %)), а в 1/5 случаев – аденомами (6 (19,4 %)). Для множественного поражения ОЩЖ при ПГПТ было характерно преобладание частоты выявления отсутствия капсулы и ободка неизменённой ткани, а также наличие адипоцитов ($p_{\chi^2} < 0,01$). Структурные компоненты морфологического строения ОЩЖ позволяют выявить изменения, характерные для множественного поражения ОЩЖ при ПГПТ, с диагностической эффективностью 76,5–90,3 %.*

Заключение. *Множественное поражение ОЩЖ при любом клиническом варианте гиперпаратиреоза характеризуется высокой частотой преобладания гиперплазии – 80 % при ПГПТ и 100 % при ВГПТ и ТГПТ. В качестве морфологических критериев множественного поражения ОЩЖ при ПГПТ установлены: наличие адипоцитов в паренхиме железы (диагностическая эффективность (ДЭ) – 90 %); отсутствие капсулы (ДЭ = 78 %) и ободка неизменённой ткани железы (ДЭ = 76 %).*

Ключевые слова: *патоморфологическая оценка, множественное поражение околощитовидных желез, гиперпаратиреоз*

Для цитирования: Ильичева Е.А., Каня О.В., Рожанская Е.В., Берсенев Г.А. Морфологические критерии множественного поражения околощитовидных желез при первичном гиперпаратиреозе. *Acta biomedica scientifica*. 2023; 8(5): 50-59. doi: 10.29413/ABS.2023-8.5.5

Статья поступила: 22.06.2023
Статья принята: 27.09.2023
Статья опубликована: 05.12.2023

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a common endocrinological disease caused by adenoma of a single parathyroid gland (PTG) in 80–85 % of cases (solitary lesion of the PTG), lesions of more than one PTG in 20–25 % (hyperplasia of all glands or double adenomas (double adenomas – multiple PTG lesions), and less than 1 % is caused by cancer of the PTG [1, 2].

The actual incidence of multiple PTG lesions in PHPT is difficult to estimate, as detection depends on the surgical approach of a particular clinic (selective single PTG excision under intraoperative monitoring of intact parathyroid hormone or routine bilateral neck revision), the alertness and experience of the operating surgeon, and the experience of the pathologist to differentiate the pathomorphological basis of hyperparathyroidism from normal PTG tissue [3].

There are no specific morphological signs of multiple lesions of the PTG at the PHPT, histological examination is limited to the determination of the substrate – adenoma or hyperplasia.

The complexity of classifying PTG adenoma from hyperplasia lies in their minor morphological differences. Distinguishing features of hyperplasia as opposed to adenoma comprise the absence of capsule and rim of unchanged PTG tissue, heterogeneous cellular composition with the presence of adipocytes and diffuse proliferative process with the growth of all cellular elements [4–7].

The use of Sudan III staining for fat cell detection has been previously recommended to help distinguish the pathomorphological basis of hyperparathyroidism. Both normal PTG morphological structure and hyperplasia are characterised by the presence of fat droplets in the main cells, while they are few or absent in hyperfunctioning adenoma cells [8].

Adenoma is considered to be a monoclonal true tumour, whereas hyperplasia is characterised by polyclonal growth that develops under the influence of external factors [9, 10]. This is the reason why during hyperplasia there is synchronous enlargement of all PTGs [4]. Revealing hyperplasia after selective parathyroidectomy is associated with a high risk of persistence or recurrence of hyperparathyroidism [11].

THE AIM OF THE STUDY

To study the structure of morphological substrate of primary, secondary and tertiary hyperparathyroidism and to assess the effectiveness of morphological criteria in the diagnosis of sporadic multiglandular disease in primary hyperparathyroidism.

MATERIALS AND METHODS

A single-centre prospective study of a continuous sample consisted of 100 cases of surgically treated patients with PHPT, secondary hyperparathyroidism (SHPT), undergoing renal replacement therapy (RRT), haemodialysis (HD), and tertiary hyperparathyroidism (THPT), undergoing RRT after kidney transplantation (KT), in the thoracic surgical department of the Irkutsk Regional Clinical Hospital in 2020–2021. The inclusion criterion was the indication for surgical treatment for diagnosed PHPT, SHPT and THPT. Exclusion criteria were age below 40 years in those diagnosed with PHPT and multiple PTG lesions, as well as suspected hereditary PHPT.

According to the criteria, 69 patients were included in the study, of which 18 patients with PHPT and multiple PTG lesions formed the main group ($n_{preparation}$ = 31) and 51 patients ($n_{preparations}$ = 104) – the comparison group. The comparison group was divided into 3 subgroups: 1) patients with PHPT and solitary PTG lesion – 26 patients ($n_{preparations}$ = 26); 2) patients with SHPT – 15 patients ($n_{preparations}$ = 48); 3) patients with THPT – 10 patients ($n_{preparations}$ = 30). Control group – 5 preparations of unchanged PTG tissue sampled as a result of intraoperative biopsy of intact PTG from patients with solitary lesions of the PTG in PHPT, recognized by a pathologist as normal PTG tissue.

Sporadic multiglandular disease in PHPT was deemed to be the removal of more than one pathologically altered parathyroid gland or detection of persistence after removal of at least one pathologically altered parathyroid gland.

The object of the study was PTG preparations obtained as a result of surgery. Standard morphological study of hematoxylin-eosin stained preparations was performed by light microscopy in 10 fields of view. This phase evaluated the efficacy of morphological criteria in the diagnosis of sporadic multiglandular disease in PHPT.

The first step was to categorize all PTG tissue preparations into three groups depending on the pathomorphological changes: adenoma, hyperplasia, and normal PTG structure. Adenoma criteria: presence of a rim of unchanged gland tissue, whose cells are in the inactive phase (light main), and a capsule that surrounds a single tumour nodule with a homogeneous cellular composition of the parenchyma, represented by a single cell type; absence of adipocytes in the parenchyma. Hyperplasia criteria: absence of unchanged tissue rim and capsule; heterogeneity of cellular composition of parenchyma and presence of adipocytes in it; formation of cell nodules with clear connective tissue borders. In the second step, three types of hyperplasia were distinguished to clarify the nature of hyperplasia: diffuse, diffuse-nodular and nodular [12]. Diffuse type of hyperplasia is characterised by a uniform increase in the number of cells of the whole gland parenchyma with preservation of the normal lobular structure. In the diffuse nodular type of hyperplasia the lobular structure of the gland parenchyma is disturbed with the formation of multiple encapsulated nodules of cells. Nodular ("pseudo-adenoma", according to the authors) type of hyperplasia is represented by a single large nodule of uniformly proliferating parenchymatous cells resembling an adenoma in PHPT and predominating over the rest of the diffusely hyperplastic PTG tissue.

Being based on the literature data concerning the PTG pathological morphology, the following structural components were used to assess the pattern of PTG morphological changes in different types of hyperparathyroidism (Table 1).

Statistical analysis of data was performed using Statistica 10.0 for Windows software package (StatSoft Inc., USA; license No. AXAR402G263414FA-V). Categorical are presented as number of observations and frequency as a percentage with 95 % confidence interval. Statistical significance was determined using Pearson's chi-square test (χ^2), Fisher's exact test. Differences were considered statistically significant at $p < 0.05$.

All patients signed informed consent to participate in the study. The study was approved by the Biomedical Ethics Committee of Irkutsk Scientific Centre of Surgery and Traumatology (protocol No 9 dated of 09.11.2012).

RESULTS

Table 2 shows the structure of morphological changes of PTG in the main group and comparison groups.

Table 2 reveals that the morphological picture of the comparison groups was homogeneous: group 1 was represented by PTG adenoma, groups 2 and 3 by hyperplasia. The majority of PTG preparations in the main group were represented by hyperplasia, and in 1/5 cases by adenomas. Among 61 PTG preparations of PHPT patients, 25 of 31 preparations (80.6 (62.5–92.5) %) of the main group

TABLE 1

STRUCTURAL COMPONENTS OF THE PARATHYROID GLAND MORPHOLOGY

PTG segments	Components	Assessment
Stroma	Capsule	Presence/absence
	Unchanged tissue rim	Presence/absence
Parenchyma	Uniformity of cellular composition	Yes/No
	Predominant cell type	• main active (dark) • main inactive (light)
	Presence of adipocytes	Yes/No
	Presence of cell nodules with clear connective tissue boundaries	Yes/No

TABLE 2

STRUCTURE OF MORPHOLOGICAL CHANGES IN PARATHYROID GLANDS IN THE MAIN GROUP AND THE COMPARISON GROUPS

Study groups	Morphological characteristics	
	Morphological basis	Number of preparations, *n* (%)
Main group: $n_{patients}$ = 18 (100) $n_{preparations}$ = 31 (100)	Hyperplasia	25 (80.6)
	Adenoma	6 (19.4)
Comparison Group 1: $n_{patients}$ = 26 (100) $n_{preparations}$ = 31 (100)	Adenoma	26 (100)
	Biopsy: normal structure	5 (100)
Comparison Group 2: $n_{patients}$ = 15 (100) $n_{preparations}$ = 48 (100)	Hyperplasia	48 (100)
Comparison Group 3: $n_{patients}$ = 10 (100) $n_{preparations}$ = 30 (100)	Hyperplasia	30 (100)

and 0 of 30 preparations (0 (0–11.5) %) of the comparison group 1 had hyperplasia ($p < 0.01$; χ^2 test).

Figure 1 shows a microphotograph of the normal PTG morphological structure.

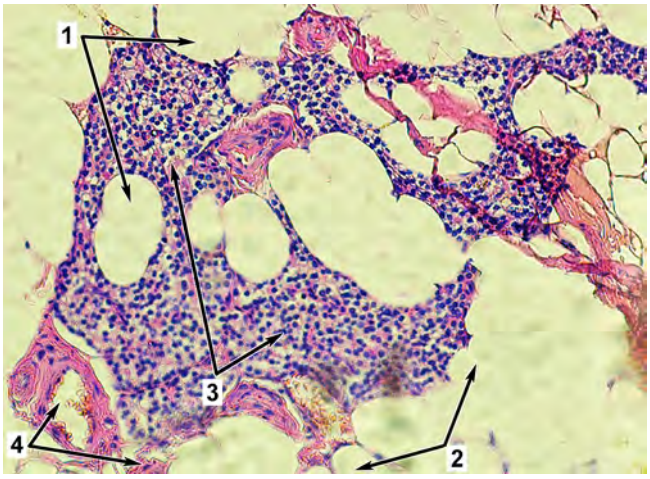

FIG. 1.
Microphotograph. Normal morphological structure of parathyroid gland tissue. Hematoxylin-eosin staining, magnification × 20.
1 *– adipocytes;* **2** *– connective tissue capsule;* **3** *– main light cells;* **4** *– vessel*

The normal morphological structure was characterised by the location of PTG tissue surrounded by adipocytes of adipose tissue. The gland was separated from the latter by a barely visible thin connective tissue capsule, which gave off tracts deep into the stroma, forming a lobular structure. The main cellular stroma consists of inactive (light-coloured) principal cells with light transparent cytoplasm and clear nuclei, grouped in the form of lobules, between which adipocytes and vessels are located.

The frequency of detection of stroma and parenchyma components of preparations in adenoma and hyperplasia was analysed using the selected structural parameters (see Table 1) (Table 3).

According to Table 3, the frequency of detection showing absence of capsule and rim of unchanged tissue was statistically significantly predominant in hyperplasia compared to adenoma ($p < 0.01$). There was no statistical significance of the frequency of the predominant cell type when comparing adenomas and hyperplasias ($p > 0.05$). The frequency of adipocyte detection was statistically significantly predominant in hyperplasia compared to adenomas ($p < 0.01$). Therefore, the structural components of PTG stroma and parenchyma as classical pathomorphological criteria allowed to distinguish adenoma from hyperplasia quite accurately.

TABLE 3

THE FREQUENCY OF DETECTION OF THE COMPONENTS OF STROMA AND PARENCHYMA OF PARATHYROID GLANDS PREPARATIONS DEPENDING ON THE PATHOMORPHOLOGICAL BASIS, *n* (%), [95% CI]

PTG components			Pathomorphologic basis		$p_{\chi 2}$
			denoma, *n* = 32 (100 %)	AHyperplasia, *n* = 103 (100 %)	
Stroma	Capsule	Yes	26 (81.2) [63.5–92.7]	14 (13.6) [7.6–21.7]	**< 0.01**
		No	6 (18.8) [7.2–36.4]	89 (86.4) [78.2–92.3]	
	Unchanged tissue rim	Yes	23 (71.8) [53.2–86.2]	–	**< 0.01**
		No	9 (28.2) [13.7–46.7]	103 (100) [96.4–100.0]	
Parenchyma	Predominant cell type	Main active (dark)	27 (84.3) [67.2–94.7]	78 (75.7) [66.2–83.6]	> 0.05
		Main inactive (light)	5 (15.6) [5.2–32.7]	25 (24.3) [16.3–33.7]	
	Presence of adipocytes	Yes	–	103 (100) [96.4–100.0]	**< 0.01**
		No	32 (100) [89.1–100.0]	–	
	Presence of cell nodules with clear borders	Yes	–	62 (60.1) [50.0–69.7]	**< 0.01**
		No	32 (100) [89.1–100.0]	41 (39.8) [30.2–49.9]	

TABLE 4

THE FREQUENCY OF DETECTION OF THE COMPONENTS OF STROMA AND PARENCHYMA OF PARATHYROID GLANDS PREPARATIONS OF THE MAIN AND COMPARISON GROUPS, *n* (%), [95% CI]

PTG components			Main group, 31 (100 %)	Comparison group 1, 26 (100 %)	Comparison group 2, 48 (100 %)	Comparison group 3, 30 (100 %)
Stroma	Capsule	Yes	6 (19.3) [7.4–37.4]	**20 (76.9) [56.3–91.0]**	6 (12.5) [4.7–25.2]	14 (46.6) [28.3–65.6]
		No	**25 (80.4) [62.5–92.5]**	6 (23.1) [8.9–43.6]	**42 (87.5) [74.7–95.2]**	**16 (53.4) [34.3–71.66]**
	A rim of unaltered tissue	Yes	5 (16.1) [5.4–33.7]	**18 (69.2) [48.2–85.6]**	–	–
		No	**26 (83.9) [66.2–94.5]**	8 (30.8) [14.3–51.1]	**48 (100) [92.6–100.0]**	**30 (100) [88.4–100.0]**
Parenchyma	Predominant cell type	Main active (dark)	30 (96.7) [83,3–99,9]	21 (80.7) [60.6–93.4]	36 (75) [60.4–86.3]	18 (60) [40.6–77.3]
		Main inactive (light)	1 (3.3) [0.1–16.7]	5 (19.3) [6.5–39.3]	12 (25) [13.6–39.6]	12 (40) [22.6–59.4]
	Presence of adipocytes	Yes	25 (80.4) [62.5–92.5]	–	48 (100) [92.6–100.0]	30 (100) [88.4–100.0]
		No	6 (19.3) [7.4–37.4]	**26 (100) [86.7–100.0]**	–	–
	Presence of cell nodules with clear boundaries	Yes	1 (3.3) [0.1–16.7]	–	**35 (72.9) [58.1–84.7]**	**26 (86.6) [69.2–96.2]**
		No	30 (96.7) [83.3–99.9]	26 (100) **[86.7–100.0]**	13 (27.1) [15.2–41.8]	4 (13.4) [3.7–30.7]

Note. Statistically significant results by χ^2 criterion (Fisher's exact test), $p < 0.05$, are shown in bold.

Table 4 shows the frequency of detection of PTG stroma and parenchyma components in the main group and in the comparison groups.

According to Table 4, the frequency of detection of capsule absence in surgical preparations significantly prevailed in the main group and in comparison groups 2 and 3 in comparison with comparison group 1 ($p < 0.01$). Moreover, the frequency of capsule detection was statistically significantly higher in comparison group 3 compared to the main group and comparison group 2 ($p < 0.05$). The capsule absence allows to distinguish the PTG pathology of multiple lesions in PHPT and SHPT patients undergoing RRT HD compared to solitary lesions in PHPT and multiple lesions in THPT patients undergoing RRT KT.

Figure 2 shows a microphotograph of the PTG adenoma morphological structure.

The frequency of detection of rim absence was statistically significantly predominant in the main group and comparison groups 2 and 3 compared to comparison group 1 ($p < 0.01$). Additionally, the frequency of capsule absence detection was statistically significantly prevalent in comparison groups 2 and 3 compared to the main group ($p < 0.01$). Similar to the capsule, detection of the absence of a rim of unchanged PTG tissue allows us to distinguish gland pathology in multiple lesions, in PHPT and SHPT patients undergoing RRT HD, compared to solitary lesions in PHPT and multiple lesions in THPT in patients undergoing RRT KT.

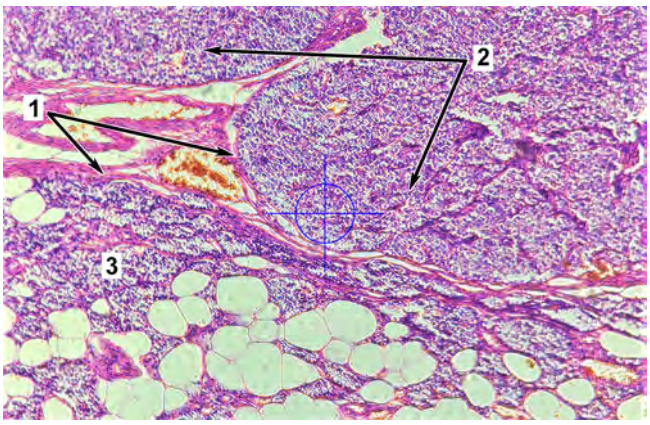

FIG. 2.

Microphotograph. Morphological structure of parathyroid adenoma at the border of adenoma and the "rim" of normal parathyroid tissue. Hematoxylin-eosin staining, magnification × 10. **1** *– connective tissue capsule;* **2** *– parenchyma of the adenoma, represented by a homogeneous cellular composition with a predominance of active (dark) main cells and the absence of adipocytes;* **3** *– stroma of the "island" of unchanged parathyroid tissue*

The frequency of prevalence of major active PTG cells was statistically significantly prevalent in the main group compared to all comparison groups (1, 2 and 3) ($p < 0.05$). In contrast, no statistically significant frequency of prevalence of active or inactive main PTGs was found by comparing comparison groups 1, 2 and 3 with each other ($p > 0.05$). In our sample, the predominance of major active cells appeared to distinguish the glandular pathology of multiple PTG lesions in patients with PHPT from other types of hyperparathyroidism.

The frequency of adipocyte detection in the gland parenchyma was statistically significantly predominant in the main group compared to comparison group 1 ($p < 0.01$). Additionally, the frequency of adipocyte detection in PTG parenchyma was statistically significantly predominant in comparison groups 2 and 3 compared to comparison group 1 ($p < 0.01$). Detection of adipocytes in the gland parenchyma allows to distinguish the pathology of multiple PTG lesions in any type of hyperparathyroidism from solitary ones in PHPT.

The frequency of cell nodule detection in the gland parenchyma was statistically significantly predominant in both comparison group 2 and comparison group 3 as compared to both the main group and comparison group 1 ($p < 0.01$). However, there was no statistically significant predominance of cell nodules in comparison group 2 compared to comparison group 3 ($p > 0.05$). Cell nodule formation appeared to be characteristic of multiple lesions in SHPT and THPT and distinguishes it from the pathology in PHPT.

TABLE 5

THE FREQUENCY OF DETECTION OF DIFFERENT TYPES OF HYPERPLASIA IN THE MAIN GROUP AND IN THE COMPARISON GROUPS 2 AND 3, *n* (%), [95% CI]

Study groups	Type of hyperplasia	Quantity
Main group 25 (100) [86.2–100.0]	Diffuse	**21 (84.0) [63.9–95.4]**
	Diffuse nodular	4 (16.0) [4.5–36.0]
Comparison group 2 48 (100) [92.6–100.0]	Diffuse	13 (27.0) [15.2–41.8]
	Diffuse nodular	**29 (60.4) [45.2–74.2]**
	Nodular	6 (12.6) [4.7–25.2]
Comparison group 3 30 (100) [88.4–100.0]	Diffuse	4 (13.4) [3.7–30.7]
	Diffuse nodular	12 (40.0) [22.6–59.4]
	Nodular	**14 (46.6) [28.3–65.6]**

Note. Statistically significant results by χ^2 criterion (Fisher's exact test), $p < 0.05$, are shown in bold.

Table 5 shows the frequency of detection of different types of hyperplasia in the main group and in comparison groups 2 and 3.

According to Table 5, the incidence of diffuse hyperplasia was statistically significantly predominant in the main group compared to comparison groups 2 and 3($p < 0.01$). There was no statistically significant predominance of the diffuse hyperplasia incidence in comparison group 2 as compared to comparison group 3 ($p > 0.05$).

Figure 3 shows a microphotograph of the morphological structure of PTG hyperplasia (diffuse hyperplasia).

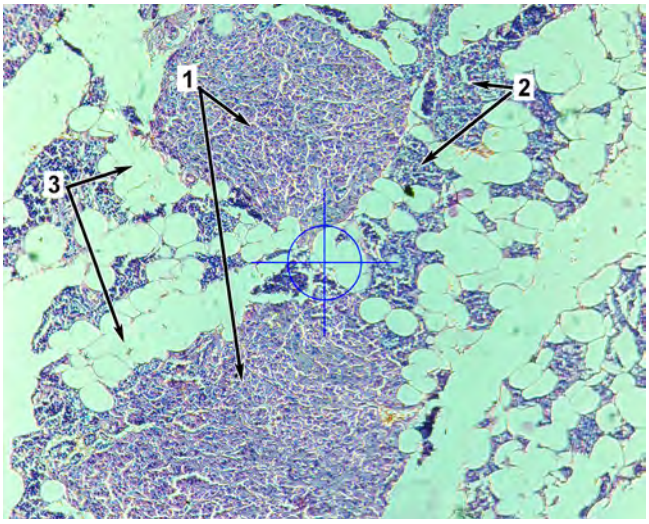

FIG. 3.

Microphotograph. Diffuse hyperplasia of the parathyroid gland. Hematoxylin-eosin staining, magnification × 10. **1** *– main dark cells;* **2** *– main light cells;* **3** *– adipocytes*

The frequency of diffuse nodular hyperplasia cases was statistically significantly higher in comparison group 2 as compared to the main group ($p < 0.01$). There was no statistically significant predominance of the diffuse nodular hyperplasia incidence in comparison group 2 as compared to comparison group 3 ($p > 0.05$).

Figure 4 shows a microphotograph of the morphological structure of PTG hyperplasia with nodule formation (diffuse nodular hyperplasia).

The frequency of detection of nodular hyperplasia was statistically significantly higher in comparison group 3 as compared to the main group and comparison group 2 ($p < 0.01$).

Figure 5 shows a micrograph of the morphological structure of PTG hyperplasia with nodule formation (nodular hyperplasia).

By comparing the histological examination data and surgical outcomes, the results of diagnostics of morphological signs of multiple PTG lesions in PHPT using the selected structural criteria were obtained (Table 6).

By comparing the data of the histological study and the results of the surgery (Table 6) the operative

characteristics of the structural components of the morphological structure of the gland in diagnosing the pathology of multiple PTG lesions in PHPT were calculated (Table 7).

Table 7 shows that the structural components of the PTG morphological structure allow us to diagnose changes characteristic of multiple PTG lesions in PHPT with a diagnostic efficiency of 57.9–90.3 %.

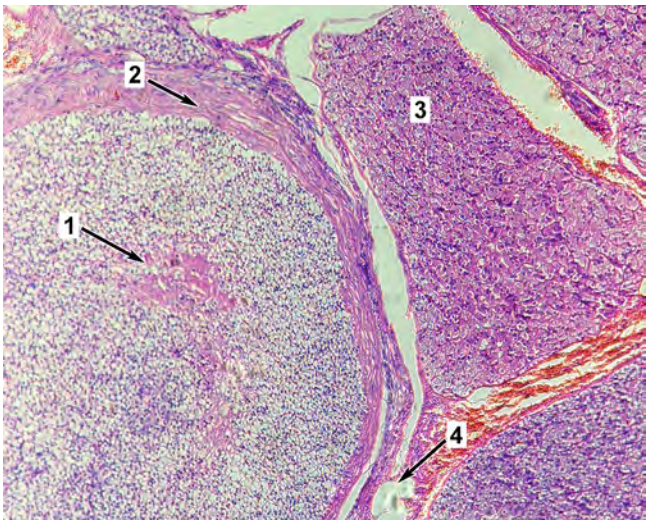

FIG. 4.
Microphotograph. Diffuse-nodular hyperplasia of the parathyroid gland. Hematoxylin-eosin staining, magnification × 10. **1** *– node of the main light cells;* **2** *– connective tissue border;* **3** *– the main parenchyma of dark smooth cells;* **4** *– adipocytes*

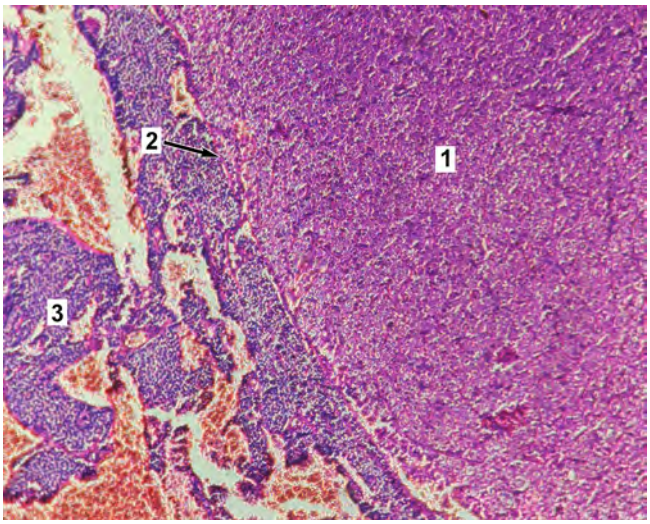

FIG. 5.
Microphotograph. Nodular hyperplasia of the parathyroid gland. Hematoxylin-eosin staining, magnification × 10. **1** *– area of nodular hyperplasia from the main light cells;* **2** *– connective tissue border;* **3** *– main parenchyma of dark smooth cells*

TABLE 6

RESULTS OF STUDY OF MORPHOLOGICAL SIGNS OF MULTIGLAND PARATHYROID DISEASE IN PRIMARY HYPERPARATHYROIDISM USING SELECTED STRUCTURAL CRITERIA

Results	True positive	False positive	False negative	True negative
Capsule absence	25	6	6	20
Rim of unchanged tissue absence	26	8	5	18
Predominance of main active cells	30	21	1	5
Presence of adipocytes	25	0	6	26

TABLE 7

OPERATIONAL CHARACTERISTICS OF THE COMPONENTS OF THE MORPHOLOGICAL STRUCTURE OF THE PARATHYROID GLAND IN THE DIAGNOSIS OF MULTIGLANDULAR PARATHYROID DISEASE, % (95% CI)

Characteristics	DSE	DSP	DE	PPV	NPV
Capsule absence	80.6 (62.5–92.5)	76.9 (56.3–91.0)	78.7 (66.5–81.6)	80.6 (62.5–92.5)	76.9 (56.3–91.0)
Rim of unchanged tissue absence	83.8 (66.2–94.5)	69.2 (48.2–85.6)	76.5 (69.4–80.9)	76.4 (58.8–89.2)	78.2 (56.3–92.5)
Predominance of main active cells	96.7 (83.3–99.9)	19.2 (6.5–35.3)	57.9 (42.5–64.2)	58.8 (44.1–72.4)	83.3 (35.8–99.5)
Presence of adipocytes	80.6 (62.5–92.5)	100.0 (86.7–100.0)	90.3 (87.5–99.9)	100.0 (86.7–100.0)	81.2 (63.5–92.7)

Note. DSE – diagnostic sensitivity; DSP – diagnostic specificity; DE – diagnostic efficiency; PPV – positive predictive value; NPV – negative predictive value.

DISCUSSION

Thus, in our sample, the majority of PHPT patients with multiple PTG lesions had hyperplasia as the morphological substrate and 1/5 had adenomas.

Previously, we retrospectively analysed the case histories of 62 patients suffering from PHPT with both solid and multiple PTG lesions (44 and 18 patients, respectively), assessing surgical outcomes and PTG morphology [13]. Multiple PTG lesions were found to be the main cause of disease persistence (16 %) [13]. The structure of the morphological substrate was heterogeneous: with a solitary PTG lesion – 52.2 % adenomas and 40.9 % hyperplasias, with multiple – 22.1 % adenomas, 72.2 % hyperplasias [13, 14]. Among 18 patients in the main group, persistence was observed in 8 out of 14 (57 %) with the morphological substrate of PTG hyperplasia and in 2 out of 4 (50 %) with adenoma ($p_{\chi 2} > 0.05$) [13, 14]. The heterogeneity of the morphological structure and its lack of influence over the outcome of surgical treatment in PHPT with solitary and multiple PTG lesions dictated this study.

The question was posed: are there pathomorphological features of multiple PTG lesions and can routine microscopy distinguish between them?

In our sample of PHPT patients with multiple PTG lesions, a heterogeneous morphological structure with a prevalence of hyperplasia of 80 (62–92) % and a hyperplasia to adenoma ratio of 4:1 was revealed. In other clinical variants of hyperparathyroidism the morphological structure was homogeneous: in PHPT with solitary lesion of PTG – adenoma (100 (86–100) %), in SHPT and THPT – hyperplasia (100 (92–100) % and 100 (88–100) %, respectively).

Morphological structural criteria known in the literature to distinguish hyperplasia and PTG adenoma [4–7] allowed us to establish that multiple glandular lesions in PHPT compared to solitary ones were characterised by a predominant frequency of absence of capsule and rim of unchanged tissue, presence of adipocytes in the parenchyma and main active (dark) cells. The diagnostic efficiency of these criteria in detecting sporadic multiglandular disease in PHPT was 57–90 %. The following criteria were found to be most effective: presence of adipocytes (90 %), absence of capsule (78 %) and rim of unchanged glandular tissue (76 %).

CONCLUSION

Sporadic multiglandular disease in any clinical variant of hyperparathyroidism is characterised by a high frequency of predominance of the morphological substrate in the form of hyperplasia – 80 % (62–92 %) in primary hyperparathyroidism and 100 % (92–100 % and 88–100 %, respectively) in secondary and tertiary hyperparathyroidism. The following morphological criteria of multiple PTG lesions in primary hyperparathyroidism were established: presence of adipocytes in the gland parenchyma (DE = 90 %), absence of capsule (DE = 78 %) and rim of unchanged gland tissue (DE = 76 %).

Funding

The study and publication of the article are carried out in accordance with the plan of research work (R&D) of Irkutsk Scientific Centre of Surgery and Traumatology No. 063 "Biomedical technologies for the prevention and treatment of organ failure in reconstructive and restorative surgery" (due dates 2013–2021) and R&D "Personalized approach to the prevention and correction of multiple organ dysfunction in the treatment of surgical diseases" (due dates 2013–2021), as well as R&D "Personalized approach to the prevention and correction of multi-organ dysfunction in the treatment of surgical diseases" (due in 2022–2026).

Conflict of interest

The authors declare no apparent and potential conflicts of interest related to the publication of the present article.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

NEUROLOGY AND NEUROSURGERY

COMPLEX NEUROIMAGING ASSESSMENT OF THE PROXIMAL SEGMENT AFTER RIGID FIXATION AND DYNAMIC STABILIZATION IN PATIENTS WITH DEGENERATIVE LUMBAR DISEASE

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Received: 07.03.2023
Accepted: 14.11.2023
Published: 05.12.2023

ABSTRACT

Background. *The development of the adjacent level syndrome and, as a consequence, adjacent segment degenerative disease are currently the most common complications of decompression and stabilization surgery with the development of segmental instability.*

The aim of the study. *To conduct a comprehensive neuroimaging assessment of the proximal adjacent segment after rigid fixation and dynamic stabilization in degenerative lumbar disease.*

Materials and methods. *We conducted a prospective multicenter study of the results of surgical treatment of 274 patients with degenerative-dystrophic diseases of the lumbar spine, who underwent monosegmental decompression and stabilization surgery using the TLIF (transforaminal lumbar interbody fusion) technique and open transpedicular rigid fixation, as well as open hemilaminectomy with stabilization of the operated segments with nitinol rods. The study included radiography, diffusion-weighted magnetic resonance imaging and computed tomography (dual-energy mode) of intervertebral discs and isolated facet degeneration of the upper adjacent level.*

Results and discussion. *Combination of the initial proximal segment degeneration in the form of facet joints degeneration (density of cartilaginous plate – 163.5 ± 14.2 HU, density of external facet – 709.35 ± 13.6 HU, density of internal facet – 578.1 ± 12.1 HU), Pfirrmann III, IV grade degeneration of intervertebral disc and a measured diffusion coefficient of less than 1300 mm^2/s cause high risks of developing adjacent segment degenerative disease, which regulates the use of monosegmental dynamic fixation with nitinol rods, or preventive rigid fixation of the adjacent segment.*

Conclusion. *Using complex neuroimaging in the preoperative period makes it possible to predict the results of surgical treatment, take timely measures to prevent degenerative diseases of the adjacent segment, and to carry out dynamic monitoring of processes in the structures of the spinal motion segment.*

Key words: *degenerative diseases of the lumbar spine, rigid fixation, dynamic fixation, adjacent segment, intervertebral disc, facet joint*

For citation: Krivoschein A.E., Kolesov S.V., Kalinin A.A., Konev V.P., Kazmin A.I., Moskovskiy S.N., Byvaltsev V.A. Complex neuroimaging study of the proximal segment after rigid fixation and dynamic stabilization in patients with degenerative lumbar disease. *Acta biomedica scientifica*. 2023; 8(5): 60-72. doi: 10.29413/ABS.2023-8.5.6

КОМПЛЕКСНАЯ НЕЙРОВИЗУАЛИЗАЦИОННАЯ ОЦЕНКА ПРОКСИМАЛЬНОГО СЕГМЕНТА ПОСЛЕ РИГИДНОЙ ФИКСАЦИИ И ДИНАМИЧЕСКОЙ СТАБИЛИЗАЦИИ У ПАЦИЕНТОВ С ДЕГЕНЕРАТИВНЫМ ЗАБОЛЕВАНИЕМ ПОЯСНИЧНОГО ОТДЕЛА

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Статья поступила: 07.03.2023
Статья принята: 14.11.2023
Статья опубликована: 05.12.2023

РЕЗЮМЕ

Введение. *Развитие синдрома смежного уровня и, как следствие, дегенеративное заболевание смежного сегмента в настоящее время являются самыми частыми осложнениями декомпрессивно-стабилизирующих вмешательств с развитием сегментарной нестабильности.*

Цель исследования. *Провести комплексную нейровизуализационную оценку проксимального смежного сегмента после ригидной фиксации и динамической стабилизации при дегенеративной патологии поясничного отдела позвоночника.*

Материалы и методы. *Проведено проспективное мультицентровое исследование результатов хирургического лечения 274 пациентов с дегенеративно-дистрофическими заболеваниями поясничного отдела позвоночника, которым выполнено моносегментарное декомпрессивно-стабилизирующее вмешательство с применением методики TLIF (transforaminal lumbar interbody fusion) и открытой транспедикулярной ригидной фиксации, а также открытой гемиляминэктомии со стабилизацией оперированных сегментов стержнями из нитинола. Исследование включало рентгенографию, диффузионно-взвешенные магнитно-резонансную томографию и компьютерную томографию (в двухэнергетическом режиме) межпозвонковых дисков (МПД) и изолированной фасеточной дегенерации верхнего смежного уровня.*

Результаты и обсуждение. *При сочетании исходной дегенерации проксимального сегмента в виде дегенерации дугоотросчатых суставов с плотностью хрящевой пластинки 163,5 ± 14,2 HU, наружной фасетки 709,35 ± 13,6 HU, внутренней фасетки 578,1 ± 12,1 HU, денегерации МПД III, IV степени по C.W. Pfirrmann и измеряемого коэффициента диффузии менее 1300 мм^2/с имеются высокие риски развития дегенеративного заболевания смежного сегмента, что регламентирует использование моносегментарной динамической фиксации с использованием стержней из нитинола, или проведение превентивной ригидной фиксации смежного сегмента.*

Заключение. *Использование комплексной нейровизуализации в предоперационном периоде позволяет проводить прогнозирование результатов хирургического лечения, своевременно принимать профилактические меры по профилактике дегенеративных заболеваний смежного сегмента и осуществлять динамическое наблюдение за процессами в структурах позвоночно-двигательного сегмента.*

Ключевые слова: *дегенеративные заболевания поясничного отдела позвоночника, ригидная фиксация, динамическая фиксация, смежный сегмент, межпозвонковый диск, дугоотросчатый сустав*

Для цитирования: Кривошеин А.Е., Колесов С.В., Калинин А.А., Конев В.П., Казьмин А.И., Московский С.Н., Бывальцев В.А. Комплексная нейровизуализационная оценка проксимального сегмента после ригидной фиксации и динамической стабилизации у пациентов с дегенеративным заболеванием поясничного отдела. *Acta biomedica scientifica*. 2023; 8(5): 60-72. doi: 10.29413/ABS.2023-8.5.6

INTRODUCTION

Lumbar spinal stenosis is the most common indication for operation in spinal surgery. The main method of surgical treatment of such pathology is the use of decompressive-stabilizing interventions, which allow to control neurological symptoms [1, 2]. At the same time, surgical treatment does not stop the progression of the disease, but is only aimed at eliminating its clinical manifestations. A number of experts note that after surgery in the long term, there is a decrease in the quality of life of patients as a result of recurrence of degenerative pathology [3–5].

The development of adjacent level syndrome and, as a consequence, adjacent segment degenerative disease (ASDD) are currently the most frequent complications of decompressive-stabilizing interventions with the development of segmental instability [6]. According to the literature, the development of ASDD 10 years after posterior rigid stabilization occurs in 6.7–80.0 % of patients, 24 % of whom require revision surgery, with the vast majority of cases involving the upper (proximal) adjacent segment [7–10]. In order to level the progression of the degenerative cascade and preserve physiological parameters of adjacent segment biomechanics, dynamic stabilizing systems [11, 12] have been introduced into the clinical practice of spinal surgeons to prevent the development of ASDD.

Along with the improvement of implants for decompressive and stabilizing interventions on the spine, a detailed preoperative assessment of not only the affected but also adjacent segments is necessary to prevent adverse clinical outcomes and the risks of repeated surgical interventions [6]. Modern preoperative neuroimaging should include standard and functional radiography, magnetic resonance imaging (MRI), and Multislice Spiral CT Scan (MSCT) [13–15], which allow proper planning of the surgical strategy and assessment of the dynamics of pathological processes after surgical intervention [16].

One of the efficient ways to assess the microstructural state of the intervertebral disc (IVD) to determine the possible surgical treatment tactics is the use of diffusion-weighted (DW) MRI with calculation of the Apparent diffusion coefficient (ADC) values [17]. An adjacent segment MDC value of less than 1300 mm^2/s was found to be statistically significantly associated with the development of ASDD [18].

The second of the main parameters in the assessment of the adjacent functional spinal unit (FSU) is the assessment of the facet joints (FJ). A correlation between morphological and radiological changes in FJ according to dual-energy computed tomography (DECT) has been established [19, 20]. The obtained numerical indices of FJ element density [21] in combination with ADC indices for IVD allow a comprehensive assessment of the affected and adjacent segments when planning surgical treatment of patients with degenerative pathology of the lumbar spine, as well as for postoperative control.

This research study aims to analyse the dynamics of degenerative changes in the IVD and FJ of the proximal adjacent segment after decompressive-stabilising interventions using different fixation systems in the context of the risks of ASDD development.

THE AIM OF THE STUDY

To conduct a comprehensive neuroimaging assessment of the proximal adjacent segment after rigid fixation and dynamic stabilization in degenerative lumbar disease.

MATERIALS AND METHODS

In the period from January 2017 to January 2022, in three clinics: Department of Traumatology No. 2 (Vertebrology) of the Clinical Medical and Surgical Center of the Ministry of Health of the Omsk region (Omsk), Department of Spinal Pathology, National Medical Research Center for Traumatology and Orthopedics named after N.N. Priorov (Moscow), Center for Neurosurgery, Clinical Hospital "Russian Railways-Medicine" (Irkutsk) – a prospective multicentre study according to a single approved protocol was conducted. The study was carried out in accordance with the Declaration of Helsinki of the World Medical Association "Ethical Principles of Scientific Medical Research Involving Human Subjects" as amended in 2000 and "Rules of Clinical Practice in the Russian Federation" approved by the Order of the Ministry of Health of Russia No. 266 dated June 19, 2003. The study was approved by the Ethical Committee of the Omsk State Medical University (protocol No. 4 dated December 12, 2016).

Medical records of 274 patients who underwent decompression-stabilizing interventions using rigid and dynamic fixation between January 2017 and January 2018 were included in the study. Informed consent was obtained from each patient before the examination. Two main groups were selected: group I (n = 139) underwent monosegmental decompression-stabilizing intervention using open median access with bilateral skeletonisation of paraspinal musculature, facetectomy, decompression of neural structures, TLIF (transforaminal lumbar interbody fusion) methodology and open transpedicular rigid fixation; group II (n = 135) underwent monosegmental decompression-stabilizing intervention using open median access with bilateral skeletonization of the paraspinal musculature, hemilaminectomy and decompression of neural structures, with stabilization of the operated segments with nitinol rods.

The inclusion criteria were monosegmental lesion at the level of L_{IV}–L_V, L_V–S_I with clinical manifestations of compression radiculopathy, high level of segmental translation in the area of the affected segment, absence of clinical and radiological signs of proximal syndrome.

The exclusion criteria were as follows: bisegmental lesions with clinical manifestations of compression radicu-

lopathy; previous surgical interventions on the lumbosacral spine; history of spinal trauma; confirmed tumour process; infectious lesions of the spinal column; spondylolysis spondylolisthesis and the presence of osteoporosis (T-test below –2.5 SD). The study design with exclusion reasons is summarised in Figure 1.

Clinical parameters were assessed using the visual analog scale (VAS) of pain for back and lower extremities, the Oswestry Disability Index (ODI) and the SF-36 questionnaire (Short Form 36).

Digital images were evaluated using the image archiving and transmission system and MultiVox DICOM Viewer software (Gammamed, Russia). Measurements were performed by three independent expert radiologists, from whom all information, including age, patients' name and imaging time, was completely concealed to prevent subjective interpretation error. The mean values of the measurements between the three observers were taken for analysis in order to ensure inter-observer consistency. Segmental translation was measured from lateral radiographs of the lumbar spine; for this measurement, a perpendicular line was drawn from the posterior edge of the lower endplate of the upper vertebra to the line of the upper endplate of the lower vertebra; the length between the two lines was defined as segmental translation, a criterion for segment instability. The study of adjacent segments (IVD) was performed using T2-mode MRI with C.W. Pfirrmann classifications and diffusion-weighted image analysis. The condition of isolated degeneration of the FJ proximal adjacent level was assessed using MSCT in DECT with determination of quantitative X-ray morphometric parameters of the FJ (optical density of the external and internal facets, cartilage plate area) according to Hounsfield unit (HU).

Clinical results and a set of instrumental parameters were evaluated before surgery and 6, 12, 36, 60 months after surgical treatment.

Statistical processing of the obtained data was performed by methods of variation statistics using standard packages Microsoft Excel 2016 (Microsoft Corp., USA), Statistica 12.0 (StatSoft Inc., USA), BioStat (AnalystSoft, USA). We also used a standard control in MS Excel to sample the values of the middle of the table to display on the chart in the infinity symbol style. The advantages and disadvantages of each method of fixation are revealed through a comparative chart. Microsoft Excel 2016 spreadsheet editor (Microsoft Corp., USA) was used to create the database. In case of non-normal distribution type, non-parametric criteria were used: intergroup analysis using Mann – Whitney test (p_{M-U}), intragroup analysis using Wilcoxon test (p_W). Statistical measurement of the relationship (strength and direction) between the signs was carried out by calculating the Spear-

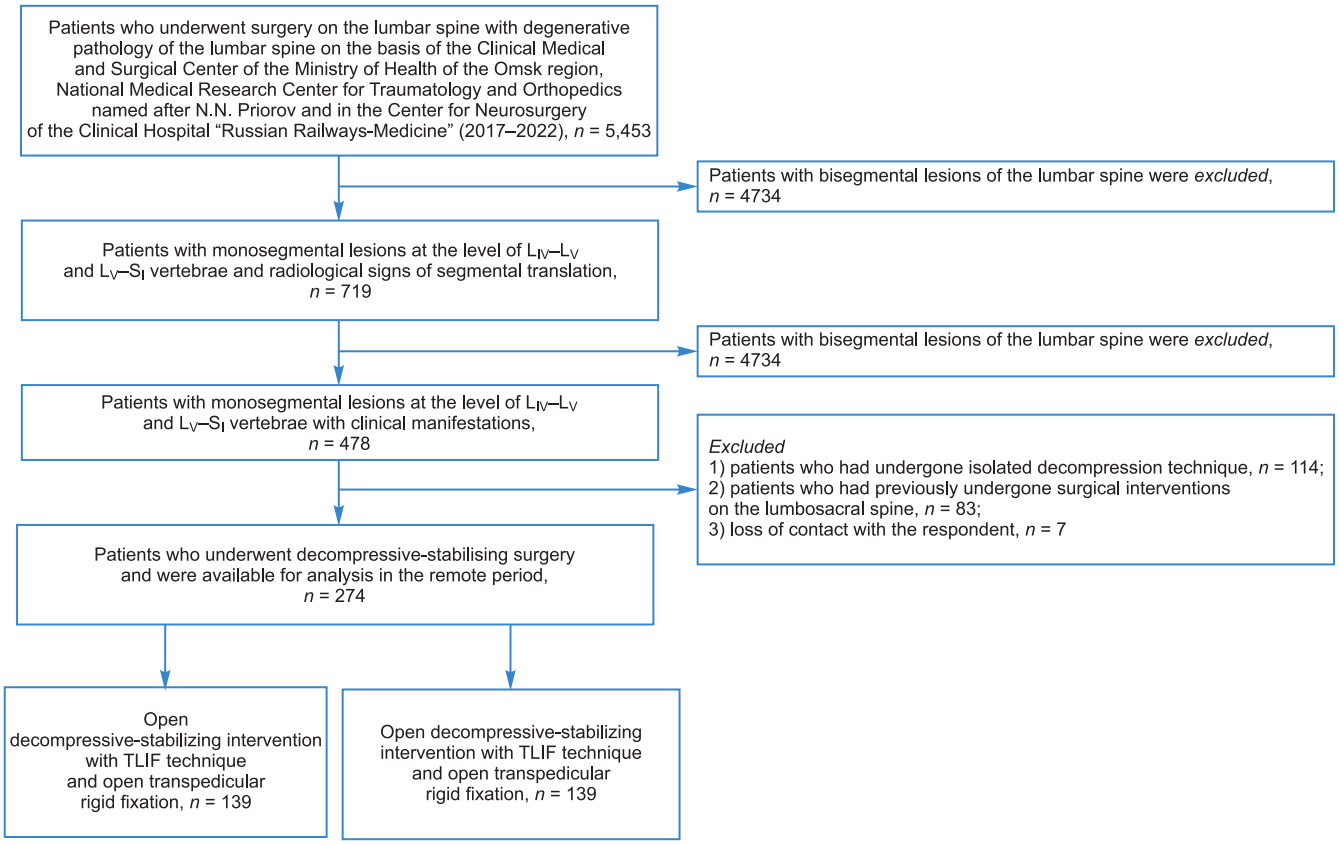


FIG. 1.
Flowchart of patients included in the study

man's rank correlation coefficient (r_s) followed by an assessment of diagnostic significance (binary logistic series, Z-test). The sample size was calculated using Lehr's formula for 80 % power and a two-sided level of statistical significance of $p < 0.05$.

RESULTS

Positive dynamics ($p_W < 0.05$) was observed in both groups of patients studied when examining changes in pain syndrome in the lumbar spine and lower extremities (Fig. 2).

Comparative assessment of functional status by ODI and SF-36 revealed a comparable level of preoperative parameters in the studied groups ($p_{M-U} > 0.05$). At the time of 6, 12, 36 and 60 months after surgical treatment, the best functional status was verified in group II ($p_{M-U} < 0.05$) compared with group I (Fig. 3, 4).

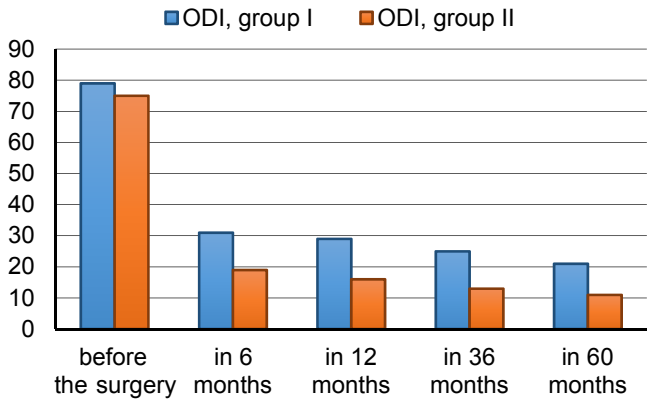


FIG. 3.
Dynamics of the functional state according to Oswestry Disability Index (0–100 %) in the studied groups of patients

An assessment of the degenerative changes severity of IVD of the proximal FSU is summarised in Table 1.

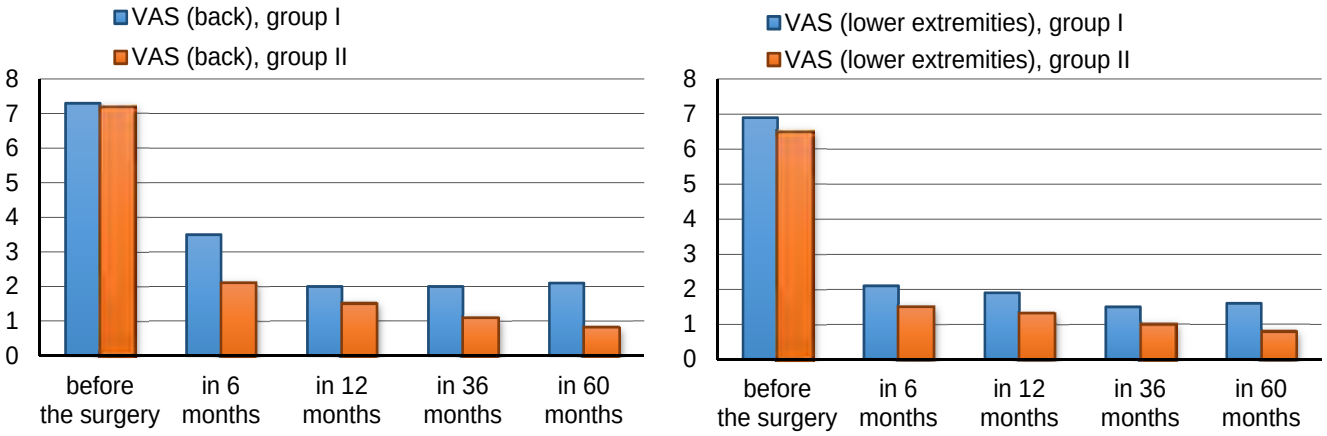


FIG. 2.
Dynamics of pain syndrome (according to visual analogue scale (0–10 cm)) in the lumbar spine and lower extremities in the studied groups of patients

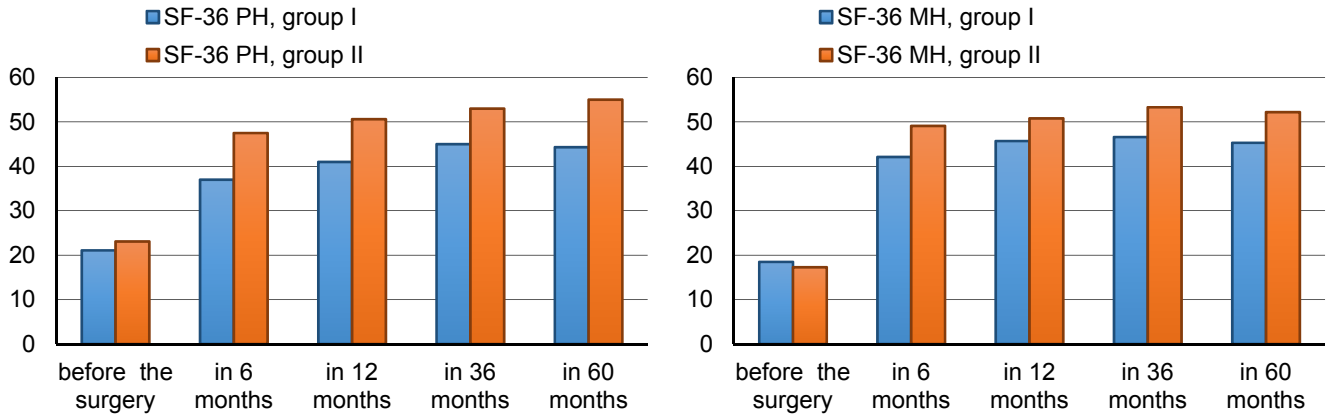


FIG. 4.
Dynamics of the functional state according to SF-36 questionnaire in the studied groups of patients: PH – Physical Health; MH – Mental Health

The analysis revealed a statistically significant change in the degree of degeneration in group I (p_W = 0.03), while in group II no significant degenerative changes were registered in the distant postoperative period (p_W = 0.47) (Table 1).

A statistically significant progression of IVD degeneration in group I (p_W = 0.01) was revealed when comparing the results of DW-MRI in the studied groups, while no significant degenerative changes of the proximal segment were observed in group II in the remote postoperative period (p_W = 0.73) (Table 2).

After surgical treatment in group I, progression of proximal IVD degeneration was detected in 24.1 % of cases. Between 12 and 60 months following surgery, 29 patients required revision interventions with prolongation of rigid fixation.

In group II, degeneration of the adjacent proximal IVD was noted in 5.8 % of cases ($p_{M–U}$ = 0.01). Revision intervention with extension of dynamic stabilisation was performed in 2 patients at 36 and 60 months after the primary intervention. The incidence of ASDD in group I patients was 20.1 %, while in group II it was 2.0 % ($p_{M–U}$ = 0.002).

When analyzing the severity of FJ degeneration according to the results of DECT before surgery, a comparable optical density of FJ between groups ($p_{M–U}$ < 0.05) was noted.

After 60 months, the progression of degenerative processes in FJ was observed: in group I, the cartilage lamina density increased by 13.4 % compared to preoperative values, the density of the external facet – by 15.1 %, the density of the internal facet – by 15.6 %. In group II, cartilage lamina density increased by 3.7 % compared to preoperative values, external facet density by 4.1 %, and internal facet density by 2.2 % ($p_{M–U}$ < 0.05) (Table 3).

In comparative analysis using a 5-point system with calculation of risk and positive outcome of the strategy according to the proposed models of surgical interventions, a heat map was used to visually detail the degree of degenerative processes in the FJ (Fig. 5, 6). Each risk is described by a number of criteria such as optical density of the external and internal facet, Hounsfield cartilage plate area. The value of each risk criterion was ranked by the probability of risk occurrence.

Therefore, when using the traditional method with monosegmental rigid fixation (group I), progression of degenerative processes in the FJ was observed, which may be a risk factor for ASDD development in 75 % of cases. In contrast, when dynamic stabilisation was used (group II), the degree of degenerative changes was 50 %

TABLE 1

DEGENERATIVE CHANGES OF PROXIMAL INTERVERTEBRAL DISC IN PATIENTS OF THE STUDIED GROUPS

Indicator		Group I (*n* = 139)		Group II (*n* = 135)	
		before the surgery	in 60 months	before the surgery	in 60 months
Degree of disc degeneration according to C.W. Pfirrmann, *n* (%)	I	–	–	–	–
	II	68 (47.3)	32 (22.1)	69 (50.1)	62 (45.3)
	III	71 (52.7)	96 (68.8)	66 (49.9)	73 (54.7)
	IV	–	11 (9.1)	–	–
	V	–	–	–	–

TABLE 2

RESULTS OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING OF PROXIMAL INTERVERTEBRAL DISC IN PATIENTS OF THE STUDIED GROUPS

Indicator	Group I (n = 139)		Group II (n = 135)	
	before the surgery	in 60 months	before the surgery	in 60 months
Apparent diffusion coefficient (mm^2/s), Me (25; 75)	1422 (1366; 1471)	1118 (1017; 1293)	1438 (1367; 1492)	1412 (1338; 1482)

TABLE 3

DENSITY INDICATORS OF THE ELEMENTS OF FACET JOINT OF THE UPPER ADJACENT LEVEL IN PATIENTS OF THE STUDIED GROUPS

Indicators	Group I (*n* = 139)		Group II (*n* = 135)	
	before the surgery	in 60 months	before the surgery	in 60 months
Cartilaginous plate density, HU	164.8 ± 14.2	221.2 ± 10.5	161.7 ± 15.8	171.2 ± 3.9
External facet density, HU	713.65 ± 13.6	1035.3 ± 21.6	702.43 ± 12.3	730.9 ± 4.8
Internal facet density, HU	582.1 ± 15.1	899.9 ± 9.2	575.5 ± 11.6	586.2 ± 4.1

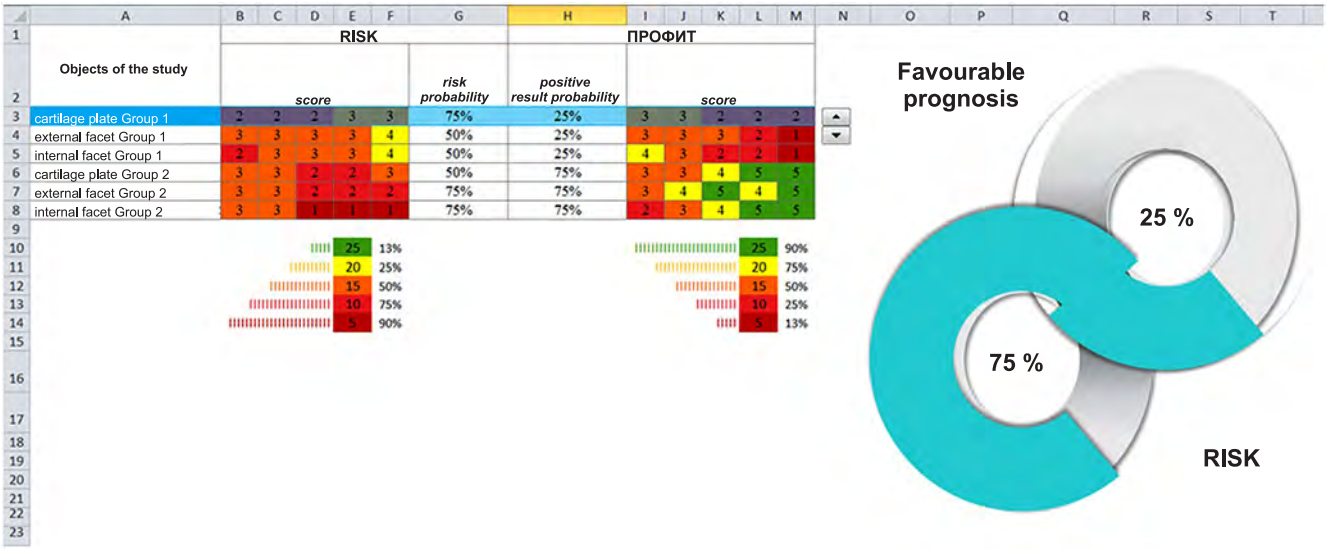


FIG. 5.

Comparative analysis of the state of facet joint with an assessment of the risks of degeneration progression and positive treatment results after rigid fixation (group I)

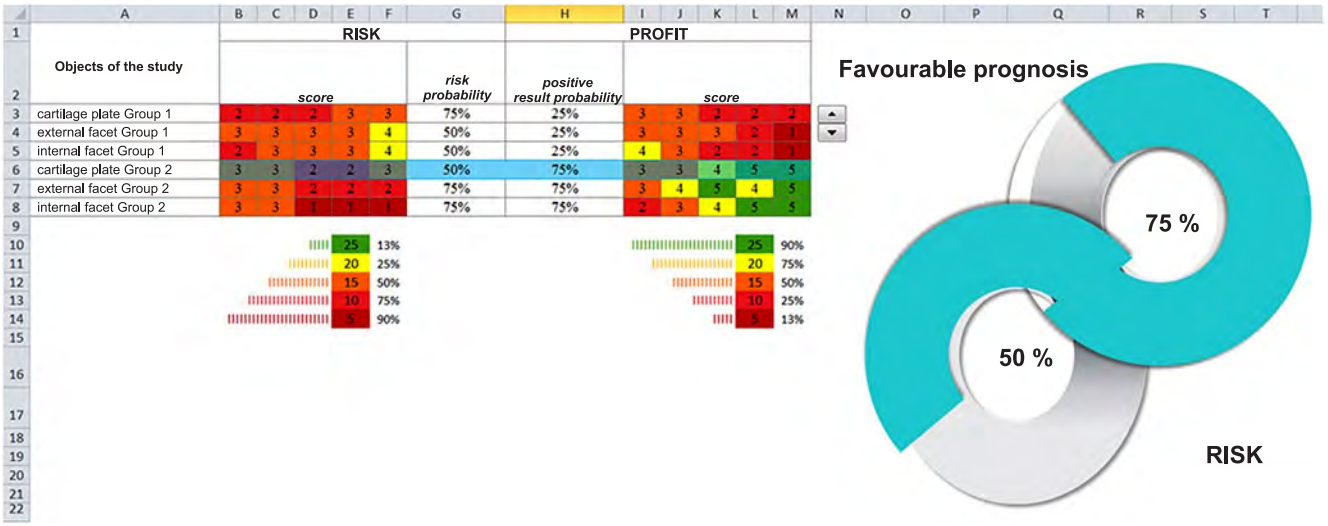
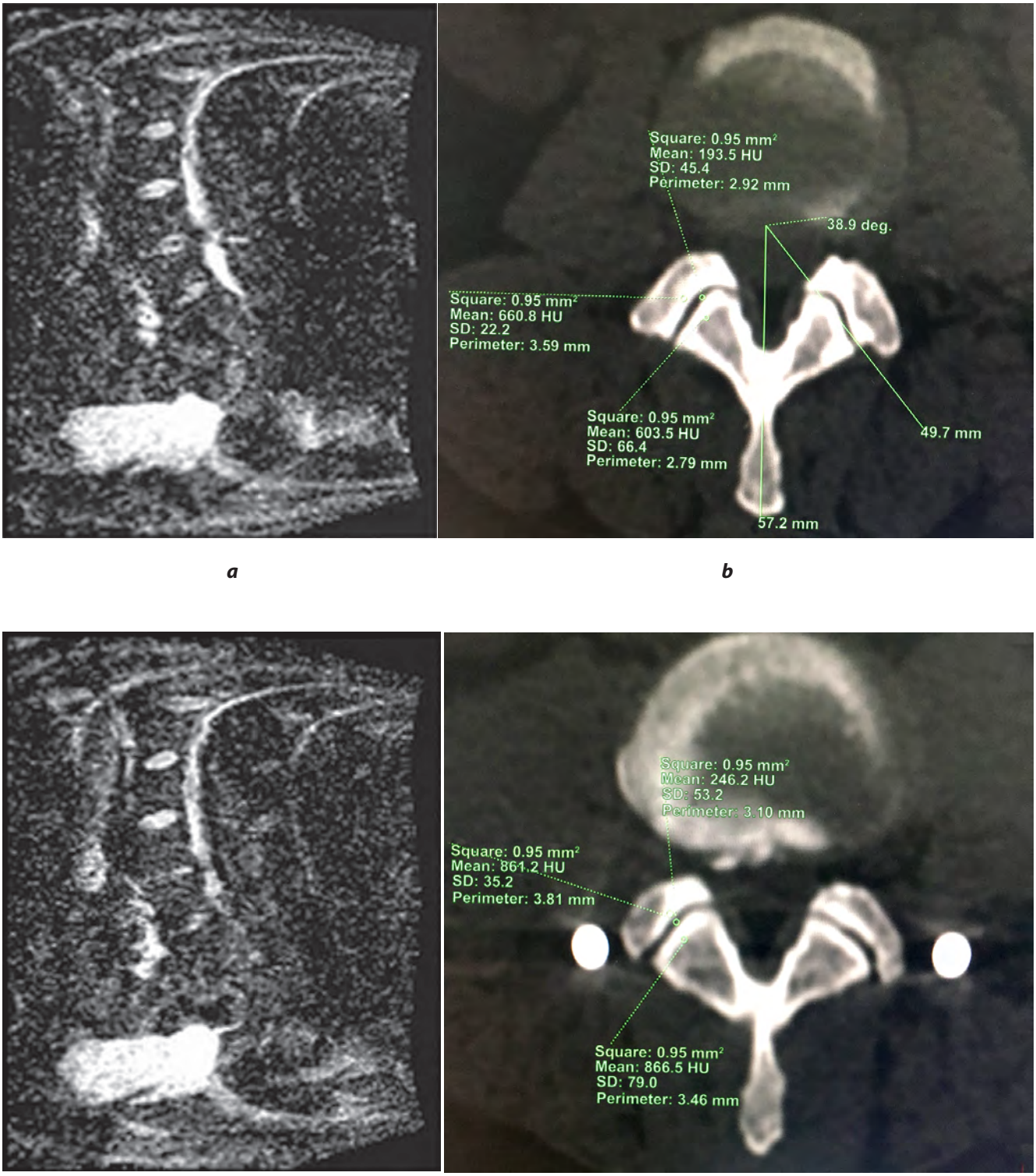


FIG. 6.

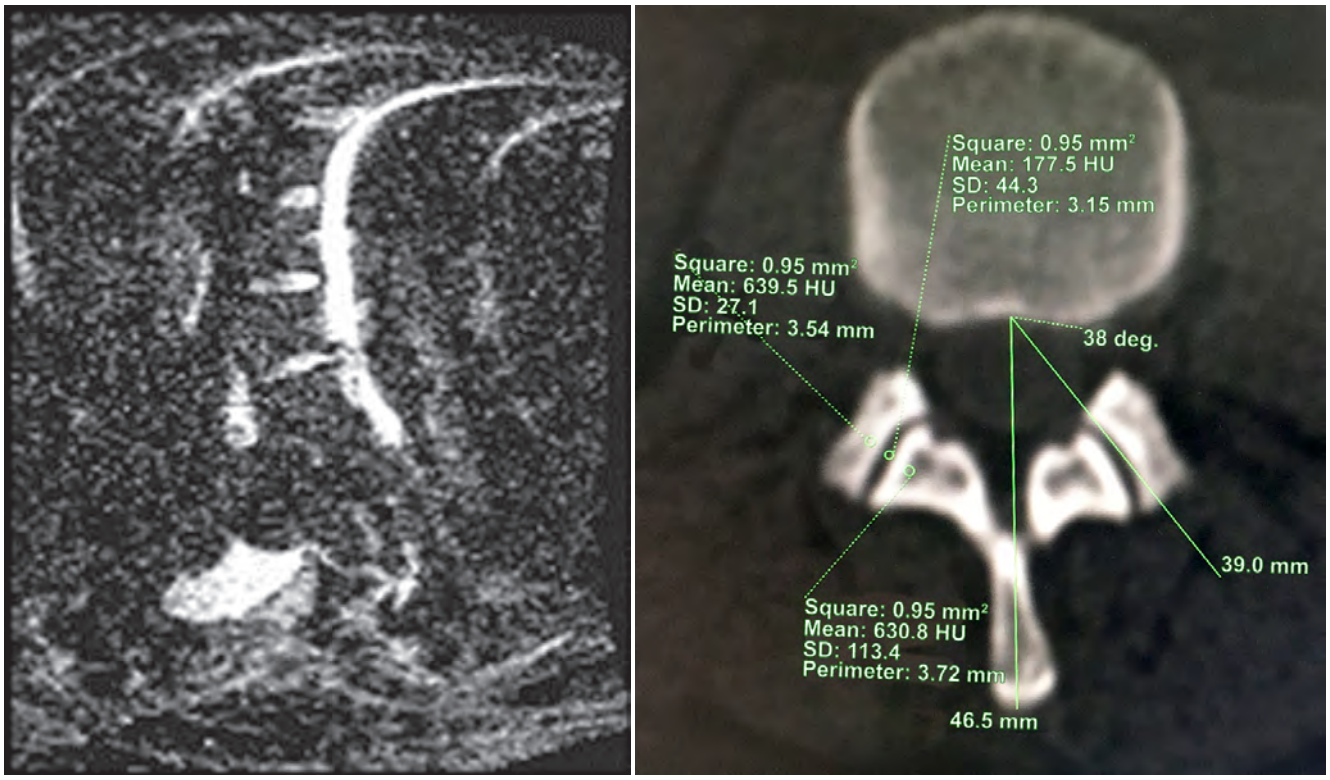
Comparative analysis of the state of facet joint with an assessment of the risks of degeneration progression and positive treatment results after dynamic stabilization (group II)



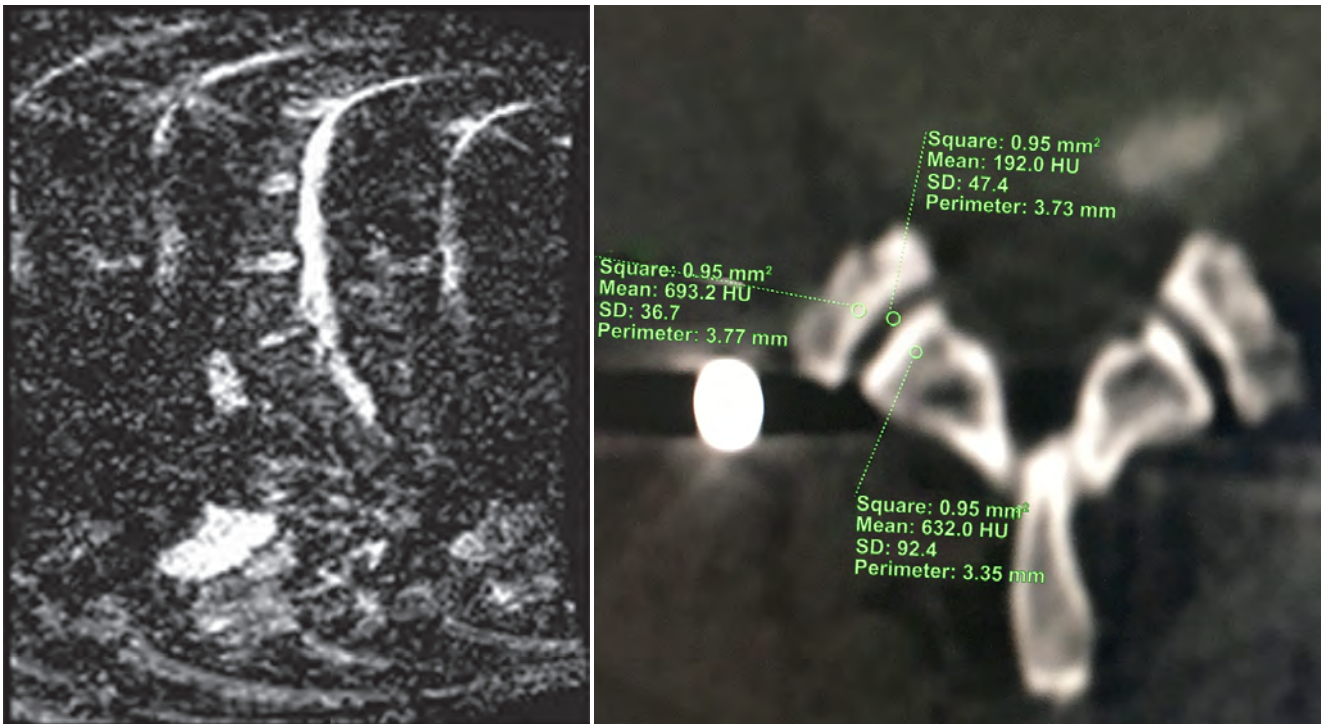
a ***b*** ***c*** ***d***

FIG. 7.

Patient S., 32 years old. Degenerative diseases of the lumbar spine in the L_V–S_I segment: ***a*** *– diffusion-weighted magnetic resonance imaging (apparent diffusion coefficient: L_V–S_I – 1102 mm²/sec, L_{IV}–L_V – 1415 mm²/sec);* ***b*** *– axial projection of computed tomography of facet joint (cartilaginous plate density – 193.5 HU, outer facet density – 660.8 HU, inner facet density – 603.3 HU);* ***c*** *– sagittal projection of diffusion-weighted magnetic resonance imaging after TLIF surgery and open transpedicular rigid fixation (apparent diffusion coefficient: L_{IV}–L_V – 1175 mm²/sec, negative dynamics);* ***d*** *– axial projection of computed tomography of facet joint after surgical intervention using TLIF technique and open transpedicular rigid fixation (cartilaginous plate density – 246.2 HU, outer facet density – 861.2 HU, inner facet density – 886.6 HU; negative dynamics of an increase in the density of facet joint of L_{IV}–L_V segment)*



a *b*



c *d*

FIG. 8.

Patient N., 36 years old. Degenerative disease of the lumbar spine in the L_V–S_I segment: ***a*** *– diffusion-weighted magnetic resonance imaging (apparent diffusion coefficient: L_V–S_I – 1141 mm²/sec, L_{IV}–L_V – 1424 mm²/sec);* ***b*** *– axial projection of computed tomography of facet joint (cartilaginous plate density – 177.5 HU, outer facet density – 639.5 HU, inner facet density – 630.8 HU);* ***c*** *– sagittal projection of diffusion-weighted magnetic resonance imaging after decompression with stabilization of the operative segment with nitinol rods (apparent diffusion coefficient: L_{IV}–L_V – 1395 mm²/sec, no progression of adjacent level degeneration according to apparent diffusion coefficient);* ***d*** *– axial projection of computed tomography of facet joint after decompression with stabilization of the operative segment with nitinol rods (cartilaginous plate density – 192.0 HU, outer facet density – 693.2 HU, inner facet density – 632.0 HU; slight progression of degenerative processes in the facet joint elements of L_{IV}–L_V segment)*

(Fig. 6), indicating proper distribution of biomechanical stress on the upper adjacent segment.

Clinical examples (Fig. 7, 8) demonstrate the dynamics of degenerative processes in IVD and FJ of the proximal segment in patients of groups I and II according to DW-MRI and DECT data before surgery and 60 months after surgery.

DISCUSSION

Unsatisfactory outcomes following rigid decompressive-stabilizing interventions are mostly associated with disruption of the natural biomechanics of adjacent segment elements [22]. It stimulates both researchers and clinicians, on the one hand, to analyze possible risk factors for ASDD development, while, on the other hand, to use devices that preserve normal biomechanics parameters of the surgically operated and adjacent segments [23, 24]. ASDD affects FJs and IVDs, which are important structural elements of the FSU. Comprehensive preoperative neuroimaging of anatomical structures of vertebral segments allows predicting long-term clinical results and implementing timely prophylactic measures to prevent ASDD development [16, 25].

In their prospective study, J. Anandjiwala et al. [26] revealed a high frequency of signs of adjacent segment degeneration in respondents with initial degeneration of IVD adjacent segments of the III degree according to C.W. Pfirrmann's classification. Similar findings were obtained in a study by J. Liang et al. [27], which clearly emphasises the initial degeneration of IVD of the 3rd degree according to S.W. Pfirrmann, which is one of the most accurate indicators of ASDD development.

The initial FJ degeneration is also important in the stability of the adjacent FSU; for instance, in the work of A.M. Wu et al. [28] it has been found that the initial degeneration of FJ 3rd degree according to A. Fujiwara is also a predictor of the development of instability in the segment. Similar results were obtained in the work of S.V. Hadlow et al. [29] and A. Fujiwara et al. [30]. The authors report insufficient assessment by surgeons of the initial degeneration severity of the adjacent FSU and, in particular, its dynamic structures. This study fully confirms the results of earlier clinical and instrumental studies, and the use of sensitive neuroimaging methods, such as DW-MRI and DECT, allows assessment of degenerative processes at all stages of treatment.

This study clearly demonstrated that patients who underwent posterior trapedicular fixation using nitinol rods had better long-term clinical outcomes; these results correlate with earlier studies demonstrating the efficacy of rod and nitinol versus rigid fixation [31, 32]. For instance, in group II, the progression of degenerative processes in IVD was 5.8 %, and ASDD was registered in only 2 % of cases. In group I, progression of degenerative changes in FJ was registered in the form of an increase in the optical density of the cartilage plate by 13.4 %, in the density of the external facet by 15.1 %, and in the density of the internal facet by 15.6 %. In group II insignificant changes were revealed in the form of increase in optical density: cartilage plate – by 5.7 %, external facet – by 7.8 %, internal facet – by 4.2 %.

Therefore, the combination of initial proximal segment degeneration in the form of FJ degeneration with cartilage plate density of 163.5 ± 14.2 HU, external facet density of 709.35 ± 13.6 HU, internal facet density of 578.1 ± 12.1 HU, IVD degeneration of III, IV degree according to C.W. Pfirrmann, and ADC less than 1300 mm^2/s, there are high risks of ASDD development, which requires the use of monosegmental dynamic fixation with nitinol rods or preventive rigid fixation of the adjacent segment. This will reduce the number of early and late revision interventions, which is consistent with previous experimental studies [33].

Complex neuroimaging in the preoperative period during planning of decompressive-stabilizing interventions makes it possible to assess the state of the proximal IVD and FJ as the main predictors of ASDD development, as well as to predict the long-term clinical results and to initiate preventive measures in a timely manner.

Study limitations

It should be noted that the study conducted has certain limitations. Firstly, the study has a small homogeneous sample without randomization procedure, which may act as a cause of systematic error. Second, the observational study did not take into account the adjacent segment facet angle parameters, FJ tropism abnormality, postoperative fatty degeneration of paraspinal muscles, and vertebro-pelvic balance parameters that influence the risk of ASDD development after lumbar spinal surgery. Third, only one method of ASDD prophylaxis using nitinol rods has been examined in this study without comparison with other types of stabilization.

CONCLUSION

The study has revealed that the combination of initial proximal segment degeneration in the form of FJ degeneration with cartilage plate density of 163.5 ± 14.2 HU, external facet density of 709.35 ± 13.6 HU, internal facet density of 578.1 ± 12.1 HU and ADC of the proximal IVD less than 1300 mm^2/s increases the risk of ASDD development in patients using rigid fixation by 24 %, whereas in patients using dynamic fixation the risk of development is 1.2 %, as the biomechanical parameters of the stabilized segment are preserved and thus there is adequate distribution to adjacent segments.

Using the complex neuroimaging in the preoperative period provides an opportunity to predict the results of surgical treatment, take timely preventive measures to avoid ASDD and perform dynamic monitoring of the processes in the FSU structures.

Conflict of interest
The authors of this study declare no conflicts of interest.

Funding
The study was not sponsored.

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EXPERIENCE OF UNILATERAL AND BILATERAL TRANSPEDICULAR FIXATION IN DEGENERATIVE DISEASES OF THE LUMBAR SPINE

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ABSTRACT

The aim. *To study the effectiveness of using monosegmental fixation systems in surgeries involving resection of part of the facet joint in patients with posterolateral and foraminal hernias in the lumbar spine.*

Materials and methods. *The study included 40 patients with degenerative diseases of the lumbar spine who underwent medial facet resection and the removal of posterolateral or foraminal disc hernia. Among them, 10 patients underwent unilateral single-level transpedicular fixation with interbody fusion using titanium cage (UTPF cage group), and the other 10 patients underwent unilateral monosegmental transpedicular fixation (UTPF group). The remaining 20 patients underwent bilateral transpedicular fixation (BTPF group). The amount of intraoperative blood loss, duration of surgery and length of hospital stay, as well as the frequency of perioperative complications in the groups were assessed. Visual analogue scale (VAS) pain score, Oswestry index and McNab score were assessed before and 6 and 12 months after surgery.*

Results. *Intraoperative blood loss in the UTPF cage and UTPF groups was less than in the BTPF group, as was the duration of surgery; the differences were statistically significant ($p < 0.05$). Indicators of VAS score and Oswestry Quality of Life Index in the studied groups indicated the effectiveness of the technology.*

Discussion. *Unilateral decompressive and stabilizing surgeries in patients with posterolateral and foraminal hernias of the lumbar spine can reduce the duration of the surgery, the volume of blood loss and the severity of pain in the postoperative period due to adequate decompression of the neurovascular formations of the spinal canal and stabilization of the spinal motion segment, which prevents the relapse of the disease and provides early rehabilitation of patients.*

Conclusion. *Unilateral transpedicular fixation is acceptable and safe for lumbar degenerative diseases and improves the quality of life of the patients.*

Key words: *unilateral transpedicular fixation, lumbar degenerative diseases, VAS score, Oswestry index*

Received: 24.04.2023
Accepted: 04.10.2023
Published: 05.12.2023

For citation: Sorokovikov V.A., Potapov V.E., Zhivotenko A.P., Gorbunov A.V., Sklyarenko O.V., Larionov S.N. Experience of unilateral and bilateral transpedicular fixation in degenerative diseases of the lumbar spine. *Acta biomedica scientifica*. 2023; 8(5): 73-80. doi: 10.29413/ABS.2023-8.5.7

ОПЫТ ОДНО- И ДВУХСТОРОННЕЙ ТРАНСПЕДИКУЛЯРНОЙ ФИКСАЦИИ ПРИ ДЕГЕНЕРАТИВНЫХ ЗАБОЛЕВАНИЯХ ПОЯСНИЧНОГО ОТДЕЛА ПОЗВОНОЧНИКА

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РЕЗЮМЕ

Цель исследования. *Изучить эффективность использования моносегментарных фиксирующих систем при операциях, сопровождающихся резекцией части дугоотростчатого сустава у пациентов заднебоковыми и фораминальными грыжами на поясничном отделе позвоночника.*

Материалы и методы. *В исследовании участвовали 40 пациентов с дегенеративно-дистрофическими заболеваниями поясничного отдела позвоночника, которым выполнены резекция медиальной фасетки и удаление задне-боковой или фораминальной грыжи диска. Среди них 10 пациентам проведена монолатеральная одноуровневая фиксация транспедикулярными винтами с межтеловым спондилодезом титановым кейджем (ОТПФ-кейдж), а другим 10 – односторонняя моносегментарная транспедикулярная фиксация (ОТПФ). Оставшимся 20 пациентам выполнена двусторонняя транспедикулярная фиксация (ДТПФ). Проводилась оценка величины интраоперационной кровопотери, длительности операции и времени госпитализации, а также частота периоперационных осложнений в группах. Оценка боли по визуально-аналоговой шкале (ВАШ), степень ограничения жизнедеятельности на основании индекса Освестри и показателя Макнаб оценивались до и через 6 и 12 месяцев после операции.*

Результаты. *Интраоперационная кровопотеря в группах с ОТПФ-кейджем и ОТПФ была меньше, чем в группе с ДТПФ, так же, как и продолжительность операции; различия были статистически значимыми ($p < 0,05$). Показатели ВАШ, индекс качества жизни Освестри в исследуемых группах свидетельствовали об эффективности технологии.*

Обсуждение. *Односторонние декомпрессивно-стабилизирующие вмешательства у пациентов с заднебоковыми и фораминальными грыжами поясничного отдела позвоночника позволяют уменьшить продолжительность операции, объём кровопотери и выраженность болевого синдрома в послеоперационном периоде за счёт адекватной декомпрессии нервно-сосудистых образований позвоночного канала и стабилизации позвоночно-двигательного сегмента, что предотвращает рецидив заболевания и обеспечивает раннюю реабилитацию пациентов.*

Вывод. *Односторонняя транспедикулярная фиксация допустима и безопасна при поясничных дегенеративных заболеваниях, способствует улучшению качества жизни пациентов.*

Ключевые слова: *односторонняя транспедикулярная фиксация, поясничные дегенеративные заболевания, оценка по ВАШ, индекс Освестри*

Статья поступила: 24.04.2023
Статья принята: 04.10.2023
Статья опубликована: 05.12.2023

Для цитирования: Сороковиков В.А., Потапов В.Э., Животенко А.П., Горбунов А.В., Скляренко О.В., Ларионов С.Н. Опыт одно- и двухсторонней транспедикулярной фиксации при дегенеративных заболеваниях поясничного отдела позвоночника. *Acta biomedica scientifica*. 2023; 8(5): 73-80. doi: 10.29413/ABS.2023-8.5.7

INTRODUCTION

Over the last decades, significant progress has been observed in the treatment of degenerative-dystrophic spine diseases associated with the development of reasonable tactics and the introduction of new instrumental technologies into surgical practice. However, difficulties in the treatment of such patients remain, as clinical manifestations are caused not only by compression of the neural structures of the spinal canal, but also by the formation of instability in both the injured and adjacent spinal-motor segments [1–3].

The cornerstone component of the degenerative spine disease pathology appears to be changes in intervertebral discs and facet joints and, as a consequence, the development of segmental instability [4, 5], which in some cases is interpreted as "discogenic instability" [6, 7]. Violation of the biomechanics of the vertebral column is accompanied not only by linear but also angular displacement of vertebrae and, as a consequence, damage to the fibrous ring, ligamentous apparatus, and sometimes by disc herniation and the development of radicular and reflex-tonic syndromes [8, 9]. The outcome of changes in the vertebral-motor segments in the failure of the anterior and posterior support complexes, as well as the development of changes in the vertebral trabecular structures and degeneration of the disc tissue of the affected segment, appears to be natural.

Discectomy represents one of the common techniques for the surgical treatment of herniated discs in degenerative-dystrophic spine diseases. However, HIVD (Herniated intervertebral disc) excision by resection of a part of the facet joint without fixation of the spinal motion segment is accompanied by recurrence of pain and unsatisfactory treatment results both as a consequence of segmental instability and recurrence of the herniation in 7–18 % of cases [10–13].

Analysis of data from the current literature with meta-analysis of treatment results indicates the effectiveness of rigid transpedicular fixation, as well as interbody spondylodesis, for stabilization of the vertebral column [14–17]. At the same time, these surgical technologies also have disadvantages such as disconnection from the biomechanics of the vertebral-motor segment with the development of the "adjacent level" syndrome, which can be reduced by unilateral transpedicular stabilization [18–20]. Attention should also be paid to the high risks of instrumental spinal fixation in patients with ankylosing spondylitis, spondyloarthritis and osteoporosis. Surgical interventions with massive paravertebral trauma are also predictors associated with worsening treatment outcomes, causing pain recurrence and prolonged duration of rehabilitation treatment [21–23]. The domestic literature practically does not cover the aspects of using unilateral monosegmental fixations, whereas the technology is widely used abroad [18, 19].

THE AIM OF THE STUDY

To study the effectiveness of using unilateral and bilateral monosegmental fixation systems during surgery with resection of part of the facet joint in patients with posterolateral and foraminal herniations in the lumbar spine.

MATERIALS AND METHODS

Forty patients with degenerative and dystrophic spine pathology have undergone surgery at the Irkutsk Scientific Centre of Surgery and Traumatology. Among them, 10 patients underwent unilateral transpedicular fixation with titanium cage interbody spondylosis (UTPF-cage) after removal of radicular compression by medial facet resection, and the other 10 patients underwent only unilateral monosegmental transpedicular fixation (UTPF). A total of 20 patients underwent bilateral transpedicular fixation (BTPF). The clinical picture of the disease in patients was dominated by pain radicular syndrome in combination with vertebrogenic musculotonic syndrome. All patients underwent clinical neurological, neurophysiological, introscopic preoperative examination. The indications for surgery were ineffectiveness of nonsurgical treatment, persistent radicular pain syndrome. In most cases, the intervertebral hernia was located at the level of L_{IV}–L_V in 26 (65 %), in 10 (25 %) – at the level of L_V–S_I, in 4 (10 %) – at the level of L_{II}–L_{III}. By sex and age, the patients were differentiated as follows: 16 (40 %) women, 24 (60 %) men; among them 30 (75 %) patients were of working age, from 38 to 65 years. Patients did not differ between groups in terms of sex, age, body mass index (BMI), and degree of intervertebral disc (IVD) degeneration (according to the C.W. Pfirrmann classification). The data are presented in Table 1.

The technology of HIVD excision was performed according to the generally accepted technique with resection of the medial facet and foraminotomy. Resection of a part of the facet joint allowed isolation of the spinal root, its displacement without gross traumatic effects and subsequent hernia excision. Unilateral transpedicular fixation was performed in 20 patients to stabilize the spinal motion segment. Among them, monolateral fixation using transpedicular screws with interbody spondylosis with a titanium cage was implemented in 10 patients (Fig. 1).

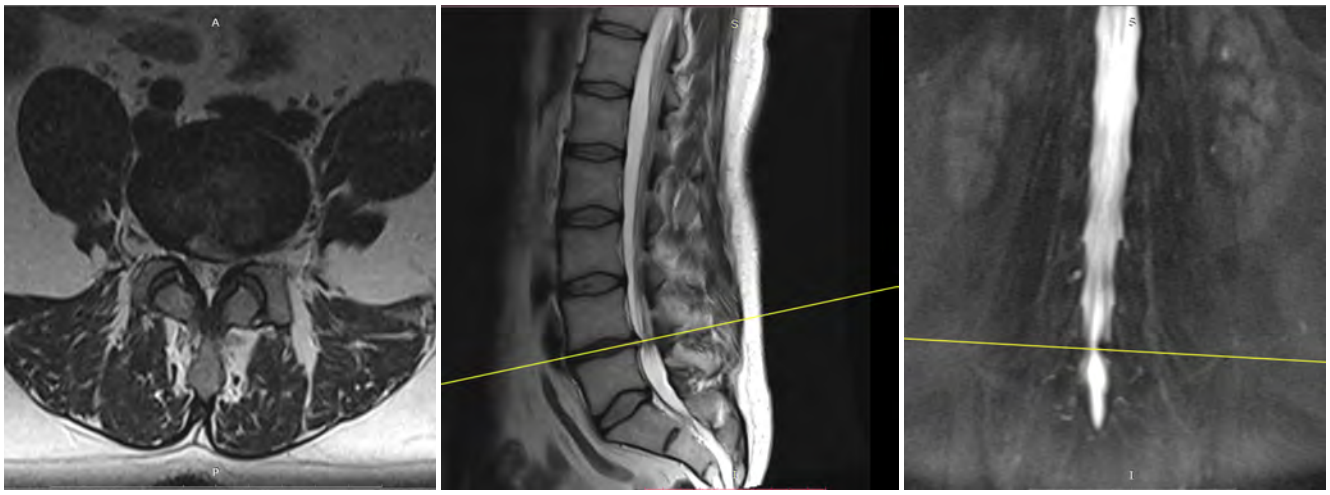
Inclusion criteria: presence of posterolateral or foraminal hernia with radicular compression; ineffectiveness of nonsurgical treatment for more than 3 months.

Exclusion criteria: obesity of the 2–3rd degree (BMI > 35 kg/m^2); spondylolisthesis of the II degree and above; lumbar degenerative scoliosis; infectious process in the acute phase; osteoporosis. Somatic and clinical manifestations in the groups had no statistically significant differences and were comparable. Patients signed informed consent. The study was authorized by the Ethical Committee of the Irkutsk Scientific Centre of Surgery and Traumatology (meeting minutes No. 9 dated December 08, 2021).

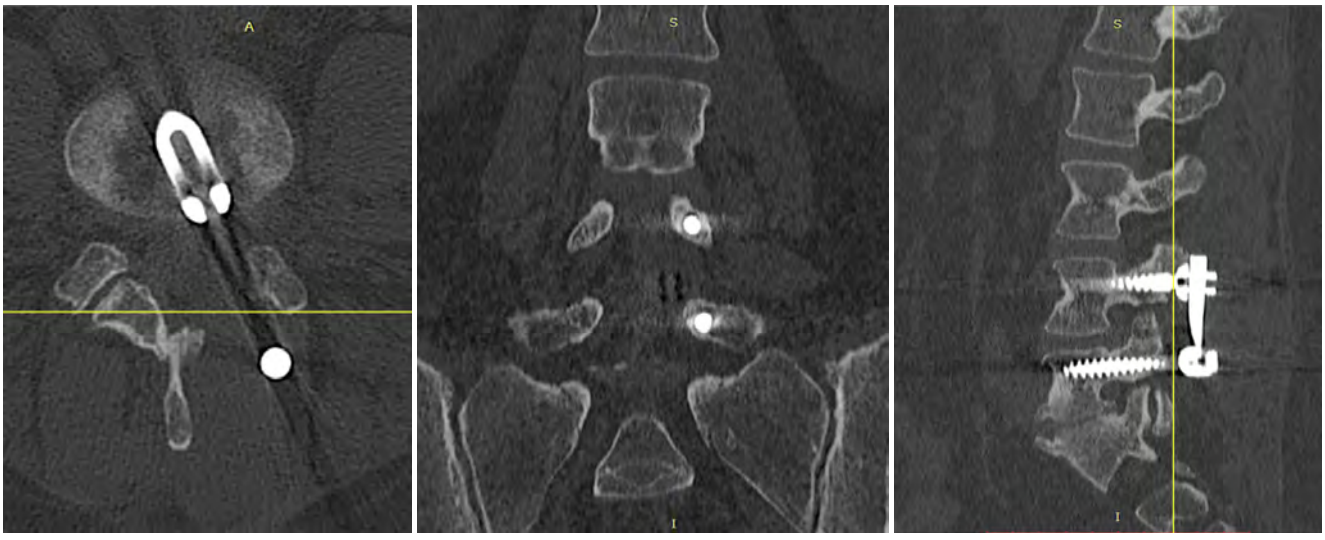
The results and patient satisfaction with treatment outcomes were assessed based on the visual analogue scale (VAS) of pain, the McNab scale, and the Russian version of the Oswestry index [24].

TABLE 1
CHARACTERISTICS OF GROUPS

Indicators		UTPF-cage (*n* = 10)	UTPF (*n* = 10)	BTPF (*n* = 20)
Sex: male/female		7/3	6/4	–/8
Age		49.22 ± 4.8	50.18 ± 2.8	50.33 ± 4.5
BMI		29.1 ± 5.58	30.1 ± 3.23	30.5 ± 3.33
Degrees of IVD degeneration (C.W. Pfirrmann classification)	II degree	3	2	7
	III degree	7	8	11
	IV degree			2



a



b

FIG. 1.
a *– MRI, T_2-weighted image, axial and sagittal sections: spondylarthrosis, left-sided L_{IV}–L_V disc herniation;* ***b*** *– MSCT of the lumbar spine: transpedicular fixation of L_{IV}–L_V on the left, interbody cage*

Statistical processing was performed using SPSS Statistics 10 program (IBM Corp., USA). Data are presented as mean and standard deviation, and differences between groups were analyzed using Pearson's χ^2 test. Statistical significance was defined as $p < 0.05$.

RESULTS

The results of surgical treatment were assessed based on the regression of vertebrogenic pain syndrome and neurological symptoms, restoration of static-dynamic function of the spine, indicators of the traumatic nature of surgery (duration, amount of blood loss), and patient satisfaction with the outcomes. The data are summarized in Table 2.

Analysis of surgical treatment revealed that intraoperative blood loss in the UTPF-cage and UTPF groups was less than that in the BTPF group, similarly to the duration of surgery. Pain regression and improved quality of life in the postoperative period were observed in all patients with a decrease in VAS score from 8.39 ± 0.3 to 2.39 ± 0.3 cm ($\chi^2 = 0.059$; $p < 0.05$), and the Oswestry index from 66 ± 0.35 to 31.7 ± 0.28 ($\chi^2 = 0.018$; $p < 0.05$). Relief of neurological symptoms (allodynia, paresthesias, weakness of foot extensors) was observed in 38 patients. All patients were intensively activated the day after surgery with mandatory lumbar fixation with a rigid orthopaedic corset. Postoperative re-

TABLE 2
THE RESULTS OF SURGICAL TREATMENT

Indicators		UTPF-cage ($n = 10$)	UTPF ($n = 10$)	BTPF ($n = 20$)	p
Surgery time (min)		60 ± 1.9	56 ± 1.4	75 ± 1.7	$p < 0.05$
Blood loss (ml)		59.22 ± 2.8	57.18 ± 1.8	75.33 ± 2.5	$p < 0.05$
VAS	before the surgery	8.35 ± 0.3	8.39 ± 0.2	8.45 ± 0.4	$p > 0.05$
	at discharge	2.45 ± 0.3	2.35 ± 0.4	2.37 ± 0.4	
	in 6 months.	1.23 ± 0.33	1.22 ± 0.36	1.41 ± 0.26	$p > 0.05$
	in 12 months.	0.90 ± 0.11	0.82 ± 0.15	0.92 ± 0.20	
Oswestry Index	before the surgery	66.3 ± 0.15	67.1 ± 0.25	64.6 ± 0.65	
	at discharge	31.7 ± 0.15	30.7 ± 0.15	32.7 ± 0.55	
	in 6 months.	18.1 ± 0.25	17.7 ± 0.15	19.7 ± 0.15	$p > 0.05$
	in 12 months.	9.16 ± 1.26	9.26 ± 1.45	12.26 ± 1.35	
McNab scale score at hospital discharge	perfect	10	9	18	
	good	–	1	2	$p > 0.05$
	satisfactory	–	–	–	
McNab scale score in 6 months after discharge	perfect	10	9	18	
	good	–	1	2	$p > 0.05$
	satisfactory	–	–	–	
McNab scale score in 12 months after discharge	perfect	10	9	17	
	good	–	1	2	$p > 0.05$
	satisfactory	–	–	1	

habilitation period in patients ranged from 1.5 to 2 months, and it was shorter in men. All patients retained their ability to work except 1 case. During the 12-month follow-up period after surgery, there was 1 case of increased pain in the lumbar spine against the background of progression of degenerative changes at the adjacent level during bilateral transpedicular stabilization. The patient was forced to change his place of employment. According to the control multispiral computed tomography, no implant failure was revealed. In summary, excellent and good results after discectomy for posterolateral and foraminal HIVD with single-level transpedicular fixation were achieved in all patients at 12-month follow-up.

DISCUSSION

Posterior accesses to the spinal canal structures during discectomy followed by monolateral instrumental stabilization of the spinal segment, as well as classical transpedicular fixation techniques, contribute to fixation of the damaged spinal segment, but at the same time avoid excessive traumatization of soft tissues [25–28]. We are aware that at the stage of decompression of the neural formations of the spinal canal in patients with posterolateral and foraminal intervertebral hernias for neurolysis and mobilization of the radicular nerve, it is reasonable to perform resection of a part of the facet joint, which predetermines segment instability. Other risks of microsurgical HIVD excision include its recurrence into a formed fibrous ring defect, increased load on the arch joints, and pain exacerbation [29]. Prevention of disc hernia recurrence can be achieved through the use of a cage or a Barricaid intervertebral disc fibrous ring prosthesis [30], whereas stabilization of the supporting structures of the spinal motion segment (SMS) is achieved by unilateral unilevel transpedicular fixation combined with or without an interbody cage [31–33].

Improvement of the technology of surgical treatment of degenerative diseases of the lumbar spine allows us to formulate the main provisions that mitigate the risks of disease recurrence. First, surgical treatment of compression forms of degenerative spinal lesions should provide full decompression of the neurovascular formations of the spinal canal. Second, fixation of the damaged spinal-motor segment prevents recurrence of the disease and ensures early rehabilitation of patients. These provisions are related to both modern spine surgery techniques and the use of microsurgical techniques.

Our experience, as well as literature data about the use of unilateral and bilateral single-level fixation systems in patients with posterolateral and foraminal lumbar herniated discs, testify to their effectiveness. Reduction of traumatism and duration of surgery, as well as the blood loss extent, are the main predictors of the effectiveness of using unilateral monosegmental systems [26, 27].

The results of the study suggest that both unilateral and bilateral fixation techniques can be applied to prevent hernia recurrence and SMS instability, however, a reduction in the traumatic nature of the intervention is evidence in favour of monolateral systems. The issue needs further detailed and multicentre study and accumulation of clinical data in both foreign and domestic practice.

CONCLUSIONS

Modern surgical techniques during surgery with resection of part of the facet joint in patients with posterolateral and foraminal herniations in the lumbar spine allow adequate decompression of the neural structures of the spinal canal and stabilization of the SMS.

Unilateral monosegmental instrumented fixation is an effective technique that allows achieving consolidation, early activation and social adaptation of patients.

Funding

The authors declare that there was no external funding in conducting the study.

Conflict of interest

The authors declare the absence of apparent and potential conflicts of interest related to the publication of this article.

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Potapov V.E. – search and analytical work; treatment and examination of patients; surgical procedure.

Zhivotenko A.P. – search and analytical work; writing the text of the article.

Gorbunov A.V. – treatment and examination of patients; surgical procedure.

Sklyarenko O.V. – dynamic monitoring and after surgery follow-up.

Larionov S.N. – discussion of the research results; writing the text of the article.

The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

ONCOLOGY

TESTICULAR DIFFUSE LARGE B-CELL LYMPHOMA. CLINICAL LECTURE AND CASE REPORT

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ABSTRACT

Lymphoma is a heterogeneous group of lymphocyte malignancies that may involve lymphatic tissue, bone marrow, or extranodal sites. The lecture provides a brief overview of the current state of the problem of diagnosis and treatment of primary testicular lymphoma. Primary testicular lymphoma (PTL) is a rare lymphoid malignancy. Though it is rare, PTL is the most common type of testicular tumor in men over 60 years of age. The most common histological type is diffuse large B-cell lymphoma. To date, there are no well-documented etiological or risk factors for PTL. In contrast to other common testicular neoplasms, there was no statistically significant association of PTL with cryptorchidism, trauma, chronic orchitis, or infertility. Ultrasound is generally the first-line imaging method used to characterize testicular lesions. PTL manifests itself in the form of a hypoechoic formation, which can take the form of either a single large formation or multiple small formations that occupy most of the testicular parenchyma or completely replace it. Systemic treatment, including orchiectomy, chemotherapy, radiation therapy, and intrathecal prophylaxis, is necessary for all patients with PTL. In addition to achieving complete remission, the goal of PTL treatment is to prevent recurrences in the contralateral testis and central nervous system. The presented information is supplemented by our own observation and images. Personal medical data is published with the written consent of the patient. In our case, the patient's age was 38 years, which does not fall into the specified age group for primary testicular lymphoma. In our opinion, the publication of this clinical case and analysis of scientific literature on this topic are relevant.

Key words: *diffuse large B-cell lymphoma, primary testicular lymphoma, non-Hodgkin lymphoma*

Received: 15.06.2023
Accepted: 08.11.2023
Published: 05.12.2023

For citation: Lelyavin K.B., Taranenko A.V., Bryukhanov V.G. Testicular diffuse large B-cell lymphoma. Clinical lecture and case report. *Acta biomedica scientifica*. 2023; 8(5): 81-91. doi: 10.29413/ABS.2023-8.5.8

ДИФФУЗНАЯ КРУПНОКЛЕТОЧНАЯ В-КЛЕТОЧНАЯ ЛИМФОМА ЯИЧКА. КЛИНИЧЕСКАЯ ЛЕКЦИЯ И НАБЛЮДЕНИЕ ИЗ ПРАКТИКИ

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РЕЗЮМЕ

Лимфома представляет собой гетерогенную группу злокачественных новообразований лимфоцитов, которые могут вовлекать лимфатическую ткань, костный мозг или экстранодальные локализации. В лекции приводится краткий обзор современного состояния проблемы диагностики и лечения первичной лимфомы яичка. Первичная лимфома яичка (ПЛЯ) является редкой лимфоидной злокачественной опухолью. ПЛЯ, хотя и встречается редко, представляет собой наиболее распространённый вид опухоли яичка у мужчин старше 60 лет. Наиболее часто встречающимся гистологическим типом является диффузная крупноклеточная В-клеточная лимфома. На сегодняшний день нет хорошо задокументированных этиологических факторов или факторов риска ПЛЯ. В отличие от других распространённых новообразований яичка, не наблюдалось статистически значимой связи ПЛЯ с крипторхизмом, травмой, хроническим орхитом или бесплодием. Ультразвуковое исследование, как правило, является методом визуализации первой линии, используемым для характеристики поражений яичка. ПЛЯ проявляется в виде гипоэхогенного образования, которое может иметь вид как одиночного крупного образования, так и множественных мелких образований, занимающих большую часть паренхимы яичка или полностью её замещающих. Системное лечение, включая орхиэктомию, химиотерапию, лучевую терапию и интратекальную профилактику, необходимо для всех пациентов с ПЛЯ. Помимо достижения полной ремиссии, целью лечения ПЛЯ является предотвращение рецидивов в контралатеральное яичко и центральную нервную систему. Представленный материал дополнен собственным наблюдением и иллюстративным материалом. Персональные медицинские данные публикуются с письменного согласия пациента. В нашем случае возраст пациента составил 38 лет, что не попадает в указанную возрастную группу для первичной лимфомы яичка. На наш взгляд, публикация данного клинического случая и анализа научной литературы по данной теме является актуальной.

Ключевые слова: *диффузная крупноклеточная В-клеточная лимфома, первичная лимфома яичка, неходжкинская лимфома*

Статья поступила: 15.06.2023
Статья принята: 08.11.2023
Статья опубликована: 05.12.2023

Для цитирования: Лелявин К.Б., Тараненко А.В., Брюханов В.Г. Диффузная крупноклеточная В-клеточная лимфома яичка. Клиническая лекция и наблюдение из практики. *Acta biomedica scientifica*. 2023; 8(5): 81-91. doi: 10.29413/ABS.2023-8.5.8

Primary testicular lymphoma (PTL) is one of the rarest and most aggressive forms of lymphoproliferative neoplasia with primary tumor growth predominantly from extracerebral lymphoid tissue, characterized by a continuous process of recurrence and with a poor prognosis. The most common histotype of PTL is diffuse large B-cell lymphoma (DLBCL) [1]. A common clinical symptom of PTL is unilateral painless testicular swelling that develops over weeks, months or even years.

Lymphoproliferative neoplasias represent a heterogeneous group of diseases with common links of pathogenesis, which are subdivided into Hodgkin's and non-Hodgkin's lymphomas. Hodgkin lymphoma is characterized by the presence of specific changes (granulomas with large multinucleated Berezovsky – Sternberg cells) in lymph nodes against the background of a primary extracerebral tumour lesion of the lymphatic system; non-Hodgkin lymphoma includes all other primary extracerebral tumours of the lymphatic system, which are divided into T- and B-cell groups and a number of subgroups [2]. Primary testicular DLBCL initially occurs only in the testis and is not associated with lymphoma elsewhere or leukaemia. Testicular involvement with a background of systemic lymphoma/leukaemia is diagnosed as secondary testicular lymphoma. As PTL is rare, attempts to elucidate its clinical characteristics, prognostic outcomes mainly rely on case reports and analyses of a small cohort of patients, and unfortunately the data have not been properly analyzed at the large population level.

HISTORICAL AND EPIDEMIOLOGICAL BACKGROUND

In the scientific literature, the first mention of primary testicular lymphoma appeared in 1856 in a practical treatise on diseases of the testis, spermatic cord and scrotum published by the British surgeon Thomas Blizard Curling (1811–1888), who was renowned for his ability to treat testicular diseases [3]. PTL was later described by M. Malassez in his article published in 1877 in the French Bulletin of the Society of Pathology [4].

Non-Hodgkin's lymphoma (NHL) is among the most commonly diagnosed haematological malignancies worldwide, comprising almost 3 % of all cancer diagnoses, occurring predominantly in white males of European and Hispanic origin over 65 years of age [5]. According to the International Agency for Research on Cancer, approximately 414,772 new cases of NHL were diagnosed worldwide in 2015 [5]. The five-year survival rate for NHL is 72.0 and 86.6 % for Hodgkin's lymphoma. Nearly 21,000 people are expected to die from lymphoma in 2023, comprising 3.5 % of all cancer deaths. The mean age at diagnosis for patients with NHL is 67 years and the mean age at death is 76 years, with Hodgkin's lymphoma most commonly detected between the ages of 20 and 34 years, and as a result of the higher survival rate among younger patients, the mean age of death is 68 years [6]. The World Health Organization classification system defines more than 90 different subtypes [7]. NHL can occur in almost every organ [8]. Further classification of the individual lymphoma subtypes is beyond the scope of this article, but ultimately each is defined by morphology, immunophenotype, genetic, molecular and clinical features.

Primary testicular lymphoma is an extremely rare form of extranodal NHL, comprising 3–9 % of testicular malignancies and 1–2 % of NHL, and tends to recur haematogenously to the central nervous system, skin, lungs, pleura, Waldeyer's ring, soft tissues and eyes, sometimes concealing the primary localization of the focus [9]. PTL is the most common type of ectranodal lymphoma affecting the genitourinary system, with an incidence of 3.04 % (kidney lymphoma 0.22 %, bladder lymphoma 0.18 %, prostate lymphoma 0.01 %) [9]. The true incidence of PTL remains precisely unknown. Foreign literature confirms the rarity of PTL with an annual incidence of 0.09 to 0.26 per 100,000 people [10]. With a mean age of diagnosis ranging from 66 to 68 years, PTL is the most frequent malignant neoplasm in men over 60 years of age, with a progressively increasing risk of disease progression with age and frequent bilateral organ involvement (8–38 %) [10]. Diffuse large B-cell lymphoma is the most common subtype of lymphoma, including testicular localisation, and it represents 30 to 40 % of all new NHL diagnoses. DLBCL includes B-cell lymphomas of moderate to high malignancy with different molecular backgrounds, clinical course and response to treatment. Up to one-third of DLBCLs have extranodal localization, most commonly the gastrointestinal tract, skin and soft tissues, bones and genitourinary organs [10]. With primary testicular lymphoma, sporadic cases (Burkitt's lymphoma, lymphoblastic lymphoma, plasmacytoma, T-cell lymphoma) of other lymphoma varieties have been described in the scientific literature [11]. Up to 90 % of DLBCLs are diagnosed at stage 1 and 2 [12].

Testicular DLBCL often infiltrates the epididymis, the spermatic cord, and retroperitoneal lymph nodes. Along with a tendency to affect the contralateral testis, the process may spread to the central nervous system (CNS), as well as to other extranodal sites: skin, lungs, kidneys, adrenal glands, gastrointestinal tract, etc. [13]. Recurrence of testicular DLBCL in the CNS occurs in 5 % of patients [14]. Twenty-five percent of patients with DLBCL have secondary spread to the heart [15, 16].

PATHOGENESIS, MOLECULAR CHARACTERISTICS OF TESTICULAR DIFFUSE LARGE B-CELL LYMPHOMA AND RISK FACTORS

PTL etiology is currently not precisely defined and remains poorly studied. To this day, there is still debate about the factors that contribute to the development of this disease. Genetic predisposition is of some importance, and infectious and inflammatory factors also increase the risk of lymphoma formation.

First-degree relatives of patients with NHL and Hodgkin's lymphoma have an increased risk of developing lym-

phoma, by a factor of 1.7 and 3.1, respectively. A family history of a particular lymphoma subtype is associated with the development of the same subtype [6]. Three principal mechanisms exist whereby infection increases lymphoma risk: direct lymphocyte transformation, immunosuppression, and chronic antigenic stimulation [6]. Rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, dermatomyositis, and celiac disease (gluten disease) are inflammatory conditions that increase the risk of developing lymphoma due to disease-specific causes and continuous intake of immunosuppressant drugs [6]. Modifiable risk factors include tobacco use and obesity (body mass index – 30 kg/m^2 or higher). Implants and prolonged exposure to pesticides are also associated with NHL [6]. HIV infection is a recognized risk factor for aggressive and primary extranodal lymphomas and is the only well-described etiologic factor for testicular DLBCL.

Testicular DLBCL is a B-cell malignancy in which normal B-cell development and differentiation are impaired. The use of cytogenetics, fluorescence *in situ* hybridization, and comparative genomic array hybridization has shown that genetic alterations in primary testicular DLBCL often include complex abnormalities such as translocation, trisomy, amplification, and deletion. Abnormalities of 3q27 and 6q deletion are the most frequently observed; the latter may be the only cytogenetic abnormality [17].

The DLBCL microenvironment plays an important role in the pathogenesis of PTL and prognosis of the disease [18]. Over the last decades, neutrophils have been shown to contribute to tumour progression, including PTL [19]. Several mechanisms have been identified suggesting a role for neutrophils in the high probability of progression. The secretion of various cytokines such as interleukin 2, interleukin 10 and high immature cell content constitutes one of them [20]. Conversely, elevated neutrophil counts are associated with potent antitumour effector cells, especially in patients with lymphoma [21]. T-lymphocytes, mainly consisting of CD4$^+$ and CD8$^+$ T-cells, play an important role in cell-mediated immunity. A small amount of tumour infiltrating CD4$^+$- and CD8$^+$ T-cells has shown in scientific studies to be associated with poor prognosis in patients with PTL (increased risk of progression and death) [22].

Primary testicular DLBCL develops in an immunoprivileged site behind the hemato-testicular barrier and has a molecular profile very similar to primary CNS lymphoma, including mutations MYD88^{L265P} (70–80 %), CD79B and CDKN2A (88 %), as well as changes in PD-1/PD-2 loci (50 %) [23]. ABC phenotype and MCD genomic subtype are found in most clinical cases [24].

The World Health Organization (WHO) defines DVCCL as a tumour of large to medium-sized B-lymphocytes with a nucleus size comparable to or larger than that of a normal macrophage or twice the size of a normal lymphocyte. The features of DLBCL include diffuse growth of tumor cells with infiltration of lymph nodes and/or non-lymphatic organs and tissues by large lymphoid B-cells. DLBCL is morphologically characterized by diffuse infiltration of medium to large sized cells with large nuclei and abundant cytoplasm, which destroy and obliterate the basic architecture of the affected lymphatic tissue. The cells typically express pan-B-cell antigens (CD19, CD20, CD22, CD79a and CD45). Most cells also express surface immunoglobulin. Approximately 14 % of lymphomas express CD30, which may indicate a favourable prognosis [25].

CLINICAL SIGNS

PTL has no specific clinical signs. The most common clinical symptom of PTL is uni- or bilateral oedema of the testis (scrotum) that develops over a long period of time (weeks, months and even years), usually painless [13]. Bilateral testicular oedema is observed in 35 % of patients with PTL [13]. PTL is associated with the development of hydrocele in 40 % of cases, and urologists are the first consultants that patients refer to. In some cases, PTL may initially manifest with the onset of sharp pain in the testicle. In addition to an increase in testicular size, systemic manifestations such as fever, anorexia, night sweats and weight loss may join, which occurs in 25–41 % of patients [13]. During the course of the disease, local spread of the process to the testicular appendages, the spermatic cord and scrotal skin, and regional retroperitoneal lymph nodes often develops [13].

DIAGNOSIS AND TREATMENT

Ultrasound examination (ultrasound) continues to be the most widely used method of imaging testicular neoplasms. As a rule, testicular DLBCL is characterized by local or diffuse "hypervascularization" on color Doppler ultrasound. It has been suggested that if colour Doppler scrotal imaging reveals hypervascularization in patients with complaints of painless scrotal oedema, testicular lymphoma/leukaemia should be considered as a differential diagnosis [26]. The mean PTL size at primary ultrasound is 5.0 cm (interquartile range 4.1–7.1 cm) [13].

Since PTLs represent a subtype of diffuse large B-cell lymphoma that is fluorodeoxyglucose-dependent, positron emission tomography-computed tomography (PET-CT) should be used to determine the extent of the lesion. Bone marrow biopsy is only required in DLBCL, in cases of discordant histological picture and in negative PET-CT results. Unfortunately, PET-CT opportunities do not allow detecting CNS lesions, as it naturally absorbs fluorodeoxyglucose; therefore, magnetic resonance imaging of the brain and lumbar puncture followed by cytology and flow cytometry are recommended to exclude CNS lesions [27]. CNS involvement (cerebral membranes, epidural space and brain parenchyma) in testicular DLBCL almost always leads to unfavourable outcomes with a median survival after diagnosis of CNS involvement of only 2–5 months [27].

Apart from achieving complete remission, treatment of primary testicular DLBCL is essentially aimed at achieving both local and systemic control of the disease, as well as preventing possible recurrence to the contralateral testis and CNS. No randomised phase III studies have been conducted since the disease is rare, and the international-

ly accepted standard of care for testicular DLBCL is based on evidence from a retrospective analysis of case series and phase II studies [28].

Nowadays, at the time of diagnosis, a patient with primary DLBCL should be offered a multimodal treatment approach including surgery in the volume of uni- or bilateral orchofunicollectomy, combined anthracycline-based chemotherapy, prophylactic intrathecal chemotherapy and craniomoshono irradiation. Orchiectomy is the main and obligatory initial method of treatment and diagnosis in all patients irrespective of the stage of the cancer process, providing morphological verification of the diagnosis, followed by cytological, histological, immunohistochemical and karyological studies of the removed testis. Furthermore, it should be considered that the persistence of the blood-testis barrier prevents the testicular tumour from being exposed to chemotherapeutic drugs, and testicular tumour cells may also express high levels of drug-resistant proteins, which also contribute to the development of resistance to chemotherapy.

Testicular DLBCL is an extremely aggressive malignancy with low overall survival and progression-free survival: 5-year progression-free survival and 5-year overall survival are 35.4 % (95% confidence interval (95% CI): 14.8–56.0 %) and 53.4 % (95% CI: 30.1–76.7 %), respectively [13]. The prognosis for testicular DLBCL is unfavorable, especially if disease dissemination occurs within the first year after diagnosis [29]. Improved survival rates (overall survival up to 85 %, progression-free survival up to 74 %) can be achieved in patients with local/limited stage primary testicular DLBCL using anthracycline-containing chemotherapy in combination with rituximab, prophylactic contralateral scrotal radiotherapy and prophylactic intrathecal chemotherapy [30]. Although there are studies that have not demonstrated improved survival in patients with testicular DLBCL [31], nevertheless, several studies have confirmed, that the addition of rituximab (375 mg/m^2) to chemotherapy according to R-CHOP regimens (cyclophosphamide 750 mg/m^2, doxorubicin 50 mg/m ^{2}, vincristine 1.4 mg/m^2, prednisone 100 mg) leads to a significant reduction in CNS relapses during PTL [32, 33]. Local/limited stage (I and II) of the process according to the international classification of Ann Arbor (1971), performance of chemotherapy after orchiectomy, and a low international prognostic index score (less than 2) are independent factors correlating with increased survival of patients with testicular DLBCL [13].

If contralateral testicular irradiation is not performed, the risk of PTL recurrence is 42 % within 15 years [34]. Numerous scientific studies have convincingly demonstrated that the absence of prophylactic contralateral irradiation is a poor predictor of prognosis [35, 36]. Whether preventive contralateral orchiectomy should be performed remains to be studied.

By using chemotherapy containing high doses of methotrexate, the risk of relapse in the CNS can be reduced [37]. High doses of methotrexate, however, comprise a resource-intensive therapy with significant toxicity, so it should be administered only to patients at high risk of CNS lesion recurrence. Rituximab improves survival but does not reduce CNS relapse rates [37].

With a view to forming experience and structuring medical knowledge among specialists involved in the treatment of urological patients, we present a clinical observation – a case of primary testicular DVCCL treated according to the SCARE (Surgical CAse REport) 2020 recommendations [38].

Patient T. born in 1984 (38 years old) came to our clinic on September 9, 2022 with the main complaint of painless enlargement of the right testicle in volume. He considered himself diseased for a year, when he discovered a change in the size of the scrotum on the right side; he was treated by an urologist at his place of residence with suspected orchoepididymitis, and took antibiotics. No effect of the treatment was observed, the right testicle continued to increase in size.

At the initial examination, the skin of the external genitalia is unchanged, pale pink in colour, wrinkled, without pathological inclusions (Fig. 1). The scrotum is asymmetrical in shape, enlarged in size on the right side; superficial palpation of the scrotal organs on the right side reveals a painless dense elastic mass measuring 4 × 6 cm. The testis is enlarged in size, ovoid in shape, dense-elastic, smooth in consistency, no free fluid is detected during deep testicular palpation on the right side. The testis on the left is elastic, of soft-elastic consistency, smooth. The testicular appendage is symmetrically located on both sides, soft in consistency, with no additional inclusions. The elements of the spermatic cord are palpated in the form of a round dense, freely displaceable mass, pathologic inclusions are not palpated. The veins of the spermatic cord are not dilated. Examination and palpation of the penis, inguinal region, lower abdomen and perineum revealed no peculiarities.

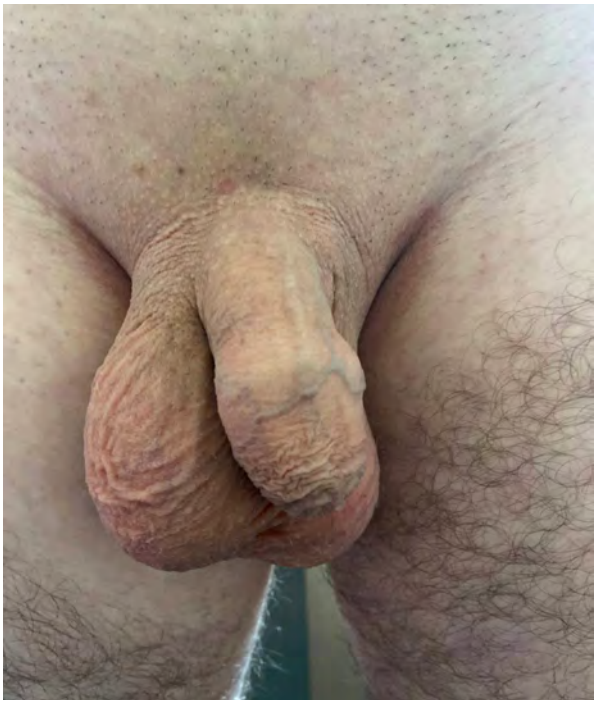


FIG. 1.
Patient T. External genital appearance

An ultrasound examination of the scrotal organs was performed at an appointment with a urologist: a voluminous hypoechogenic mass of the right testicle, occupying ¾ of the organ, was revealed. The size of the right testicle is 36.7 cm^3, with clear contours. Doppler reveals diffuse hypervascularisation of the right testis. No changes were found in the contralateral testis. Laboratory findings, including testicular tumor markers, were within reference values. Endoscopic examination of the upper and lower gastrointestinal tract revealed no pathology. On October 13, 2022, an ultrasound examination of the veins of the lower extremities was performed: no pathology was revealed.

A native high-resolution multi-layer spiral computed tomography of the chest, abdomen, and pelvic organs with primary collimation of 64 × 0.6 mm, slice reformat thickness of 1.0–5.0 mm, and subsequent 3D image analysis was performed on October 12, 2022 (Fig. 2). In the scan area, the right testis is enlarged in size (56 × 43 mm), inhomogeneous structure (up to 14–33 HU). No other pathological findings were observed. A preliminary diagnosis was determined following the above-mentioned findings: Malignant neoplasm of the right testicle of the 1a clinical group (C62.2).

In the first stage on October 27, 2022, the patient underwent radical right-sided orchofuniculectomy with high ligation of the seminal vein under general anaesthesia (Fig. 3).

Macroscopically, the right testicular tumour which was excised as a solid, homogeneous grey-white mass with a lobular appearance, replacing the testis completely, not adherent to the surrounding tissues (Fig. 4). Twelve months have elapsed since the initial medical treatment and verification of the diagnosis.

According to the results of histological examination dated November 15, 2022, the microdrugs of the excised tumour of the right testis revealed diffuse growth of non-Hodgkin lymphoma from large and medium-sized cells. The tumour of the right testis was formed by large lymphoid

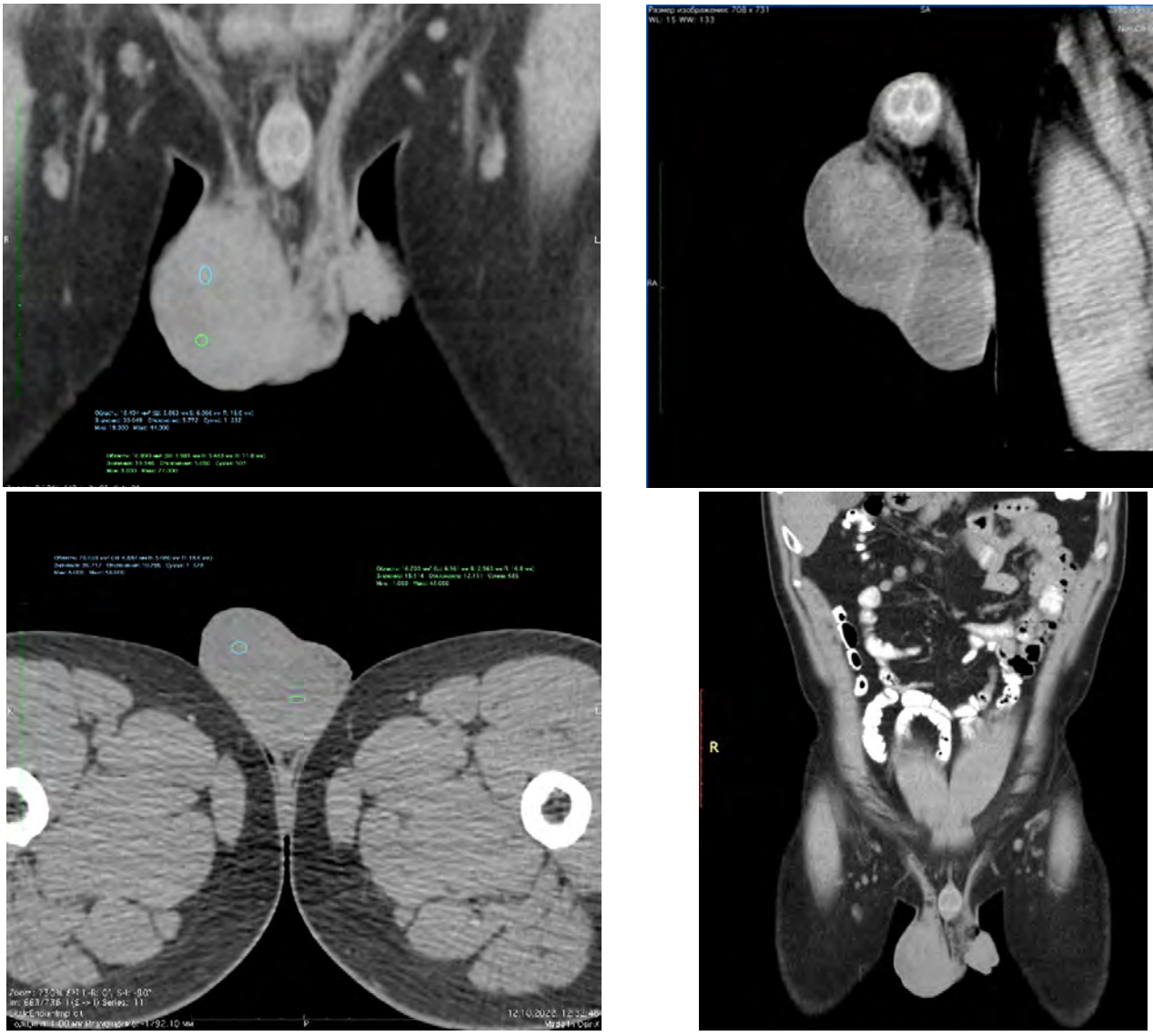


FIG. 2.

Patient T. Primary testicular diffuse large B-cell lymphoma of the testis. Contrast-enhanced computed tomography: enlarged right testis (56 × 43 mm)

cells, the diameter of which exceeded the size of a small lymphocyte by 4–5 times, with a diffuse growth pattern. Morphologically, the predominant cell population was centroblasts characterised by a vesicular chromatin structure, 2–4 nuclei located near the nuclear membrane and moderately developed amphophilic cytoplasm (Fig. 5).

Additionally, an immunohistochemical study of the right testicular tumor was performed (November 17, 2022) immunohistochemical study of the right testicular tumor on Bond-maX immunohistostainer (Leica Microsystems, Germany) using a panel of Novocastra/Leica antibodies to CD20 (L26 clone), CD3 (LN10 clone), CD10 (56C6 clone), CD5 (4C7 clone), Cyclin D1 (D1-GM), CD23 (1B12 clone), bcl-6 (LN22 clone), MUM1 (MuM1p clone) and Ki-67 (MM1 clone). The immunophenotype of the lymphoma was represented by expression of pan-B-cell antigen CD20 as well as CD23,

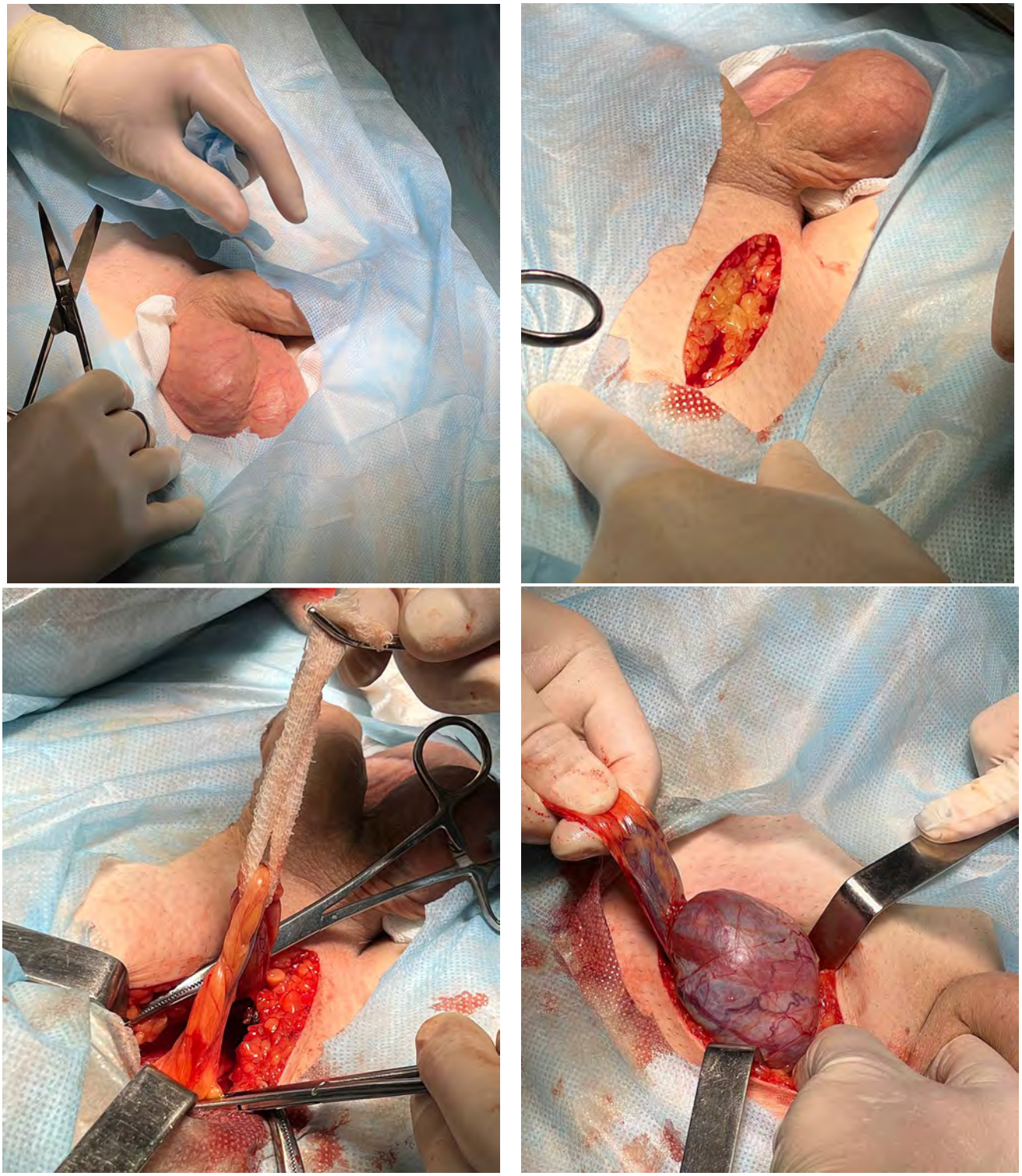


FIG. 3.
Patient T. Intraoperative images: right-side radical inguinal orchiofuniculectomy

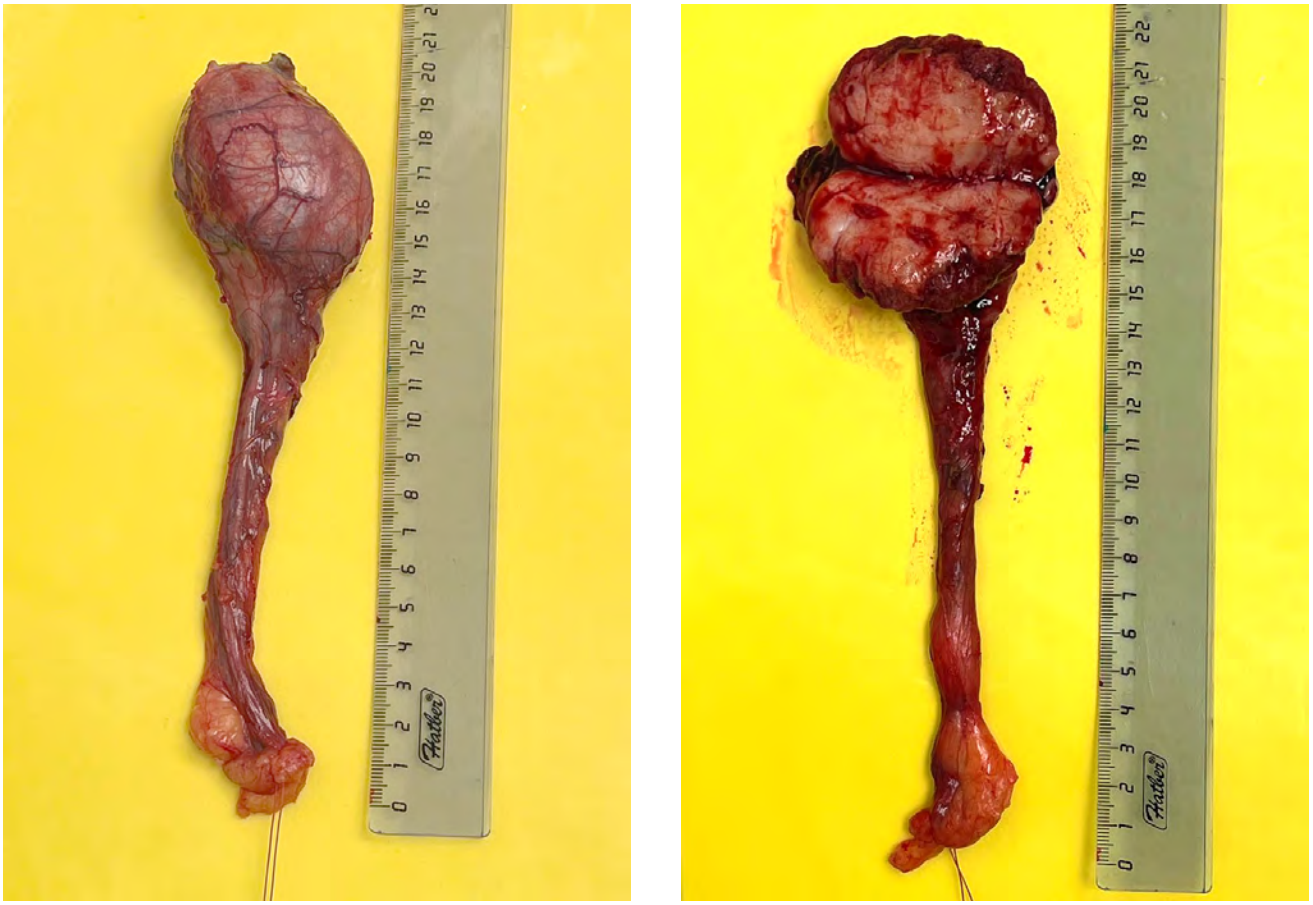


FIG. 4.
Patient T. Primary testicular diffuse large B-cell lymphoma of the testis: macroscopic preparation

bcl-6 and MUM1 and absence of expression of the rest of the above antigens. The proliferative activity of the tumour by Ki-67 expression was about 80 %. The tumour cells were characterized by the following immunophenotype: $CD20^+$, $CD3^-$, $CD10^-$, $CD5^-$, cyclin $D1^-$, $CD23^+$, $bcl\text{-}6^+$, $MUM1^+$ and $Ki\text{-}67^+$ (about 80 %). Considering the histological picture and immunohistochemical findings, the right testicular neoplasm was classified as a diffuse large B-cell lymphoma of non-germ cell origin (activated cells).

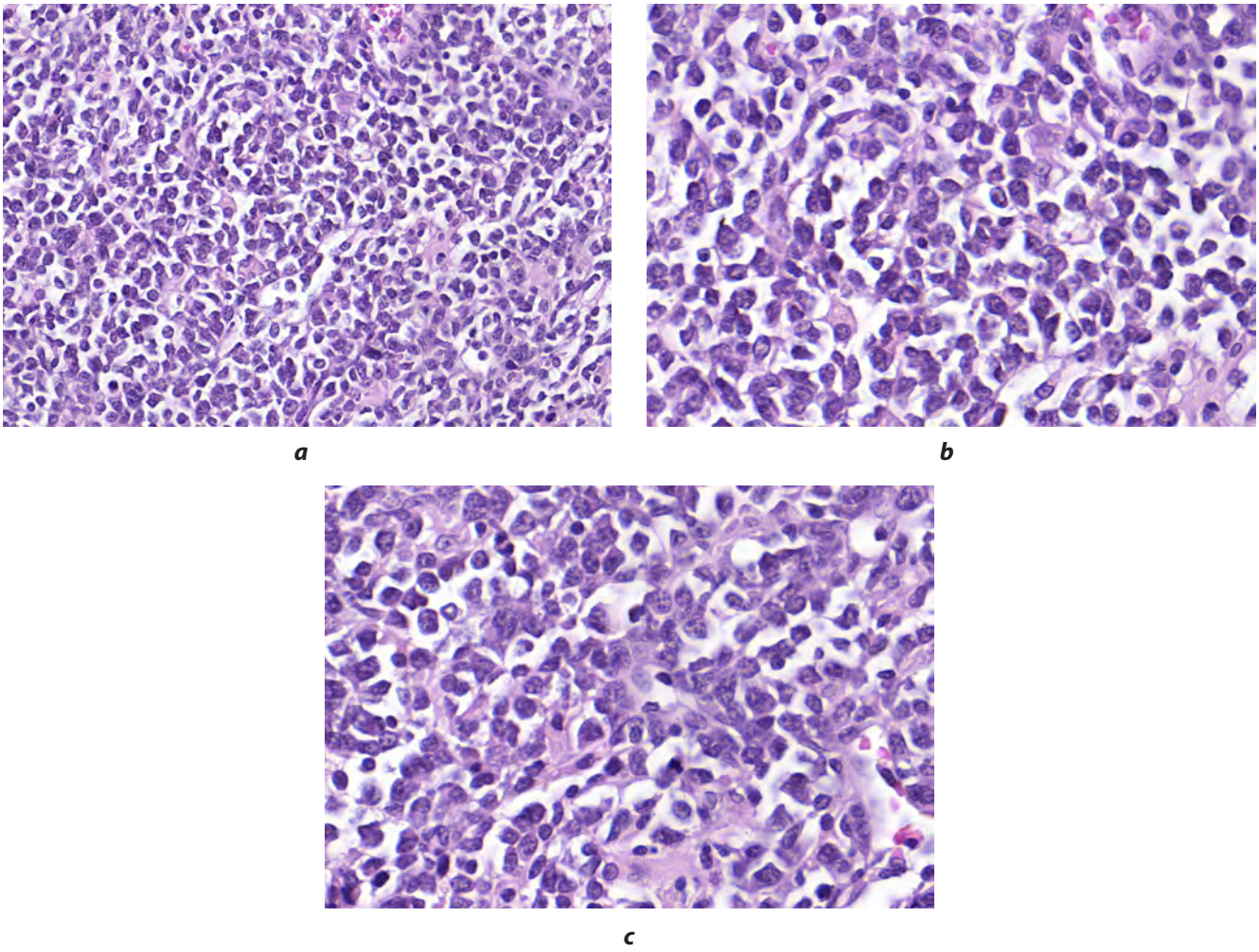
Postoperative period (day 3) was complicated by left lower lobe infarction-pneumonia S 7/8/DN0 (according to Clavien – Dindo 1 scale), with clinical manifestations (confirmed on the basis of laboratory and instrumental examinations), as a result of acute phlebothrombosis of the popliteal tibial segment on the left and peripheral left-sided pulmonary artery thromboembolism. Conservative treatment was received in the department of vascular surgery; he was discharged with improvement in satisfactory condition to continue treatment of the underlying disease.

Primary diagnosis: diffuse large B-cell lymphoma, non-GCB type, with right testicular involvement (C83.3). IE stage. Status post orchofuniculectomy on the right; palliative chemotherapy (1 course of R-CHOP regimen), clinical group II. Morphological conclusion: diffuse large B-cell lymphoma, non-GCB type, $CD20^+$, $CD23^+$, $bcl\text{-}6^+$, $MUM1^+$, proliferative activity index Ki-67 = 80 %. Status post right-sided radical inguinal orchofuniculectomy. Complication: acute phlebothrombosis of the popliteal tibial segment on the left (I80.2). Peripheral left-sided pulmonary artery thromboembolism (I26.9). Left-sided lower lobe infarction pneumonia S 7/8/DN0 (J18.8).

Systemic chemotherapy according to the R-CHOP scheme is planned as the second stage after a radically removed primary lesion. No invasion to other localisations was observed within 3 months following diagnosis.

CONCLUSION

Primary testicular DLBCL is a unique form of aggressive B-cell lymphoma with a characteristic genetic profile. The submitted clinical case of primary testicular DLBCL convincingly demonstrates that the tumour occurs not only in men after 60 years of age, but also at an earlier age; it indicates the importance of pathomorphological diagnosis and the use of additional immunohistochemical methods of investigation for the accurate diagnosis and differential diagnosis. However, physical assessment of the external genitalia continues to be the most important step in the diagnosis of urological diseases. Since there are no standardized protocols for the management of patients with prima-



a ***b*** ***c***

FIG. 5.

*Patient T. Primary testicular diffuse large B-cell lymphoma of the testis. Histological examination: the image demonstrates a testicular tumour consisting of diffuse layers and discrete medium to large sized atypical cells with pale eosinophilic or clear cytoplasm. The predominant cell population is centroblasts characterised by a vesicular chromatin structure, 2–4 nuclei located near the nuclear membrane and a moderately developed amphophilic cytoplasm. Hematoxylin and eosin staining; magnification ×200 (**a**), ×400 (**b**, **c**)*

ry testicular lymphoma, it is essential that these clinical cases continue to be analyzed and discussed in routine urological practice.

The treatment evolution of primary testicular DLBCL during the last decade is an excellent example of successful translational studies, through which a better understanding of the pathogenesis of the disease has contributed to the development of the most effective treatments. Recurrence to the central nervous system remains a serious problem, however, and future studies should focus on determining the best treatment strategy to reduce the risk of its occurrence.

Conflict of interest

The authors of this article declare no conflicts of interest.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

TRAUMATOLOGY

VERTICALIZATION OF PATIENTS AND AXIAL LOAD ON THE LOWER LIMBS AFTER SURGICAL TREATMENT OF UNSTABLE PELVIC RING INJURIES (BRIEF REVIEW OF THE LITERATURE)

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ABSTRACT

The article provides a theoretical review of scientific publications devoted to the rehabilitation of patients with unstable pelvic ring injuries; the features of pelvic ring damage are considered based on the specifics of the traumatic injury, the frequency of occurrence and the severity of the consequences. It is emphasized that prolonged pain syndrome due to pelvic ring injuries and the duration of the rehabilitation period negatively affect the physical and psycho-emotional state of a patient. At the same time, pelvic ring injuries are most relevant among the working population, and their consequences are quite serious, including disability and death. Consequently, the possibility of optimizing rehabilitation measures for patients with unstable injuries, aimed at restoring the functions of the musculoskeletal system in static conditions and while walking, is currently one of the urgent tasks of theoretical and practical traumatology. The possibilities of verticalization of patients and the use of axial load on the lower limbs in the postoperative period are considered as the main rehabilitation measures. It is noted that in the case of resolving the issue of axial load in case of unstable pelvic ring injury, the intensity of such load and the timing of the start of its use should be determined individually, depending on the physical condition of a patient, the characteristics of the injury and the presence of concomitant injuries. Treatment for unstable pelvic ring injuries most commonly is carried out in most cases through the use of various methods of surgical treatment and restoration of the pelvic anatomy. Based on the results of the theoretical study, it is necessary to state that, despite the obvious significance of postoperative treatment, the adequate organization of which largely determines its final result, it was revealed that the material for studying this issue is insufficient due to specific approaches to verticalization and axial load on the lower limbs, depending on type of pelvic ring injury, taking into account the individual characteristics of the injury in a particular patient.

Key words: *pelvic trauma, pelvic ring injury, pelvic bones fracture, verticalization of patients, axial load on the lower limbs*

Received: 12.02.2023
Accepted: 09.11.2023
Published: 05.12.2023

For citation: Melkostupov A.A., Komogortsev I.E., Vinogradov V.G., Angarskaya E.G. Verticalization of patients and axial load on the lower limbs after surgical treatment of unstable injuries of the pelvic ring (brief review of the literature). *Acta biomedica scientifica*. 2023; 8(5): 92-99. doi: 10.29413/ABS.2023-8.5.9

ВЕРТИКАЛИЗАЦИЯ ПАЦИЕНТОВ И ОСЕВАЯ НАГРУЗКА НА НИЖНИЕ КОНЕЧНОСТИ ПОСЛЕ ОПЕРАТИВНОГО ЛЕЧЕНИЯ ПАЦИЕНТОВ С НЕСТАБИЛЬНЫМИ ПОВРЕЖДЕНИЯМИ ТАЗОВОГО КОЛЬЦА (КРАТКИЙ ОБЗОР ЛИТЕРАТУРЫ)

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РЕЗЮМЕ

В статье выполнен теоретический обзор научных публикаций, посвящённых вопросам реабилитации пациентов с нестабильными повреждениями тазового кольца, рассмотрены особенности его повреждения исходя из специфики травматического повреждения, частоты встречаемости и серьёзности последствий. Подчёркивается, что длительный болевой синдром при повреждениях тазового кольца и длительность реабилитационного периода негативно влияют на физическое и психоэмоциональное состояние пациента. При этом повреждения тазового кольца наиболее актуальны среди трудоспособного населения, а последствия их достаточно серьёзны, вплоть до инвалидизации и летального исхода. Следовательно, возможность оптимизации мероприятий по реабилитации пациентов с нестабильными повреждениями, направленных на восстановление функций опорно-двигательного аппарата в статике и при ходьбе, является в настоящее время одной из актуальных задач теоретической и практической травматологии. В качестве основных реабилитационных мероприятий рассматриваются возможности вертикализации пациентов и применения осевой нагрузки на нижние конечности в послеоперационном периоде. Отмечено, что в случае решения вопроса осевой нагрузки при нестабильном повреждении тазового кольца величина такой нагрузки и сроки начала её применения должны определяться индивидуально, в зависимости от физического состояния пациента, особенностей травмы и наличия сопутствующих повреждений. Лечение при нестабильных повреждениях тазового кольца, как правило, проводится в большинстве случаев посредством использования различных методов оперативного лечения и восстановления анатомии таза. По результатам выполненного теоретического исследования необходимо констатировать, что, несмотря на очевидную значимость послеоперационного лечения, адекватная организация которого во многом определяет конечный его результат, выявлено, что материала для изучения данного вопроса недостаточно вследствие специфических подходов к вертикализации и осевой нагрузке на нижние конечности в зависимости от типа повреждения тазового кольца с учётом индивидуальных характеристик травмы у конкретного пациента.

***Ключевые слова**: травма таза, повреждение тазового кольца, перелом костей таза, вертикализация пациентов, осевая нагрузка на нижние конечности*

Для цитирования: Мелкоступов А.А., Комогорцев И.Е., Виноградов В.Г., Ангарская Е.Г. Вертикализация пациентов и осевая нагрузка на нижние конечности после оперативного лечения пациентов с нестабильными повреждениями тазового кольца (краткий обзор литературы). *Acta biomedica scientifica*. 2023; 8(5): 92-99. doi: 10.29413/ABS.2023-8.5.9

Статья поступила: 12.02.2023
Статья принята: 09.11.2023
Статья опубликована: 05.12.2023

UNSTABLE PELVIC RING INJURIES: PECULIARITIES OF OCCURRENCE, ROLE OF REHABILITATION MEASURES

The incidence of pelvic ring injuries has increased in recent decades in populations worldwide, as a result of the increased rhythm of modern life, which contributes to an increased risk of injury. As a consequence, the issue of preventing post-traumatic pelvic injuries, which are the cause of subsequent disability, has also become relevant [1–3].

The main cause of pelvic ring injuries, including unstable injuries, is usually high-energy trauma, the variety and severity of which have increased with significant advances in science and technology. Currently, the main factor in the occurrence of unstable pelvic ring injuries is road traffic accidents, catatrauma (falls from height), and high-force impacts of various mechanisms [4, 5].

Anatomically, the pelvis is a complex of two iliac bones, two sciatic bones, two bosom bones and the sacrum – all these anatomical elements form the so-called pelvic ring. Pelvic fracture classifications are based on these anatomical and biomechanical features [6].

The first description of pelvic ring injuries was proposed by the prominent French surgeon J.F. Malgaigne in the century before last, and over the past almost three centuries; about fifty different classifications have been proposed [7].

The classification of A.V. Kaplan based on the integrity of the pelvic ring is the best known in our country [8]. This classification is quite accurate in showing the specificity of this type of injury, but only considers the integrity of the bony components of the pelvic ring injuries, not reflecting the damage to the capsular ligamentous apparatus and the resulting instability.

In 1961, G. Reppal and S. Sutherland proposed a classification of pelvic ring injuries [9, 10] based on the directions of mechanical force acting on the pelvic ring: frontal (external rotation), lateral compression (internal rotation), and vertical shear. Since this classification did not take into account pelvic ring instability, it did not allow us to recommend any treatment methods [11].

In the course of further study of biomechanics based on the approach of G. Reppal and S. Sutherland led to the development of the M. Tile classification of pelvic ring injuries, which takes into account the increasing degree of instability (partial and complete) of the pelvic ring [12]. Association for the Study of Internal Fixation (AO, Arbeitsgemeinschaft für Ostesinthesefragen), better known in Russia, as an AO Association, improved the classification of M. Tile [13], and the stability of the dorsal bone ligamentous complex was the main classification criterion.

According to the M. Tile AO/ASIF (Association for the Study of Internal Fixation) classification, pelvic ring injuries are divided into stable (type A) and unstable (types B and C). Unstable pelvic injuries are damage to the pelvic ring, provoking bone mobility. They occur in most cases as a result of high-energy injuries, mainly caused by road traffic accidents (64.37 %), falls from a significant height (25.32 %) or sports injuries (about 2 %) [14, 15]. Such fractures are often accompanied by associated life-threatening injuries [16, 17]. Type B pelvic ring injuries are open and lateral compression fractures. There is partial destruction of the posterior pelvic ring elements, including sacral fractures and injuries to the sacroiliac complex, in cases where the pelvic ring is vertically stable but rotationally unstable.

In unstable C-type pelvic ring injuries, there is complete destruction of the posterior semicircle and displacement of bone fragments in three planes, which leads to rotational and vertical instability, accompanied by high mortality in the acute period of injury and disability in the long-term period [18, 19]. In unstable pelvic ring injuries, two or more fractures may be simultaneously involved, with displacement of the pelvic fractures causing risk of damage to internal organs, provoking the possibility of haemorrhage [20], up to and including death. Optimal patient rehabilitation tactics for pelvic bone fractures and capsular ligamentous apparatus injuries along with treatment determines the effectiveness of the implemented measures, allowing to reduce the treatment and recovery period, accelerate the restoration of joint function of the lower extremities and minimize the risk of patient disability [21, 22].

Treatment of patients with unstable pelvic ring injuries is one of the urgent and unsolved problems of modern traumatology. Pelvic ring injuries can be characterized by significant pain syndrome and cause a long-term reduction in the patient's physical activity both at the household level and in terms of social adaptation, including reduced quality of life and psychological health due to prolonged immobilization and rehabilitation, as well as the development of possible complications [23]. Provision of lower extremity support and preservation of movement in the lower extremities in the case of pelvic ring injuries should be accompanied by stable fixation with preservation of adequate repositioning [24, 25], which should ensure early activation of the patient [26–28]. The use of nonsurgical methods, which are technically simple and involve prolonged immobilization of patients with pelvic ring injuries, does not allow early activation and verticalization, which makes these methods ineffective for the treatment of these types of injuries [29]. Active surgical tactics in case of pelvic ring injuries, however, with certain technical difficulties, are accompanied by significant blood loss and excessive surgical aggression [4, 29].

The severity of pelvic ring injuries, their variety, unsatisfactory results of nonsurgical treatment methods and surgical interventions require further in-depth study of this issue [30–32]. Thereby, the issues of treatment of patients with pelvic ring injuries at all stages: preoperative, immediate operative and postoperative periods are becoming more relevant [33].

PECULIARITIES OF PATIENTS' VERTICALIZATION AND SPECIFICITY OF AXIAL LOAD IN THE POSTOPERATIVE PERIOD IN UNSTABLE PELVIC RING INJURIES: CURRENT STATE OF THE ISSUE

Immobilization syndrome accompanying patients with pelvic ring injuries, which is a set of multi-organ disorders associated with non-physiological restriction of motor activity and prolonged horizontal position of patients, remains relevant nowadays. Such condition can lead to musculoskeletal, respiratory, endocrine-metabolic, cardiovascular disorders.

Verticalization as a leading method of prevention and therapy of immobilization syndrome [34] in pelvic ring injuries allows to restore (preserve) adequate afferentation from muscle-tendon and joint receptors, to preserve the activity of reflex reactions and automatisms caused by post-tonic mechanisms, in particular, to ensure preservation of the reflex mechanism of bladder and bowel emptying, and ultimately allows to significantly reduce the recovery period and minimize the development of possible complications [35, 36].

The importance of verticalization being a mechanism of early activation of patients after surgical manipulations, the meaning of which is stable fixation and adequate repositioning of fragments in case of pelvic ring injuries, lies in maintaining or restoring the maximum possible value of the gravitational gradient – the highest angle of elevation of the patient, which does not lead to the development of signs of orthostatic insufficiency [37], i. e. the essence of which lies in the ability to maintain vital parameters stable in any position

The verticalization objective is to achieve the highest value of gravitational gradient (more than 80°), which is a prerequisite for maintaining the patient's functioning in the rehabilitation process. Verticalization is the only way to overcome immobilization syndrome – a complex of multi-organ disorders associated with non-physiological restriction of the patient's motor and cognitive activity [38]. The frequency of verticalization in relation to ways of overcoming the gravitational gradient is significant, allowing the patient's normal body function to be optimized as much as possible.

Effective treatment in cases of unstable pelvic ring injuries of AO/ASIF types B and C in order to achieve restoration of the pelvic anatomy is performed using various surgical methods by external fixation with osteosynthesis or a combination of these devices. External fixation of the pelvic ring is a minimally invasive method of osteosynthesis and is performed using various devices, the development of which has been the subject of numerous studies. They can be of various designs and modifications, used both as a temporary and definitive method of osteosynthesis [39]. When the patient's condition is unstable or critical, manipulation is limited to fixation of the pelvic ring with external fixation devices to a minimum extent. At the same time, unfortunately, the modifications of external fixation devices proposed today are not stable enough to fix the posterior pelvis [40–43], which is the main condition for reliable fixation of the pelvic ring injury and, consequently, for the successful treatment of this injury [44].

In the stable condition of the patient, it is possible to use extramedullary and immersion fixators [23, 45, 46]. A number of authors consider ORIF (open reduction and internal fixation) as the gold standard for pelvic ring injuries [47, 48]. The open technique allows good repositioning and rigid fixation, but it is complicated, traumatic and accompanied by intraoperative blood loss [4, 49]. The implementation of these types of manipulations requires the use of expensive fixators, which are not available in all medical centres. The detailed planning of these types of surgical interventions is also performed using three-dimensional reconstruction of pelvic fractures, which entails the complexity of logistical organization, which limits the use of ORIF for pelvic ring injuries in many medical institutions [28, 50].

Irrespective of the method of surgical treatment, however, early surgical fixation in cases of unstable pelvic ring injuries allows rehabilitation measures to be initiated through verticalization and early axial loading as soon as possible. This reduces the incidence of hypostatic complications associated with prolonged bed rest and hypodynamia: pressure injuries, decompensation of comorbidities, pneumonia, muscle hypotrophy, joint contractures, phlebothrombosis and thromboembolism.

Early verticalization and axial loading of the lower extremities can reduce mortality in cases of polytrauma as well as improve functional outcomes. Additionally, the minimal surgical invasiveness of these manipulations and early rehabilitation can reduce the probability of possible complications and the duration of hospital treatment [51, 52]. All these positive factors of the therapeutic process make it possible to significantly reduce logistical and economic costs for medical institutions.

There are no reliable studies in Russia and worldwide that could show the dependence of early verticalization and early axial load on the lower extremities on the choice of the method of surgical treatment of pelvic ring injuries. There is also no universally recognized algorithm for the treatment of patients with these injuries.

Verticalization of patients in the postoperative period is performed after 2–3 months in average, depending on the type of injury and the treatment performed. Verticalization is allowed after X-ray control to assess the state of consolidation, the standing of transosseous elements and bone fragments, and subsequent axial load on the lower extremities is implemented as the pain syndrome decreases. The duration and specifics of training are determined individually and depend on the patient's age, physical condition, type of pelvic trauma, as well as the specifics of the surgical intervention performed. In the initial stages, it is necessary to maximize the patient's mobility under the supervision of the attending physician and physical therapy instructor, using various rehabilitation devices, including support devices (walkers, crutches, etc.). It is essential when using crutches

to avoid the development of "crutch paresis" [23], which occurs when crutches apply prolonged pressure to the radial nerve or part of the brachial plexus.

In unstable pelvic ring injuries, the timing of onset and magnitude of axial loading should be determined. In terms of determining the value of axial load, the patient's ability to perform a single lift of the extremity against gravity or a single repetition of a task is used as the basis for this definition [38]. The magnitude of the axial load must be high enough to be effective, on the one hand, and on the other hand, re-injury must be avoided. Axial load dosing in the postoperative period is determined based on the results of radiological examination or computed tomography of the pelvic bones using special computer programmes, which is currently one of the main issues in the rehabilitation of patients with unstable pelvic ring injuries [53, 54].

During the verticalization phase, the patient should be trained to practice the self-care features. Physiotherapeutic treatment, therapeutic exercise aimed at gradually increasing the physical load on the musculoskeletal system are carried out. After consolidation of pelvic fractures and capsulo-ligamentous apparatus of the pelvis, measures aimed at the patient's full physical recovery or impact on persistent residual phenomena (application of a special orthosis for pelvic stabilization, spa treatment) are implemented [55].

CONCLUSION

The possibility of recovery of the musculoskeletal apparatus functions in statics and walking after treatment of unstable pelvic ring injuries in the shortest possible time is a determining factor in the choice of rehabilitation measures. The postoperative period largely determines the final result of the performed treatment, influences the possible consequences and quality of life of the patient. Axial load on the lower extremities and verticalization should be performed immediately after pain relief, while considering the physiological characteristics of the patient's condition and the peculiarities of possible multi-organ injuries. Considering this theoretical study, the issues related to verticalization and axial load on the lower extremities depending on the type of pelvic ring injury have been insufficiently studied and require further research.

Conflict of interest

The authors of this article declare no conflicts of interest.

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EFFECTS OF LOW-DOSAGE RADIOTHERAPY FOR KNEE OSTEOARTHRITIS ON THE INCIDENCE OF KNEE ARTHROPLASTY: RESULTS OF A RANDOMIZED CONTROLLED TRIAL WITH 9-YEAR FOLLOW-UP

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Received: 02.04.2023
Accepted: 13.11.2023
Published: 05.12.2023

ABSTRACT

The aim. *To compare the incidence of knee arthroplasty in patients receiving standard treatment with non-steroidal anti-inflammatory drugs (NSAIDs) in combination with symptomatic slow acting drugs for osteoarthritis (SYSADOA), or combination of NSAIDs and SYSADOA with low-dose radiation therapy (LDRT) in patients with stage 0–2 knee osteoarthritis (OA).*

Materials and methods. *The article presents the results of randomized controlled study of 292 patients with confirmed knee OA according to Altman's criteria (1991) and Kellgren – Lawrence radiographic stages 0–2 who were randomized into two groups. The control group (n = 146) received standard therapy of NSAIDs + SYSADOA. Patients of the study group (n = 146) received combination of standard therapy and LDRT up to a total dose of 4.5 Gy. The cumulative risk of knee arthroplasty was assessed using actuarial analysis and the Kaplan – Meier method. Attributable (AF) and population attributable (PAF) fractions were calculated to assess LDRT preventive potential.*

Results. *The total observation period was 2131.2 person-years. Knee arthroplasty was performed in 4.1 % (n = 6) of patients in the study group against 7.5 % (n = 11) in the control group. The incidence density ratio was 0.60 (95% CI: 0.18–1.88), which corresponds to a risk reduction by 67 %, but the differences were not statistically significant due to the small number of cases (p = 0.340). The AF was 40 % while the PAF was 21 %.*

Conclusions. *The use of LDRT reduces the risk of knee arthroplasty by two-thirds and has the potential to prevent 21 % cases of knee arthroplasty in patients with knee OA. A study on a larger sample is required.*

Key words: *osteoarthritis, knee joint, joint arthroplasty, low-dose radiation therapy*

For citation: Makarova M.V., Valkov M.Yu., Grjibovski A.M. Effects of low-dosage radiotherapy for knee osteoarthritis on the incidence of knee arthroplasty: Results of a randomized controlled trial with 9-year follow-up. *Acta biomedica scientifica*. 2023; 8(5): 100-106. doi: 10.29413/ABS.2023-8.5.10

ВЛИЯНИЕ НИЗКОДОЗНОЙ ЛУЧЕВОЙ ТЕРАПИИ ОСТЕОАРТРИТА КОЛЕННОГО СУСТАВА НА ЧАСТОТУ ЭНДОПРОТЕЗИРОВАНИЯ: РЕЗУЛЬТАТЫ РАНДОМИЗИРОВАННОГО КОНТРОЛИРУЕМОГО ИСПЫТАНИЯ С 9-ЛЕТНИМ НАБЛЮДЕНИЕМ

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Статья поступила: 02.04.2023
Статья принята: 13.11.2023
Статья опубликована: 05.12.2023

РЕЗЮМЕ

Цель исследования. *Сравнить частоту эндопротезирования коленного сустава у больных, получавших стандартное лечение нестероидными противовоспалительными препаратами (НПВП) в комбинации с симптоматическими лекарственными средствами замедленного действия (SYSADOA, symptomatic slow acting drugs for osteoarthritis) либо их сочетание с низкодозной лучевой терапией (НДЛТ), при остеоартрите коленных суставов 0–2-й стадий.*

Материалы и методы. *Представлены отдалённые результаты рандомизированного контролируемого испытания в выборке из 292 пациентов с подтверждённым остеоартритом (ОА) коленных суставов по критериям Altman (1991), рентгенологической стадией 0–2 по Kellgren – Lawrence, случайным образом распределённых в две группы. Контрольная группа (n = 146) получала терапию комбинацией НПВП и SYSADOA. В группе исследования (n = 146) пациенты дополнительно к стандартному лечению получали НДЛТ до суммарной дозы 4,5 Гр. Кумулятивный риск эндопротезирования оценивали с помощью актуарного анализа и метода Каплана – Майера. Для оценки профилактического потенциала НДЛТ рассчитывали предотвратимые доли для выборки (AF, attributable fraction) и для генеральной совокупности (PAF, population attributable fraction).*

Результаты. *Общее время наблюдения составило 2131,2 человеко-лет. 4,1 % (n = 6) пациентам группы исследования проведено эндопротезирование против 7,5 % (n = 11) в контрольной группе. Отношение плотностей инцидентности составило 0,60 (95% ДИ: 0,18–1,88), что соответствует снижению риска на 67 %, но результаты не достигали уровня статистической значимости по причине малого числа эндопротезирований (p = 0,340). Предотвратимая доля эндопротезирований составила 40 % для выборочной совокупности и 21 % для генеральной совокупности пациентов с рентгенологической стадией 0–2.*

Заключение. *Применение НДЛТ снижает риск эндопротезирования на две трети и потенциально способно снизить частоту эндопротезирования на 21 % у больных ОА коленного сустава. Требуется исследование на большей выборке.*

Ключевые слова: *остеоартрит, коленный сустав, эндопротезирование, низкодозная лучевая терапия*

Для цитирования: Макарова М.В., Вальков М.Ю., Гржибовский А.М. Влияние низкодозной лучевой терапии остеоартрита коленного сустава на частоту эндопротезирования: результаты рандомизированного контролируемого испытания с 9-летним наблюдением. *Acta biomedica scientifica*. 2023; 8(5): 100-106. doi: 10.29413/ABS.2023-8.5.10

INTRODUCTION

Osteoarthritis (OA) of the major joints, more commonly affecting those over 40 years of age, is the most common musculoskeletal disease. In 2020, it is estimated that 654 million people worldwide could have knee OA [1]. According to Russian statistics, up to 13 % of the adult population suffer from knee and hip OA [2].

Current OA therapy is primarily aimed at pain relief. Traditionally, non-steroidal anti-inflammatory drugs (NSAIDs) have been prescribed for this purpose [3, 4]. Following the clinical recommendations of the Association of Rheumatologists of Russia, symptomatic slow acting drugs for osteoarthritis (SYSADOA), including tissue repair stimulators (chondroitin sulfate, glucosamine, etc.), as well as bone and cartilage metabolism correctors, can also be used to treat knee OA [4]; in the anatomical-therapeutic-chemical classification they are included along with NSAIDs and anti-rheumatic drugs in "basic therapy" [3]. However, meta-analyses of studies conducted without the support of pharmaceutical companies have not confirmed the benefits of using chondroitin sulfate and glucosamine, so many international professional communities of rheumatologists do not recommend their use [3, 5].

Osteoarthritis often progresses steadily to advanced stages, resulting in a high incidence of disability and referral for surgical treatment. Among all reported cases of permanent disability, 30 % are associated with OA progression [1]. Among them, about 15 % of patients are referred for total knee replacement [6]. Meanwhile, the long-term results of knee arthroplasty cannot be recognized as completely satisfactory. As many as 25 % of patients are dissatisfied with the results of surgery, as several studies have reported. Within two to five years, revision surgeries are performed in 60–80 % of cases [7, 8]. In more than half of all cases of unsatisfactory results caused by endoprosthetics, patients are suffering from pain in the operated joint [9]. The incidence of infectious complications after surgery is 0.2–4.5 % in primary prosthetics and 4.5–12 % in revision (repeat) prosthetics [6, 7].

As a result, a search for more effective techniques for conservative treatment of OA is required. Since the 1970s, low-dose radiation therapy (LDRT) has been used for the OA treatment of various localisations, which is able to provide long-term pain relief [10, 11]. LDRT has been successfully used in Germany and Spain for the therapy of gonarthritis [12, 13]. Russia has a long experience with this approach [14], but further evidence of its efficacy is required for inclusion of this treatment. LDRT has been previously demonstrated in a randomized study that it could prevent the progression of pain syndrome and pathological changes in the joint over a horizon of three years [15, 16]. A long-term preservation of the analgesic effect has the potential to delay the need for surgical treatment.

THE AIM OF THE STUDY

To conduct a comparative analysis of the knee arthroplasty incidence in patients who received low-dose radiation therapy in combination with baseline therapy with non-steroidal anti-inflammatory drugs in combination with symptomatic slow-acting drugs or standard treatment alone, in patients with osteoarthritis of knee joints of stages 0–2 within the framework of an open randomized trial with long-term prospective follow-up.

MATERIAL AND METHODS

Patient characteristics

The details of the patient sample have been described previously [15, 16]; briefly, they can be summarized as follows. The study, conducted from October 2012 to October 2014, included patients with clinically confirmed OA of the knee joints of stage 0–2 according to the criteria of Altman, 1991 [17] Kellgren – Lawrence [18] in combination with or without laboratory and radiological manifestations and baseline pain level of 30 mm or more on the visual analogue scale (VAS).

Treatment regimen

Randomisation using a number generator was used for allocation into groups. In the control group, the patients received basic therapy with selective NSAIDs and combined preparation SYSADOA glucosamine (500 mg) and chondroitin sulphate (400 mg) according to the scheme: 1 capsule 3 times a day for 3 weeks, from the fourth week – 1 capsule 2 times a day for up to 12 weeks. After an 8-week break, a repeat course in the same regimen was administered for 12 weeks. Low-dose orthovoltage X-ray therapy to the affected joint at a dose of 4.5 Gy in 10 sessions every 48 hours was administered to the patients of the study group against the background of standard treatment similar to that in the first group.

A total of 292 patients were included in the analysis, 146 in each treatment group. Patients in the comparison groups were comparable in terms of age-sex composition and baseline disease characteristics. Female patients were 48 % and the mean age was 36–40 years. The mean body mass index was 27 kg/m^2 in both groups, and the duration of pain syndrome before treatment varied from 9.2 to 9.7 months. Radiological stages 0 (symptomatic OA with changes characteristic of OA according to magnetic resonance imaging (MRI) but no changes on radiographs), 1 and 2 were established in 15 (10.3 %), 89 (60.9 %) and 42 (28.8 %) patients of the control group and in 24 (16.4 %), 86 (58.9 %) and 36 (24.7 %) patients of the study group, respectively. No statistically significant differences between the two groups were observed for all the compared indices.

Statistical analysis

The cumulative risk of endoprosthetic replacement was assessed using actuarial analysis and the Kaplan – Meier method. Knee arthroplasty, the data on which were obtained from the Unified State Information System in the sphere of healthcare of the Arkhangelsk region as of December 31, 2021, was considered as an event.

The incidence of endoprosthetic replacement in both groups was calculated per 100 person-years. Relative (AF,

attributable fraction) and population (PAF, population attributable fraction) fractions were calculated to estimate the proportion of endoprosthetic replacements that could have been prevented if all patients had received LDRT in addition to standard treatment in the study and in the general population. Differences in the incidence of outcome between groups were assessed using the Wilcoxon – Jihan test.

The results of the analyses are presented with 95 % confidence intervals (95% CI) as they are more informative than traditional levels of statistical significance [19]. The Stata software package version 17 (Stata Corp., USA) was used for all calculations [20].

The study was approved by the Ethical Committee of the Northern State Medical University (minutes No. 10 dated December 21, 2011), informed consent was obtained from all patients.

RESULTS

The number of patients who underwent knee arthroplasty by radiological stage is summarized in Table 1. The cumulative risk of endoprosthetic replacement for the two groups is summarized in Figure 1.

The incidence of knee arthroplasty was significantly associated with the initial OA stage. In the initial absence of radiological signs of OA, none of the patients required surgery during 9 years of follow-up. Endoprosthesis was performed half as often in more advanced OA stages when LDRT was used. The total time to either endoprosthesis or censoring was 2131.2 person-years. A total of 4.1 % ($n = 6$) of patients in the study group underwent endoprosthetics as compared to 7.5 % ($n = 11$) of patients in the control group. The incident density ratio was 0.60 (95% CI: 0.18–1.88), meaning that the use of the new method has the potential to significantly reduce the time to need for endoprosthesis, but the results did not reach the level of statistical significance as the number of endoprosthetics was not significant ($p = 0.340$).

Calculation of the preventable fractions (AF and PAF) of the studied outcome showed that 40 % of knee arthroplasties could have been prevented in the study sample population if all patients had received the experimen-

TABLE 1

THE TOTAL NUMBER OF JOINT REPLACEMENTS IN PATIENTS WITH KNEE OSTEOARTHRITIS OVER A A 9-YEAR PERIOD

Baseline stage	Control group	Study group
X-ray stage 0, abs. (%)	0/24 (0.0 %)	0/15 (0.0 %)
X-ray stage 1, abs. (%)	2/86 (2.3 %)	1/89 (1.1 %)
X-ray stage 2, abs. (%)	9/36 (25.0 %)	5/42 (11.9 %)

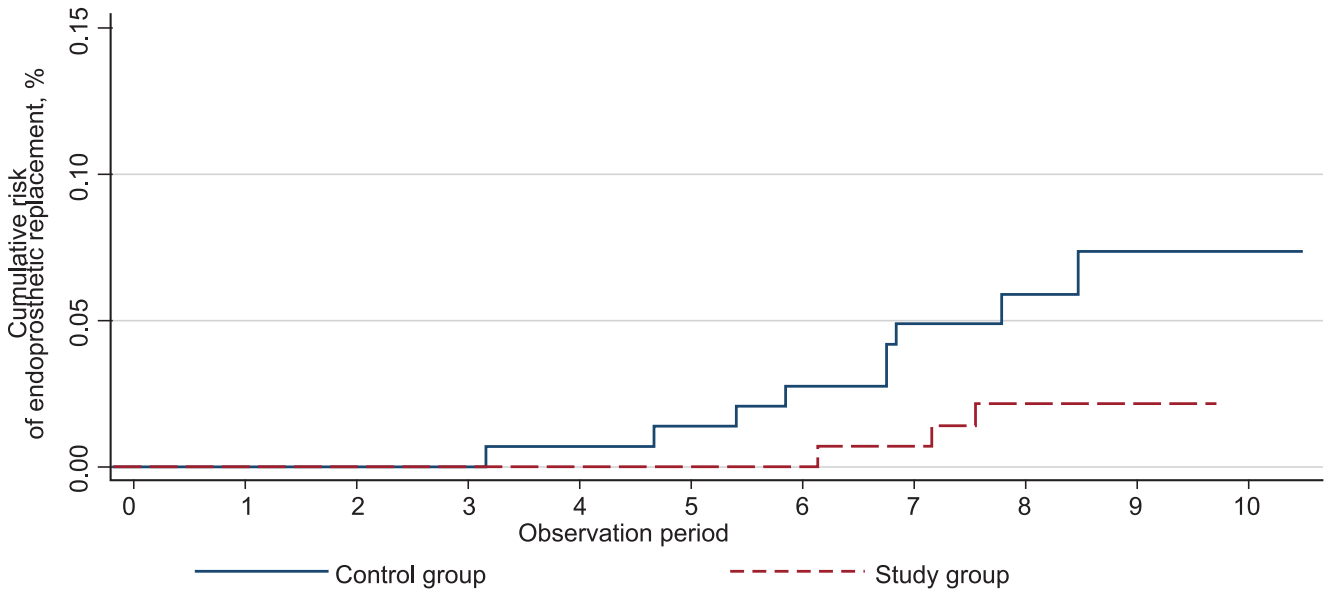

FIG. 1.

Cumulative risk of total knee replacement as affected by treatment of osteoarthritis

tal treatment, while in the general population of patients with knee osteoarthritis with radiological stage 0–2 this proportion would have been 21 %.

DISCUSSION OF RESULTS

The article contains a comparative analysis of the knee arthroplasty frequency in patients in the framework of an open randomized trial depending on the previous treatment of knee OA stages 0–2. The study's inclusion of data from symptomatic knee OA allowed us to follow the results of therapy for the disease when changes are not yet radiologically evident (stage 0). There were no adverse effects of low-dose radiation therapy on the disease course in symptomatic OA, which confirms our results of no endoprosthetic incidence in both the control and study groups. A two-fold reduction in the risk of arthroplasty was observed in patients treated with LDRT compared with the control group, but despite the magnitude of the effect, no differences reached the level of statistical significance for conventional alpha and beta error rates as a result of the small number of outcomes studied.

Low-dose radiation therapy is not a common approach in the treatment of knee OA. A major obstacle in the expansion of its use is the lack of evidence from high quality studies. This is, for example, the conclusion reached by the authors of a recently published systematic review of the literature [12]. They analyzed heterogeneous studies, the earliest of which was dated 1980; a total of 26 studies were included in the analysis. Many of the studies analyzed were retrospective in nature with an observational design, had no control group and / or contained a small number of observations.

Up to date, a very few randomized studies examining the effect of LDRT in knee OA have been published [11, 13, 16]. A positive effect of LDRT was obtained in a study from Germany. In a retrospective analysis, S. Keller et al. evaluated the clinical response to LDRT in 1,037 patients with painful knee OA immediately or within two months after completion of irradiation. Pain reduction after LDRT was observed in 79.3 % (10.5 % complete response, 68.8 % partial response) [21]. O.J. Ott et al. assumed that LDRT is less effective for the treatment of severe pain syndrome in advanced OA with already documented destruction of the bone joint and damage to periarticular soft tissues, which may be resistant to the anti-inflammatory effect of LDRT [22].

By contrast, in a double-blind randomised trial from the Netherlands, the authors observed no reduction in pain among patients in the study group compared with the control group of simulated irradiation (relative risk, 1.09; 95% CI: 0.37–3.19), and no significant synovial changes or reduction in synovitis volume on MRI. One should note that the total number of observations ($n = 55$ in both groups) and the limited follow-up period (3 months) do not allow a definitive conclusion about the efficacy of the approach [11].

Our randomized trial has a high degree of maturity. LDRT for the included knee OA patients was performed 8–10 years ago. It has previously been demonstrated that the addition of orthovoltage radiotherapy to standard conservative treatment leads to a persistent reduction in pain syndrome, improvement of joint function and, in general, quality of life of patients for a horizon of at least three years [15, 23, 24].

The decision to proceed with a joint endoprosthesis is determined not only by the radiological stage, but also, to a greater extent, by the severity of the pain syndrome and the patient's disability with persistent impairment of static and dynamic functions (third and fourth). With an initial more severe radiological stage of OA, the deterioration of statico-dynamic functions in these patients occurs more rapidly [25]. In Europe, the incidence of arthroplasty among patients over 65 years of age was an average of 0.6 per 1,000 population in the 2010s [6, 8]; in Russia, this rate was somewhat lower during the same period, being up to 0.2 per 1,000 adults [2].

This study was the first to analyze data about the incidence of total knee arthroplasty depending mainly on the previous treatment received in a randomized analysis; thus, assessing the impact of a specific therapy on the course of OA. Patient outcomes were followed over a long period of time, which is an important feature of our study. In most other studies, the duration of follow-up is limited to one, maximum three years of follow-up [11, 13] without studying the long-term outcomes of the disease. From this study, it was demonstrated that one in five cases of endoprosthetic replacement could be prevented if all patients in the general population received the experimental treatment.

The comparatively small total number of observations (292 patients in total) and 17 events represent limitations of the study. Considering, however, that the incidence of knee arthroplasty was half as frequent in the study group compared with the control group, a longer follow-up period is required, as well as replication of the study in other studies using larger sample populations.

Other limitations include the fact that there is no mandatory patient registration for OA to date, so there is a risk of patients "dropping out" of the study. However, in the present study, we had access to patients' personal data; they were called personally for appointments and evaluated for long-term treatment outcomes. However, when analyzing larger data sets, such personalization may not be available; this is an important motivation for mandatory registration of OA patients and possibly the creation of an OA registry along the lines of population-based cancer registries [26].

CONCLUSION

The integration of LDRT into OA treatment regimens can not only permanently reduce pain syndrome and improve the quality of life of such patients, but also potentially reduce the risk of knee arthroplasty by two-fold. With few-

er patients requiring endoprosthetics, the financial burden on the health care system is potentially reduced.

Conflict of interest

The authors of this article declare no conflicts of interest.

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THE POSSIBILITY OF A FAVOURABLE OUTCOME AND REVERSIBILITY OF SEVERE ANKLE JOINT DAMAGE ON THE EXAMPLE OF A CLINICAL OBSERVATION

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ABSTRACT

The problem of aseptic talus necrosis consists of the following features: a) manifestation of the disease in the form of acute articular syndrome without typical symptoms; b) inevitable serious consequences in the form of disfiguring deforming arthrosis of the ankle joint, development of gross deformities of the rear foot, etc., resulting in disability. The lack of methods for monitoring the dynamics of the disease also plays an important role. This is particularly so with such an important issue as the substantiation of stopping immobilization and allowing the load on the foot in order to avoid collapsed talus and subsequent complications. It is believed that treatment started before radiographic changes helps to avoid severe complications, but for a number of reasons patients arrive already at the stage of late severe destructive changes. All of the above explains the high relevance of the problem of treatment of patients with aseptic talus necrosis. The importance of the presented clinical case and the value of this information can be considered several points: its example demonstrates the possibility of early diagnosis of severe talus damage cause by aseptic necrosis; based on objective data, a substantiation was made for allowing the load on the leg with body weight in the complex of rehabilitation measures; the possibility of regression of pathological changes associated with aseptic talus necrosis and the dynamics of the course of aseptic talus necrosis with a favorable outcome were demonstrated, which is confirmed by modern research methods. Thus, the need for magnetic resonance imaging has been confirmed for all referred patients with a clinical picture of local articular syndrome in the ankle joint, the possibility of complete regression of avascular necrosis symptoms in case of nonsurgical treatment at the early stages and the possibility of resolving the load on the leg in the complex of rehabilitation treatment have been demonstrated.

Key words: *clinical case, aseptic necrosis, talus, pre-radiological changes, regression of changes, MRI changes in the talus, MSCT changes in the ankle bone*

Received: 11.07.2023
Accepted: 14.11.2023
Published: 05.12.2023

For citation: Skuratova L.K., Gudi S.M., Luchshev M.D., Zhidkov S.K., Prokaev F.V., Pakhomov I.A. The possibility of a favourable outcome and reversibility of severe ankle joint damage on the example of a clinical observation. *Acta biomedica scientifica*. 2023; 8(5): 107-115. doi: 10.29413/ABS.2023-8.5.11

ВОЗМОЖНОСТЬ ХОРОШЕГО ИСХОДА И ОБРАТИМОСТЬ ТЯЖЁЛОГО ПОРАЖЕНИЯ ГОЛЕНОСТОПНОГО СУСТАВА НА ПРИМЕРЕ КЛИНИЧЕСКОГО НАБЛЮДЕНИЯ

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РЕЗЮМЕ

Проблематика асептического некроза таранной кости складывается из следующих особенностей: а) манифестация заболевания в виде острого суставного синдрома без типичных симптомов; б) неизбежные тяжёлые последствия в виде обезображивающего деформирующего артроза голеностопного сустава, развития грубых деформаций заднего отдела стопы и т. д. с исходом в инвалидность. Важную роль играет отсутствие методики контроля за динамикой развития заболевания. Особенно это касается такого важного вопроса, как обоснование прекращения иммобилизации и разрешения нагрузки на стопу во избежание коллапса таранной кости и последующих осложнений. Считается, что лечение, начатое на стадии «дорентгеновских» изменений, позволяет избежать тяжёлых осложнений, но по ряду причин пациенты приходят уже на стадии поздних тяжёлых деструктивных изменений. Всё перечисленное объясняет высокую актуальность темы лечения пациентов с асептическим некрозом таранной кости. Важностью представленного клинического случая и ценностью информации о нём можно считать несколько положений, а именно: на его примере продемонстрирована возможность ранней диагностики тяжёлого поражения таранной кости асептическим некрозом; на основании объективных данных проведено обоснование разрешения возобновления нагрузки на ногу весом тела в комплексе реабилитационных мероприятий у пациента; продемонстрированы возможность регресса патологических изменений, связанных с асептическим некрозом таранной кости, и динамика течения асептического некроза таранной кости с благоприятным исходом, что подтверждено современными методами исследования. Таким образом, подтверждена необходимость проведения магнитно-резонансной томографии всем обратившимся пациентам с клиникой локального суставного синдрома в области голеностопного сустава, продемонстрирована возможность полного регресса симптоматики асептического некроза при консервативном лечении на ранних стадиях и показана возможность разрешения нагрузки на ногу в комплексе реабилитационного лечения.

Ключевые слова: *клинический случай, асептический некроз, таранная кость, «дорентгеновские изменения», регресс изменений, МРТ-изменения таранной кости, МСКТ-изменения таранной кости*

Статья поступила: 11.07.2023
Статья принята: 14.11.2023
Статья опубликована: 05.12.2023

Для цитирования: Скуратова Л.К., Гуди С.М., Лучшев М.Д., Жидков С.К., Прокаев Ф.В., Пахомов И.А. Возможность хорошего исхода и обратимость тяжёлого поражения голеностопного сустава на примере клинического наблюдения. *Acta biomedica scientifica*. 2023; 8(5): 107-115. doi: 10.29413/ABS.2023-8.5.11

JUSTIFICATION FOR THE NEED TO DEMONSTRATE A CLINICAL CASE

Epidemiology

Aseptic necrosis of the ankle bone is known to be caused by fractures in 75 % of cases [1]. The object of study in this article is a patient with secondary ankle bone aseptic necrosis of non-traumatic genesis. No separate code for secondary ankle bone aseptic necrosis exists in the ICD-10 system; therefore, a number of generalized codes have been proposed for coding: M87.0, M87.1, M87.2, M87.3, M87.8, M87.9, M90.3, M90.4, M90.5. According to the international classification, osteonecrosis is included in the group of diseases of class XIII, subgroup M87. Bone osteonecrosis is a high incidence disease and registries are being kept in economically developed countries. Unfortunately, in Russia, aseptic necrosis has not been isolated in the structure of musculoskeletal morbidity in the adult population; accurate data on osteonecrosis of ankle bones are also not available. Meanwhile, there are many publications about the high incidence of the disease with a tendency to an increasing incidence [2, 3].

Diagnostics

The literature suggests that there are no pathognomonic clinical symptoms of ankle bone aseptic necrosis, but it is considered very likely that any patient who comes to the hospital with persistent localized inflammatory syndrome of the ankle joint without an apparent cause will probably have ankle bone aseptic necrosis [4]. X-rays, MSCT (multislice spiral CT scan) and magnetic resonance imaging (MRI) are the main diagnostic methods being used. These methods are used as complementary, allowing to establish a complete picture of the lesion [1]. Examination methods such as bone scintigraphy, densitometry, etc. are recommended for differential diagnosis. However, the aseptic necrosis diagnosis is currently usually late and occurs against the background of already developed complications [5].

Treatment

Treatment of patients with an ankle bone aseptic necrosis at ARCO (Association Research Circulation Osseous) stage 1 or less is offered both nonsurgically and surgically [6]. The basis of nonsurgical treatment is, first of all, unloading of the foot against the background of medication with various groups of drugs (non-steroidal anti-inflammatory drugs, anticoagulants, vasodilators, etc.). The time required for complete revascularisation of the ankle bone is up to 2 years, while the recommended time for unloading the lower extremity is up to 8 months; there is no justification for these terms in the literature, which is unacceptable nowadays, considering the high demands of patients to reduce treatment time, increase its comfort and reduce traumatism [5]. The results of surgical treatment according to ARCO stage 1 aseptic necrosis of the ankle bone by subchondral osteoplasty have been reported in the literature; however, this procedure has been shown to aggravate the course of osteonecrosis [6]. Other treatment methods (necrosis core decompression, corrective joint arthrodesis, mosaic osteochondroplasty, endoprosthetic joint replacement, etc.) are intended for use at later stages and in cases of complications [7–9].

Resume

In summary, the relevance of the presented issues is confirmed by the importance of early diagnosis of aseptic necrosis of the ankle bone, the lack of clear criteria of the disease course dynamics necessary for making tactical decisions, and the lack of treatment effect evidence.

In view of the above, there were a number of tasks to be accomplished at the beginning of the treatment of the patient in the submitted clinical case:

1. To confirm the severity of aseptic necrosis of the ankle bone and assess its stages.
2. As the treatment progresses, to reveal indications for authorising foot loading.
3. To undertake nonsurgical treatment, to evaluate its result, to confirm good clinical effect by the data of objective methods of study.

STUDY MATERIAL

The material for the study was the patient's outpatient card, which reflects his outpatient visits to physicians of different specialties, therapeutic manipulations performed, and the prescription of medicines. In addition, MSCT and MRI images were assessed in dynamics and during the treatment process until the patient recovered.

The study was approved by the local ethical committee of the Novosibirsk Research Institute of Traumatology and Orthopedics n. a. Ya.L. Tsivyan (extract No. 012/23 from the minutes of the meeting No. 005/23 dated May 26, 2023).

Patient information

Patient V., a 51-year-old man, clerical worker, a resident of a million-strong city, visited the clinic of Novosibirsk Research Institute of Traumatology and Orthopedics n. a. Ya.L. Tsivyan for an outpatient appointment. The patient signed consent to participate in the study, according to the World Medical Association Declaration of Helsinki, and to publish the results of the study without identification. The medical history revealed that 4 weeks before the patient encounter, following a COVID-19 infection (and hormone therapy) severe pain and swelling in the ankle area on the left side, and claudication were observed. The patient was visually inspected and examined.

The following methods were used to diagnose and treat the patient.

Clinical method

The presence of pain according to the visual analogue scale (VAS), ankle swelling (with ligature at the level of ankle poles), hyperaemia (visually), temperature difference (with infrared laser thermometer), range of active and passive motions in the ankle joint (with an angle meter) were assessed. The above measurements were performed at the examination day, 1, 2, 3, 4, 6 and 9 months from the onset of the disease.

Radiological method

The patient underwent X-ray of the ankle joint in the straight and lateral projections in the standing position at the time of patient encounter, 6 months after patient encounter, and at the end of treatment.

Tomographic method

The patient underwent MSCT and MRI at the time of patient encounter, as well as 1, 2, 3, 4, 6, 9, 12 months after patient encounter.

Functional method

The result was assessed according to AOFAS (American Orthopaedic Foot & Ankle Society) at the end of treatment, after 12 months.

CASE HISTORY

The disease onset was swelling, redness, fever and sharp pain of the left ankle joint area 4 weeks after COVID-19 infection and massive hormone therapy. Approximately one week after the onset of the disease, the patient encountered to the clinic of foot and ankle surgery of Novosibirsk Research Institute of Traumatology and Orthopedics n. a. Ya.L. Tsivyan. Physical examination revealed a provisional diagnosis of secondary aseptic necrosis of the ankle bone. The diagnosis was confirmed with X-ray, MSCT and MRI studies of the ankle bone being performed (Fig. 1–3).

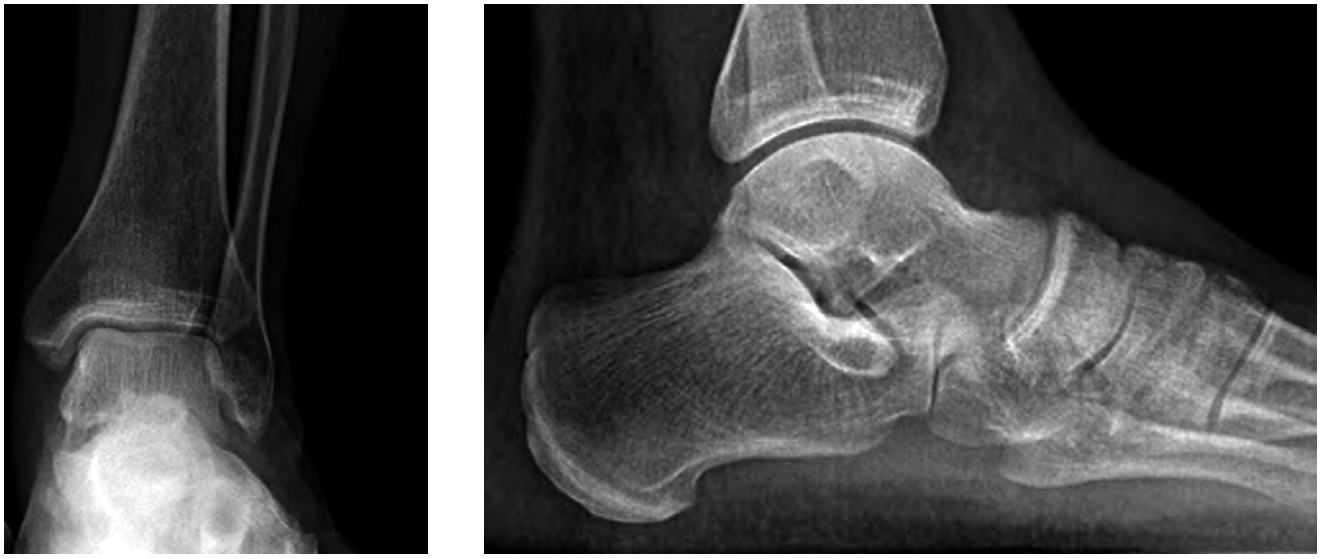

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FIG. 1.

*Patient V. Left ankle joint X-ray in straight (**a**) and lateral (**b**) projections: no pathological changes in the ankle bone were revealed*

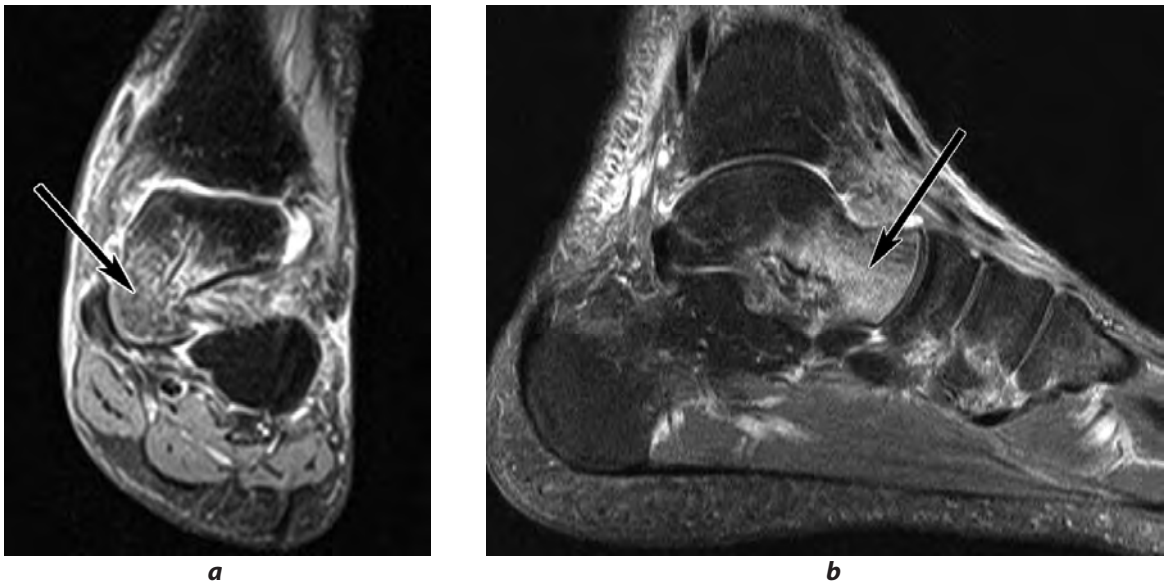

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FIG. 2.

*Patient V. MRI of the patient's ankle joint, coronal (**a**) and sagittal (**b**) scans: severe bone marrow swelling with epicentre in the area of the head of the ankle bone, spreading to the block of the ankle bone (indicated by the white arrow); ankle joint synovitis. Aseptic talus necrosis, the stage of edema*

Examined jointly by a rheumatologist and endocrinologist, diagnosed as secondary aseptic osteonecrosis of the ankle bone at the stage of oedema. After the diagnosis was confirmed, treatment was carried out, which began with puncture of the ankle joint (seeding of synovial fluid – sterile). Complete unloading of the leg with orthosis immobilization. Drug therapy was initiated, including selective cyclooxygenase inhibitors, calcium metabolism regulators, bone resorption inhibitors, and cartilage metabolism regulators. The patient underwent a course of physical therapy, therapeutic exercises under the supervision of a physiotherapist.

In 4 weeks, there was a decrease in pain syndrome by 6 (60 %) VAS points, swelling subsided and the thickness of the tibia in the supra-ankle area decreased from 32 to 28 cm (by 25 %). Control MRI and MSCT examinations of the ankle bone were performed. Despite the clear positive clinical dynamics of the disease, however, the stage studies rather indicated the opposite. Preservation of signal brightness was observed on control MRI (Fig. 4).

Signs of bone resorption appeared on the control MSCT (Fig. 5). The prescribed treatment was continued with special emphasis on foot unloading.

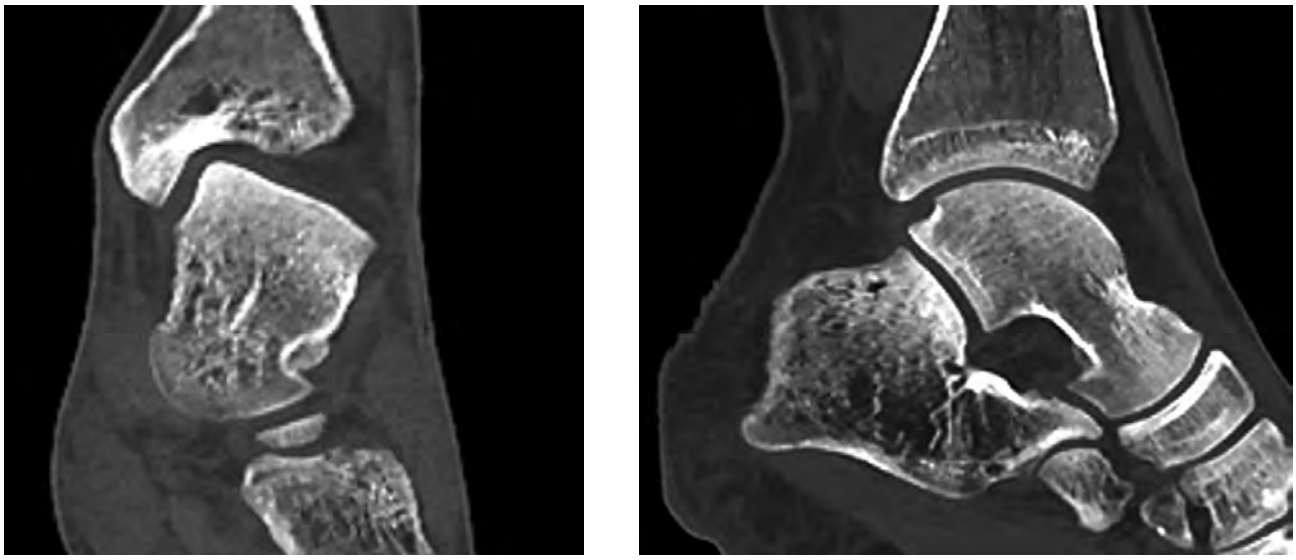

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FIG. 3.

*Patient V. MSCT of the ankle joint, coronal (**a**) and sagittal (**b**) scans: no signs of destruction of the ankle bone are observed*

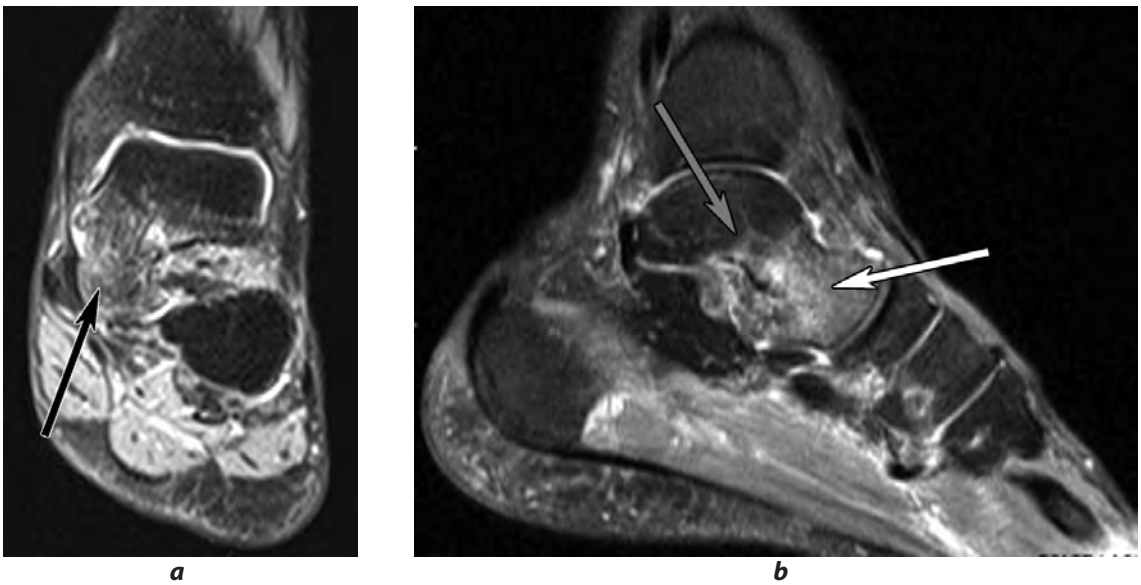

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FIG. 4.

*Patient V. MRI of the ankle joint, coronal (**a**) and sagittal (**b**) scans. Bone marrow oedema (black arrow) persists. A cyst formation in the area of the head of the ankle bone is observed. Bone marrow swelling persists in the area of the head of the ankle bone (white arrow) with spreading to the trochlea of talus; small cysts (grey arrow). Ankle joint synovitis*

The next follow-up examination was performed 4 weeks later. The clinical picture demonstrated complete relief of pain syndrome in the ankle joint. Positive dynamics was observed on control MSCT and MRI. There was a decrease in the brightness of the signal from the bone marrow of the ankle bone, the appearance of a "spotty structure" of the bone substance, which was explained by "focal" suppression of the inflammatory process (Fig. 6).

The patient underwent control MSCT, which revealed signs of not only cyst formation cessation, but also restoration of the ankle bone trabecular structure (Fig. 7). The patient's favourable combination of clinical and imaging findings justified the patient to allow a dosed load on the lower limb with gradual weaning off the means of additional support over a period of 2–3 weeks.

Treatment was extended and was accompanied by positive dynamics of the course of the disease; the patient regained full support of the lower extremity 2.5 months after the treatment onset. Control examinations were continued once a month: positive dynamics was observed in the form of clinical improvement and gradual reduction of MR signal brightness with complete clinical recovery to the degree of asymptomlessness and to the restoration of normal MR signal from the bone substance of the head

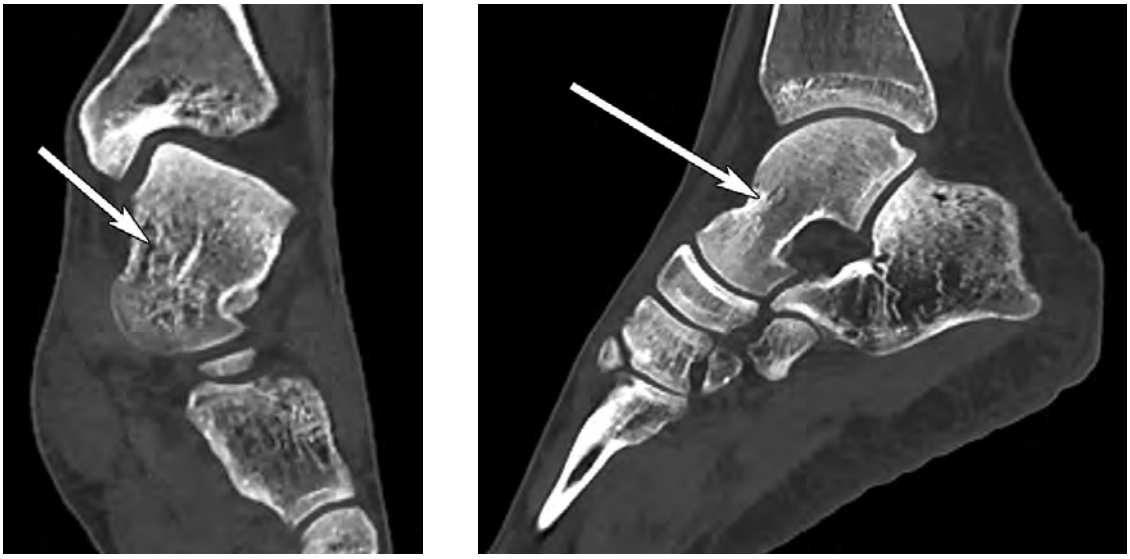

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FIG. 5.

*Patient V. MSCT of the ankle joint, coronal (**a**) and sagittal (**б**) scans. The bony structure of the head and neck of the ankle bone is observed to be disturbed (white arrow). Evidence of small cysts in the head and neck of the ankle bone*

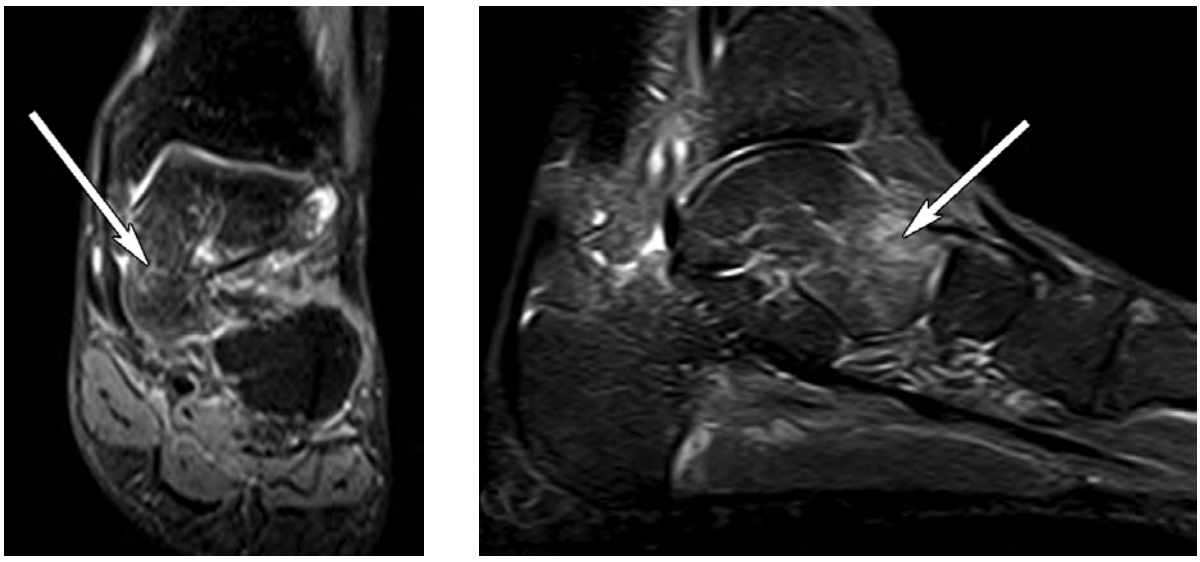

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FIG. 6.

*Patient V. MRI of the ankle joint, coronal (**a**) and sagittal (**b**) scans. A decrease in signal intensity is observed; mosaicism of the image of the head of the ankle bone appears (white arrow). Decreased brightness of the MRI signal in the area of the ankle bone head, appearance of "mosaicism" of the ankle bone head area. A cyst formation in the area of the head of the ankle bone is observed*

of the ankle bone by September 2022, i. e. by the 8th month from the treatment onset (Fig. 8).

Treatment result

The swelling, pain and hyperaemia in the ankle joint had completely resolved by the time the lower extremity was loaded. The range of motion in the ankle joint, reduced by 25 % compared to the healthy one, was fully restored after 12 months (35°/0°/23°). Foot support was restored, the positive dynamics as measured by VAS was 6 points, AOFAS score was 38 points. A good treatment result was obtained. It should be mentioned that the patient was examined 1 year after the treatment: the achieved result was preserved in the form of practically asymptomatic clinical picture, which was confirmed on control MRI and MSCT. The tomographic picture was favourable, had no dynamics compared to controls after 6 months and is therefore not being reported.

DISCUSSION

Numerous studies directly or indirectly suggest that changes in aseptic necrosis of the ankle bone are fatal [8, 9]. It is considered that nonsurgical treatment is indicat-

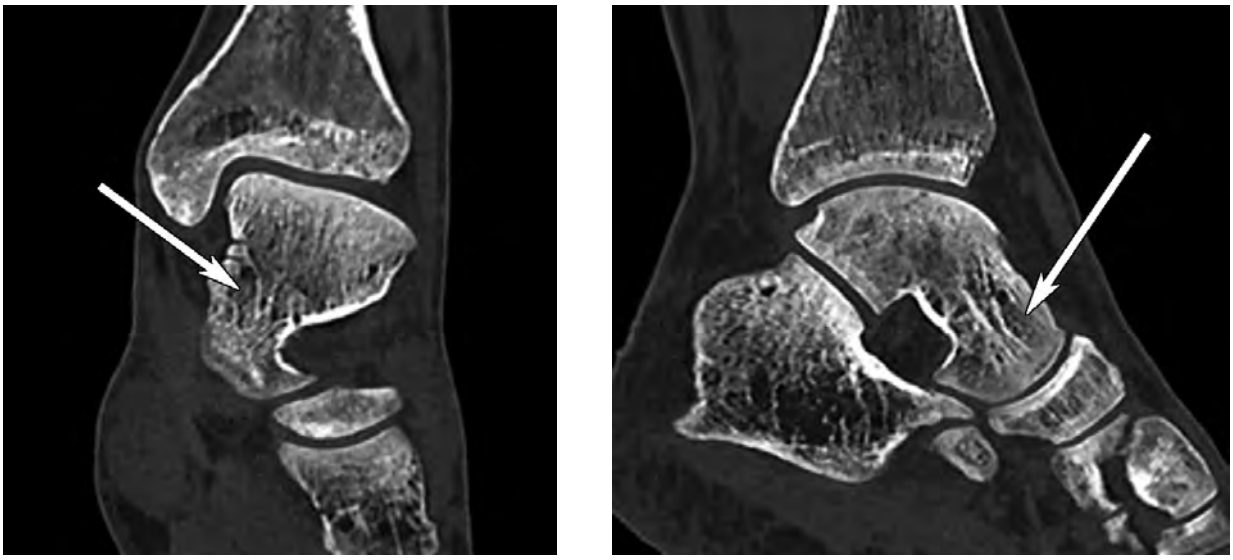

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FIG. 7.

*Patient V. MSCT of the ankle joint, coronal (**a**) and sagittal (**b**) scans. Restoration of the "bar" (beamed) structure of the head and neck of the ankle bone is observed (white arrow). Confirmation of bone structure restoration of the ankle bone head and neck (white arrow) and regression of small cyst formation in the ankle bone head and neck*

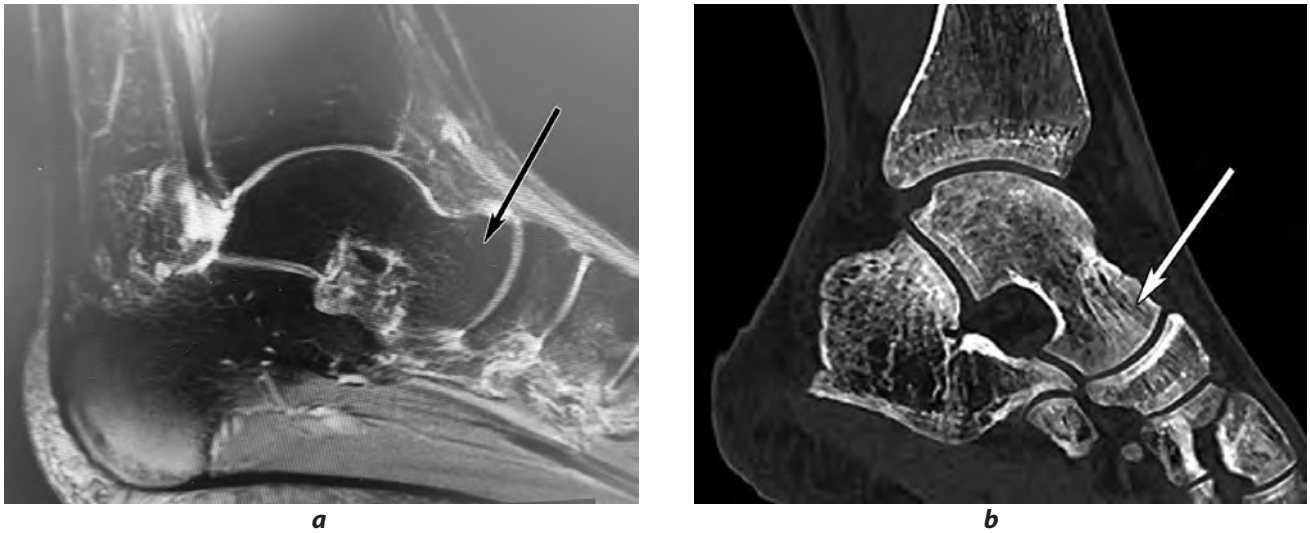

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FIG. 8.

*Patient V. **a** – MRI of the ankle joint, sagittal scan: uniformity of the MRI signal from the ankle bone in the area of the former lesion (black arrow). **b** – MSCT of the ankle joint, sagittal scan: confirmation of the restoration of the bone structure of the head and neck of the ankle bone (white arrow) and regression of the formation of small cysts in the head and neck of the ankle bone, areas of osteosclerosis. Good treatment resultss*

ed in a number of cases, but it is impossible to preserve the anatomy of the ankle bone, and its collapse with severe outcome is inevitable [2, 3]. Presumably this can be considered to be true in some cases, but this example rather supports the idea that early pathogenetic treatment can preserve the anatomical shape of the ankle bone. Early diagnosis and treatment is the key to success, which is important for primary care physicians to be aware of. Considering that aseptic necrosis has no specific clinical picture in the early stages, the classic diagnostic technique of X-ray is not successful for diagnosis; however, X-ray in pain of unclear origin is indicated to exclude findings such as platypodia, mass lesions, ligamentous injuries, cysts, fatigue fractures [4]. A debate comparing multislice computed tomography and magnetic resonance imaging is a controversy in the pages of the printed media. The answer is unequivocal: both examinations are indicated. The closer to the time of disease onset, the more valuable MRI data are the further away – the more valuable MSCT data are due to their purpose [1]. The question of surgical tactics in the early period of osteonecrosis of the ankle bone has not been definitively resolved. From one side, there are many reports about the advantage of the nonsurgical method [1, 4]. No guidance is however provided as to which indicators should be used to decide whether to allow loading of the foot, whether to reduce the process, and so on. [5]. The proposed "subchondral osteoplasty" surgery, developed for the treatment of early-stage osteonecrosis, has not lived up to expectations: there are reports that its use aggravates the course of aseptic necrosis [9]. The described clinical case in our study demonstrates the possibility of early nonsurgical treatment of the patient.

CONCLUSIONS

In summary, the described clinical case provides evidence of the possibility for complete regression of clinical and imaging symptoms; the importance of early diagnosis of aseptic necrosis of the ankle bone is evident. The key success factor in this case was the alertness of the traumatologist, outpatient rheumatologist in terms of early detection of aseptic necrosis. The X-ray method familiar to traumatology and orthopaedics does not demonstrate its positive properties for the diagnosis of aseptic necrosis in the early stages. A team approach involving a rheumatologist, endocrinologist, led by an orthopaedic trauma surgeon was the basis of success in treating the patient. Interruption of acute inflammation in the bone marrow of the ankle bone by complete unloading, immobilization of the affected extremity, prescription of nonsteroidal anti-inflammatory drugs, physiotherapy, metabolic therapy, paraarticular blockades with glucocorticosteroids served as the basic principle of treatment. The clinical case is of particular value in assessing the dynamics of the course of the disease using objective methods and forming actions against this basis. For instance, the beginning of clear reduction of MR-signal intensity on T2 weighted images (T2-VI) and restoration of bone substance in the necrosis zone, confirmed by MSCT and MRI examinations, allowed to start foot loading, and complete restoration of MR-signal on T2-VI as well as restoration of the bone structure of the ankle bone in combination with the clinical picture of no symptoms allowed to consider the patient as recovered.

The following conclusions can therefore be stated:

1. If a patient encounters with unexplained localized joint syndrome of the ankle joint, aseptic necrosis of the ankle bone should be considered and examined, including MRI if there are no changes observed with conventional X-rays.

2. The basis of nonsurgical treatment of a patient with an aseptic necrosis of the ankle bone is immobilisation and unloading of the leg in the conditions of "multidisciplinary approach", dynamic MRI and MSCT control when making a decision about the change of therapeutic methods.

3. If the basic principles outlined in the article are followed, changes in the ankle bone are reversible until complete clinical recovery and radiological symptoms.

Conflict of interest

The authors of this article declare no conflicts of interest.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

CLINICAL CASE OF THE SURGICAL TREATMENT OF COMPLETE RUPTURE OF DISTAL BICEPS TENDON USING TWO CORTICAL BUTTONS

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ABSTRACT

Distal biceps tendon injuries mainly occur in men from the active groups of population. Among the athletes and military personnel, the incidence rate is 2–10 % of the upper limb tendon injuries. Comparative studies have shown the achievement of better functional results in surgical treatment, while maintaining overall complication rate of 4.6–25 %.

The aim. *To demonstrate a new reinsertion technique with two cortical buttons in case of complete rupture of distal biceps tendon as part of a clinical case.*

Materials and methods. *The article presents a clinical case of surgical treatment of a patient with complete rupture of dominant limb distal biceps tendon which was more than 2 weeks old and was accompanied by lacertus fibrosus provocation and persistent muscle retraction.*

Results. *We obtained the following clinical results by the week 24 after the surgery: VAS (Visual Analogue Scale) score – 1 cm, ASES (American Shoulder and Elbow Surgeons) score – 99 points, DASH (Disabilities of the Arm, Shoulder and Hand) score – 15 points. Dynamometry results: Dex. 85; sin. 90 (2daN); range of motion corresponds to the same of a healthy joint. MRI at 1.5 T shows no signs of synostosis or heterotopic ossification; MSCT shows no signs of migration of cortical buttons in comparison with intraoperative X-ray control.*

Discussion. *Extracortical methods of distal biceps tendon positioning in anatomical reinsertion have lower strength indicators, comparable with the use of transosseous sutures and anchor fixators. A larger area of contact of the studied zone in case of minimal tendon compression in the area of proximal radioulnar space or inside the formed radial bone canal provides high strength indicators and reduces the risk of repeated injury.*

Conclusion. *The scores of the scales (VAS, DASH, ASES) turned out to be better than when using other common methods. The technique of dipping distal biceps tendon stump into the formed oval canal of the "anatomical impression" using the proposed method meets the objectives of careful attitude to the tendon and provides the largest area of its contact with the bone.*

Key words: *elbow joint, lacertus fibrosus, distal tendon, biceps, sports medicine, cortical button*

Received: 07.06.2023
Accepted: 26.10.2023
Published: 05.12.2023

For citation: Medvedchikov A.E., Anastasieva E.A., Prokhorenko V.M., Kirilova I.A. Clinical case of the surgical treatment of complete rupture of distal biceps tendon using two cortical buttons. *Acta biomedica scientifica*. 2023; 8(5): 116-124. doi: 10.29413/ABS.2023-8.5.12

КЛИНИЧЕСКИЙ СЛУЧАЙ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ ПОЛНОСЛОЙНОГО ПОВРЕЖДЕНИЯ ДИСТАЛЬНОГО СУХОЖИЛИЯ ДВУГЛАВОЙ МЫШЦЫ ПЛЕЧА С ПРИМЕНЕНИЕМ ДВУХ КОРТИКАЛЬНЫХ ПУГОВИЦ

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РЕЗЮМЕ

Введение. *Повреждения дистального сухожилия двуглавой мышцы плеча (ДСДМП) в основном встречаются у мужчин в активных категориях населения. Среди спортсменов и военнослужащих частота случаев составляет 2–10 % от сухожильных травм верхней конечности. Сравнительные исследования показали достижение лучших функциональных результатов при хирургическом лечении с сохранением общего уровня осложнений 4,6–25 %.*

Цель исследования. *Демонстрация новой техники реинсерции двумя кортикальными пуговицами при полнослойном повреждении дистального сухожилия двуглавой мышцы плеча в рамках клинического случая.*

Материал и методы. *Представлен случай хирургического лечения пациента с полнослойным повреждением ДСДМП на доминантной конечности давностью свыше 2 недель, провокацией lacertus fibrosus и стойкой мышечной ретракцией.*

Результаты. *Клинические результаты к 24-й неделе после операции по шкалам: VAS (Visual Analogue Scale) – 1 см, ASES (American Shoulder and Elbow Surgeons) – 99 баллов и DASH (Disabilities of the Arm, Shoulder and Hand) – 15 баллов. Динамометрия: Dex. 85; Sin. 90 (2daN); амплитуда движений соответствует здоровому суставу. Инструментальная оценка: магнитно-резонансная томография при 1,5 Тл – признаки синостозирования или гетеротопической оссификации не выявлены; мультиспиральная компьютерная томография – миграция кортикальных пуговиц в сравнении с интраоперационным рентген-контролем не выявлена.*

Обсуждение. *Накостные методы позиционирования ДСДМП при анатомической реинсерции имеют меньшие показатели прочности, сравнимые с таковыми при использовани трансоссальных швов и якорных фиксаторов. Бóльшая площадь контакта изучаемой зоны при минимальной компрессии сухожилия в области проксимального радиоульнарного пространства или внутри сформированного канала лучевой кости даёт высокие прочностные показатели и снижение риска повторного повреждения.*

Заключение. *Результаты шкал (VAS, DASH, ASES) оказались лучшими, чем при использовании иных распространённых методик. Методика погружения культи ДСДМП в сформированный овальный канал «анатомического оттиска» предлагаемой техникой отвечает задачам бережного отношения к сухожилию и обеспечивает наибольшую площадь его контакта с костью.*

Ключевые слова: *локтевой сустав, lacertus fibrosus, дистальное сухожилие, бицепс плеча, спортивная медицина, кортикальная пуговица*

Для цитирования: Медведчиков А.Е., Анастасиева Е.А., Прохоренко В.М., Кирилова И.А. Клинический случай хирургического лечения полнослойного повреждения дистального сухожилия двуглавой мышцы плеча с применением двух кортикальных пуговиц. *Acta biomedica scientifica*. 2023; 8(5): 116-124. doi: 10.29413/ABS.2023-8.5.12

Статья поступила: 07.06.2023
Статья принята: 26.10.2023
Статья опубликована: 05.12.2023

INTRODUCTION

Injuries to the distal biceps brachii tendon (DBBT) are mainly found in active males, with an incidence of 1.2–5.4 cases per 100,000 in the general population [1]. Among athletes and military personnel, the incidence ranges from 2–10 % of tendon injuries of the upper extremity [2]. As a consequence of spontaneous eccentric action on the flexed elbow joint – forearm supination – strength and endurance can be reduced by more than 40 %, while constant tension on the degeneratively damaged *lacertus fibrosus* or DBBT stump can lead to persistent pain syndrome [3]. Injuries are more frequent in males (> 95 %) than females (≤ 5 %); the mean age of those addressing is 46.3 years [4]. In sport, nosology affects younger categories at the peak of their career (38.3 years) [5].

The pathogenesis of the focal degenerative processes formation as a result of DBBT hypovascularisation during mechanical impingement accompanying forearm bone rotation continues to be mentioned in the literature as the main cause of damage in the area of the "anatomical impression" on the radial tuberosity. Histopathological findings of the injured area revealed increased proteoglycans, collagen type III, matrix metallopeptidase-1 and matrix metallopeptidase-3, indicating pre-existing tendinopathy [6]. Besides, abuse of anabolic androgenic steroids (androstane and estrene derivatives), corticosteroids, statins (HMG-CoA reductase inhibitors) leads to an increased risk of degenerative processes in the enthesis area [7].

There is an evidence that > 26 % of professional athletes are unable to return to their usual level of exertion after DBBT injury, whereas > 89 % of injured patients from physical labour can recover complex motor patterns in postoperative work [5]. Numerous comparative studies have shown better functional results with surgical treatment of this type of injury (acceleration of strength and endurance indices) compared to a conservative approach.

The emphasis of surgical techniques is now shifting towards minimally invasive anatomical reinsertion, allowing not only the restoration of flexion and supination strength, but also the avoidance of desmogenic contractures. The overall post-treatment complication rate, however, is still in the range of 25 % which is associated with the complex architectonics of the neurovasal structures of the *fossa cubiti* [8]. Heterotopic ossification and synostosis of the proximal radioulnar space (PRUS) are common with the "classic" Dobbie access or the "minimally invasive" Boyd – Anderson access. Systematic reviews also report ≥ 5 % posterior interosseous nerve injuries (PIN), lateral antebrachial cutaneous nerve injuries (LABCN) ≤ 40 % in common surgical approaches [9–11]. The alternative DBBT repair technique of anterior double incision approach (ADIA) has recently gained popularity due to its low postoperative complication rate. Reinsertion methods have also evolved – from transosseous suture to complex variants of "anchor" fixation, which are conceptually divided into the following groups: 1) extramedullary and intracanalicular (by DBBT position); 2) intramedullary and extramedullary (by implant positioning).

According to a series of topographic-anatomical studies by S. Siebenlist et al. the maximum strength values of DBBT fixation in the area of "anatomical impression" under cyclic loads are possible only with anatomical reinsertion of DBBT with a cortical button [12]. A single intramedullary cortical button can withstand forces of 275 ± 44 N at break, two intramedullary buttons 455 ± 103 N, and one extramedullary button 305 ± 27 N (the common Bain method), while anchor type and ligature fixation ("bone tunnels") can withstand 180 ± 20 and 150 ± 20 N, respectively. As a consequence, the strength performance of intracanalicular fixation permits aggressive postoperative rehabilitation protocols and allows for shorter periods of disability. Recurrent DBBT damage incidence remains rare (0.7 %), but the risk increases 7-fold (5.4 %) when a combination of implants (cortical button + interference screw) is used and a greater fixation strength is sought [8, 9].

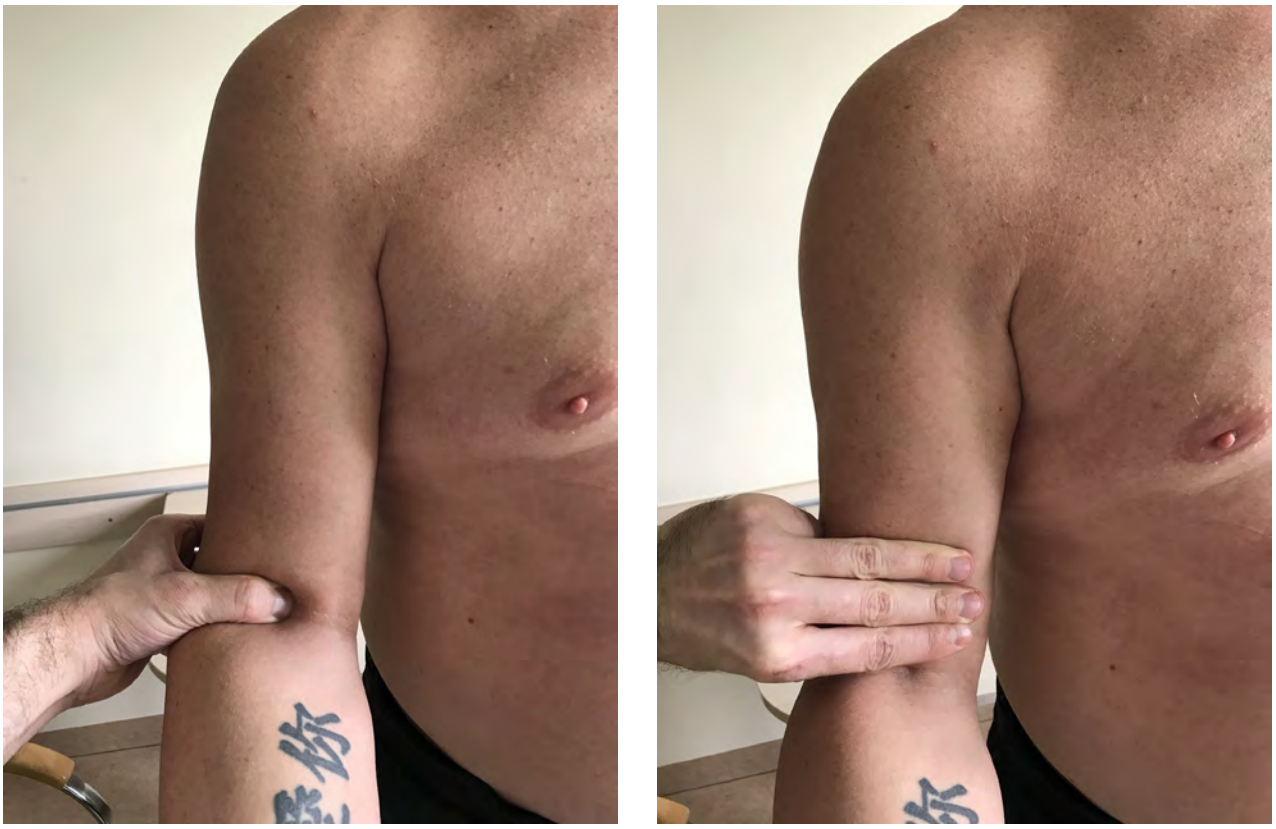
This study is based on an earlier biomechanical study by S. Siebenlist et al. and consists of the fact that extramedullary methods of DBBT reinsertion in the area of the "anatomical impression" have lower strength values comparable to those of transosseous sutures or anchor fixators; therefore, it is still relevant to develop an effective implant combination for the intracanalicular variant.

The **aim** of this clinical case presentation is to demonstrate a new technique of reinsertion with two cortical buttons (hereinafter referred to as RTB) for a full-thickness injury of the distal biceps brachii tendon.

MATERIAL AND METHODS

Patient M., 44 years old, engaged in physical labor, went for an outpatient appointment with an orthopedic traumatologist at the Novosibirsk Research Institute of Traumatology and Orthopedics n. a. Ya.L. Tsivyan on October 16, 2022 with complaints of pain, deformity of the biceps muscle, presence of a spilled hematoma and muscle weakness. Clinical tests: Ruland "+"; O'Driscoll "–"; subcutaneous defect by reverse Popeye type (Fig. 1). Morphometry: flexion /extension 40°/90°; pronation/supination 50°/45°; palpable stump of distal biceps tendon at the level of the tendon-muscular junction. Assessment of force by mechanical dynamometer: Dex. 35; Sin. 90 (2daN). After clinical examination, magnetic resonance imaging (MRI) at 1.5 Tesla of the elbow joint was performed, revealing a full-thickness DBBT lesion.

Additionally, *lacertus fibrosus* provocation and muscle retraction (45 mm), the size of the PRUS (4.8 mm) were visualized (Fig. 2). Orthopedic scales survey: VAS (Visual Analogue Scale) – 5 cm; ASES (American Shoulder and Elbow Surgeons) – 30 points; DASH (Disabilities of the Arm, Shoulder and Hand) – 49 points. Classifications: type 3 according to L. Perera and type 3b according to J. Fuente. Anamnesis morbi: work-related injury; prescription of injury < 3 weeks; right hand, dominant side. A topographic-anatomical study on cadaveric material was performed be-



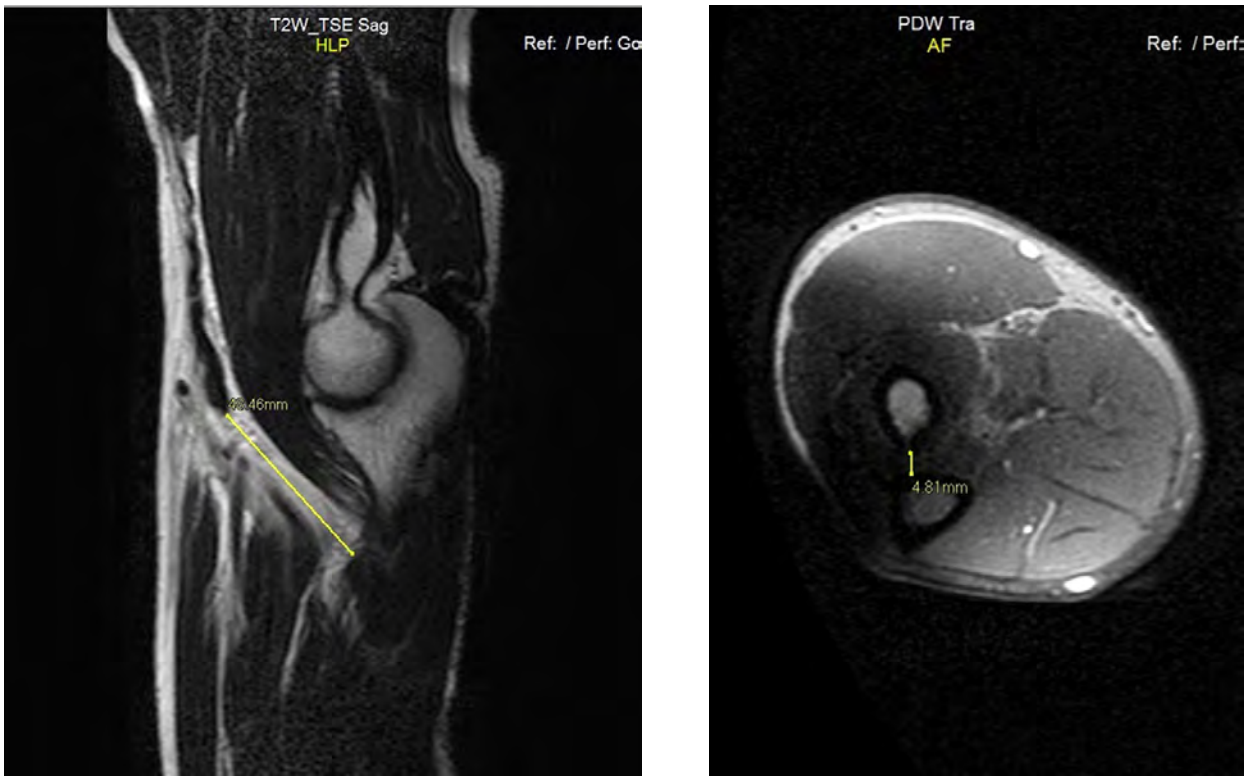
a ***b***

FIG. 1.
*Patient M. Specific O'Driscoll test "–" (**a**) and Ruland test "+" (**b**) in case of complete rupture of distal biceps tendon*

fore surgical treatment in clinical practice in 2022. The obtained results made it possible to perform calculations of the DBBT contact area on the radial tuberosity for different reinsertion methods. With the consent of the ethical committee of February 2023 Novosibirsk Research Institute of Traumatology and Orthopedics n. a. Ya.L. Tsivyan, an article was published and a patent for the invention of surgical technique was received [13, 14]. The patient has signed an informed voluntary consent (IVC) for the medical intervention, as well as an IVC for the release of personal medical information in an anonymized form. RTB treatment was performed on the day of admission on October 24, 2022.

Surgical intervention was performed under combined anaesthesia: regional intercostal anaesthesia (brachial plexus blockade from supraclavicular access with Ropivacaine 0.5 % – 20 ml) combined with intubation anaesthesia.

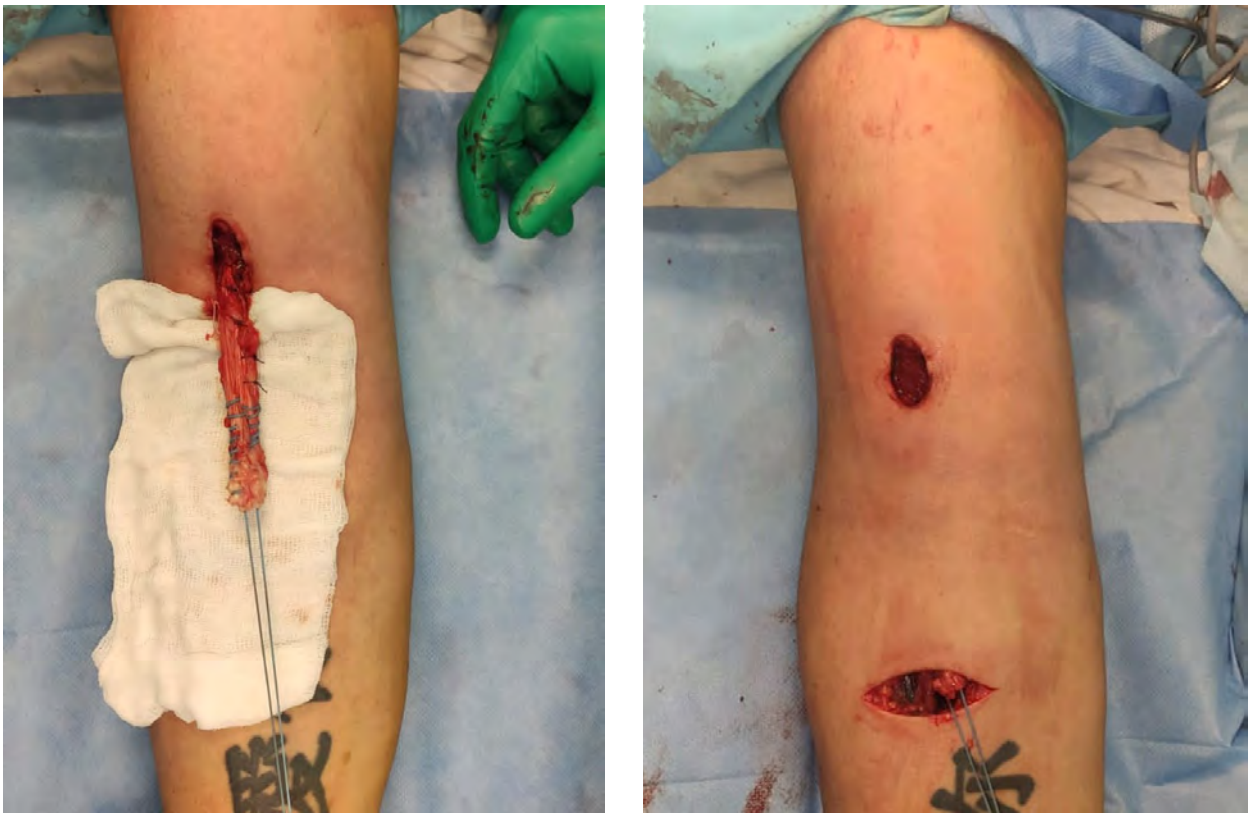
Laying the patient on the orthopaedic table in the supine position with the arm resting 90° at the shoulder joint on an attachment shelf. Strict forearm supination in the elbow extension position was monitored throughout the session. Anatomical landmarks were labelled before using the incision film under the X-ray guidance of an electron optical converter (EOC): DBBT stump, proximal "search" and distal "main" access (ADIA), radial head and *n. radialis* marking. A 3 cm transverse skin incision was made on the palmar surface at the marking site in the projection of the radial tuberosity. In the interval between *M. brachioradialis* and *M. pronator teres*, *N. radialis* was visualized and moved to the lateral side for free skeletonization of the "anatomical impression". A 2 mm Kirschner spoke (hereinafter referred to as a guide spoke) was positioned through the upper edge of the radius tuberosity by means of power equipment. Then, a through channel was drilled using a 4.5 mm bone drill along the guide spoke. Following 2 cm distally, which corresponds to the lower edge of the radius tuberosity, the second guide spoke was inserted in a similar manner with the sequential formation of a 4.5 mm through channel. Keeping the guide spokes in place, the bone drill was changed to 7 ± 2 mm and the palmar cortical layer of the radius was drilled out to form a blind-ended oval hole. Subsequently, a 2 cm longitudinal skin incision was made in the lower third of the upper arm above the area of the retracted DBBT stump. The isolated stump was sutured with nonabsorbable thread (gauge 5 Ti-Cron, braided tape variant) according to the Krackow method for 3–4 cm. A partial lesion of the *lacertus fibrosus* was revealed in the distal parts of the residual limb, which required suturing. The free ends of the nonabsorbable thread were inserted into the first cortical button to form a self-tightening loop. Between the ADIA access "windows", the stump was guided through the myofascial canal formed with the Mikulich clamp to the "anatomical impression" (Fig. 3). A second cortical button was then tak-



a ***b***

FIG. 2.

*Patient M. Patient M. T1-weighted MRI in case of complete rupture of distal biceps tendon in sagittal (**a**) and coronal (**b**) sections, with measurement of the proximal radioulnar space the level of middle third of the tuberosity anatomical impression of the right radial bone and of the muscle retraction degree*



a ***b***

FIG. 3.

*Patient M. Stump suturing with lacertus firbrosus suture (**a**) and passage of the restored complex between the "windows" of anterior double incision approach (ADIA) (**b**)*

en and a free nonabsorbable thread was inserted into it to form a similar self-tightening loop. Through the distal skin incision, a medical instrument (e. g., Mosquito clamp) was used to insert the first cortical button in an upright position through the distal through channel in the cortical layer of the radius; the free ends were left outside.

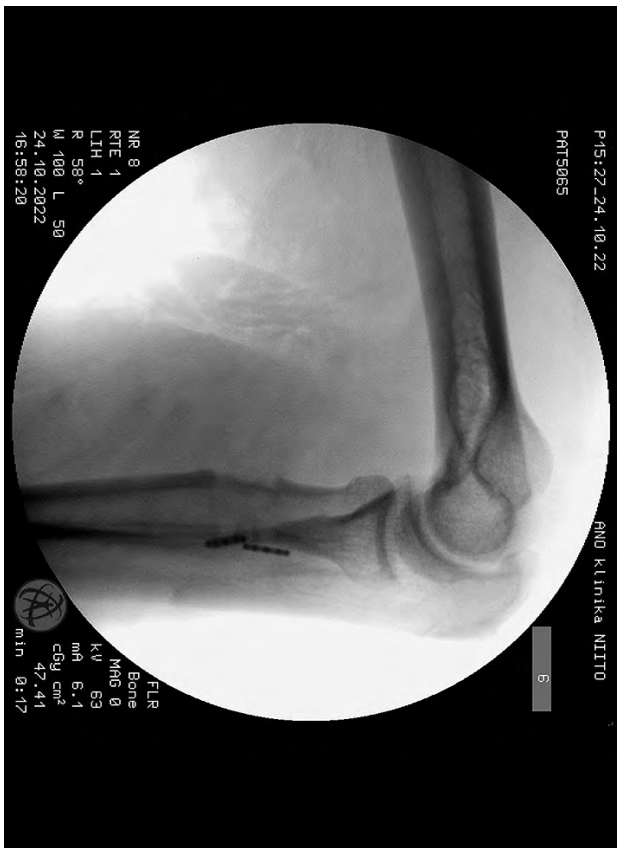
A second cortical button was inserted through the proximal through channel in a similar manner. Both cortical buttons were placed in a horizontal position by the rotation method with mandatory EOC control. The elbow joint of the operated extremity was brought to the 60–90° flexion position, and the DBBT was lowered with self-tightening loops into the formed oval opening of the radial tuberosity. The achieved correction was fixed with 3–4 locking knots. A uniform immersion of the DBBT stump with the repetition of the "anatomical impression", a high degree of fixation strength and a larger area of tendon-bone contact were visually observed compared to the known methods. Surgical wounds were sutured and aseptic dressings were applied. The operated limb was not immobilized. Intraoperative EOC monitoring was supplemented within 1 day by multilayer spiral computed tomography (MSCT) with 3D reconstruction to exclude splitting of the bony "isthmus" between the 4.5 mm technical canals and migration of cortical buttons (Fig. 4).

The patient was discharged under the supervision of an outpatient unit doctor on October 28, 2022, there were no signs of septic complications. The rehabilitation protocol included immobilization with kinesiotape (sequential change of stabilizing and lymphatic drainage variants every 5 days for 4 weeks), cryotherapy, non-steroidal anti-inflammatory drugs *per os*, physical therapy – I period, apparatus mechanotherapy on the Kinetec Centura training appliance (Kinetec, France).

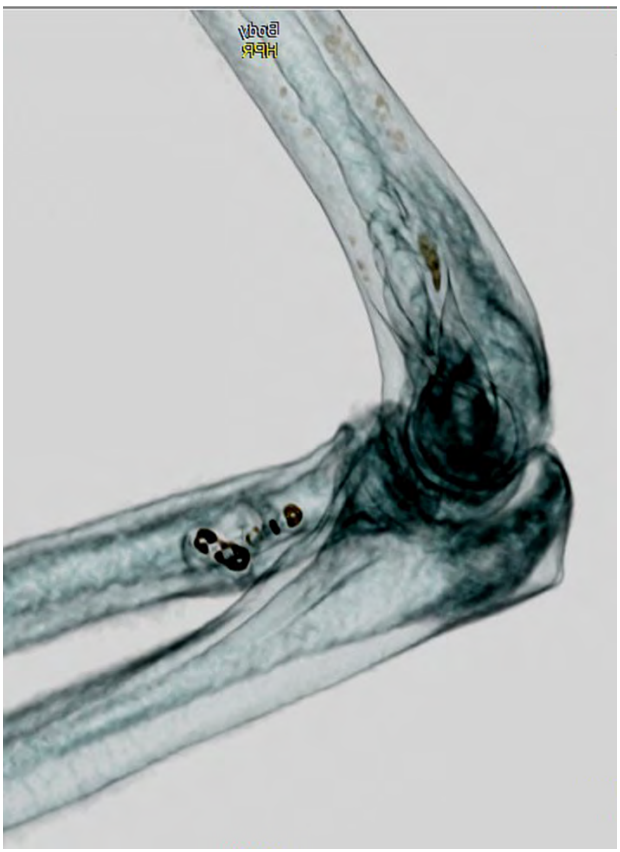
RESULTS

The results of treatment of full-thickness DBBT lesions with RTB technique were analysed using a universal method of personalized assessment by questionnaire with the use of scales (VAS, DASH, ASES), the first of which was conducted on an outpatient basis at the Novosibirsk Research Institute of Traumatology and Orthopedics n. a. Ya.L. Tsivyan after 6 weeks, the second – after 24 weeks. The absence of persistent pain syndrome (VAS < 2 cm), statistically significant difference in comparative dynamometry, Ruland and O'Driscoll tests was considered as a positive result (Fig. 5).

Initial clinical examination: flexion/extension 10°/120°; pronation/supination 80°/70°. Second follow-up exami-



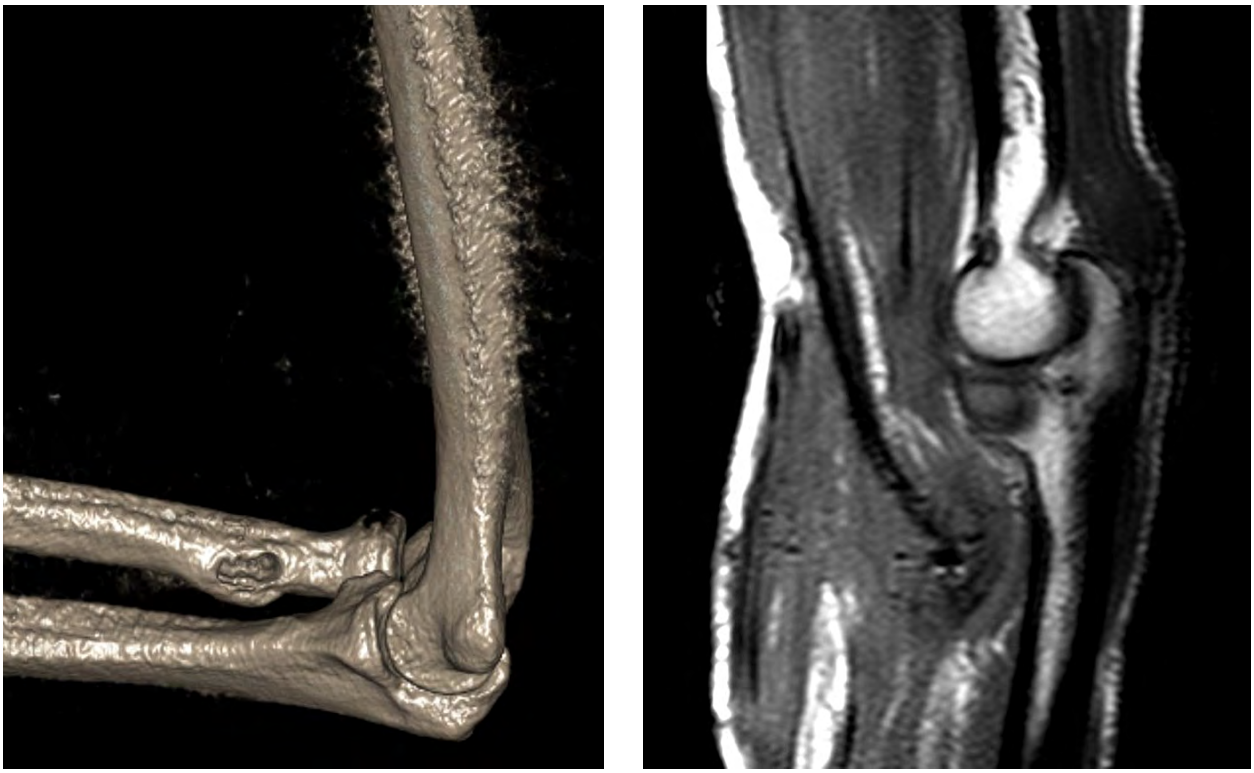
a



b

FIG. 4.

*Patient M. Intraoperative X-ray imaging of the operated elbow joint under the control of the light image converter (**a**) and multispiral computed tomography with 3D visualization of the cortical implants position 6 months after surgery using reinsertion with two cortical buttons (**b**)*



a ***b***

FIG. 5.

*Patient M. Multispiral computed tomography with 3D visualization of the "anatomical impression" (**a**) and MRI visualization of tendon tension (**b**) 6 months after surgical treatment using reinsertion with two cortical buttons*

nation (24 weeks): VAS – 1 cm, ASES – 99 points, DASH – 15 points. Dynamometry: Dex. 85; Sin. 90 (2daN); comparative movement amplitudes correspond to a healthy joint. Postoperative complications were assessed at two postoperative checkpoints. First point – 30 days: heterotopic ossification "–", neuropathy "–", contracture "+", muscle hypotrophy "+". Second point – 90 days: heterotopic ossification "–", neuropathy "–", contracture "–", muscle hypotrophy "–". Instrumental assessment of the results: 1.5 Tesla MRI of the operated joint with visualisation of the tendon course to the "anatomical impression" – absence of inflammatory changes of the *lacertus fibrosus*, previous size of the PRUS (4.8 mm) without signs of synostosis or heterotopic ossification; MSCT with 3D reconstruction – absence of cortical button migration in comparison with intraoperative EOC-control.

The patient returned to domestic activities after 4 weeks and to occupational activities after 6 weeks of the above rehabilitation.

DISCUSSION

Extramedullary methods of DBBT positioning during anatomical reinsertion have lower strength values comparable to the use of transosseous sutures and anchor fixators, even with the intramedullary use of one or two cortical buttons proposed by S. Siebenlist et al. [12, 15]. Comparative measurements of the tendon-bone contact index at the radial tuberosity revealed an advantage of intracanal methods (2.09 ± 0.2 cm^2) over extramedullary methods (0.49 ± 0.2 cm^2) in a recent topographic-anatomical study [14]. The large contact area of the study area with minimal compression of the tendon in the area of the PRUS or inside the formed radial canal ensures that high strength values are achieved and the risk of re-injury is reduced. Similar DBBT fixation methods accompanied by technically complicated *lacertus fibrosus* sutures or additional use of an interference screw are also available from the literature, which have risks of high intracanalicular compression and ischaemia, as well as direct traumatization of the degeneratively changed tendon by the implant blades [16].

A case of successful surgical treatment of a full-thickness DBBT lesion using a new technique with effective use of implants is described in this clinical observation. The technique of immersing the DBBT stump into the formed oval canal of the RTB "anatomical impression" meets the objectives of gentle treatment of the tendon and has the largest area of contact with the bone. No publications about such an experience were found in the foreign and domestic literature.

CONCLUSION

The vast majority of full-thickness DBBT lesions are treated surgically, while the incidence of periopera-

tive complications and re-injury varies widely depending on the specific technique and patient demographics. The choice of cutaneous access and reinsertion method continues to be the question that's been debated a lot in the search for universal solutions. The RTB technique, performed as suggested, is effective in the treatment of the full-thickness variant of the lesion, but a longer time frame and number of observations will reveal the advantages and disadvantages, thus determining its place in clinical practice.

Funding

The work was carried out within the framework of the State Assignment No. 122032200266-8.

Conflict of interest

The authors of this article report the absence of obvious and potential conflict of interests related to the publication of materials.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

ACUTE KIDNEY INJURY AFTER PRIMARY TOTAL HIP REPLACEMENT

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ABSTRACT

Surgical interventions that do not directly affect the urinary system can cause excretory dysfunction of kidneys.

The aim. *To establish the prevalence, risk factors and clinical significance of acute kidney injury after primary hip replacement performed in the clinic of the Irkutsk Scientific Centre of Surgery and Traumatology.*

Materials and methods. *We carried out a retrospective analysis of the case histories of 109 patients who underwent primary total hip replacement under conditions of subarachnoid anesthesia in the clinic of the Irkutsk Scientific Centre of Surgery and Traumatology in 2021.*

Results. *Postoperative changes in serum creatinine in 8 patients of the study group met the KDIGO (The Kidney Disease: Improving Global Outcomes) criteria for acute kidney injury. Initial indicators of renal excretory function in the subgroup with acute kidney injury were not different from those in the entire group.*

Statistically significant correlation was established between acute kidney injury and indicators of oxygen-carrying capacity of blood – initial and minimal postoperative hemoglobin concentration.

Acute kidney injury in patients of the study group had a minimal effect on the clinical course of the early postoperative period. None of the patients required renal replacement therapy, re-transfer from the specialized unit to the intensive care unit or any specific treatment. The duration of postoperative stay of patients with acute kidney injury in the clinic did not increase.

Conclusions. *Acute kidney injury was detected in 7.3 % of patients who underwent primary total hip replacement. Risk factors for the development of postoperative acute kidney injury in patients of the study group included relatively low initial and minimal postoperative blood hemoglobin concentrations, which may indicate prerenal mechanism of acute kidney injury pathogenesis. Implementation of the main steps of the "renal protocol" in patients with initial glomerular filtration rate over 45 ml/min/1.73 m^2 allows avoiding the development of severe clinically significant forms of postoperative acute kidney injury and complications associated with it in the early postoperative period of primary total hip replacement.*

Key words: *acute kidney injury, primary hip replacement, blood hemoglobin concentration*

Received: 05.06.2023
Accepted: 30.10.2023
Published: 05.12.2023

For citation: Lebed M.L., Kirpichenko M.G., Novikova E.V., Lebed T.G., Mankov A.V. Acute kidney injury after primary total hip replacement. *Acta biomedica scientifica*. 2023; 8(5): 125-132. doi: 10.29413/ABS.2023-8.5.13

ОСТРОЕ ПОВРЕЖДЕНИЕ ПОЧЕК ПОСЛЕ ПЕРВИЧНОГО ТОТАЛЬНОГО ЭНДОПРОТЕЗИРОВАНИЯ ТАЗОБЕДРЕННОГО СУСТАВА

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РЕЗЮМЕ

Оперативные вмешательства, напрямую не затрагивающие мочевыделительную систему, могут вызывать нарушение экскреторной функции почек.
Цель исследования. *Установить распространённость, факторы риска и клиническую значимость острого повреждения почек после первичного эндопротезирования тазобедренного сустава у пациентов клиники ФГБНУ «Иркутский научный центр хирургии и травматологии» (ИНЦХТ).*
Материалы и методы. *Ретроспективному анализу подвергнуты истории болезни 109 пациентов, которым в 2021 г. в клинике ИНЦХТ в условиях субарахноидальной анестезии выполнено оперативное вмешательство в объёме первичного тотального эндопротезирования тазобедренного сустава (ТЭТС).*
Результаты исследования. *У 8 пациентов исследуемой группы послеоперационная динамика показателей креатинина в сыворотке крови соответствовала критериям KDIGO (The Kidney Disease: Improving Global Outcomes) острого повреждения почек (ОПП). Исходные показатели экскреторной функции почек в подгруппе ОПП были не хуже, чем во всей группе.*
Статистически значимая корреляция установлена между ОПП и показателями кислородной ёмкости крови – исходной и минимальной послеоперационной концентрацией гемоглобина.
ОПП у пациентов исследуемой группы после первичного ТЭТС оказывало минимальное влияние на клиническое течение раннего послеоперационного периода. Ни одному из пациентов не потребовалось проведение заместительной почечной терапии, повторный перевод из профильного отделения в палату интенсивной терапии и реанимации, специфическое лечение. Продолжительность послеоперационного пребывания пациентов с ОПП в клинике не увеличивалась.
Выводы. *Острое повреждение почек выявлено у 7,3 % пациентов, перенёсших первичное ТЭТС. Факторами риска развития послеоперационного ОПП у пациентов исследуемой группы были относительно низкие показатели исходной и минимальной послеоперационной концентрации гемоглобина крови, что может свидетельствовать в пользу преренального механизма патогенеза ОПП. Реализация основных положений «ренального протокола» у пациентов с исходной скоростью клубочковой фильтрации более 45 мл/мин/1,73 м^2 позволяет избежать развития тяжёлых клинически значимых форм послеоперационного ОПП и связанных с ним осложнений в раннем послеоперационном периоде первичного ТЭТС.*

Ключевые слова: *острое повреждение почек, первичное эндопротезирование тазобедренного сустава, концентрация гемоглобина крови*

Статья поступила: 05.06.2023
Статья принята: 30.10.2023
Статья опубликована: 05.12.2023

Для цитирования: Лебедь М.Л., Кирпиченко М.Г., Новикова Е.В., Лебедь Т.Г., Маньков А.В. Острое повреждение почек после первичного тотального эндопротезирования тазобедренного сустава. *Acta biomedica scientifica*. 2023; 8(5): 125-132. doi: 10.29413/ABS.2023-8.5.13

INTRODUCTION

Surgical interventions that do not directly affect the urinary system can cause excretory dysfunction of kidneys. The clinical and economic aspects of postoperative acute kidney injury (AKI) have been the cause of intense research attention. The relevance of the problem for modern surgery in general and for traumatology and orthopaedics in particular is confirmed by statistical data considering the worsening of formal indicators of the postoperative period – the frequency of postoperative complications, exacerbations of concomitant pathology, the duration of patients' stay in the intensive care unit (ICU) and hospital, re-hospitalisation, hospital mortality, and the cost of treatment [1–4].

"Acute kidney injury" (this term has replaced the previously used term "acute renal failure") refers to a sudden onset of renal dysfunction under the influence of any exo- or endogenous factors, limited in time to 7 days [5]. The absence of a clear AKI cause is not uncommon and indicates a multifactorial pathogenesis [6]. The commonly accepted criteria for AKI include increased serum creatinine concentration and decreased diuresis rate [5].

Literature suggests that even transient AKI has potential long-term consequences ranging from the development of chronic kidney disease (CKD) to increased hospitalization rates, short- and long-term mortality [6, 7].

As the problem is significant and there are no obvious solutions, the need for a specific multidisciplinary approach to prevent AKI in the perioperative period has been recognized [8].

THE AIM OF THE STUDY

To determine the prevalence, risk factors and clinical significance of acute kidney injury after primary hip arthroplasty in patients of the Irkutsk Scientific Centre of Surgery and Traumatology.

MATERIALS AND METHODS

The case histories of 109 patients who underwent surgical intervention for primary total hip replacement (THR) under subarachnoid anaesthesia at the clinic of the Irkutsk Scientific Centre of Surgery and Traumatology in 2021 were retrospectively analysed. Summary results are presented as median (Me), 25th (P_{25}) and 75th (P_{75}) percentiles.

As Table 1 summarizes, the study group was predominantly female; as a rule, patients had a physical status corresponding to ASA (American Society of Anesthesiologists) class 3 and were of elderly age.

TABLE 1

DISTRIBUTION OF PATIENTS BY SEX, AGE AND PHYSICAL STATUS

Indicators		Values
Age, Me (P_{25}; P_{75})		63 (56; 68)
Physical status according to ASA, Me (P_{25}; P_{75})		3 (3; 3)
Sex, *n* (%)	female	62 (57 %)
	male	47 (43 %)

The disease that caused surgical intervention was idiopathic deforming osteoarthritis in the majority of cases (Table 2).

TABLE 2

PATHOLOGY FOR WHICH THE PATIENTS OF THE STUDY GROUP UNDERWENT SURGERY

Pathology	*n* (%)
Idiopathic deforming arthrosis	97 (89 %)
Femoral neck fracture	11 (10.1 %)
Rheumatoid arthritis	1 (0.9 %)

During pre-hospital examination, patients were expectedly diagnosed with concomitant age-related somatic pathology, most often arterial hypertension, chronic gastritis, coronary heart disease (CHD), and diabetes mellitus (Table 3). Number of nosologies of comorbidities per patient is 2 (1; 3).

TABLE 3

CONCOMITANT SOMATIC PATHOLOGY IN PATIENTS OF THE STUDY GROUP

Concomitant somatic pathology	Prevalence, *n* (%)
Arterial hypertension	81 (74.3 %)
Chronic gastritis	69 (63.3 %)
CHD	17 (15.6 %)
Diabetes mellitus	15 (13.8 %)
Chronic cholecystitis	8 (7.3 %)
LEVVD	4 (3.7 %)
Chronic pyelonephritis	1 (0.9 %)

Note: LEVVD – lower extremity varicose vein disease.

Using baseline and postoperative serum creatinine concentration values, glomerular filtration rate (GFR) was measured using the CKD-EPI formula as the most correct calculation method according to the KDIGO (The Kidney Disease: Improving Global Outcomes) recommendations [9].

Blood haemoglobin concentration was recorded: preoperatively and minimally during postoperative hospital follow-up. Tranexamic acid infusion of 15 mg/kg 10–20 min before the surgical procedure was administered for haemostatic purposes in case of absence of contraindications (5 patients had such contraindications). External perioperative blood loss (visually intraoperative haemorrhage in the aspirator plus postoperative drainage discharge) was considered. Peri-operative estimated blood loss was determined by the decrease in blood haemoglobin concentration [10].

Spearman's rank correlation method was used to establish a connection between the phenomena. The Wilcoxon test was used to assess the statistical significance of the differences between the indicators at different stages of the study; in case of multiple comparisons, the Bonferroni correction was used.

Statistical processing was performed using Statistica 10 software package (StatSoft Inc., USA).

The study was performed within the framework of the research work "Systemic approach in the development of personalized methods of diagnosis and treatment of patients with injuries and diseases of the musculoskeletal system" (state registration number 122022200210-2; approved by the Ethical Committee of the Irkutsk Scientific Centre of Surgery and Traumatology, Minutes No. 9 dated December 16, 2021), meets the ethical standards of the World Medical Association Declaration of Helsinki "Ethical Principles for Conducting Scientific Medical Research Involving Human Subjects" as amended in 2000 and the "Rules of Clinical Practice in the Russian Federation" approved by Order of the Ministry of Health of Russia No. 266 dated June 19, 2003.

STUDY RESULTS

Notwithstanding the fact that the diagnosis of renal pathology was preliminarily confirmed in only 1 patient, an initial decrease (from slight to moderate) in renal excretory function was revealed in the majority of patients in the study group (Table 4). If CKD levels above C3a or equivalently GFR < 45 ml/min/1.73 m^2 were detected at the outpatient preoperative stage, patients were referred for a consultation with a nephrologist to prescribe specific therapy.

Considered in a single array the data of the patients of the studied group are the evidence of at least preser-

TABLE 4

STRATIFICATION BY BASELINE GLOMERULAR FILTRATION RATE ACCORDING TO CHRONIC KIDNEY DISEASE CLASSIFICATION [11]

Stages of CKD	Global kidney function characteristics	GFR level, ml/min/1.73 m^2	Number of patients, *n* (%)
Norm or C1	High or optimal	> 90	34 (31.2 %)
C2	Slightly reduced	60–89	59 (54.1 %)
C3a	Moderately reduced	45–59	16 (14.7 %)
C3b	Significantly reduced	30–44	–
C4	Sharply reduced	15–29	–
C5	End-stage renal disease (ESRD)	< 15	–

TABLE 5

POSTOPERATIVE DYNAMICS OF GLOMERULAR FILTRATION RATE AND SERUM CREATININE CONCENTRATION

Follow-up period	GFR, ml/min/1.73 m^2		Creatinine, μmol/l	
	entire group	AKI sub-group	entire group	AKI sub-group
At baseline	80.8 (67.2; 91.0)	87.7 (77.1; 98.3)	79.0 (70.0; 90.0)	72.5 (50.1; 79.5)
Day 1	82.3 (67.4; 93.4) *p* > 0.05	**59.4 (56.9; 66.3)** ***p* = 0.027**	80.0 (66.0; 93.5) *p* > 0.05	**102.5 (85.8; 117)** ***p* = 0.028**
Day 5	**83.7 (69.4; 94.2)** ***p* = 0.014**	77.8 (56.9; 90.4) *p* > 0.05	**75.0 (64.0; 89.0)** ***p* = 0.039**	81.0 (63.8; 99.8) *p* > 0.05

vation of excretory renal function in the postoperative period and even of its statistically significant improvement by the day 5 of observation (Table 5).

Perioperative blood loss expectedly led to the development of mild anemia: hemoglobin concentration decreased from the initial 134 (125; 143) g/L to 116 (107; 124) g/L on the day 1 and to 112 (102; 119) g/L on the day 5 of follow-up.

The estimated (according to the decrease in haemoglobin concentration) perioperative blood loss in the study group was 989 (809; 1350) mL or 18 % (16 %; 23 %) of the circulating blood volume (CBV). In the meantime, external perioperative blood loss was much lower, 200 (100; 320) mL or 4 % (2 %; 6 %) of the CBV; the clinical value of this indicator in most cases is very low [10]. Erythrocyte suspension transfusion was performed intraoperatively in 1 (0.9 %) patient and in another 2 (1.8 %) patients postoperatively.

In other words, in general, the system of perioperative anaesthesia support in total hip replacement works effectively.

In 8 (7.3 %) patients of the study group, however, the postoperative dynamics of serum creatinine values met the KDIGO criteria for acute kidney injury (Table 5). A statistically significant increase in creatinine concentration and corresponding decrease in GFR were observed in all of these patients on the first day after surgery, with subsequent recovery on the day 5 of follow-up.

Of particular note is the fact that baseline renal excretory function in the AKI subgroup was at least as good as in the whole group (not statistically significant).

To determine the influence of possible risk factors in postoperative AKI development, a correlation analysis was performed (Table 6).

No statistically significant relationships were found between postoperative AKI on the one hand and age, sex, and calculated blood loss on the other.

Statistically significant correlation was established between the fact of postoperative AKI development and blood oxygen capacity indices – initial and minimal postoperative haemoglobin concentration.

In the AKI subgroup, the estimated blood loss was 1098 (949; 1217) mL or 21 % (19 %; 24 %) of the CBV. The minimum postoperative hemoglobin values were not critical and amounted to 99 (95; 105) g/L. Of significance, no transfusion was performed on any of the patients in the AKI subgroup. No AKI and oliguria were observed in patients of the subgroup on the day 1 after surgery; diuresis on the background of perioperative infusion was 1600 (1600; 2700) mL.

Bone cement containing gentamicin was used for implant fixation in 41 (37.6 %) patients of the study group. In the AKI subgroup, cemented endoprosthetic components were implanted in 3 (37.5 %) of 8 patients. In summary, the results of this study do not provide a reasonable conclusion about the possible effect of potentially nephrotoxic components of bone cement on the development of postoperative AKI.

AKI in patients of the study group after primary THR had minimal effect on the clinical course of the early postoperative period. None of the patients required renal replacement therapy, repeated transfer from the specialized department to the intensive care and intensive care unit, or specific treatment. The correction of postoperative therapy consisted in the cancellation of drugs with nephrotoxic effect (most often non-narcotic analgesics were prescribed instead of non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief). The duration of postoperative stay of AKI patients in the clinic did not increase.

DISCUSSION

Significant advances in surgical and anaesthetic technology have made replacement arthroplasty the treatment of choice, statistically significantly improving the quality of life of patients with a wide range of diseases and injuries of major joints of the lower extremity. The large array of total replacement arthroplasty surgeries of major joints of the lower extremity, as well as the global trend towards further increase in their number, provide an opportunity to reveal the patterns of influence of stereotypical trauma of the musculoskeletal system, which in essence is surgical intervention, on the life support systems of the organism. In contrast to unintentional injury, dur-

TABLE 6
THE RESULTS OF CORRELATION ANALYSIS

Risk factors	Correlation with AKI	*p*
Age	0.13	> 0.050
Sex	–0.03	> 0.050
Estimated blood loss, % CBV	0.12	> 0.050
Baseline blood hemoglobin	**–0.19**	**< 0.050**
Minimum postoperative blood hemoglobin	**–0.22**	**< 0.050**

ing surgical intervention the injury is inflicted under conditions of anaesthesia and blood loss compensation, which together avoid traumatic shock. The effects of musculoskeletal trauma on the body, however, are more complex, more multifaceted, and far from being limited to local destruction, nociceptive afferentation, and decreased circulating blood volume.

The risk of acute kidney injury is one of the non-obvious consequences of trauma and orthopaedic surgeries that affect the course of the postoperative period.

Literature data concerning AKI after orthopaedic interventions are extremely inconsistent [12].

First of all, the authors use at least three modern AKI criteria systems: RIFLE (Risk, Injury, Failure, Loss of kidney function, End-stage kidney disease) [13], AKIN (Acute Kidney Injury Network) [14] and KDIGO [9]. Comparing data from a small sample of a single-centre study with the results of a synthesis of data from regional and national registers is also a challenging task [12]. In addition, the database used may only cover patients with severe AKI, creating the illusion of low morbidity and high mortality [15]. KDIGO criteria were used in this study according to the current domestic guidelines [5].

The reported incidence of AKI after replacement arthroplasty of lower extremity joints varies from 0.16 to 19.9 % [12, 15, 16]. Meanwhile, studies using KDIGO criteria demonstrate serum creatinine dynamics corresponding to AKI closer to the upper limit of this interval – in 10–19.9 % of patients [12, 16]. Small single-centre studies tend to report higher AKI rates [12, 16]. Obviously, the true incidence of AKI according to KDIGO criteria in patients undergoing primary total major joint replacement arthroplasty of the lower extremity may be approximately 10 % [12].

According to the researchers, the risk factors for AKI after replacement arthroplasty of large joints of the lower extremity are: male gender; elderly age; obesity; low baseline hematocrit, blood haemoglobin and plasma albumin; concomitant diabetes mellitus, arterial hypertension, congestive heart failure, chronic obstructive pulmonary disease, liver pathology; auscultated preoperative heart murmurs; high ASA risk; use of renin-angiotensin system inhibitors; long duration of surgery; one-stage bilateral intervention; significant and prolonged postoperative decrease in blood haemoglobin level; perioperative blood transfusion; use of nephrotoxic drugs – vancomycin and gentamicin – for antibiotic prophylaxis [4, 12, 15–24].

There is evidence from a number of studies that a predictor of AKI after replacement arthroplasty of lower extremity joints is initially diagnosed CKD, most commonly defined as a decrease in calculated GFR rate less than 60 ml/min/1.73 m^2 [1, 16, 17, 19, 20, 23, 25, 26]. The incidence of postoperative AKI is increased 2.3–3.7-fold with initial CKD [17, 25, 26]. Even if the diagnosis of CKD is not definitively confirmed, a lower preoperative estimated GFR rate is associated with an increased risk of postoperative AKI [15]. Statistically, preoperative GFR rates of less than 60 mL/min/1.73 m^2 are accompanied by a 5- to 6-fold increase in the incidence of AKI [27].

GFR rate is used to stratify changes in renal function. Direct measurement of this indicator in clinical practice has been replaced by a calculated method for reasons of practicality, since direct measurement is time-consuming and expensive [15].

An apparently technically simple process of identifying patients with an initially reduced GFR rate is unexpectedly challenging in itself. The defined proportion of patients with baseline GFR rate reduction may differ significantly – by 7–8 times – which is depending on the formula used to calculate GFR rate [15]. This leads to significant discrepancies in the assessment of renal function, both at baseline and during postoperative follow-up, and thus to non-comparability of conclusions.

Modern domestic recommendations suggest calculating GFR rate using the CKD-EPI formula [5]. However, literature sources refer to GFR rate calculated according to the Mayo formula as a more accurate predictor of postoperative AKI [15].

This complexity and multifactorial nature of the pathogenesis of postoperative AKI predetermine the importance of the technologies used in the treatment process, which in turn may differ significantly from one medical centre to another. A consequence of this is the additional discrepancy in the reported incidence of postoperative AKI and the value of each orthopaedic clinic's experience.

More specifically, the introduction of technologies to optimize postoperative rehabilitation may have an impact on the incidence of postoperative AKI [3]. ERAS (Enhanced Recovery After Surgery) protocols are intended to minimize postoperative infusion, which may be associated with the development of AKI, especially since similar concerns have been raised in other surgical procedures [3, 28]. The undoubted achievements of ERAS associated with early patient mobilization and shorter hospital stays are coupled with reports of an increasing proportion of patients with abnormally low GFR rates postoperatively as new rehabilitation protocols are implemented [3, 29].

Generally, AKI is mainly likely to develop by a prerenal mechanism secondary to hypovolaemia as a result of renal ischaemia [3, 27]. Renal mechanisms, which may be mediated by direct damaging effects, also cannot be excluded [3].

The clinical significance of postoperative AKI has been the impetus for optimizing the perioperative management of patients in total joint replacement arthroplasty of the lower extremity.

The early detection of decreased renal excretory function has the potential to stratify the risks of complications before surgery and to modify the postoperative treatment programme [15].

The proposed perioperative "renal protocol" provides preoperative detection of CKD (GFR < 60 ml/min/1.73 m^2), as well as risk factors from comorbidities, correction of preoperative anaemia, restriction up to complete withdrawal of nephrotoxic drugs (NSAIDs, antibiotics, hypotensive drugs and diuretics), minimization of blood loss, control

of systemic hemodynamics and hydrobalance, postoperative GFR rate control [12, 30]. Implementation of the "renal protocol" serves to reduce the incidence of postoperative AKI and improve clinical and economic outcomes of treatment [30].

Referring to our own experience, the "renal protocol" for primary THR at the Irkutsk Scientific Centre of Surgery and Traumatology clinic includes:

- pre-hospital identification of patients with CKD, consultation with a nephrologist if CKD level is above C3a (GFR rate < 45 ml/min/1.73 m^2), treatment of concomitant pathology, restriction of nephrotoxic drugs (primarily NSAIDs);
- anaemia diagnosis and correction at the outpatient preoperative stage;
- perioperative hemodynamic control, minimization of hemorrhagia, timely effective replenishment of blood loss;
- use of subarachnoid anaesthesia with preserved consciousness, which leads to enteral replenishment of physiological fluid requirements immediately after the end of surgery and when the patient is admitted to the postoperative observation room;
- the cancellation of nephrotoxic drugs at the diagnosis of postoperative AKI.

Being clearly aware of the limitations in using the results of the present study (relatively small sample in one medical centre), we nevertheless consider it possible to formulate statements summarising our long-term experience (649 primary THR surgeries performed at the Irkutsk Scientific Centre of Surgery and Traumatology clinic in 2021 only).

CONCLUSIONS

Acute kidney injury was detected in 7.3 % of patients undergoing primary total hip replacement arthroplasty. Risk factors for the development of postoperative acute kidney injury in patients of the study group included relatively low baseline and minimal postoperative blood hemoglobin concentrations, which may indicate prerenal mechanism of acute kidney injury pathogenesis. Implementation of the main provisions of the "renal protocol" in patients with initial GFR rate more than 45 ml/min/1.73 m^2 allows to avoid the development of severe clinically significant forms of postoperative AKI and related complications in the early postoperative period of primary THR.

Funding

The study was not sponsored.

Conflict of interest

The authors of this article declare the absence of a conflict of interest.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

ASSESSMENT OF THE EFFECTIVENESS OF SURGICAL TREATMENT OF PATIENTS WITH MASSIVE TEARS OF THE ROTATOR CUFF TENDONS USING ARTHROSCOPICALLY ASSISTED TRANSPOSITION OF THE LATISSIMUS DORSI TENDON

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ABSTRACT

Rotator cuff tears are one of the most common musculoskeletal injuries and account for about 20 %. Massive rotator cuff tears account for up to 40 % of all tears. There is no single approach in the treatment of patients with massive rotator cuff tears. We have developed a new method of surgical treatment of these patients – arthroscopically assisted transposition of the latissimus dorsi tendon using 1/2 of the tendon of the long peroneal muscle.

The aim of the study. *To assess the effectiveness of surgical treatment of patients with massive rotator cuff tears who had arthroscopically assisted transposition of the latissimus dorsi tendon using an autograft of a 1/2 of the tendon of the long peroneal muscle.*

Materials and methods. *The study included 15 patients with Patte stage III and Thomazeau grade 2–3 massive rotator cuff tears, who had arthroscopically assisted transposition of the latissimus dorsi tendon using 1/2 of the tendon of the long peroneal muscle.*

Results. *The article presents the long-term results of surgical treatment of patients using the developed method. The following criteria were evaluated: average age; time since injury; duration of surgery. Functional outcome was assessed using the ASES (American Shoulder and Elbow Surgeons) scale. Taking into account the indicators on the ASES functional scale 1 year after surgical treatment, the following results were obtained: excellent – in 14 (93.3 %) patients, satisfactory – in 1 (6.7 %) patient.*

Conclusion. *The developed method allows us to restore the function of the shoulder joint as early as it possible, to reduce the severity of the pain syndrome and to improve the quality of life of patients.*

Key words: *transposition of the latissimus dorsi tendon, massive ruptures of the rotator cuff, tendon of the long peroneal muscle*

Received: 05.05.2023
Accessed: 05.10.2023
Published: 05.12.2023

For citation: Menshova D.V., Ponomarenko N.S., Kuklin I.A., Tishkov N.V., Puseva M.E. Assessment of the effectiveness of surgical treatment of patients with massive tears of the rotator cuff tendons using arthroscopically assisted transposition of the latissimus dorsi tendon. *Acta biomedica scientifica*. 2023; 8(5): 133-143. doi: 10.29413/ABS.2023-8.5.14

ОЦЕНКА ЭФФЕКТИВНОСТИ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ ПАЦИЕНТОВ С МАССИВНЫМИ РАЗРЫВАМИ СУХОЖИЛИЙ ВРАЩАТЕЛЬНОЙ МАНЖЕТЫ ПЛЕЧА С ИСПОЛЬЗОВАНИЕМ АРТРОСКОПИЧЕСКИ-АССИСТИРОВАННОЙ ТРАНСПОЗИЦИИ СУХОЖИЛИЯ ШИРОЧАЙШЕЙ МЫШЦЫ СПИНЫ

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РЕЗЮМЕ

Разрывы вращательной манжеты плеча входят в число наиболее распространённых травм опорно-двигательного аппарата: их частота составляет около 20 %. Доля массивных разрывов вращательной манжеты среди всех разрывов достигает 40 %. Единого подхода в лечении пациентов с массивными разрывами вращательной манжеты плечевого сустава (МРВМПС) на сегодняшний день не существует. Нами разработан новый способ хирургического лечения такой категории пациентов: артроскопически-ассистированная транспозиция сухожилия широчайшей мышцы спины с использованием 1/2 сухожилия длинной малоберцовой мышцы.

Цель исследования. *Оценить эффективность хирургического лечения пациентов с массивными разрывами вращательной манжеты плечевого сустава, которым выполнена артроскопически-ассистированная транспозиция сухожилия широчайшей мышцы спины с использованием аутотрансплантата 1/2 сухожилия длинной малоберцовой мышцы.*

Материалы и методы. *В исследование включено 15 пациентов с МРВМПС III стадии по Patte и 2–3-й степени по Thomazeau, которым выполнена артроскопически-ассистированная транспозиция сухожилия широчайшей мышцы спины с использованием 1/2 сухожилия длинной малоберцовой мышцы.*

Результаты. *В статье представлены отдалённые результаты хирургического лечения пациентов по разработанному способу. Оценивались следующие критерии: средний возраст; давность с момента травмы; длительность операции. Функциональный результат оценивался по шкале ASES (American Shoulder and Elbow Surgeons). Учитывая показатели по функциональной шкале ASES через 1 год после оперативного лечения, получены следующие результаты: отличные – в 14 (93,3 %) случаях, удовлетворительные – в 1 (6,7 %).*

Заключение. *Разработанный способ позволяет в более ранние сроки восстановить функцию плечевого сустава, уменьшить выраженность болевого синдрома и улучшить качество жизни пациентов.*

Ключевые слова: *транспозиция сухожилия широчайшей мышцы спины, массивные разрывы вращательной манжеты плеча, сухожилие длинной малоберцовой мышцы*

Для цитирования: Меньшова Д.В., Пономаренко Н.С., Куклин И.А., Тишков Н.В., Пусева М.Э. Оценка эффективности хирургического лечения пациентов с массивными разрывами сухожилий вращательной манжеты плеча с использованием артроскопически-ассистированной транспозиции сухожилия широчайшей мышцы спины. *Acta biomedica scientifica*. 2023; 8(5): 133-143. doi: 10.29413/ABS.2023-8.5.14

Статья поступила: 05.05.2023
Статья принята: 05.10.2023
Статья опубликована: 05.12.2023

Rotator cuff ruptures are among the most common musculoskeletal injuries. Their incidence is 20 % [1]. Rotator cuff pathology is more commonly caused by degenerative processes in the tendons. According to the literature, up to 54 % of ruptures occur in individuals over 60 years of age [2]. The prevalence of rotator cuff massive ruptures (RCMR) comprises 40 % of all cuff ruptures [3]. No single classification of rotator cuff ruptures currently exists. Patients with massive ruptures have complaints of pain and limitation of movement, but they can also be asymptomatic [4]. In large and massive ruptures, there is a change in the biomechanics of the shoulder joint. An antero-superior dislocation of the head of the humerus is formed, and at later stages, progression of osteoarthritis and, as a consequence, atropathy of the shoulder joint. In 20 % of RCMR cases, pseudoparalysis of the upper extremity results [5]. No single approach in the treatment of this pathology currently exists. Nonsurgical therapy is aimed at pain control, but has a short-term effect. Surgical treatment options favoured include: subacromial balloon angioplasty, proximal rotator cuff plasty, musculotendinous transfers and reverse endoprosthesis. According to the literature, however, the complication rate after surgical repair of massive ruptures ranges from 20 to 94 % [6–8].

Considering the literature data, all advantages and disadvantages of the existing methods of treatment of patients with RCMR, a new method of surgical treatment was developed in our clinic: arthroscopic-assisted latissimus dorsi tendon transposition using autograft of the 1/2 of the peroneus longus tendon – and the long-term results of surgical treatment are being summarised.

THE AIM OF THE STUDY

To assess the efficacy of surgical treatment of patients with massive ruptures of the rotator cuff to which an arthroscopically-assisted latissimus dorsi tendon transposition using autograft of a 1/2 of the peroneus longus tendon was performed.

MATERIALS AND METHODS

The clinical study was approved by the local ethical committee of the Irkutsk Scientific Centre of Surgery and Traumatology (Minutes No. 2 dated February 25, 2023). In 2021, 15 patients (10 men and 5 women) who were admitted to the clinic with the diagnosis of chronic massive injury of the tendons of the rotator cuff have undergone surgery on the basis of the traumatology and orthopedics department No. 1 of the Irkutsk Scientific Centre of Surgery and Traumatology. According to magnetic resonance imaging (MRI), all patients had tendon retraction of the supraspinous muscle (stage III according to Patte with fatty atrophy of the supraspinous muscle of the grades 2 and 3 according to Thomazeau). All patients had undergone surgery according to the developed method: atroscopic-assisted latissimus dorsi tendon transposition using autograft by 1/2 of the peroneus longus tendon (patent for invention No. 2779219 C1) [9]. The patients were residents of the Irkutsk region; the mean age was 61.2 ± 6.7 years. In all patients, the cause of rupture was domestic trauma, more often a fall on the hand. The mean time from injury to admission was 3.5 ± 2.6 years.

Inclusion criteria:

- patients with massive ruptures of the rotator cuff (Patte stage III and Thomazeau grade 2–3);
- the age of the patients is 45–70 years;
- patients with recurrent rotator cuff tendon ruptures after surgical treatment – tendon reinsertion.

Exclusion criteria:

- patients with rotator cuff tendon ruptures (Patte stage I–II and Thomazeau grade 1);
- age of patients – over 70 years;
- patients with infectious lesions in the area of surgical intervention;
- upper extremity neurological disorders;
- patients' refusal to undergo surgical intervention.

Surgical treatment was performed as follows. Under anesthesia, the shoulder joint is accessed under aseptic conditions in the patient's side position through standard arthroscopic ports. The condition of the articular cartilage and the degree of retraction of damaged tendons are assessed. The insertion site area on the head of the humerus is refreshed to pinpoint bleeding.

The next step is a mini-access to latissimus dorsi tendon along the posterior axillary line (Fig. 1) and its excision, not reaching 4 cm to the fixation point (Fig. 2).

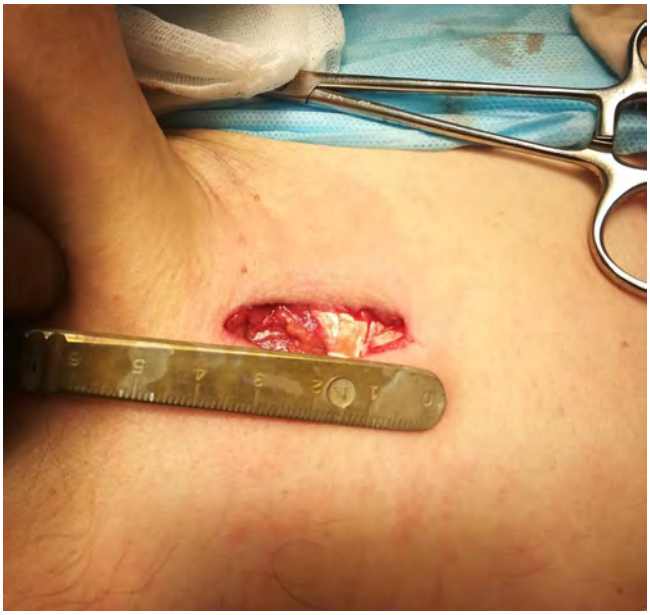

FIG. 1.
Limited incision to access latissimus dorsi tendon

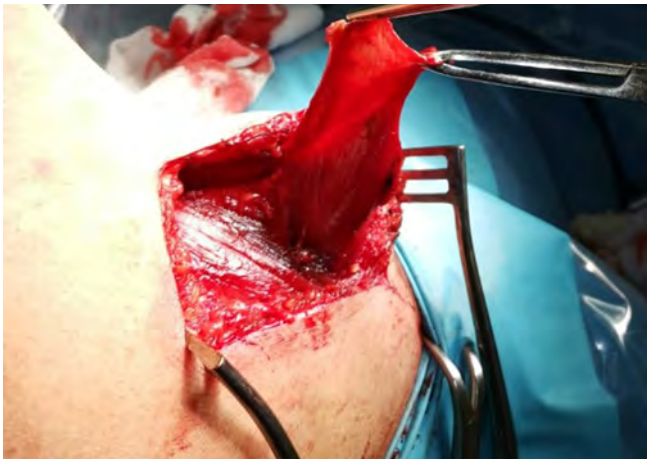

FIG. 2.
Isolation and dissection of the latissimus dorsi tendon from the fixation point

A separate access in the lower third of the tibia is used to take 1/2 of the peroneus longus tendon (Fig. 3).

The fourth stage – lengthening of the tendon of the latissimus longus dorsi by inserting 1/2 of the tendon of the peroneus longus tendon (Fig. 4) and suturing it with a spike suture – thus, a tendon autograft was formed (Fig. 5).

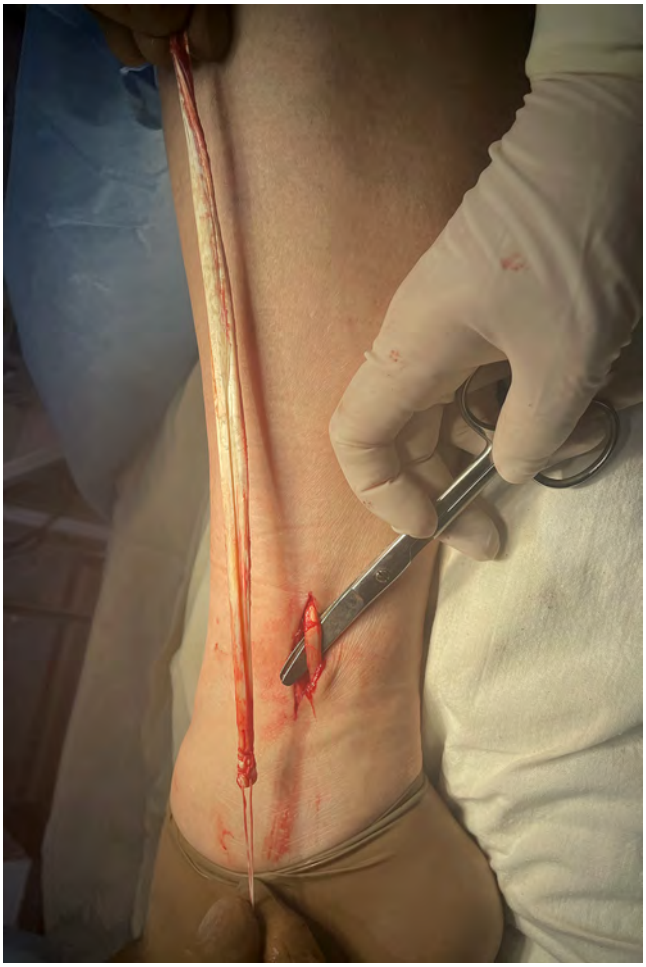

FIG. 3.
Retrieval of 1/2 of long peroneal muscle

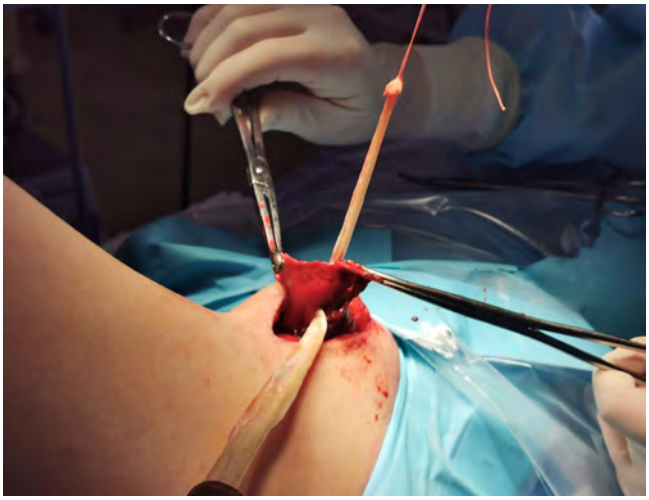

FIG. 4.
Integration of 1/2 of the long peroneal muscle tendon into the latissimus dorsi tendon

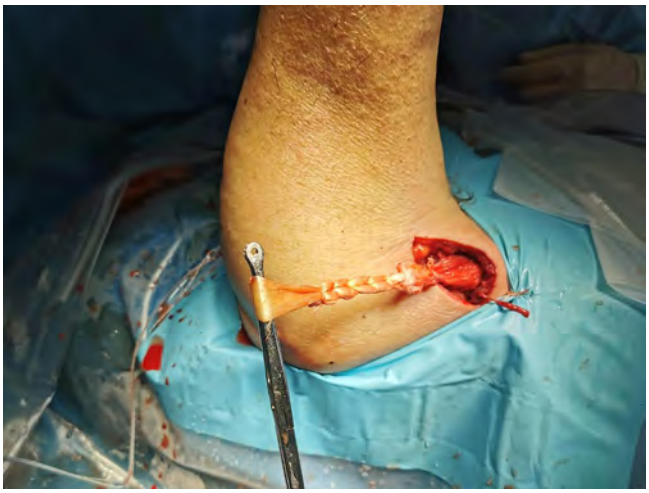

FIG. 5.
Suturing of the prepared autograft

A channel is formed through the posterior arthroscopic port under the posterior portion of the deltoid muscle, through which the free end of the tendon autograft is passed into the subacromial space and its fixation with anchor fixators on the insertion site of the humeral head is performed. The shoulder joint is washed with saline solution, haemostasis is performed, skin sutures and aseptic dressing are applied. The upper extremity is fixed with a 60° abduction splint for 6 weeks. From the day 2 patients start passive exercises of the shoulder joint on an abduction splint. After the cessation of immobilization, the active phase of physical therapy of the shoulder joint begins.

RESULTS

As a result of the analysis of surgical treatment efficiency, the following criteria were evaluated: duration

of surgical intervention; volume of intraoperative blood loss; and length of hospital stay. The level of pain syndrome in the area of surgical intervention was assessed according to the visual analogue scale (VAS). Functional outcomes were assessed using the American Shoulder and Elbow Surgeons' Shoulder Assessment Questionnaire (ASES).

The duration of surgery was 93.6 ± 16.5 min. Intraoperative blood loss was 34.6 ± 28.7 ml. The patients' length of hospital stay was 9.5 ± 3.3 days.

Pain intensity and functional outcome scores were assessed at 3, 6, and 12 months postoperatively. The preoperative pain level in patients was 7.6 ± 0.7 points. Three months after surgical treatment, patients complained of minor pain syndrome at rest, which increased after physical activity. The mean pain scores 3 months after surgery were 2.0 ± 0.9. At 6 months after surgery, the intensity of pain syndrome was 1.3 ± 1.0 points. After 12 months, patients reported a significant reduction or absence of pain syndrome. The mean pain intensity scores were 1.1 ± 1.0 points. Figure 6 summarizes the dynamics of pain syndrome intensity.

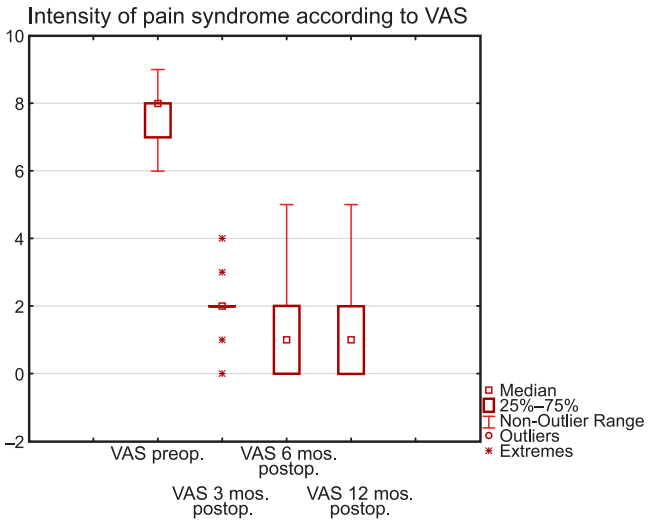

FIG. 6.
Dynamics of pain syndrome intensity

Functional outcomes were assessed using the ASES score. Figure 7 summarizes the results from the ASES evaluation questionnaire.

The mean preoperative functional scores according to the ASES score were 20.6 ± 5.3 points. Functional results 1 year after surgical treatment were 89.2 ± 10.4 points. There was a positive improvement in functional outcomes; Wilcoxon criterion for related groups $p < 0.0004$.

Considering the ASES functional scale scores 1 year after surgical treatment, the following results were obtained: excellent in 14 (93.3 %) cases. Patients had no complaints of pain and discomfort in the operated shoulder joint or minor pain syndrome after physical activity. The range

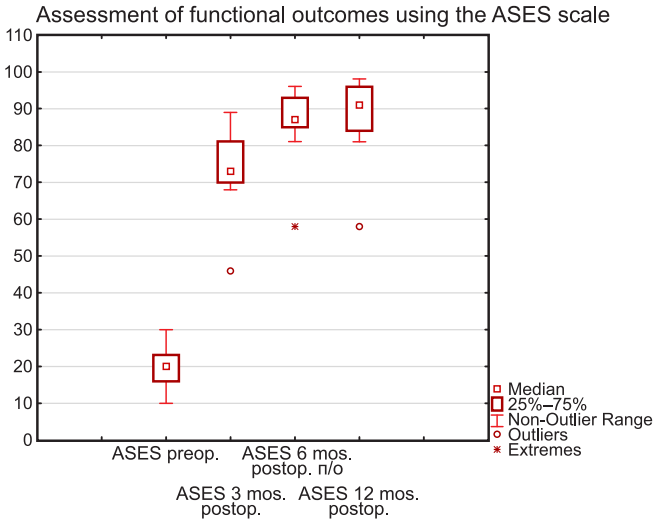

FIG. 7.
Assessment of the functional results according to ASES score

of motion in the shoulder joint: flexion and abduction – in the range of 160–180°. All patients in this group returned to their daily activities, and 3 patients continued to undertake physical activity at an amateur level. Satisfactory results were obtained in 1 (6.7 %) case. 1 patient had moderate pain and limitation of abduction and flexion in the range of 90–100°.

CLINICAL CASE STUDY

Patient M., 56 years old, addressed the diagnostic and counselling department of Irkutsk Scientific Centre of Surgery and Traumatology with complaints of pain and restriction of motion in the right shoulder joint. Past medical history: in 2013, the patient suffered a traumatic dislocation of the right shoulder joint. The dislocation was suppressed at the community clinic. The patient was re-injured in 2017; the injury was domestic – she slipped and fell on her right hand. The patient was admitted to the local clinic with dislocation of the acromial end of the clavicle, ligament grafting was performed. The postoperative period was uneventful. Subsequently, the patient continued to be bothered by pain syndrome with progressive limitation of movement in the right shoulder joint. Nonsurgical therapy: physiotherapy and non-steroidal anti-inflammatory drugs had no positive effect. Considering the clinical examination and MRI findings of the shoulder joint, the patient was diagnosed with a long-standing massive injury of the right rotator cuff tendon. A combined contracture of the right shoulder joint was detected. Surgical treatment has been recommended.

Local status: right upper extremity is involved in locomotor act of walking, not immobilised. The skin of the shoulder joint is of normal colour. There is a 10 cm postoperative scar without signs of inflammation in the projection of the clavicular-acromial articulation. Hypotrophy of the soft tissues of the right shoulder joint

is observed. Palpatory – pain in the area of the supraspinous fossa, pain and weakness when making abduction. Positive Leclerc's symptom, falling arm test, Jobe test. Active movements in the right shoulder joint: 70° abduction, 70° flexion. No neurovascular abnormalities of the right upper extremity were revealed. The preoperative ASES functional score was 20 points.

Preoperative radiographs revealed upper subluxation of the head of the right humerus, grade II osteoarthritis of the right shoulder joint, and grade II osteoarthritis of the clavicular-acromial joint (Fig. 8).

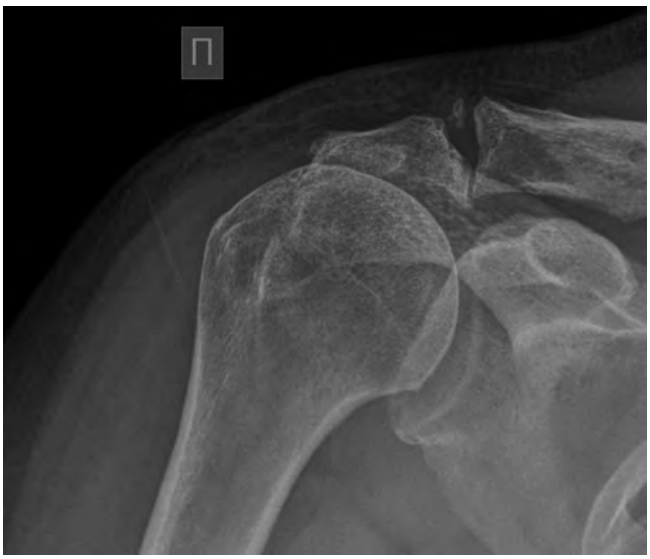

FIG. 8.
Patient M. X-ray of the right shoulder joint before the surgery

MRI of the right shoulder joint revealed subacromial narrowing up to 0.2 cm, rupture of the tendon of the supraspinous muscle with retracted tendon fibres at the glenoid level (Patte stage III). Muscular abdomen of the supraspinous muscle – with signs of atrophy (grade 3 according to Thomazeau) (Fig. 9).

Following the results of instrumental studies and clinical examination, the patient was considered to undergo arthroscopic-assisted latissimus dorsi tendon transposition using autograft of 1/2 tendon of the peroneus longus tendon. The postoperative period was uneventful. The patient was discharged from the hospital on the day 7 to the outpatient stage with recommendations. The right upper extremity was immobilized with an abduction splint for 6 weeks. During the period from 2 days to 6 weeks, the patient performed a set of passive shoulder exercises. From week 7 postoperatively, the patient started active right shoulder physical therapy and was provided with a course of physiotherapy.

At 3 months after surgery, the patient has a minor pain syndrome – 2 points according to VAS. Right shoulder joint full range of motion: 180° of abduction, 180° of flexion. Functionality was rated at 89 according to the ASES scale (Fig. 11).

Six months after surgery, the patient noted insignificant pain syndrome after physical activity – 1 point according to VAS, full recovery of working efficiency. Functionality was rated at 91 according to the ASES scale (Fig. 12).

After 12 months, the patient has no complaints. Pain syndrome is insignificant after heavy physical activity – 1 point according to VAS. Complete restoration of working efficiency. Functionality is rated at 93 according to the ASES scale. The patient is satisfied with the results of surgical treatment (Fig. 13).

One year after surgery, MRI of the right shoulder joint revealed that the tendon of the supraspinous muscle was not visualized, and a graft of 1/2 of the peroneus longus tendon, fixed with anchors in the head of the humerus, was detected in its projection (Fig. 14).

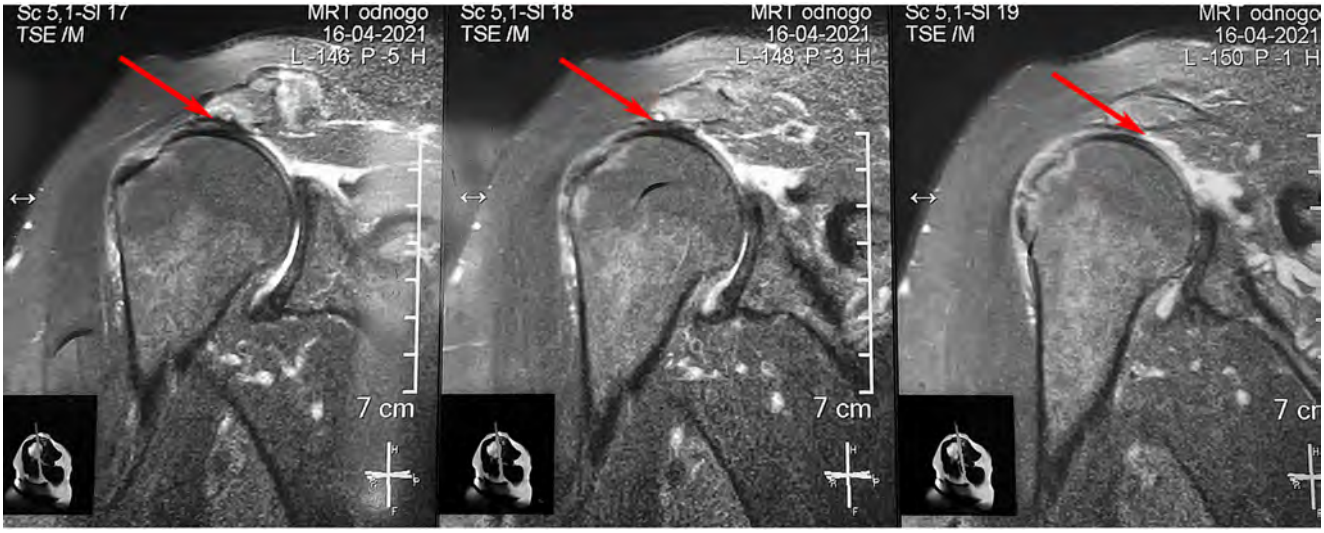

FIG. 9.
Patient M. MRI of the right shoulder joint before the surgery

FIG. 10.
Patient M. Functional result before the surgery

FIG. 11.
Patient M. Functional result in 3 months after the surgery

FIG. 12.
Patient M. Functional result 6 months after the surgery

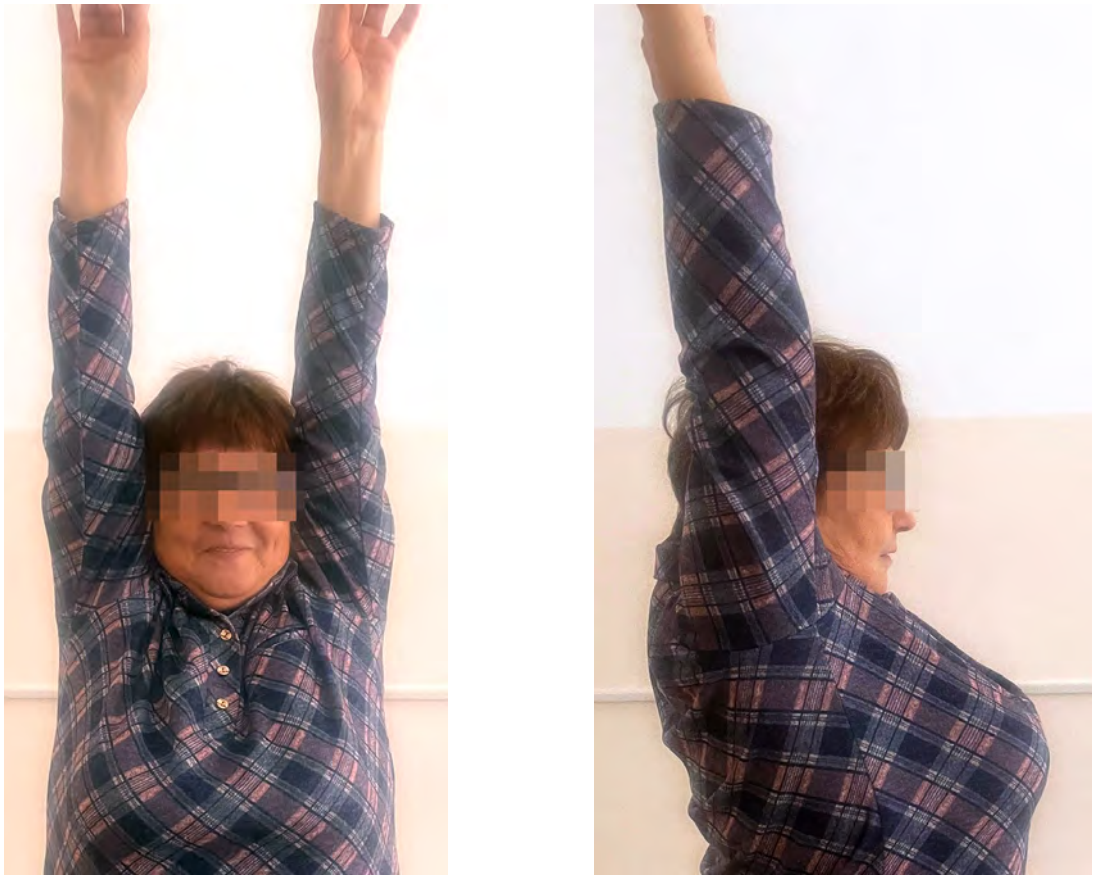

FIG. 13.
Patient M. Functional result 12 months after the surgery

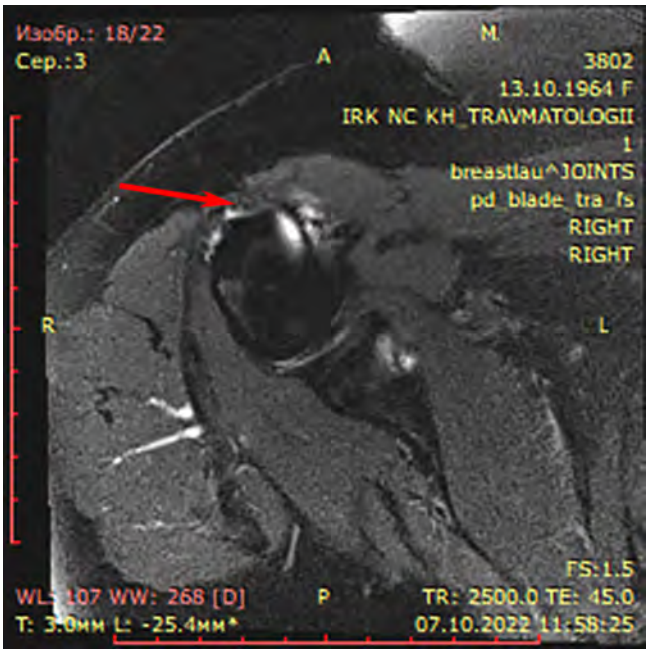

FIG. 14.
Patient M. MRI of the right shoulder joint 12 months after the surgery

DISCUSSION

The most common surgical treatment options for RCMR, according to the literature, can be considered to be subacromial balloon angioplasty, proximal rotator cuff plasty, musculotendinous transfers, namely latissimus dorsi tendon transposition, and reverse endoprosthesis. The essence of subacromial balloon angioplasty is the introduction of a balloon spacer into the subacromial space, which is subsequently filled with physiological solution. This device is designed to increase the acromion-shoulder interval, lower the humeral head and thereby eliminate secondary subluxation. Studies prove that the subacromial spacer is destroyed within 12 months [10, 11]. Much attention is currently being paid to such a surgical treatment option as proximal rotator cuff plasty. Defects are substituted with both allografts and autografts. The fasciae latae muscle is more often used as autografts. R.W. Jordan et al. conducted a systematic review of the literature of reconstruction of the upper part of the rotator cuff with the fasciae latae muscle and cell-free dermal collagen matrix. 9 studies were included in the review. Five studies reported about transplantation of the fasciae latae muscle, and 4 studies focused on cell-free dermal collagen matrix. The average follow-up time ranged from 10.9 to 42.4 months. The results were assessed using X-ray techniques. Dermal matrix failure was observed from 5.5 to 55 % of cases, fasciae latae muscle failure was 4.2–36.1 % [8]. When the articular cartilage of the humeral head is preserved, muscle-tendon transfers are one of the surgical treatment options for RCMR. The most common is the transfer of latissimus dorsi tendon. In 1998, C. Gerber et al. were the first to propose and perform latissimus dorsi tendon transposition to the head of the humerus in cases of massive ruptures of the rotator cuff. The results of treatment of 16 patients with tendon defects of the supraspinous and infraspinatus muscles, secondary subluxation of the head of the humerus, and limitation of abduction and flexion were analyzed. Biomechanically, the essence of the surgery was to change the force vector to relegate the head of the humerus and restore the biomechanics of the joint. Positive treatment results were reported in 80 % of cases [12]. K.P. Shea et al. conducted a systematic literature review between 1992 and 2010 to determine the outcomes of latissimus dorsi tendon transposition. Ten studies were analysed; mean follow-up was 45.5 months. Functional scores improved from 45.9 to 73.2 points. There was an improvement in flexion from 101.9° to 130.7° postoperatively. The overall reported complication incidence was 9.5 %, including infectious complications, neuropathy, ruptures of transferred tendons, haematomas, and wound discrepancies [13]. Currently, latissimus dorsi tendon transposition using the arthroscopic technique has become more common in the literature. Its main advantage is the preservation of the acromiohumeral muscle. In the postoperative period, patients retain muscle strength, which contributes to faster rehabilitation. Patients also experience less pain syndrome in the postoperative period when using minimally invasive technique in comparison with open surgical intervention technique [14]. Muscle-tendon transfers can be considered the technique of choice for young and active patients. The risk of iatrogenic damage to the neurovascular bundle during tendon excision from the crest of the humerus remains high, however, as well as high risks of graft detachment both after primary transposition and after revision intervention. According to the literature, the clinical failure incidence after latissimus dorsi tendon transposition stands at 36 % [15]. Another treatment option for massive ruptures of the rotator cuff tendons is reverse shoulder arthroplasty. Common indications for endoprosthesis are pain and "pseudoparalysis" of the shoulder joint, which develops against the background of massive ruptures of the rotator cuff [16]. According to the authors, endoprosthesis is not suitable for the treatment of young and active patients because of functional limitations, as well as because of the rapid wear of the endoprosthesis and, consequently, the need for repeated revision surgery [17].

Modern scientific literature analysis reveals that there are no unified approach and algorithm for the treatment of patients with massive ruptures of the rotator cuff. Each treatment method has its own pros and cons. In severe cases of RCMR, when there is maximum diastasis between the end of the damaged tendon of the supraspinous muscle and its attachment area (Patte stage III), the muscle itself is in fatty involution (Thomazeau grade 2–3) and becomes unable to fulfil its function. The surgical treatment method suggested by this study makes it possible to replace the function of the supraspinous tendon with the function of the latissimus dorsi. Access to the tendon is minimal (5.0–7.0 cm), thus reducing the risk of one of the complications of this surgery – damage to the neurovascu-

lar bundle – by excising the tendon of the latissimus dorsi before reaching the neurovascular bundle. Half of the peroneus longus tendon is used as the graft, minimizing damage in the donor area and reducing the risk of graft lysis in the area where the graft is used. Lengthening the tendon of the latissimus dorsi with a graft allows to reduce the tension of the muscle and, consequently, to reduce the probability of failure of its new attachment on the head of the humerus. As a result of the latissimus dorsi transfer, the head of the humerus is lowered and the biomechanics of the shoulder joint is restored. The use of arthroscopic technique reduces the traumatic nature of surgical intervention. The autograft also provides an opportunity to cover the entire insertion area of the humeral head and thereby further eliminate subacromial impingement syndrome.

CONCLUSIONS

The developed method of arthroscopic-assisted latissimus dorsi tendon transposition using 1/2 of the peroneus longus tendon allows to restore the function of the shoulder joint earlier, reduce the severity of pain syndrome and improve the quality of life of patients.

Conflict of interest

The authors of this article declare no conflicts of interest.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

MICROCIRCULATION PARAMETERS OF THE DAMAGED SEGMENT OF THE LOWER EXTREMITY AFTER TREATMENT OF DIAPHYSEAL FRACTURES USING A LOCKED INTRAMEDULLARY NAIL

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ABSTRACT

Background. *An in-depth analysis of the scientific works of scientists and medical practitioners allows us to conclude that locked nail intramedullary osteosynthesis is the optimal and the most effective method of treating closed diaphyseal fractures of the lower leg bones, which is caused by the high stability of osteosynthesis and minimal damage to soft tissues during surgery. The processes of microcirculation changes in the early postoperative period by various metal structures, including a locked intramedullary nail, still remain unexplored. In particular, there is insufficient data on the use of a locked intramedullary nail.*

The aim of the study. *To identify the features of changes in microcirculation indices of injured lower leg bones during fixation of fragments with a locked intramedullary nail in the early postoperative period.*

Materials and methods. *The microcirculation of the lower limb segment was studied in 25 patients using laser Doppler flowmetry. Data from 25 healthy volunteers were used as a comparison group.*

Results. *It was found that in the early postoperative period, from day 1 to day 10, in patients with diaphyseal fractures of the lower leg bones operated with locked nail intramedullary osteosynthesis, there is a decrease in the cardiac range, an increase in the share of the shunt component of microcirculation compared to the nutritional share, as well as an increase in more than 1 ratio of the cardiac and respiratory range amplitude, which indicates an ischemia type of local circulatory disorder. Compensation of ischemia is done by anastomoses, since the bypass rate is increased.*

Conclusion. *In case of surgical treatment with locked nail intramedullary osteosynthesis, in the early postoperative period, an ischemic type of compensated local circulatory disorder develops. The regeneration process takes place under conditions of reduced arterial microcirculation blood flow and stable venous outflow, as well as the inclusion of anastomoses to compensate for destroyed vessels, which is associated with nail damage to the internal blood flow of the bone endosteum and intraosseous nutrient artery during the surgery.*

Key words: *microcirculation, laser Doppler flowmetry, diaphyseal fracture of the lower leg bone, locked nail intramedullary osteosynthesis*

Received: 13.12.2022
Accepted: 18.10.2023
Published: 05.12.2023

For citation: Plakhov A.I., Korytov L.I., Vinogradov V.G., Darenskaya M.A., Makarov S.V. Microcirculation parameters of the damaged segment of the lower extremity after treatment of diaphyseal fractures using a locked intramedullary nail. *Acta biomedica scientifica*. 2023; 8(5): 144-149. doi: 10.29413/ABS.2023-8.5.15

ПАРАМЕТРЫ МИКРОЦИРКУЛЯЦИИ ПОВРЕЖДЁННОГО СЕГМЕНТА НИЖНИХ КОНЕЧНОСТЕЙ ПОСЛЕ ЛЕЧЕНИЯ ДИАФИЗАРНЫХ ПЕРЕЛОМОВ С ПОМОЩЬЮ БЛОКИРУЕМОГО ИНТРАМЕДУЛЛЯРНОГО ГВОЗДЯ

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РЕЗЮМЕ

Обоснование. *При глубоком анализе научных трудов учёных и практикующих врачей можно прийти к выводу, что блокируемый интрамедуллярный остеосинтез является оптимальным и наиболее эффективным методом лечения закрытых диафизарных переломов костей голени, что обусловлено высокой стабильностью остеосинтеза и минимальным повреждением мягких тканей при операции. До сих пор остаются не изученными процессы изменения микроциркуляции в раннем послеоперационном периоде различными металлоконструкциями, в том числе и блокируемым интрамедуллярным гвоздём. В частности, недостаточно сведений об использовании блокируемого интрамедуллярного гвоздя.*

Цель исследования. *Выявить особенности изменений показателей микроциркуляции травмированных костей голени при фиксации фрагментов блокируемым интрамедуллярным гвоздём в раннем послеоперационном периоде.*

Материалы и методы. *У 25 пациентов с помощью лазерной допплеровской флоуметрии проведено исследование микроциркуляции сегмента нижней конечности. В качестве группы сравнения использовались данные 25 здоровых добровольцев.*

Результаты. *Установлено, что в раннем послеоперационном периоде, с 1-х по 10-е сутки, у пациентов с диафизарным переломами костей голени, прооперированных металлостеосинтезом блокируемым интрамедуллярным гвоздём, происходит уменьшение сердечного диапазона, увеличение доли шунтового компонента микроциркуляции по сравнению с нутритивной долей, а также увеличение больше 1 отношения амплитуды сердечного и дыхательного диапазона, что свидетельствует о местном нарушении кровообращения по типу ишемии. Компенсация ишемии осуществляется за счёт анастомозов, так как показатель шунтирования увеличен.*

Заключение. *При оперативном лечении блокируемым интрамедуллярным остеосинтезом в раннем послеоперационном периоде развивается нарушение местного кровообращения по ишемическому типу с компенсацией. Процесс регенерации протекает в условиях сниженного артериального кровотока микроциркуляции и стабильного венозного оттока, а также включения анастомозов для компенсации разрушенных сосудов, что связано с повреждением гвоздём внутреннего кровотока эндоста кости и внутрикостной питательной артерии в ходе операции.*

Ключевые слова: *микроциркуляция, лазерная допплеровская флоуметрия, диафизарный перелом голени, блокируемый интрамедуллярный остеосинтез*

Статья поступила: 13.12.2022
Статья принята: 18.10.2023
Статья опубликована: 05.12.2023

Для цитирования: Плахов А.И., Корытов Л.И., Виноградов В.Г., Даренская М.А., Макаров С.В. Параметры микроциркуляции повреждённого сегмента нижних конечностей после лечения диафизарных переломов с помощью блокируемого интрамедуллярного гвоздя. *Acta biomedica scientifica*. 2023; 8(5): 144-149. doi: 10.29413/ABS.2023-8.5.15

INTRODUCTION

It has been established that in the structure of bone fractures of all localisations, tibia fractures are predominant (ranging from 20 to 37.3 %); they also account for up to 60 % of the total number of fractures of long bones [1].

A deep analysis of the scientific works of scientists and practicing physicians leads to the conclusion that locked intramedullary osteosynthesis (LIOS) is the optimal and most effective method of restoring bone integrity in closed diaphyseal fractures of the tibia, which is caused by high stability of osteosynthesis and minimal damage to soft tissues during surgery [1, 2]. The fundamental reason for the development of various complications in the treatment of traumatological diseases is a violation of microcirculatory processes in the damaged extremity segment. As is well known, the above-mentioned soft tissue injuries are possible both during direct trauma and during surgical intervention; accordingly, the more serious the volume of surgical intervention, the deeper the soft tissue injuries the patient receives. It is essential to correct local tissue microcirculation disorders in the area of the affected extremity, as high-quality haemodynamics is essential for restoring the viability of damaged tissues, their subsequent regeneration and the course of inflammation [3, 4].

Consequently, an objective recording of the microcirculation disorders manifestations is necessary for effective recovery after surgery, which will allow noninvasively determining the state of local microcirculation disorders in the tissues of the affected extremity [3, 4].

Laser Doppler flowmetry (LDF) is one of the unique highly sensitive and non-invasive methods providing wide diagnostic possibilities in the study of microcirculation disorders [5]. The LDP method, according to the research data of domestic and foreign literature, allows to determine quite accurately various links of microcirculatory channel disorders and to determine quite accurately the development of pathophysiological processes in extremities [6]. However, the processes of microcirculation changes after surgical treatment of extremity bone fractures in the early postoperative period with various metal structures, including intramedullary locking nail, remain to be studied. In particular, there is insufficient information about the use of the method of surgical treatment of tibia bone fractures in the diaphysis area using an intramedullary locking nail, which predetermined the purpose of this study.

THE AIM OF THE STUDY

To reveal the peculiarities of changes in the microcirculation indices of traumatized tibia bones during fragment fixation with intramedullary locking nail in the early postoperative period.

MATERIALS AND METHODS

This study was conducted on the basis of Irkutsk City Clinical Hospital No. 3 in 2014–2016. The data describing the microcirculation in the main group consisting of 25 patients being under treatment in a trauma hospital were recorded and carefully analyzed. The study group was formed by the continuous sampling method. The criteria for entering the group were: being in a trauma hospital; age up to 59 years; and primary trauma to the tibia bones. The exclusion criteria for the study were described in a previous study [6]. The examined patients differed in the severity of injuries (Table 1). All patients on admission with closed diaphyseal fractures of the tibia bones underwent preliminary skeletal traction. After further examination, the patients underwent surgery aimed at matching the broken bone fragments – closed repositioning followed by an intraosseous metal osteosynthesis using an intramedullary locking nail. The same conventional drug therapy including disaggregants, antibacterial agents, and topical drug therapy, etc. were used in the whole group of patients during treatment. The surgical access site was also treated and dressed (Table 1).

TABLE 1

DISTRIBUTION OF PATIENTS ACCORDING TO THE NATURE OF FRACTURES AND THEIR LOCALIZATION (ACCORDING TO THE AO/ASIF CLASSIFICATION)

Number of patients	42A1	42A2	42B1	42C1	Total
abs.	16	1	4	4	25
%	64 %	4 %	16 %	16 %	100 %

Patients with tibial diaphysis fractures according to the AO/ASIF (Albeitgemeinshaft fur Osteosynthenfragen/Association for the Study of Internal Fixation) classification of group 42A1 (64 %) made up the largest group of the study population.

The clinical comparison group consisted of 25 healthy volunteers statistically significantly comparable in age and sex.

Experimental study of microcirculatory parameters indices was performed using a non-invasive LDF method with the LAKK-OP device (version 2) (SPE "Lazma", Russia). The advantages and operation mechanisms of this analyser are more detailed discussed in the previous articles devoted to this subject [6, 7].

LDF-diagrams were recorded for at least 10–11 min, with the transducer placed on the dorsal surface of the foot in the projection of the proximal part of the 1st metatarsal bone of the injured extremity. The microcirculation index (M) was assessed; a specific feature of this device is also

the registration of additional narrowly focused parameters, such as: shunt index (SI), maximum amplitudes of cardiac (Ah) and respiratory (Ar) oscillation ranges.

LDF diagnostics was performed at the same time of day, at the same room temperature (21–23 °C). Before the microcirculation study, the examinees did not ingest food or liquids, did not smoke, and did not assume an upright position.

All studies were performed in the early postoperative period, from the day 1 to the day 10 on daily basis. Based on the shunt index (SI) and microcirculation, the shunt component of the microcirculation index (M shunt.) and nutritive microcirculation index (M nutr.) were determined using the same formulas as in the previous study [7].

The cumulative analysis of the obtained data is the optimal study of microcirculation, since the isolated assessment of one of the parameters does not give a complete picture of the ongoing pathophysiological processes [8]. Thus, for a comprehensive complete and objective study in LDF-diagnostics of local disorders of microcirculatory processes the index of microcirculation, including the state of oscillatory processes associated with arterial inflow (Ah) and venous outflow (Ar) is of great importance.

It was obligatory for patients to sign informed consent to participate in the study in accordance with the ethical principles of the World Medical Association Declaration of Helsinki (1964, 2013 ed.). The study was approved by the Ethical Committee of the Irkutsk State Medical University (extract from minutes No. 2 dated April 16, 2014).

For the purpose of statistical data processing, MS Excel 2010 (Microsoft Corp., USA) and Statistica 10.0 for Windows (StatSoft Inc., USA) software were used. Based on the distribution of data, non-parametric (Mann – Whitney) or parametric (Student's t-test) criteria were used in the analysis. The data obtained were summarized using median, 25th and 75th percentiles or mean values and standard deviation.

RESULTS AND DISCUSSION

In this study we will dwell in more detail on the local blood circulation disorders using the interpretation of the laser Doppler flowmeter LAKK-OP (version 2) (NPP "Lazma", Russia).

Table 2 summarizes the studies of the clinical comparison group and the main group.

The study revealed that the microcirculation index had no statistically significant difference between the patients of the main group who underwent LIOS surgery and the clinical comparison group in the early postoperative period (days 1–10). These findings indicate local circulatory disorders of the compensatory ischaemia type. The experiment also revealed that the ratio of the proportions of the shunt and nutritive components of the microcirculation indices evidenced the violation of local circulatory disorders of ischaemic type, and the proportion of the shunt component compared to the nutritive component was 18.32 % higher.

An important point to be noted is that a striking parameter confirming the presence of ischaemia is a 39.01 % decrease in cardiac range amplitude (Ah) in the main group compared to the clinical comparison group.

No statistically significant difference was revealed when interpreting the respiratory range amplitude (Ad) amplitude parameters, indicating the absence of congestion and compensation of the ischaemic form as a result of the processes discussed further.

The ratio of heart rate and respiratory amplitude is unequivocally greater than 1 in the main group, which also evidences the existence of ischaemia [8].

TABLE 2

MICROCIRCULATION PARAMETERS IN THE MAIN AND THE COMPARISON GROUPS

Parameters	Main group		Clinical comparison group	
	I	II	III	IV
M	5.86 (5.77–6.37)	5.95 ± 0.33	6.46 (5.2–8.38)	6.72 ± 2.26
SI	2.27 (1.39–1.76)×	2.45 ± 0.36×	1.65 (0.83–2.04)×	1.57 ± 0.32×
The proportion of M nutr.	2.43	2.43	–	–
The proportion of M shunt.	3.52	3.52	–	–
Ah	0.15 (0.11–0.16)×	0.14 ± 0.01×	0.23 (0.19–0.28)×	0.24 ± 0.04×
Ar	0.11 (0.10–0.13)	0.11 ± 0.01	0.13 (0.1–0.16)	0.13 ± 0.02
Ah/Ar	1.26	1.26	–	–

Note. Data from the first (I) and third (III) columns are presented as median with lower and upper quartiles (25th and 75th percentiles); data from the second (II) and fourth (IV) columns are presented as mean values and standard deviation; × – statistically significant differences between groups ($p < 0.05$).

A statistically significant increase of 56.1 % in the shunt rate in the main group reveals the inclusion of shunt vessels and evidences the significant role of shunts in compensating ischaemia to restore blood circulation within the bone, since during surgery, the nail being inserted disrupts blood flow in the endosteum, which is not contrary to the basic study "Bone Regeneration and Blood Supply" [9].

We hypothesize that LIOS is followed by destruction of endosteal internal blood flow during surgery, after which the arterial supply to the operated extremity is impaired. This change is registered by a 39.01 % decrease in heart range amplitude (Ah). The other parameters confirming ischaemia in the injured extremity include such parameters as the proportion of shunt component of microcirculation compared to nutritive component, increased by 18.32 %, and increase in the ratio of heart to respiratory range amplitude greater than 1. This is followed by additional mechanisms that activate anastomoses or shunts, causing the values of the shunt index parameter to be 56.1 % higher than those of the clinical comparison group (healthy individuals). As a result, the blood circulation of the injured extremity is replenished, which is reflected by the value of the microcirculation index (M), which is not statistically significantly different from that in the clinical comparison group. No circulatory stasis was also observed, as the amplitude of respiratory range of variation (Ar) was not statistically significantly different from that of the clinical comparison group.

Considering the wide variety of obtained indicators of microcirculatory disorders, a compensatory ischaemia type of local blood circulation was revealed. These values indicate a decrease in arterial blood inflow to the extremity, which is associated with damage to the bone endosteum and intraosseous feeding artery by the internal blood flow nail during the surgery with subsequent compensation of ischaemia by including anastomoses, since during this surgery there is minimal damage to soft tissues and periosteum, and there is no surgical access at the fracture site, due to which the deficit of blood supply to the extremity is levelled, and the healing process is accompanied by a stable venous outflow of blood throughout the entire study period.

CONCLUSION

According to the present study, it was revealed that patients with diaphyseal fracture of the tibia bones who underwent surgery with an intramedullary locking nail have a compensated ischaemic-type circulatory disturbance in the injured extremity in the early postoperative period. Consequently, tissue regeneration occurs under conditions of reduced arterial blood flow, decreased microcirculation and normalized venous outflow caused by the inclusion of anastomoses to compensate for the destroyed vessels, which seems to be related to the nail damage of the internal blood flow to the bone endosteum and intraosseous feeding artery during surgery.

Conflict of interest

The authors of this article confirm that there is no conflict of interest.

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Изменения показателей микроциркуляции в ранний послеоперационный период при лечении диафизарных переломов костей голени с помощью пластины с ограниченным контактом. *Acta biomedica scientifica.* 2019; 4(3): 58-62]. doi: 10.29413/ABS.2019-4.3.8

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Plakhov A.I. – collection of practical material; processing of the obtained data; preparation of the article for publication.

Korytov L.I. – editing of the article; preparation of the article for publication; analysis of study results.

Vinogradov V.G. – scientific supervision for the postgraduate student; discussion of clinical material and significance for practical healthcare.

Darenskaya M.A. – assistance in statistical processing of the obtained results.

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ROTATOR CUFF TENDON RUPTURES (LITERATURE REVIEW)

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ABSTRACT

Rotator cuff injury is a common disorder: up to 20 % of the population over the age of 45 have tears of varying severity, of which up to 40 % are large and massive ruptures. The gradual development of tendon degeneration and fatty degeneration of muscle tissue and the asymptomatic course of the disease often lead to late medical attention when secondary arthropathy of the shoulder joint develops. With age, the probability of having a rupture increases, reaching 51 % in people over 80 years of age. The main diagnostic tools are radiography and magnetic resonance imaging of the shoulder joint combined with clinical examination. Nonsurgical treatment for massive injuries is ineffective, and the risk of worsening rotator cuff tendinopathy to rupture reaches 54 %. There are three main directions in the surgery of rotator cuff injuries: tendon reconstruction or replacement of their defect with grafts; muscle transfer; shoulder arthroplasty. Subacromial balloon spacer and tenogenic patches are also used. Each of these methods has a number of disadvantages and limitations. The frequency of repeated ruptures of reconstructed tendons reaches 45 %. Muscle transfer is extremely demanding on the skill of the surgeon and is associated with high risks of neurological complications. Arthroplasty imposes a number of significant restrictions on the patient, reducing the quality of life, and prosthesis components wear increases the risk of complications, especially during revision interventions. The use of the subacromial spacer is limited by its high cost and lack of long-term follow-up of treatment outcomes. Tenogenic patches have not undergone clinical trials, being an experimental technique.

There is no single approach to the treatment of massive rotator cuff ruptures. The results are contradictory, the advantages of each of the methods are balanced by their disadvantages, which provides a wide window of opportunity in the studying, optimizing classical and introducing new methods of treatment of this pathology.

Key words: *rotator cuff, surgical treatment, conservative treatment, massive ruptures*

Received: 06.07.2023
Accepted: 04.10.2023
Published: 05.12.2023

For citation: Slaikovskiy E.N., Ponomarenko N.S., Kuklin I.A. Rotator cuff tendon ruptures (literature review). *Acta biomedica scientifica*. 2023; 8(5): 150-156. doi: 10.29413/ABS.2023-8.5.16

ПОВРЕЖДЕНИЯ ВРАЩАТЕЛЬНОЙ МАНЖЕТЫ ПЛЕЧА (ОБЗОР ЛИТЕРАТУРЫ)

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РЕЗЮМЕ

Повреждение вращательной манжеты – распространённое заболевание: до 20 % населения старше 45 лет имеют разрывы разной степени выраженности, из них до 40 % – большие и массивные. Постепенное развитие процессов дегенерации сухожилий и жировой дистрофии мышечной ткани и бессимптомное течение заболевания часто приводят к поздним обращениям за медицинской помощью, когда развивается вторичная артропатия плечевого сустава. С возрастом вероятность наличия разрыва увеличивается, достигая 51 % у лиц старше 80 лет. Основными инструментами диагностики являются рентгенография и магнитно-резонансная томография плечевого сустава в совокупности с клиническим осмотром. Консервативное лечение при массивных повреждениях малоэффективно, а риск усугубления тендинопатии вращательной манжеты до разрыва при нём достигает 54 %. В хирургии повреждений вращательной манжеты плеча можно выделить три основных направления: восстановление сухожилий или замещение их дефекта трансплантатами; мышечный трансфер; эндопротезирование плечевого сустава. Также применяются субакромиальной баллонный спейсер, теногенные пластыри. У каждого из методов есть ряд недостатков и ограничений. Частота повторных разрывов рефиксированных сухожилий достигает 45 %. Мышечный трансфер крайне требователен к квалификации хирурга и сопряжён с высокими рисками неврологических осложнений. Эндопротезирование накладывает ряд существенных ограничений на пациента, снижая качество жизни, а износ компонентов протеза увеличивает степень риска осложнений, особенно при ревизионных вмешательствах. Применение субакромиального спейсера ограничено его высокой стоимостью и отсутствием длительного наблюдения за результатами лечения. Теногенные пластыри не проходили клинических испытаний, являясь экспериментальной методикой.
Таким образом, единого подхода к лечению массивных разрывов вращательной манжеты не существует, результаты противоречивы, преимущества каждой из распространённых методик уравновешиваются недостатками, что предоставляет широкое окно возможностей в области изучения, оптимизации классических и внедрения новых методов лечения данной патологии.

Ключевые слова: *вращательная манжета, хирургическое лечение, консервативное лечение, массивные разрывы*

Статья поступила: 06.07.2023
Статья принята: 04.10.2023
Статья опубликована: 05.12.2023

Для цитирования: Слайковский Е.Н., Пономаренко Н.С., Куклин И.А. Повреждения вращательной манжеты плеча (обзор литературы). *Acta biomedica scientifica*. 2023; 8(5): 150-156. doi: 10.29413/ABS.2023-8.5.16

INTRODUCTION

Rotator cuff injury is the most common pathology of the shoulder joint: up to 20 % of the population over 45 years of age have ruptures of various degrees of severity, of which up to 40 % have large and massive ruptures [1]. The disease is often asymptomatic and in only one third of patients is accompanied by pain and dysfunction of the affected shoulder joint [2]. The prevalence of rotator cuff ruptures increases with age since degenerative changes in the tendon will prevail with increasing age, occurring in 20 % of people aged 60 to 69 years, 31 % of those aged 70 to 79 years and 51 % of those over 80 years [3, 4].

The most severe category of rotator cuff tendon ruptures in terms of prognosis is massive, non-repairable ruptures, which account for up to 40 % of all ruptures. It is caused by the impossibility to perform reinsertion of rotator cuff tendons on the insertion surface, and even in case of partial adaptation of the damaged tendon, the muscle remains unable to fulfil its function as a result of fatty degeneration, the consequence of which is progressive arthropathy of the shoulder joint [5]. Currently, there are many ways to treat patients with massive, irreparable tendon ruptures of the rotator cuff with their own advantages and disadvantages, and each surgeon prefers one or another technique as a result of his or her experience and professional skills, and there is currently no single consensus and algorithm for the treatment of this severe pathology.

Several criteria shall be carefully considered in order to determine the treatment tactics and choose the optimal surgical approach: the degree of proximal displacement of the humeral head, which is reflected in the radiological classification by K. Hamada; the degree of retraction of the supraspinous muscle tendon and assessment of the volume of tendons involved in the injury according to the D. Patte classification; MRI classification of the fatty dystrophy degree of the rotator cuff muscles according to D. Goutallier; MRI classification of supraspinous muscle atrophy by H. Thomazeau.

The classification of K. Hamada, proposed by him in 1990, is based on the acromiohumeral interval AHI and the degree of degenerative changes in cartilage and subchondral bone of the articular cavity of the scapula and humeral head: stage I – AHI > 6 mm; stage II – AHI < 5 mm; stage III – concave deformation of the acromial scapular process (acetabulation) with AHI; stage IV – acetabulation with narrowing of the subacromial space; stage V – collapse of the humeral head. This classification primarily reflects the degree of shoulder arthropathy, which is of principal importance when indicating endoprosthesis replacement. The extent of rotator cuff tendon injury according to this classification is determined empirically, but it is always massive, as only such lesions cause X-ray significant changes in the position of the humeral head [6].

The D. Patte classification, proposed by him in 1990, assesses the degree of retraction of the rotator cuff tendons in the frontal plane and the involvement of the rotator cuff elements in the sagittal plane based on the results of magnetic resonance imaging (MRI). In the first case, D. Patte distinguished three stages: stage I – tendon stump is located near the place of attachment to the humerus; stage II – tendon stump is located at the level of the humeral head; stage III – tendon stump is located at the level of the glenoid. The stage directly indicates the length of time that has elapsed since the rotator cuff tendon detached from the shoulder and the degree of retraction of the corresponding muscle. In the second case, six segments were identified: segment 1 – isolated tendon injury of the subscapular muscle; segment 2 – isolated rupture of the coracohumeral ligament; segment 3 – isolated tendon rupture of the supraspinous muscle; segment 4 – complete rupture of the supraspinous muscle and partial rupture of the infraspinatus muscle tendon; segment 5 – complete rupture of the tendons of the supraspinous and infraspinatus muscles; segment 6 – complete rupture of the tendons of the supraspinous, infraspinatus and subscapular muscles [7].

The D. Goutallier classification, proposed by him in 1994, assesses the degree of fatty dystrophy of the rotator cuff muscles by dividing it into four stages: stage 0 – normal, unchanged muscle tissue; stage 1 – insignificant fat layers in the muscle thickness; stage 2 – the volume of fat layers is less than 50 % of the muscle volume; stage 3 – the volume of fat layers is 50 %; stage 4 – the volume of fat layers is more than 50 % of the muscle volume [8].

As opposed to this, H. Thomazeau et al. in their classification, proposed in 1996, assess the degree of fatty dystrophy of the supraspinous muscle by the volume of muscle tissue, distinguishing three stages: stage 1 – normal or mild atrophy (muscle tissue volume – 60–100 %); stage 2 – moderate atrophy (muscle tissue volume – 40–60 %); stage 3 – severe atrophy (muscle tissue volume – less than 40 %) [9].

DIAGNOSTICS

Clinical examination, X-ray, ultrasound and MRI of the shoulder joint are the main methods used to diagnose rotator cuff injuries.

The clinical picture of the disease is dominated by pain syndrome, impaired abduction, flexion and rotation of the shoulder, as well as decreased strength in the affected arm. The history usually includes a fall on an outstretched arm or excessive physical exertion. The professional activities associated with prolonged work with arms raised upwards or in static tension of the thoracic girdle being one of the factors. During visual examination, asymmetry of the shoulder joints as a result of muscle hypotrophy of the deltoid and infraspinatus muscles is observed. Assessment motion test (simultaneous abduction and raising of both hands, raising hands behind the head and putting them behind the back) and comparison of the range of active and passive motions allow to reveal the functional deficit and its degree. Resis-

tive tests allow a more accurate localisation of the injury by the appearance of pain when counteracting active hand motions. Pain in resistive abduction indicates a tendon of the supraspinous muscle, in resistive external rotation – tendon of the infraspinatus muscle, in resistive internal rotation – tendon of the subscapularis muscle. A "falling arm" positive test (smooth lowering of the arm from the abduction position up to 120° is not feasible) also indicates rotator cuff damage [10–12].

Comparative X-ray of both shoulder joints in direct projection will be uninformative in small ruptures, but in old large and massive ruptures the clear signs will be a decrease in the height of the subacromial space and upper subluxation of the humeral head. This examination method also reveals the presence and degree of arthropathy developed as a result of rotator cuff rupture (according to K. Hamada classification).

Ultrasound examinations are of little use in routine practice. Generally, this method is used when there are contraindications with an MRI. In large and massive tendon injuries, its accuracy and specificity are higher than in smaller volume injuries [13, 14].

MRI is currently the most informative and used diagnostic method. Its accuracy and specificity are maximised as a result of the clear visualisation of soft tissue structures and the possibility of evaluating the image in all dimensions. Apart from being able to directly visualise the area of injury, it is possible to assess its volume, the degree of tendon retraction and the degree of muscle fatty dystrophy. The use of classifications assessing these parameters (Patte, Thomazeau) facilitates the prediction of the course of the disease and the planning of a particular treatment method.

NONSURGICAL TREATMENT

Nonsurgical treatment of rotator cuff tears is primarily intended to improve quality of life by reducing pain, strengthening the shoulder girdle muscles, resulting in stabilisation of the shoulder joint and increased range of motion. Therapies include physical therapy, local injection therapy, and physiotherapy. Unfortunately, this approach requires a long period of time and its effectiveness is not high enough. In 2015, C. Schmidt et al. analyzed the effectiveness of this method. The course of nonsurgical treatment was followed for 3 months, with 75 % of patients experiencing improvement between the 6th and 12th week of treatment, but 25 % of patients did not show a positive effect of therapy and underwent surgical treatment [15]. P.O. Zingg et al. in their study also indicate that despite the apparent positive effect, its duration is not to be long-term [16].

Local injection therapy with glucocorticosteroid preparations, despite the rapid achievement of analgesic effect, is associated with the risk of aggravation of degenerative processes in the tendon tissue, its loosening and the appearance of local necrosis [17]. The use of hyaluronic acid preparations in this pathology also demonstrates low efficacy, requires prolonged use and is unable to ensure the absence of pain syndrome recurrence for a long period of time [18].

Among patients with symptomatic rotator cuff tendinopathy persisting for at least 1 year, 39 % had progression to partial or complete rupture by follow-up MRI. When patients were grouped by time between scans (1 to 2 years, 2 to 5 years, or more than 5 years), the incidence of tendinopathy before rupture was 32 %, 37 %, and 54 %, respectively [19].

SURGICAL TREATMENT

There are three main areas of surgery in rotator cuff injuries: tendon restoration, muscle transfer and shoulder endoprosthesis replacement.

The first mention of surgical treatment in rotator cuff injury is over a century old. In 1911, A. Codman performed open tendon reinsertion to the humerus. Further development of the technique was proposed by N. McLaughlin, O. Debeyre and D. Patte, who performed an extensive release of the injured tendons and muscles with their complete excision from the scapula body and subsequent covering of the defect. The rapid spread of arthroscopic techniques and the advent of anchor fixators has revolutionized reconstructive shoulder surgery since the 1990s [20]. Acute, long-standing partial injuries may respond well to this method, but in massive defects with significant tendon retraction and marked fatty muscle dystrophy, the risk of recurrence is significantly increased [21]. According to J.C. Yoo et al. the incidence of recurrent ruptures during arthroscopic refixation reaches 45.5 % [22]. A study conducted by A. Green et al., consisting of a long-term (up to 15 years) follow-up of a patient group aged up to 61 years, revealed that functional outcomes assessed by questionnaire were relatively stable at long-term follow-up after rotator cuff restoration irrespective of instrumentally confirmed tissue deterioration, and few statistically significant relationships between structural and functional outcomes were found. This indicates that rotator cuff restoration is not effective in stopping the progression of degenerative processes, but can slow it down, as well as that patients adapt to structural changes with age and preserve a subjectively high level of their life quality [23].

As a result, the idea of plasty of massive ruptures with significant tendon rupture with grafts from similar tissues of the patient or with allografts of dermal matrix was further developed. According to J.L. Bond et al. the frequency of allograft rejection reaches 36 % [24, 25]. Notwithstanding these reasons, the allograft is widely used in foreign practice, particularly as a consequence of its higher strength characteristics in comparison with own tendon tissues [26]. Often this intervention is combined with acromioplasty to reduce graft pressure in the subacromial space. Furthermore, T. Mihata in 2012 proposed capsuloplasty with fixation of the proximal edge of the graft not to the tendon stump of the rotator cuff, but directly to the articular process of the scapula. In this way,

a "hammock" effect is obtained, centring the head relative to the articular socket of the scapula [27, 28].

Muscle transfer has also emerged as an answer to the problem of long-standing massive rotator cuff injuries. It was first used by J. I'Erissoro, who in 1934 performed transposition of tendons of the latissimus dorsi and teres minor muscle in a patient with Duchenne-Erb's palsy. Further development of the technique using different variations of the transfer was proposed by C. Gerber and A. Gilbert., who finally came to an isolated open transposition of the latissimus dorsi tendon in 1988 in order to restore external rotation of the shoulder and provide shoulder abduction due to the work of the deltoid muscle [29]. Thanks to improvements in surgical technique in 2003 E. Gervasi performed arthroscopically associated transposition of the latissimus dorsi tendon. However, this method has not been widely used in practice since its technical complexity and high requirements for the surgeon's qualification [30]. Even less common is the greater pectoral muscle tendon transfer proposed by M.A. Wirth and S.A. Rockwood in 1997. The statistics collected by various authors are contradictory. The authors note a high success rate (up to 84 %) in primary intervention, but at the same time a high probability of graft rupture at the site of its fixation to the humerus (up to 38 %) and up to 61 % of complications in revision surgeries.

Shoulder endoprosthesis replacement serves as an alternative to reconstructive surgery and muscle transfer. This surgery was first performed in 1893 by J.E. Pean. Having undergone many evolutions in both prosthetic concepts and surgical techniques, three main types of prosthetics have now emerged: anatomical, superficial, and reverse prosthetics. Anatomical and superficial prosthetics involve preserving the integrity of the rotator cuff, while reverse prosthetics are applicable in cases of rotator cuff injuries, including shoulder arthropathy. The first mention of this type of prosthesis was made in 1972 by B. Reeves. Although it was not used in clinical practice, the design served as a source of further technique development until 1987, when P.M. Grammont proposed his reversible system, the main advantage of which was optimal involvement of the deltoid muscle, which compensated for the deficit of abduction associated with rotator cuff dysfunction. Modern reversible Delta shoulder prostheses, the prototype of which is the Grammont prosthesis, are widely used in world practice [31]. Chronic pain syndrome and pseudoparalysis of the upper extremity, which are manifestations of arthropathy of the shoulder joint developed as a consequence of a large or massive rupture of the rotator cuff, constitute the main indications for reverse endoprosthesis replacement. Recently, the indications for this surgery have been expanding to include massive non-repairable rotator cuff ruptures without signs of degeneration and destruction of the cartilage of the humeral head and articular surface of the scapula [32]. It is associated primarily with the accumulation of positive statistics about the effectiveness of this intervention. However, there are disadvantages of endoprosthesis replacement that significantly limit its use. First of all, it is a significant limitation of loads on the prosthetic extremity, which is unacceptable in young patients with a high level of physical activity. The range of motion in the shoulder joint is also reduced, especially its flexion. A further negative factor involves the need to perform revision surgeries as the prosthesis components wear out mechanically. There is a high risk of implant instability, dislocation, paraprosthetic infections, especially in the case of rheumatoid joint surgery. The incidence of complications in reverse shoulder endoprosthesis replacement after massive rupture of the rotator cuff and concomitant arthropathy can be as high as 20 % according to some reports [33, 34].

The use of a subacromial balloon spacer should be emphasised separately. This method was first described by E. Savarese and R. Romeo in 2012. The essence of the method consists of inserting a biodegradable inflatable balloon into the subacromial space after revision of the subacromial space, which pushes the humeral head downwards, thus levelling the subacromial conflict. An obvious advantage of it lies in the least complicated and least traumatic surgical technique as compared to classical techniques. At the same time, however, its mass application has significant limitations that narrow the indications for its use: preserved active shoulder abduction up to 90°; intact tendon rupture of the teres minor muscle; absence of arthropathy of the shoulder joint on the background of the rotator cuff massive rupture; patient's age over 65 years [35].

Also noteworthy is the development of tenogenic patches (TENOPatch), which serve as a matrix for the formation of collagen fibres binding tendon residual limb and bone. The technique has been tested using laboratory animals, but has not been subjected to clinical trials [36].

CONCLUSION

Surgery of massive rotator cuff injuries is a dynamic branch of modern orthopedics. MRI and modern optics have made it possible to make a qualitative transition in the diagnosis and treatment of this pathology, and provided a key in understanding the biomechanics of the shoulder joint, the reasons for the aggravation of the pathological process and the development of complications. There are still unresolved issues, however, the methodologies used are imperfect, the advantages of each are balanced by the disadvantages, and the advantages are not obvious. Literature data are often conflicting in assessing treatment outcomes. The combination of these circumstances provides a wide world of opportunities in the field of research, optimisation of classical and introduction of new methods of treatment of this pathology. In the authors' opinion, the rational approach is sequential treatment with a preference for organ-preserving interventions; shoulder endoprosthesis replacement remains a last resort when other surgical options have been exhausted.

Conflict of interest

The authors of this article declare no conflicts of interest.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

REVISION SURGERY FOR FAILURE OF THE DYNAMIC STABILIZATION SYSTEM OF THE LUMBAR SPINE

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ABSTRACT

The aim of the study. *To study the frequency and treatment options for dysfunction of the dynamic stabilization system of the lumbar spine.*
Materials and methods. *We carried out a retrospective analysis of the treatment of 58 patients with degenerative pathology of the lumbar spine and instability of the spinal motion segments, who were treated at the neurosurgical unit of the Irkutsk Scientific Centre of Surgery and Traumatology in 2011–2020. The stability of spinal motion segment was assessed using X-ray imaging, magnetic resonance imaging and tomography of the lumbar spine. Revision surgery was performed in 7 out of 58 previously operated patients using the Coflex dynamic fixation system of spinal motion segments (Paradigm Spine LLC, Germany).*
Results. *Revision surgery was performed in 7 out of 58 patients with dynamic fixation of the spinal motion segments with an interosseous implant due to an increase in pain syndrome. In 1 patient, the reason for repeated surgery was primary instability of the fixation system caused by a fracture of the spinous process. In the delayed period, 4 patients had an X-ray picture with heterotopic ossification of the implant and instability of spinal motion segments. In two observations, a recurrence of intervertebral hernia was diagnosed at the level of the operated spinal motion segment. During revision surgery, a facetectomy was performed with stabilization by a peek cage, followed by pain management and clinical manifestation regression.*
Conclusion. *The conducted study shows that a number of patients after discectomy and dynamic stabilization of the spine using "Coflex" system have inconsistency and heterotypic ossification of the implant and neoarthrosis. Implantation of a lumbar peek cage while maintaining the "Coflex" device makes it possible to form a rigid interbody fusion, which means it is sufficient and justified surgical technology for treating the failure of the dynamic stabilization system.*

Key words: *segmental instability of the spine, dynamic stabilization, heterotypic ossification, repeated surgical interventions, revision surgery*

Received: 31.05.2023
Accepted: 01.11.2023
Published: 05.12.2023

For citation: Potapov V.E., Larionov S.N., Zhivotenko A.P., Gorbunov A.V., Sorokovikov V.A. Revision surgery for failure of the dynamic stabilization system of the lumbar spine. *Acta biomedica scientifica*. 2023; 8(5): 157-165. doi: 10.29413/ABS.2023-8.5.17

РЕВИЗИОННАЯ ХИРУРГИЯ ПРИ НЕСОСТОЯТЕЛЬНОСТИ СИСТЕМЫ ДИНАМИЧЕСКОЙ СТАБИЛИЗАЦИИ ПОЯСНИЧНОГО ОТДЕЛА ПОЗВОНОЧНИКА

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РЕЗЮМЕ

Цель исследования. *Изучить частоту и варианты лечения дисфункции системы динамической стабилизации поясничного отдела позвоночника.*
Материалы и методы. *Проведён ретроспективный анализ лечения 58 пациентов с дегенеративной патологией поясничного отдела позвоночника и нестабильностью позвоночно-двигательных сегментов (ПДС), находившихся на лечении в отделении нейрохирургии ФГБНУ «Иркутский научный центр хирургии и травматологии» в период с 2011 по 2020 г. Оценка стабильности ПДС осуществлялась при рентгенографии, магнитно-резонансной томографии и мультиспиральной компьютерной томографии поясничного отдела позвоночника. Ревизионные вмешательства выполнены 7 из 58 ранее оперированных пациентов с применением системы динамической фиксации ПДС «Coflex» (Paradigm Spine LLC, Германия).*
Результаты. *Ревизионные хирургические вмешательства выполнены 7 из 58 пациентов с динамической фиксацией ПДС межостистым имплантом в связи нарастанием болевого синдрома. У одного больного поводом к повторной операции послужила первичная нестабильность металлоконструкции, обусловленная переломом остистого отростка. В отсроченном периоде у 4 пациентов выявлена рентгенологическая картина гетеротипической оссификации конструкции и нестабильность ПДС. В двух наблюдениях на уровне оперированного ПДС диагностирован рецидив межпозвонковой грыжи. При ревизионном вмешательстве проведена фасетэктомия со стабилизацией peek-кейджем с последующим купированием болевого синдрома и регрессом клинических проявлений.*
Заключение. *Проведённое исследование свидетельствует о том, что у ряда пациентов после дискэктомии и динамической стабилизации позвоночника системой «Coflex» развивается несостоятельность и гетеротипическая оссификация импланта, формируется неоартроз. Имплантация поясничного peek-кейджа при сохранении устройства «Coflex» позволяет сформировать ригидный межтеловой спондилодез, то есть является достаточной и обоснованной хирургической технологией лечения несостоятельности конструкции динамической стабилизации.*

Ключевые слова: *сегментарная нестабильность позвоночника, динамическая стабилизация, гетеротипическая оссификациия, повторные хирургические вмешательства, ревизионная хирургия*

Статья поступила: 31.05.2023
Статья принята: 01.11.2023
Статья опубликована: 05.12.2023

Для цитирования: Потапов В.Э., Ларионов С.Н., Животенко А.П., Горбунов А.В., Сороковиков В.А. Ревизионная хирургия при несостоятельности системы динамической стабилизации поясничного отдела позвоночника. *Acta biomedica scientifica*. 2023; 8(5): 157-165. doi: 10.29413/ABS.2023-8.5.17

INTRODUCTION

One of the actual problems of spinal neurosurgery is the treatment of degenerative pathology of the lumbar spine. The existing methods of surgical treatment of degenerative-dystrophic spine diseases, unfortunately, cannot be considered ideal [1, 2]. The use of microsurgical techniques and modern instrumental technologies in spine surgery does not exclude the recurrence of pain syndrome [3–5]. Attempts to improve outcomes and avoid exacerbation of pain have motivated specialists to search for new solutions to the problem [6–8]. Biomechanically based technologies of dynamic and rigid stabilization of the spinal motion segment (SMS) have been actively used over the last decades. The range of surgical interventions is quite diverse and includes techniques of transpedicular fixation and articular, interspinous or anterior spondylodesis with implants of various modifications [9–12].

THE AIM OF THE STUDY

To study the incidence and treatment options for failure of the posterior dynamic stabilization system.

Lumbar spine herniation surgery is often accompanied by structural transformation of the SMS support complex and disturbance of the spine biomechanics. A recent study has established a correlation between degenerative changes in SMS structures and sagittal balance or spatial stability, while the volume of active and passive movements of the vertebral column is usually dependent on the severity of bone and joint transformations [11, 13]. The study by D. Butler et al. was a prerequisite for the use of dynamic spinal segment stabilization [14], in which the authors revealed the interdependence of degenerative changes in the facet joints and intervertebral discs. The results of studies have shown that as a result of impaired SMS biomechanics, the intervertebral disc is primarily affected. Further limitations of segment mobility, rearrangement processes and redistribution of mechanical loads cause damage to facet joints, development of osteoarthritis and joint instability.

Dynamic stabilization devices are used to unload the posterior support complex, which includes the facet joints, spinous processes and part of the fibrous ring of the intervertebral disc, in order to preserve the range of physiological motions and prevent adjacent level pathology [11, 15]. The need to preserve the biomechanics of the supporting structures of the spinal motion segments and prevent disease progression was the basis for the use of the dynamic interspinous system [15]. Interosseous fixators are made of titanium alloy, which ensures sufficient strength, stiffness, and biocompatibility with a low risk of artefact formation during magnetic resonance imaging (MRI) [16–19]. The main objectives of the design include reducing the load on the facet joints, preserving the physiological volume of movement in the SMS with adequate stress distribution over the pathologically altered and adjacent SMS.

MATERIAL AND METHODS

The study was based on a retrospective analysis of treatment of 58 patients with degenerative lesions of the lumbar spine who underwent surgery using dynamic spinal stabilization with the Coflex system (Paradigm Spine LLC, Germany) and were treated at the Department of Neurosurgery of the Irkutsk Scientific Center for Surgery and Traumatology from 2011 to 2020. They included 18 females and 40 males aged 17 to 63 years (47.4 ± 9.4 years). Instrumental and neuroimaging methods of spinal examination included review and functional radiography, computed tomography (CT) (42 cases), MRI (58 cases), and CT-myelography (27 cases) of the lumbar spine. The functional state of the SMS was assessed by analyzing lumbar spine radiography data with loading tests in the 30° and 90° flexion positions. To study the biomechanical stability of the operated spinal segment with the implanted interosseous fixation system at adjacent levels, morphometric parameters were studied: frontal, oblique, and sagittal dimensions of the spinal canal; dimensions and angular indices of the facet joints conjugation.

Surgical treatment – excision of disc herniation or bone and cartilage formation with stabilization of the segment with the Coflex interosseous dynamic system was performed in 58 patients.

The indications for revision surgery were persistent pain syndrome that could not be treated with nonsurgical methods of treatment; MRI or CT data showing radicular compression in the area of the degeneratively altered segment; detection of SMS instability. Interosseous fixation at the level of L_{IV}–L_V was performed in 48 (83 %) patients, at the level of L_{II}–L_{III} – in 2 (3 %) patients, at the level of L_{III}–L_{IV} – in 3 (5 %) patients, at the lumbosacral L_V–S_I level – in 5 (9 %) patients. In 35 cases, the implant was installed during revision intervention, of which 6 patients had posterior interosseous stabilization due to recurrence of herniated disc L_{IV}–L_V and L_V–S_I; in 11 cases, degenerative spinal canal stenosis at an adjacent level due to spondyloarthrosis with marginal osteophyte growths; in 18 patients, a combination of herniation occurred or protrusions with degenerative stenosis. Surgical intervention with dynamic fixation using the Coflex system was performed initially in 23 patients in the course of disc herniation excision.

Revision intervention in patients with device failure, neoarthrosis and heterotopic ossification of the Coflex system included anterior stabilisation using an interbody lumbar peek cage. In one patient, the reason for a second surgery was the primary instability of the surgical hardware associated with a fracture of the implant-fixed spinous process. During a delayed period, 2 and 4 years after surgery, 4 patients revealed a radiological picture of heterotopic ossification of the structure and SMS instability; recurrence

of the intervertebral hernia was diagnosed in 2 patients. The study protocol was approved by the local ethical committee of Irkutsk Scientific Centre of Surgery and Traumatology (minutes No. 1 dated January 22, 2019).

All data are submitted as quantities and percentages. Differences between groups were assessed using Chi-square with Yates correction and Fisher's criterion.

RESULTS AND DISCUSSION

Repeated intervention in cases of dynamic stabilisation system failure was performed in 7 (12 %) out of 58 patients, and spondylodesis was formed using a lumbar peek-cage and retaining the Coflex device integrated with the osseous tissue of the spinous processes.

Progressive intervertebral disc degeneration was diagnosed by CT and MRI based on the detection of hypertrophy of the articular processes, the presence of gas in the joint cavity (vacuum phenomenon) in 6 patients and spinal canal stenosis in 2 patients.

A complete regression of neurological deficit after revision surgery was observed in 6 (86 %) patients. The dynamics of sensory and motor impairments in the early and remote postoperative periods is summarised in Table 1.

Analysis of the treatment results revealed that in the process of intervertebral disc degeneration, its cushioning properties are impaired, which is a prerequisite for the development of linear and angular displacement of adjacent vertebral bodies and, subsequently, the formation of segment instability. The use of an interosseous implant is aimed at prosthetic disc properties, preventing further SMS degeneration and instability. The tissue ossification in the area of the working surfaces of the fixator eventually causes a significant decrease in the Coflex's shock-absorbing properties, and the device acquires the characteristics of a fixation spacer.

The fact that interosseous implants are not biologically inert cannot be ignored. Furthermore, such factors as metal stress and, as a consequence, micromobility cause changes in the implant structure and are a predisposing factor in the formation of imbalance of mechanical loads on the articular processes with the development of clinical manifestations of construct failure [20, 21].

Prolonged use of the Coflex fixator leads to the formation of another specific complication, namely, heterotopic ossification of the interosseous stabilization de-

TABLE 1
DYNAMICS OF SENSORY AND MOTOR IMPAIRMENTS (*n* = 7)

Impairments revealed	Before the surgery	9, 24 months after surgery	48 months after surgery
Vertebrogenic syndrome	7 (100 %)	5 (71 %)	1 (14 %)
Sensation disorders			
hypesthesia	7 (100 %)	2 (29 %)	1 (14 %)
anesthesia	4 (57 %)	1 (14 %)	1 (14 %)
hyperesthesia	2 (29 %)	1 (14 %)	–
paresthesia	3 (43 %)	1 (14 %)	–
Decreased muscle strength in the lower extremity:			
weakness of the thigh and lower leg muscles	4 (57 %)	1 (14 %)	1 (14 %)
foot muscle weakness	5 (71 %)	2 (29 %)	2 (29 %)
paresis of the extensor muscles of the foot	3 (43 %)	–	–
Reflex disorder:			
knee	5 (71 %)	2 (29 %)	1 (14 %)
Achilles'	2 (29 %)	1 (14 %)	1 (14 %)
Straight leg raise	7 (100 %)	–	–

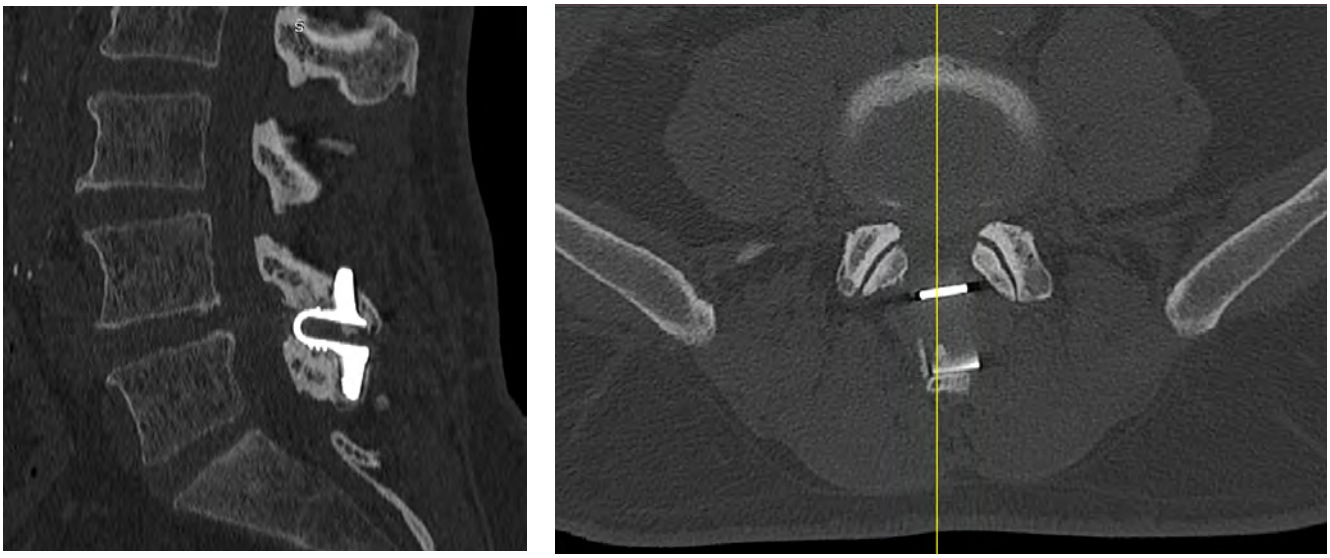
vice, which leads to the development of "adjacent level" pathology. For instance, implant failure with ossification was reported in 3 out of 35 cases in repeat surgeries and in 1 out of 23 cases in primary surgeries. Chi-square with Yates' correction ($p = 0.928$) and Fisher's two-sided test ($p > 0.05$) were used to identify the dependency of the risk of implant failure with the incidence of surgery. The results of the analyses indicate that the relationship of implant failure with repeat or primary surgery is very weak. Consequently, repeated intervention does not have a statistically significant effect as regards the risk of construct dysfunction. The problem requires further investigation, however, to identify the cause-and-effect relationships of the dynamic stabilization system failure.

The clinical observation presented below is a clear evidence of this postulate.

CLINICAL CASE STUDY

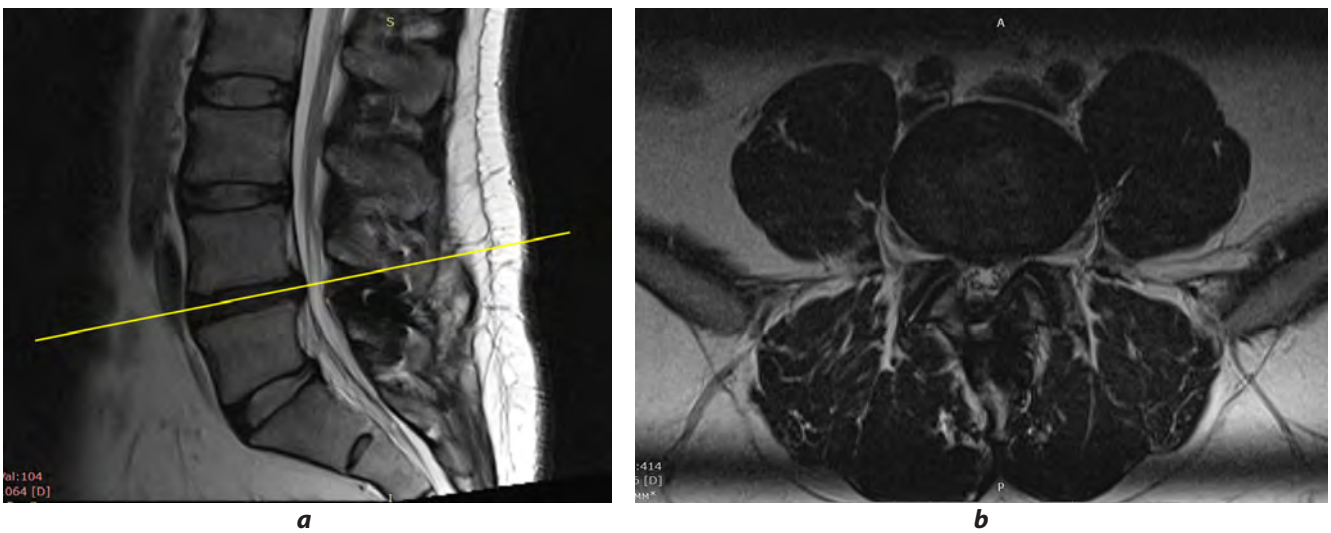
Patient P., 48 years. Diagnosis: degenerative lateral (foraminal) stenosis of the spinal canal at the level of L_{IV}–L_V on the left. Bone and cartilage junction L_{IV}–L_V. Deforming spondylosis. Spondyloarthrosis. Postoperative epidural fibrosis, the presence of a system of interosseous dynamic fixation of the spine at the level of L_{IV}–L_V. L_5 radiculopathy on the left. Severe pain and musculotonic syndromes.

Pain in the lumbar spine and the left lower limb has been bothering for 3 months. The pain is accompanied by restriction of active movements in the lumbar spine, intensifies in the vertical position and when walking, irradiates to the outer surface of the left thigh and lower leg.



a ***b***

FIG. 1.
*Patient P. Computed tomography of the lumbar spine. Multiplanar reconstruction in the sagittal plane (**a**), axial section (**b**)*



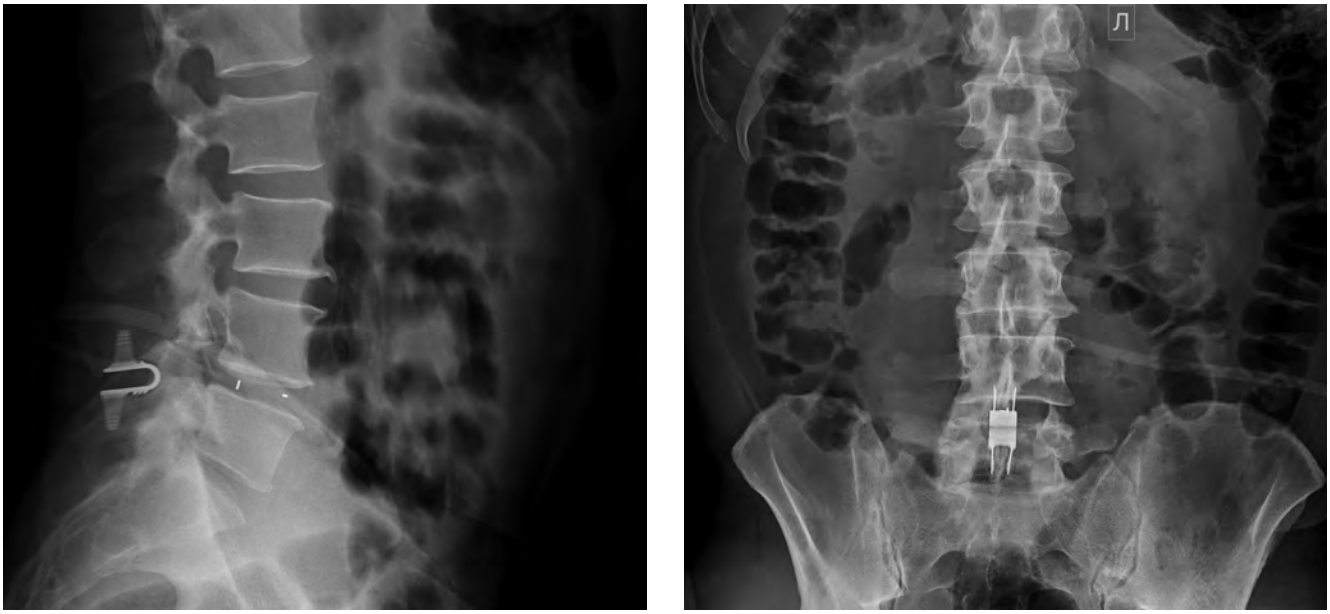
a ***b***

FIG. 2.
*Patient P. MRI of the lumbar spine. T2 weighted images: sagittal (**a**), axial section (**b**)*

Past medical history: twice underwent surgery on the lumbar spine: in 2011 – excision of L_{IV}–L_V disc herniation on the left side with installation of Coflex dynamic system (Paradigm Spine LLC., USA). In 2014, a revision and microsurgical foraminotomy was performed along the L_5 root on the left.

According to the patient, over the past year, he began to notice an increased in pain in the lumbar spine associated with physical exertion. The conservative treatment performed by a neurologist has no effect. According to MRI of the lumbar spine, the patient had a recurrence of median herniated disc L_{IV}–L_V (Fig. 2).

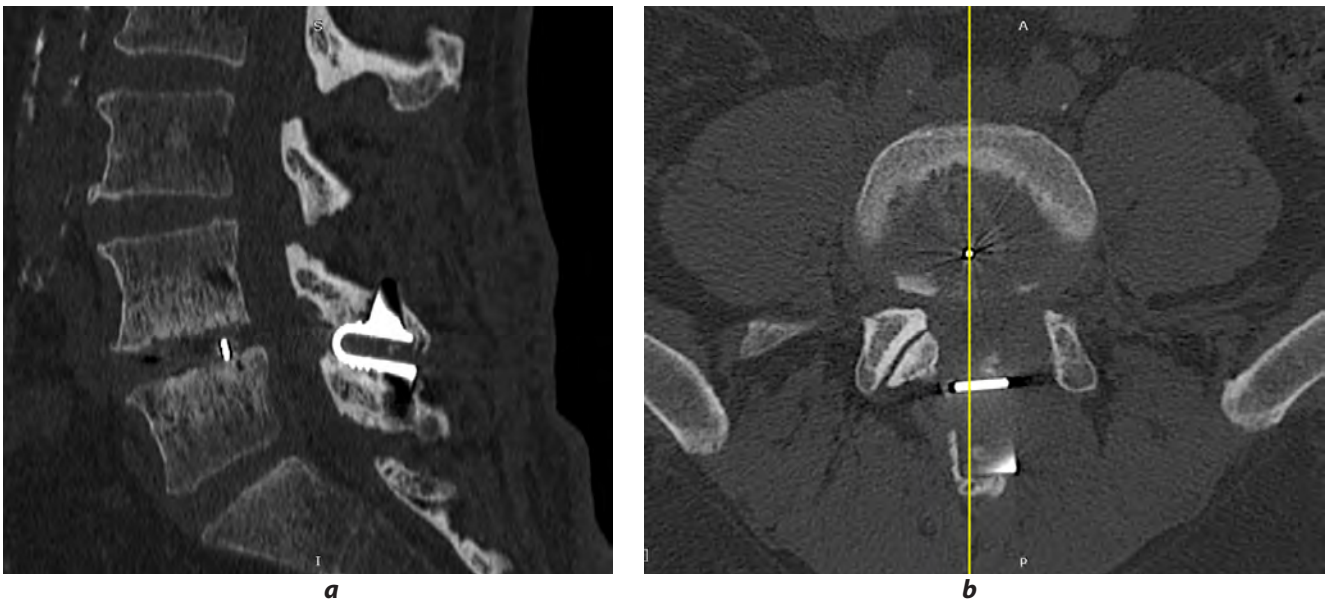
CT of the lumbar spine revealed a number of features of the condition of the interosseous fixator, which integrated into the bone tissue of the spinous processes; the space of the working dynamic loop of the metal structure was filled connective tissue with elements of bone restructuring (Fig. 1).



a ***b***

FIG. 3.

*Patient P. Spondylograms in lateral (**a**) and frontal (**b**) view in the postoperative period*



a ***b***

FIG. 4.

*Patient P. Computed tomography of the lumbar spine 6 months after the surgery. Multiplanar reconstruction in the sagittal plane (**a**), axial section (**b**). The marks of the anterior and posterior edges of the interbody cage are determined. Formation of the anterior fusion*

Surgery (June 18, 2020): interlaminectomy, medial facetectomy, microsurgical decompression of the L_5 root on the left. Removal of the osteochondral junction L_{IV}–L_V. L_{IV}–L_V interbody spondylodesis with lumbar peek cage.

The postoperative period proceeded without complications. Activated on the day 2 after surgery. Regression of pain vertebrogenic and radicular syndromes was observed. Discharged from the department for rehabilitation treatment on the day 7 in a satisfactory condition. No complaints during the follow-up period, the implant and interosseous fixator are stable radiologically (Fig. 3, 4).

DISCUSSION

Analysis of the treatment results of patients who underwent discectomy with dynamic fixation of the spinal motion segment using an interosseous implant demonstrates its effectiveness and ability to prevent recurrence of pain syndrome as well as the development of pathology at the adjacent level. At the same time, although the dynamic interosseous fixation system does not result in closure of the spinal motion segment, the radiological signs of degeneration of the intervertebral disc and the facet joints of the overlying segments revealed indicate a risk of spinal canal stenosis. The interosseous dynamic implant becomes functionally deficient over time and is involved in the formation of heterotopic ossification or posterior "bone-metallic" pseudoarthrosis [15]. According to A.E. Simonovich (2005) and C. Thome et al. (2005) [13, 22], the dynamic systems' design features do not simultaneously ensure the preservation of biomechanics and reliable support of the spinal segment.

Additional implantation of a lumbar peek cage while retaining the Coflex system created a rigid interbody spondylosis without the use of SMS transpedicular fixation. This tactic is justified both from the point of view of preserving the support of the anterior complex and from the point of view of treating segment instability. The spinal canal and intervertebral disc are accessed by interlaminectomy and medial facetectomy, which reduces the traumatic nature of the surgery itself.

Formation of spondylodesis without removal of the Coflex system using an intervertebral cage is a sufficient and reasonable technique, but in some cases it can be supplemented with monosegmental transpedicular fixation.

The implant's integration with the spinous process bone tissue, as well as the peek-cage with the closing plates of the adjacent vertebrae, ensures consolidation sufficient for spondilodesis. The existence of hollow spaces in the body of the cage, filled with bone material, favours the formation of a solid spondylodesis and accelerated formation of the bone block. The posterior interosseous dynamic stabilization technique can be used as an alternative and in some cases as a preliminary stage of spondylodesis formation.

CONCLUSION

This study reveals that a number of patients after discectomy and dynamic spine stabilisation with the Coflex system suffer from segmental instability as a consequence of heterotypic ossification and neoarthrosis formation and often require revision intervention. Formation of a spondylodesis using an intervertebral cage and retention of the Coflex system is an effective means of resolving the problem.

Funding

The authors declare that there was no external funding in conducting the study.

Conflict of interest

The authors declare the absence of apparent and potential conflicts of interest related to the publication of this article.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

THE RESULTS OF TREATMENT OF FEMORAL DIAPHYSIS FRACTURES USING LOCKED INTRAMEDULLARY OSTEOSYNTHESIS AND EXTRAMEDULLARY OSTEOSYNTHESIS (RESULTS FOR 10 YEARS)

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ABSTRACT

Background. *Femoral diaphysis fractures are one of the most common and significant injuries to the bones of the limbs. Locked intramedullary osteosynthesis makes it possible to reduce the injury rate of the surgery and its length, as well as to carry out early rehabilitation of patients.*

The aim of the study. *To conduct a continuous retrospective single-purpose comparative study of the results of treatment of patients with femoral diaphysis fractures treated with locked intramedullary osteosynthesis and extramedullary osteosynthesis for 10 years. This study did not include patients with double femoral fractures treated by osteosynthesis using a combination of two implants – locked intramedullary implant and extramedullary implant.*

Material and methods. *We conducted a retrospective study of the results of treatment of patients from 2011 to 2020. During this period, we treated 794 patients aged from 16 to 77 years with femoral diaphysis fractures. The share of people of working age was 75 %. The patients were divided into two groups depending on the method of surgical treatment. Group 1 included 500 patients who had surgical treatment using locked intramedullary osteosynthesis. Group 2 included 294 patients who had surgical treatment using extramedullary osteosynthesis.*

Results. *In patients of group 1 treated with locked intramedullary osteosynthesis, good anatomical and functional treatment results were achieved in 70 % of cases; satisfactory treatment results – in 25.2 % of cases, unsatisfactory results – in 4.8 %. In the group 2, good results were achieved in 61.9 % of cases, satisfactory – in 29.6 %, unsatisfactory – in 8.5 %.*

Conclusion. *The obtained results of treatment of femoral diaphysis fractures show the undeniable advantage of using locked intramedullary osteosynthesis compared to extramedullary osteosynthesis.*

Key words: *femoral diaphysis fracture, extramedullary osteosynthesis, locked intramedullary osteosynthesis, complications of femoral osteosynthesis*

Received: 12.02.2023
Accepted: 01.11.2023
Published: 05.12.2023

For citation: Fedorov V.G., Kuzin I.V. The results of treatment of femoral diaphysis fractures using locked intramedullary osteosynthesis and extramedullary osteosynthesis (results for 10 years). *Acta biomedica scientifica*. 2023; 8(5): 166-173. doi: 10.29413/ABS.2023-8.5.18

РЕЗУЛЬТАТЫ ЛЕЧЕНИЯ ПЕРЕЛОМОВ ДИАФИЗА БЕДРЕННОЙ КОСТИ БЛОКИРУЕМЫМ ИНТРАМЕДУЛЛЯРНЫМ И НАКОСТНЫМ ОСТЕОСИНТЕЗОМ (ИТОГИ ЗА 10 ЛЕТ)

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РЕЗЮМЕ

Обоснование. *Переломы диафиза бедренной кости являются одними из наиболее распространённых и значимых повреждений костей конечностей. Блокируемый интрамедуллярный остеосинтез (БИОС) позволяет уменьшить травматичность операции и время её проведения, а также проводить раннюю реабилитацию пациентов.*

Цель исследования. *Провести сплошное ретроспективное одноцелевое сравнительное исследование результатов лечения пациентов с переломами диафиза бедренной кости, лечившихся способом блокируемого интрамедуллярного остеосинтеза (БИОС) и способом накостного остеосинтеза пластинами, за 10 лет. Не включены в данное исследование пациенты с двойными переломами бедренной кости с остеосинтезом сочетанием двух имплантов – БИОС и накостного.*

Материал и методы. *Нами проведено ретроспективное исследование результатов лечения пациентов с 2011 по 2020 г. В отделении за данный период было пролечено 794 пациента в возрасте от 16 до 77 лет с переломами диафиза бедренной кости. Доля лиц трудоспособного возраста составила 75 %. Пациенты были разделены на две группы в зависимости от применённого метода оперативного лечения. Первая группа – оперативное лечение методом интрамедуллярного блокируемого остеосинтеза (500 пациентов). Вторая группа – оперативное лечение методом накостного остеосинтеза пластинами (294 пациента).*

Результаты. *В первой группе пациентов, пролеченных методом БИОС, хорошие анатомо-функциональные результаты лечения были достигнуты в 70 % случаев; удовлетворительные результаты лечения – в 25,2 % случаев, неудовлетворительные результаты – в 4,8 %. Во второй группе хорошие результаты достигнуты в 61,9 % случаев, удовлетворительные – в 29,6 %, неудовлетворительные – в 8,5 %.*

Заключение. *Полученные результаты лечения переломов диафиза бедренной кости показывают неоспоримое преимущество применения блокируемого интрамедуллярного остеосинтеза по сравнению с накостным остеосинтезом.*

Ключевые слова: *перелом диафиза бедренной кости, накостный остеосинтез, блокируемый интрамедуллярный остеосинтез, осложнения остеосинтеза бедренной кости*

Статья поступила: 12.02.2023
Статья принята: 01.11.2023
Статья опубликована: 05.12.2023

Для цитирования: Федоров В.Г., Кузин И.В. Результаты лечения переломов диафиза бедренной кости блокируемым интрамедуллярным и накостным остеосинтезом (итоги за 10 лет). *Acta biomedica scientifica*. 2023; 8(5): 166-173. doi: 10.29413/ABS.2023-8.5.18

INTRODUCTION

Femoral shaft fractures are among the most common and significant injuries of extremity bones. These fractures are particularly common in victims with multiple and combined trauma. The frequency of these injuries has remained high in recent years [1, 2]. Femoral shaft fractures comprise up to 20 % of femoral shaft injuries [3, 4]. The technically correct and timely surgical treatment of these fractures directly affects the quality of life and further ability of patients to work. The incidence of various complications can range from 5 % to 35 % [5, 6]. Many different techniques are available and used for surgical treatment, the priority of which has changed with the passage of time and advances in technology. Since the mid-20th century, the emphasis was mainly focused on the use of external osteosynthesis with external fixation devices, which, despite their effectiveness, remained rather inconvenient and labour-intensive to use, required constant care of spokes and rods, and brought discomfort and inconvenience to patients. At the end of the 20th century, the priority in the treatment of these fractures shifted towards immersion extra-cortical osteosynthesis with plates [7–10].

A less invasive and more functional in the postoperative period method of treatment of femoral shaft fractures with an intramedullary locking nail became actively used in the early XXI century and subsequently became the gold standard of treatment.

This technique used in surgical treatment significantly reduces injuries to soft tissues during surgical access and the surgical access itself, eliminates the need for external immobilisation, allows for stable strong fixation, reduces the operation time. Locked intramedullary osteosynthesis (LIOS) can provide early activation and rehabilitation measures from the first days after surgery, which significantly reduces the risk of complications in the postoperative period [11, 12].

THE AIM OF THE STUDY

To conduct a continuous retrospective single-targeted comparative study of the treatment results in patients with fractures of the femoral shaft treated by locked intramedullary osteosynthesis and extra-cortical osteosynthesis with plates over a period of 10 years. All surgeries during the years under study were performed by surgical teams of the traumatology department, formed from physicians with the highest and first qualification category.

The work was approved at the meeting of the Local Ethical Committee of the Izhevsk State Medical Academy (Minutes No. 763 dated October 24, 2022), was carried out in accordance with the ethical standards of the World Medical Association Declaration of Helsinki "Ethical Principles of Scientific Medical Research Involving Human Subjects" as amended in 2013 and "Rules of Clinical Practice in the Russian Federation" approved by the order of the Ministry of Health of Russia dated June 19, 2003 No. 266. All patients signed informed consent to undergo a surgery and to publish the findings without identifying themselves.

MATERIAL AND METHODS

In the traumatology department of the First Republican Clinical Hospital of the Ministry of Health of the Udmurt Republic, locked intramedullary osteosynthesis has been used since 2010 along with extra-cortical osteosynthesis. A comparative analysis of the patient outcomes with femoral shaft fractures (according to AO fracture classification: 32A, 32B, 32C) between 2011 and 2020 was performed.

The study excluded patients with double femur fracture who were being treated with two methods of operative treatment – locked intramedullary osteosynthesis and extra-cortical osteosynthesis [13].

Statistical processing of the research was carried out in two directions. Firstly, the hypothesis of the equality of samples of the analyzed signs (Pearson's Chi-squared test) and the hypothesis of the difference in the effectiveness of the treatment methods used (Student's T-test) were tested. All calculations were performed using a personal computer.

During this period, 794 patients aged 16 to 77 years with femoral shaft fractures were treated in the department. The proportion of working-age individuals was 75 per cent.

Open fractures were observed in 24 (3 %) patients, multisegmental fractures in 27 (3.4 %) patients, and pathological fractures (benign and malignant tumors) in 8 (1 %) patients.

Patients were divided into two groups depending on the surgical treatment method they underwent. The first group included patients whose surgical treatment was implemented by the method of locked intramedullary osteosynthesis – 500 patients. The second group included patients who underwent extra-cortical osteosynthesis with plates – 294 patients.

The number of patients treated in different years is summarised in Table 1.

The table reveals that at the beginning of the second decade of the 21st century, LIOS of the femoral shaft is gradually becoming the main method of surgical treatment being used. Extra-cortical osteosynthesis of femoral shaft fractures has been gradually phased out since 2014. By the end of the second decade, LIOS was already being used in 3/4 of patients in our department.

According to the type of fracture received, the patients were distributed as follows (Table 2).

In terms of fracture type, simple A1–A3 type fractures were predominant in both groups (± 56.8 %). The low number of compound fractures of the C1–C3 type (< 5 %) is to be mentioned (Table 3).

In terms of gender composition, males predominated in both groups.

The mean age of patients in the first group was 49.76 ± 20.36 years and in the second group it was 47.04 ± 16.6 years.

TABLE 1

NUMBER OF PATIENTS WITH FEMORAL SHAFT FRACTURES OVER A 10-YEAR PERIOD (LIOS AND EXTRA-CORTICAL OSTEOSYNTHESIS)

Surgical treatment method	Year										Total (patients)
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	
LIOS	15	50	44	36	40	47	50	65	77	76	500
Extra-cortical osteosynthesis using plates	49	43	44	39	32	27	18	16	13	13	294

TABLE 2

DISTRIBUTION OF PATIENTS BY FRACTURE TYPE

Fracture type according to AO classification	Patients who underwent LIOS treatment	Patients who underwent extra-cortical osteosynthesis treatment
A1–A3 type fractures	291 (58.2 %)	163 (55.4 %)
B1–B3 type fractures	189 (37.8 %)	125 (42.5 %)
C1–C3 type fractures	20 (4 %)	6 (2.1 %)
Total	500 (100 %)	294 (100 %)

TABLE 3

AGE AND SEX DISTRIBUTION OF PATIENTS

Age (years)	Patients who underwent LIOS treatment	Men	Women	Patients who underwent extra-cortical osteosynthesis treatment	Men	Women
16–18	10 (2 %)	5 (50 %)	5 (50 %)	8 (2.7 %)	5 (62.5 %)	3 (37.5 %)
19–45	172 (34.4 %)	95 (55.2 %)	77 (44.8 %)	115 (39.1 %)	63 (54.8 %)	52 (45.2 %)
46–60	180 (36 %)	94 (52.2 %)	86 (47.8 %)	105 (35.7 %)	59 (56.2 %)	46 (43.8 %)
61 years and older	138 (27.6 %)	71 (51.5 %)	67 (48.5 %)	66 (22.5 %)	37 (56 %)	29 (46 %)
Total	500 (100 %)	265 (53 %)	235 (47 %)	294 (100 %)	164 (57.3 %)	130 (42.7 %)

In terms of age and gender composition, the groups were comparable to each other, as statistical analysis revealed no statistically significant differences ($p > 0.05$).

Patients were admitted to the hospital both initially for emergency indications and by transfer from central district hospitals (CDH) for surgical treatment in the first few days after injury. During hospitalisation standard manipulations and examinations were performed in accordance with the accepted standards – in case of fractures of bones of the lower extremity, ultrasound examination (US) of the lower extremity vessels to exclude blood clots in the veins was obligatory included. Our initial assumption for lower extremity venous ultrasound is that according to the Caprini scale of individual risk assessment for venous thromboembolic complications, all our patients had moderate or high risk of venous thromboembolic complications (bed rest for more than 72 hours and severity of operative treatment) [14]. Prior to surgery, patients with lower extremity injuries were under skeletal traction, and either osteosynthesis with external fixation apparatus as a stage of preoperative preparation was performed as an emergency indication.

The surgeries were performed after the acute period subsided after the patients recovered from shock, in average on the days 5–10. In case of venous thrombosis in the veins of the lower extremity, treatment with anticoagulants followed by ultrasound control of the veins was performed.

Early rehabilitation was used in the postoperative period no matter the method of femoral osteosynthesis. Motion in the joints adjacent to the fracture were commenced from the first day after surgery. Axial load (walk-

TABLE 4

LUBOSHITZ – MATTIS – SCHWARTZBERG FEMORAL FRACTURE TREATMENT OUTCOME ASSESSMENT SYSTEM

Indicator	Score, points		
	4	3	2
Pain	none	with heavy physical activity	with light physical activity
Radiological signs of fracture consolidation	fusion at mid-physiological term	slow consolidation	false joint
Shortening (anatomical)	none	up to 2 cm	over 2 cm
Segment deformation	none	up to 10°	over 10°
Range of motion in adjacent joints	full	minor restrictions	pronounced restrictions
Thigh muscle atrophy	none	up to 2 cm	over 2 cm
Vascular disorders	none	hypostatic edema	edema and other disorders
Neurological disorders	none	nerve paresis	nerve paralysis
Infectious complications	none	soft tissue	osteomyelitis
Functional fitness of the extremity, ability to work	restored, no means of additional support required	use of a walking stick, orthopedic shoes	loss of extremity support; need to use crutches

ing) was allowed on the next day after surgery or after the oedema had subsided, with the use of unloading aids on the days 3–4 depending on the somatic and functional status of the patient and the method of osteosynthesis. In case of LIOS, partial loading up to 30 % of the patient's weight (lightly stepping in) is permissible on the second or third day, and in case of extra-cortical osteosynthesis – after two months. When discharged from the hospital, the recommendations in case of LIOS included the necessity of dynamisation 2 months after surgery, as timely dynamisation is a preventive measure for delayed consolidation and formation of a false joint [15, 16].

Treatment results and the anatomo-functional state of the extremity were assessed according to the Luboshitz – Mattis – Schwartzberg outcome scorecard [17–19], considering the degree to which the patient returned to the premorbid level of extremity function. A comprehensive assessment of the obtained treatment results was performed using the clinical parameters summarised in Table 4. Ten parameters characterising the adequacy of reparative osteogenesis and its X-ray image, as well as the result of patient rehabilitation were assessed during the study of anatomo-functional results. Each of these indicators was evaluated in points – 4, 3, 2. Treatment outcome was assessed by dividing the sum of the numerical expressions of all indicators by the number of indicators studied. The resulting mean numerical expression for the anatomo-functional outcome (index) corresponded to the defined treatment outcome. An anatomo-functional result was considered good if the treatment index was 3.5–4, satisfactory if the index was 2.6–3.4, and unsatisfactory if the index was 2.5 points or less (Table 4).

RESULTS

The results of surgical treatment were monitored in all patients in 8–12 months (Table 5).

In the first group of patients treated by LIOS method, good anatomo-functional results of treatment were achieved in 350 (70 %) patients, satisfactory in 126 (25.2 %) patients, and unsatisfactory in 24 (4.8 %) patients.

Complications in the form of non-union of the fracture and formation of a false joint were revealed in 23 (4.6 %) cases. These complications were mainly observed in the group of patients of working age, from 19 to 60 years old. The causes of these complications were: soft tissue interposition; insufficiently accurate repositioning; combined trauma in the patient; lack of load on the operated extremity; not performed or not timely performed dynamisation of the fracture area. According to literature data, infectious complications comprise up to 4 % [20]; according to our data, these complications occurred in 1.4 % of patients underwent surgery (7 patients) for open fractures and against the background of, as a rule, high-energy trauma. Conventional antibiotic therapy after necrectomy resulted in cure. This is associated with the fact that patients with a suspicion of the possibility of infectious complications after the performed operation were under constant dynamic observation.

Patients with signs of non-union formation underwent the following surgeries at an early stage (1.5 time periods from the proper average physiological fusion of a particular bone, i. e. after 5–6 months): rod replacement with a larger diameter with reaming of the medullary canal; open re-

TABLE 5

TREATMENT OUTCOMES OF PATIENTS IN BOTH GROUPS AND INCIDENCE OF COMPLICATIONS

Patient group	LIOS treatment method		Extra-cortical osteosynthesis treatment with plates	
	n	%	*n*	%
Treatment results				
Good	350	70 %	182	61.9 %
Satisfactory	126	25.2 %	87	29.6 %
Unsatisfactory	24	4.8 %	25	8.5 %
Total	500	100 %	294	100 %
Complications that have arisen				
False joint formation	23	4.6 %	26	8.8 %
Infectious complications	7	1.4 %	6	2 %
Implant migration and failure	11	2.2 %	10	3.4 %
Total	41	8.2 %	42	14.2 %

positioning with elimination of displacement and elimination of soft tissue interposition; Khakhutov bone grafting without removal of the blocked rod.

Complications in the form of migration and fracture of the locked rod and screws were observed in 11 (2.2 %) cases. These complications are associated with errors in surgical technique, failure to dynamise the fracture and excessive activity in the form of full early loading (failure to comply with the recommendations of the attending physician when the patient is discharged from hospital). Treatment in this case included removal of the broken structure and rheosteosynthesis with a larger diameter nail.

In the second group of patients treated by extra-cortical osteosynthesis with plates, good anatomo-functional treatment results were achieved in 182 (61.9 %) patients, satisfactory treatment results – in 87 (29.6 %) patients, unsatisfactory treatment results – in 25 (8.5 %) patients.

Non-unions and false joint formation were observed in 26 (8.8 %) patients. These complications were caused by: unstable and inaccurate fixation of bone fragments, interposition of soft tissues between the fragments; too early loading of the operated extremity; ineffective immobilisation [21, 22].

The following surgical procedures were performed to correct the non-union: repeated rheosteosynthesis with a plate after excision of scar tissue; plate removal; bone grafting according to Khakhutov; osteosynthesis with a lockable rod.

Infectious complications were observed in 6 (2 %) patients. Migration and breakdown of metal structures were observed in 10 (3.4 %) patients. These complications were caused by insufficiently stable fixation, excessive early loading of the operated extremity and inadequate immobilisation.

DISCUSSION

In summary, the ten-year experience of treatment of 794 patients with femoral shaft fractures has shown high efficacy of the applied treatment techniques. Generally, good and satisfactory anatomo-functional treatment results were achieved in 745 (93.8 %) patients. The risk of various types of complications was significantly lower with locked intramedullary osteosynthesis than with extra-cortical osteosynthesis with plates. The number of non-unions and false joint formations is 4.2 % lower, and the number of infectious complications is 0.8 % lower. As well, the interlocking nail is more resistant to loads and the risk of failure and migration of steel structures is lower by 2 % [23–25]. These results were proved by statistical analysis, in which the value of the Student's t-test was 2.50, that is, the differences were statistically significant ($p = 0.012664$). The Student's t-test critical value was 1.972 at a significance level of $\alpha = 0.05$.

Locked intramedullary osteosynthesis has become the gold standard for the treatment of diaphyseal femoral fractures for a number of reasons. The use of this method allows early loading of the operated extremity and does not require additional immobilisation, which is a key factor enabling early rehabilitation of patients, which is especially important for elderly and senile patients and those with comorbidities. The use of LIOS approach also reduces the risk of infectious complications and migration of metal structures. LIOS is obviously a less traumatic method of surgical treatment, requiring minimal operative access, minimising blood loss during surgery and, when used correctly and with the necessary experience, reducing operative time compared to extra-cortical osteosynthesis. All these factors make it possible to reduce the period of stay of pa-

tients in hospital and thereby increase the bed turnover and economic efficiency of the department.

CONCLUSION

The best results of femoral shaft fractures treatment were achieved using locked intramedullary osteosynthesis (95.2 %) compared to extra-cortical osteosynthesis with plates (91.5 %).

This method of surgical treatment is considered to be the "gold standard of treatment" for diaphyseal fractures of long tubular bones.

Notwithstanding its advantages and effectiveness, it is not always possible to apply this method of treatment due to various factors, and therefore an individual approach to the choice of surgical treatment method remains relevant.

Conflict of interest

The authors of the article declare no conflict of interest.

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FOREFOOT RECONSTRUCTION IN BRACHYMETATARSIA

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ABSTRACT

Background. *Brachymetatarsia is a rare disease characterized by abnormal shortening of one or more metatarsal bones. The clinical picture is most often dominated by complaints of aesthetic dissatisfaction, as well as pain in the forefoot caused by mechanical dysfunction. A radical way to solve the problem is surgical treatment.*
The aim of the study. *To demonstrate a rare clinical observation of a patient with bilateral brachymetatarsia of both feet.*
Materials and methods. *The article presents a case of stepwise treatment of a patient with bilateral brachymetatarsia with shortening of the III and IV metatarsal bones in combination with hallux valgus.*
Results and discussion. *According to the protocol, the patient underwent stepwise reconstruction of the forefoot of both feet with intervention on all five metatarsal bones. After all the rehabilitation measures, there was a complete restoration of all functions of both lower limbs after the surgery, and the patient was satisfied with the aesthetic result of the surgical treatment.*
Conclusions. *The obtained result of treatment of a patient with bilateral brachymetatarsia allows us to conclude that the use of this group of techniques is acceptable with the obligatory preoperative calculation of the necessary shortening and lengthening of the metatarsal bones, focusing on the parameters of the metatarsal formula of the forefoot, even in combination with other deformities.*

Key words: *brachymetatarsia, hallux valgus, forefoot deformity, surgical treatment*

Received: 02.11.2023
Accepted: 21.11.2023
Published: 05.12.2023

For citation: Usoltsev I.V., Leonova S.N., Kosareva M.A. Forefoot reconstruction in brachymetatarsia. *Acta biomedica scientifica*. 2023; 8(5): 174-181. doi: 10.29413/ABS.2023-8.5.19

РЕКОНСТРУКЦИЯ ПЕРЕДНЕГО ОТДЕЛА СТОПЫ ПРИ БРАХИМЕТАТАРЗИИ

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РЕЗЮМЕ

Введение. *Брахиметатарзия – редкий порок развития, характеризующийся аномальным укорочением одной или нескольких плюсневых костей. В клинической картине чаще всего преобладают жалобы на эстетическую неудовлетворённость, а также на боли в переднем отделе стопы, вызванные механической дисфункцией. Радикальным способом решения проблемы является хирургический метод лечения.*

Цель исследования. *Продемонстрировать редкое клиническое наблюдение пациента с двусторонней брахиметатарзией обеих стоп.*

Материалы и методы. *В статье представлен случай этапного лечения пациентки с двусторонней брахиметатарзией с укорочением III и IV плюсневых костей в сочетании с вальгусным отклонением первого пальца.*

Результаты и их обсуждение. *Согласно протоколу, пациентке была выполнена этапная реконструкция переднего отдела обеих стоп с вмешательством на всех пяти плюсневых костях. По прошествии всех реабилитационных мероприятий произошло полное восстановление всех функций обеих нижних конечностей после операции, а также отмечена удовлетворённость пациентки эстетическим результатом выполненной операции.*

Выводы. *Полученный результат лечения пациентки с двусторонней брахиметатарзией позволяет сделать вывод о приемлемости использования данной группы методик с обязательным предоперационным расчётом необходимого укорочения и удлинения плюсневых костей, ориентируясь на параметры метатарзальной формулы переднего отдела стопы, даже в сочетании с другими деформациями.*

Ключевые слова: *брахиметатарзия, вальгусное отклонение I пальца, деформация переднего отдела стопы, хирургическое лечение*

Статья поступила: 02.11.2023
Статья принята: 21.11.2023
Статья опубликована: 05.12.2023

Для цитирования: Усольцев И.В., Леонова С.Н., Косарева М.А. Реконструкция переднего отдела стопы при брахиметатарзии. *Acta biomedica scientifica*. 2023; 8(5): 174-181. doi: 10.29413/ABS.2023-8.5.19

INTRODUCTION

Brachymetatarsia is a rare malformation characterised by abnormal shortening of one or more metatarsal bones with disruption of the metatarsal parabola by more than 5 mm [1–3]. The incidence of this disease, according to the literature, ranges from 0.02 to 0.05 %; it develops more commonly in women, with a ratio of 25:1 [2, 4–6]. Brachymetatarsia results from stunted height or premature closure of the epiphyseal plate [7]. An underlying cause of this condition may be congenital, post-traumatic, post-infectious, iatrogenic or secondary to systemic disease such as malignancy, sickle cell anaemia, pseudohyperparathyroidism, Turner syndrome, Down syndrome, Apert syndrome, atyreosis or osteodystrophy.

The fourth metatarsal bone is affected in most cases, varying from 36 to 72 % of cases, resulting in bilateral pathology [1, 7, 8]. Complaints of aesthetic dissatisfaction as well as forefoot pain associated with mechanical dysfunction predominate in the clinical picture most commonly [9, 10].

The deformity usually manifests at the age of 5–7 years, gradually progressing with growth, and by the age of 12 years the shortening is 15–45 % of the metatarsal bone length [11].

Brachymetatarsia treatment can be either nonsurgical or surgical. Nonsurgical treatment includes wearing comfortable shoes; however, this does not solve the cosmetic problem. Various surgical treatments have been described: gradual lengthening distraction with external fixation apparatus (EFA) and single-step lengthening. No consensus currently exists concerning surgical treatment, however, as each treatment has its own advantages and disadvantages.

THE AIM OF THE STUDY

The article presents *a* case of stepwise treatment of a patient with bilateral brachymetatarsia with shortening of the III and IV metatarsal bones in combination with hallux valgus.

MATERIALS AND METHODS

Patient S., 21 years old. Was admitted to the clinic of Irkutsk Scientific Centre of Surgery and Traumatology for surgical treatment with the diagnosis: bilateral congenital brachymetatarsia. Absolute shortening of the III–IV metatarsal bones. Hallux valgus. Pain syndrome. The patient signed informed consent and authorisation for her data to be processed for scientific research.

From the patient's history: the patient considers herself sick since childhood, when at the age of 6 years, against the background of complete well-being, she first noticed shortening of the III and IV toes of both feet. The shortening of the above-mentioned toes only progressed over time, and nonsurgical treatment had no proper effect. In addition to brachymetatarsia, in adolescence the patient developed hallux valgus of both feet, which by the time of hospitalization reached 35°, which in turn only aggravated the overall aesthetic defect and was an additional source of complaints. The combination of hallux valgus and brachymetatarsia required simultaneous intervention on all five metatarsal bones (Fig. 1, 2). Stepwise surgical rehabilitation was decided: first perform surgery on the right foot, then on the left foot.

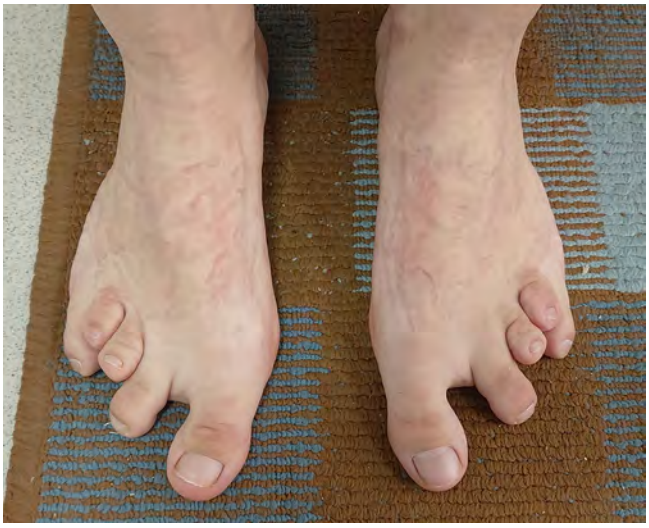

FIG. 1.
Patient S. External view of both feet before the surgery (top view)

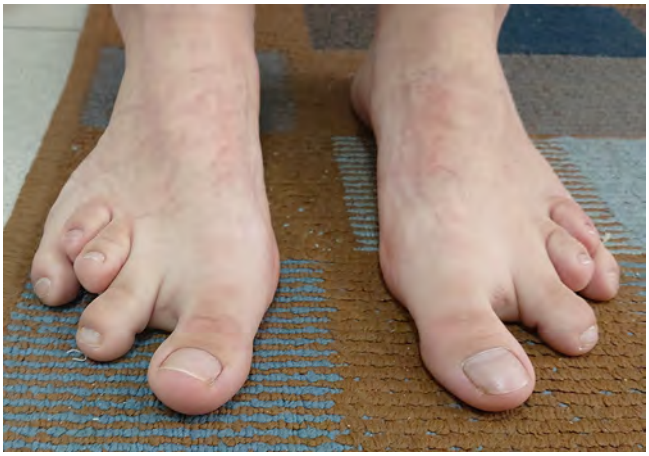

FIG. 2.
Patient S. External view of both feet before the surgery (front view)

PREOPERATIVE PLANNING

The original technique of L.G. Makinyan et al. was considered as the method of surgical intervention [12], developed for the treatment of brachymet-

atarsia of the IV metatarsal bone only, which implied increasing its length by free bone grafting with a cylindrical fragment taken from the neighbouring V metatarsal bone. Intramedullary fixation of both osteotomized bones using cannulated screws was performed. The size of the graft was determined so that the IV metatarsal bone was 3–5 mm shorter than the III metatarsal bone. The clinical observation described here was the shortening of two metatarsal bones (III and IV) at once, which required additional grafting from the II metatarsal bone to increase the length of the III metatarsal bone (Fig. 3).

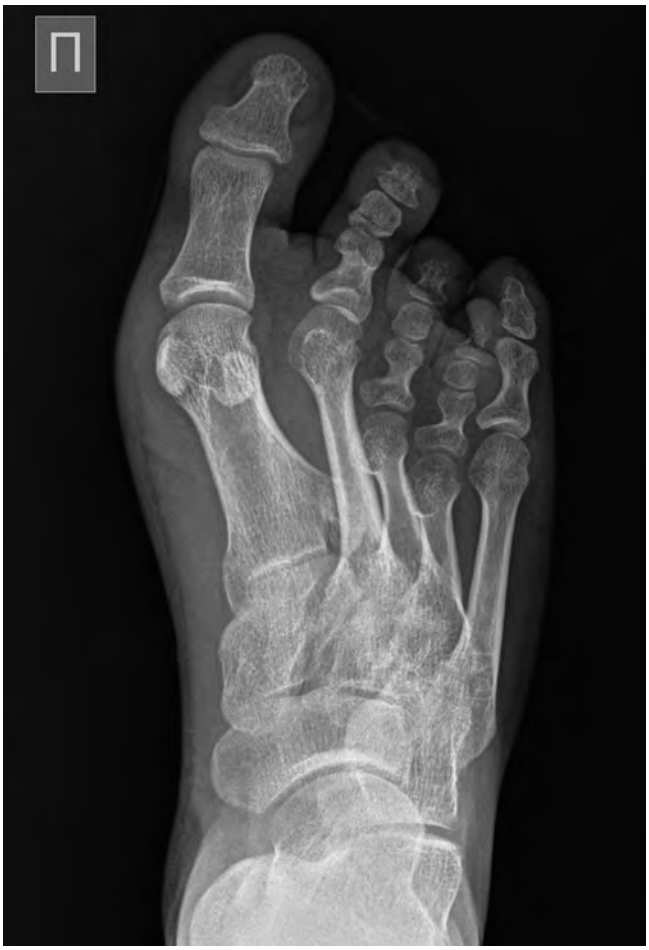

FIG. 3.
Patient S. X-ray of the right foot before the surgery (anteroposterior view)

The required shortening/lengthening of the metatarsal bones is determined by the metatarsal formula: I ≤ II > III > IV > V [13], and in this example it was calculated that the required shortening of the II metatarsal bone and the required lengthening of the III metatarsal bone corresponds to 10 mm. Subsequently, the required shortening length of the V metatarsal bone and the required lengthening of the IV metatarsal bone was determined, which also corresponded to 10 mm. Considering the associated hallux valgus, it was necessary to determine the length of the required shortening of the I metatarsal bone, equal to 10 mm.

SURGERY TECHNIQUE

Surgical intervention was performed using a pneumatic tourniquet in the lower third of the thigh. After three times treatment with antiseptic solution of the right foot with three projection incisions on the inner and dorsal surface, the metatarsal bones of the foot were accessed. Surgical treatment was initially performed to correct the hallux valgus, the standard steps of which were: medial exostosectomy, release of the lateral aspect of the I metatarsophalangeal joint, and corrective scarf-osteotomy of the I metatarsal bone with a planned shortening by 10 mm. Bone fragments were fixed with a cannulated screw with a diameter of 2.5 mm and length of 22 mm. Additionally, an Akin osteotomy was performed on the first toe with fixation with a cannulated screw with a diameter of 2.5 mm and length of 22 mm.

Subsequently, from a separate 5.0 cm long projection incision in the second intertarsal space, access to the II–III metatarsophalangeal joint, proximal metadiaphysis of the II–III metatarsal bone was performed. Two transverse osteotomies of the II metatarsal bone were performed: the first one at the level of the distal metadiaphysis. To perform the second, a cylindrical graft was obtained by indenting 10 mm proximally and immersed in physiological solution. The fragments of the II metatarsal bone were juxtaposed and fixed with a cannulated screw. From the same accessible area at the level of the distal metadiaphysis, an osteotomy of the III metatarsal bone was performed, the fragments were separated along the axis, and a graft 10 mm long from the II metatarsal bone was inserted between them. Intramedullary fixation of all fragments of the III metatarsal bone with a cannulated screw was performed. Subsequently, from an additional 5.0 cm incision in the fourth intertarsal gap, access to the IV–V metatarsophalangeal joint, proximal metadiaphysis of the IV–V metatarsal bone was performed. Similarly, a cylindrical graft was harvested from the V metatarsal bone, measuring 10 mm. The fragments of the V metatarsal bone were juxtaposed and fixed with a cannulated screw. From the same accessible area at the level of the distal metadiaphysis, an osteotomy of the IV metatarsal bone was performed, the fragments were separated along the axis, and a graft 10 mm long from the V metatarsal bone was inserted between them. Intramedullary fixation of all fragments of the IV metatarsal bone with a cannulated screw was performed. Final control of osteosynthesis stability in osteotomized bones was performed, wounds were lavaged with antiseptic solutions; the wounds were sutured in layers (Fig. 4). Aseptic bandages were applied. Elastic bandaging of the lower extremities, immobilization of the right foot with an orthopaedic boot, and radiological control were performed (Fig. 5).

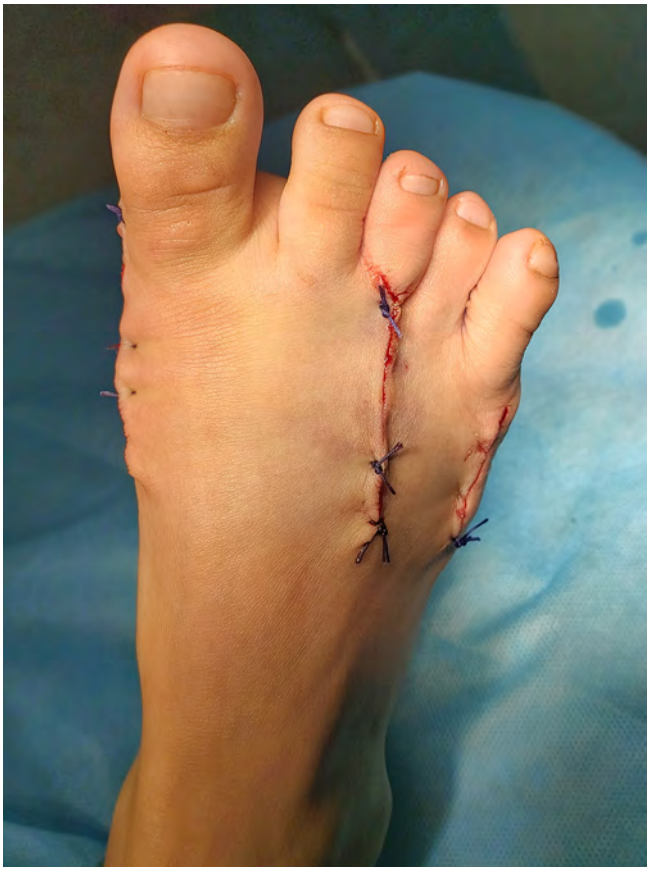

FIG. 4.
Patient S. External view of the right foot after the surgery

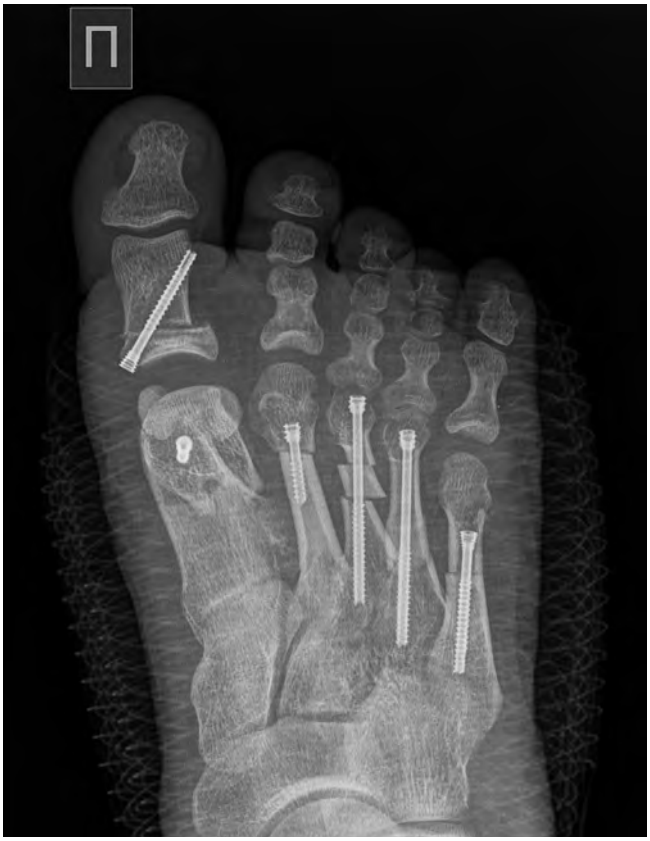

FIG. 5.
Patient S. X-ray of the right foot after the surgery (anteroposterior view)

POSTOPERATIVE CARE

According to the case management protocol after such surgeries, immobilization of the operated foot for 6 weeks in an orthopaedic boot with forefoot offloading was recommended. No deviations in the patient's condition, clinical and laboratory parameters were observed during her treatment at the clinic, which allowed her to be discharged to the outpatient stage of treatment. The sutures were removed on the 14th day. After control X-ray radiography, immobilization was discontinued and walking was allowed with gradual increase of load, and courses of physiotherapy and lymphatic drainage massage were recommended. Suppression of postoperative oedema and restoration of foot bearing capacity allowed the patient to return to her normal lifestyle without any restrictions (Fig. 6, 7).

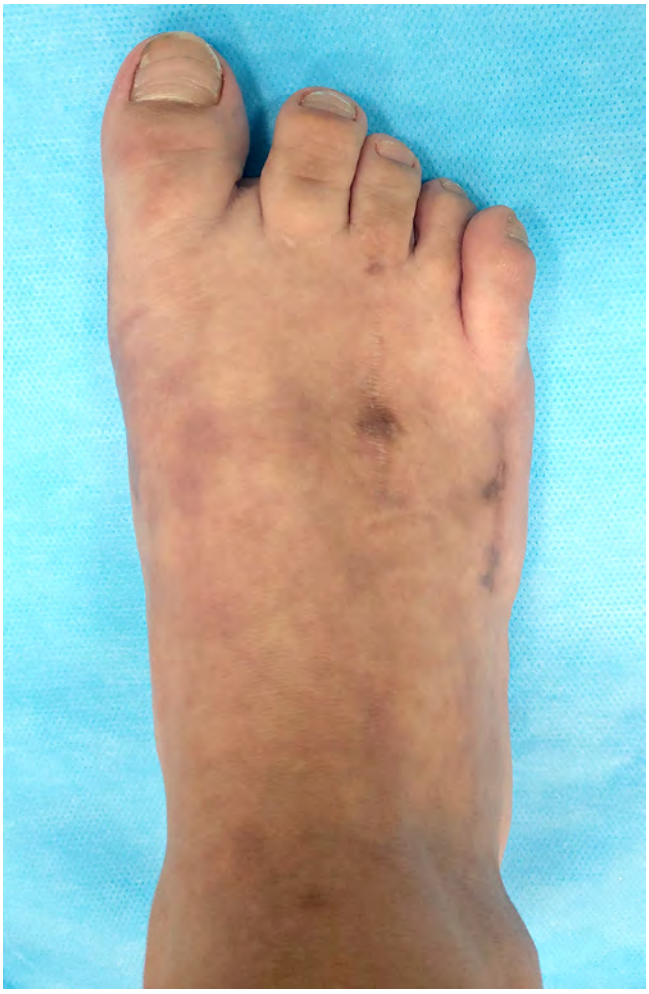

FIG. 6.
Patient S. External view of the right foot 1 year after the surgery

One year after the right foot surgery, the left foot surgery was performed according to a similar algorithm (Fig. 8–10).

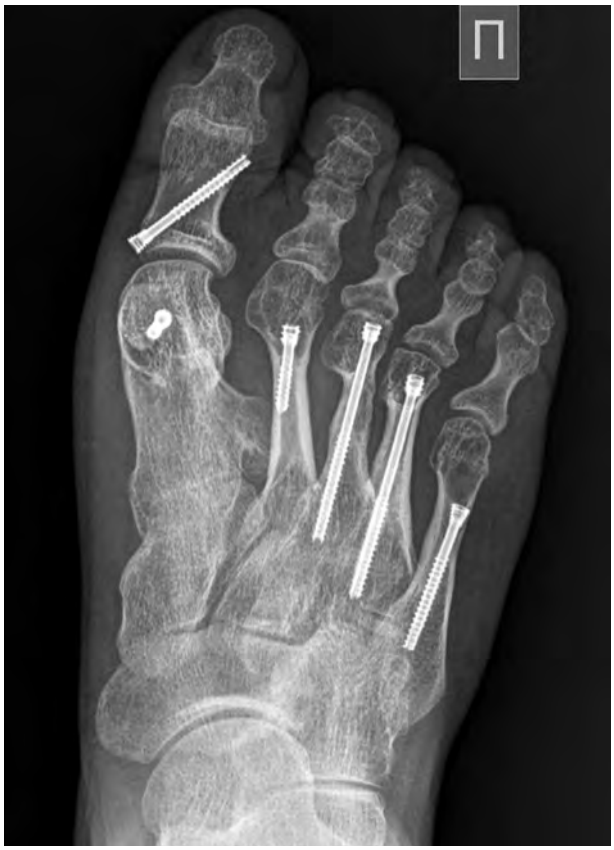

FIG. 7.
Patient S. X-ray of the right foot 1 year after the surgery (anteroposterior view)

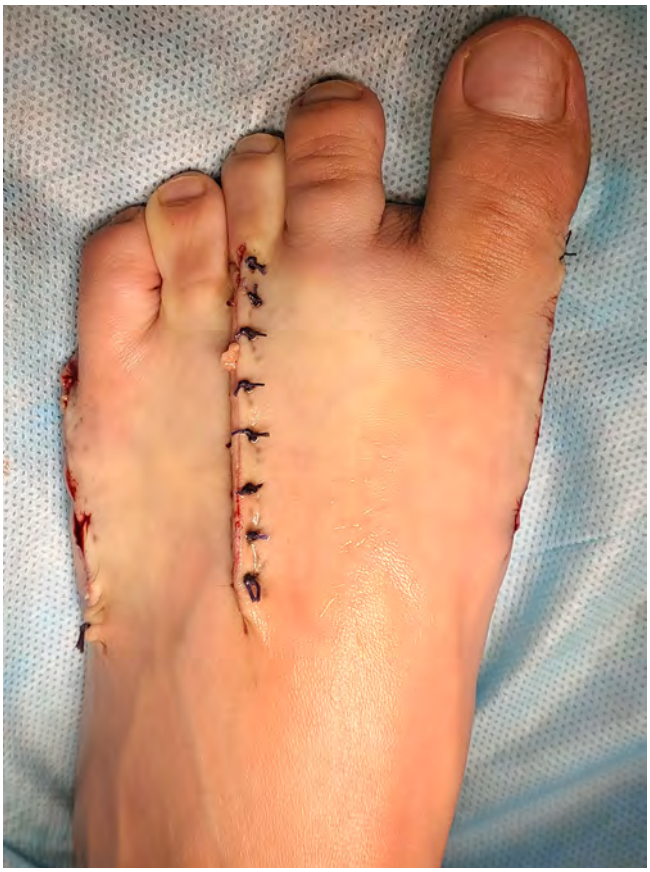

FIG. 9.
Patient S. External view of the left foot after the surgery

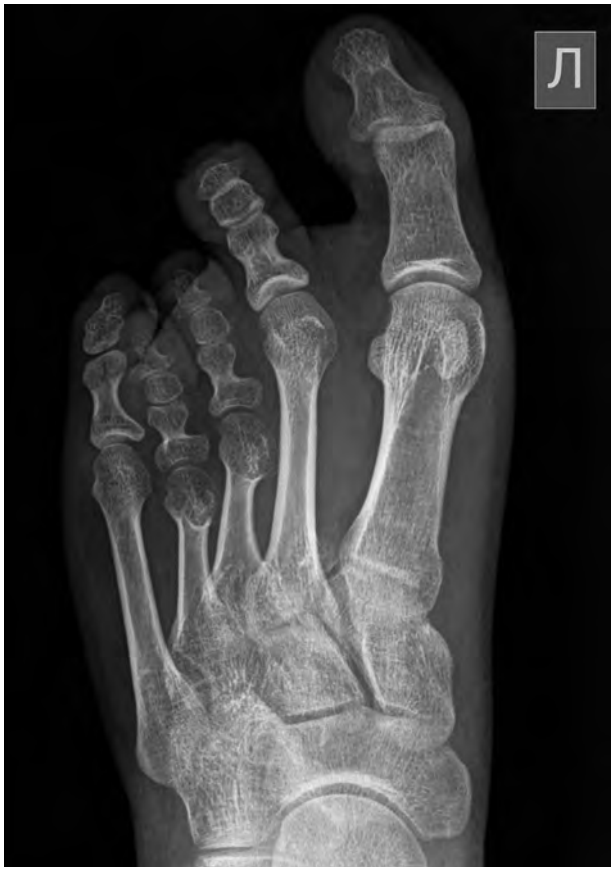

FIG. 8.
Patient S. X-ray of the left foot before the surgery (anteroposterior view)

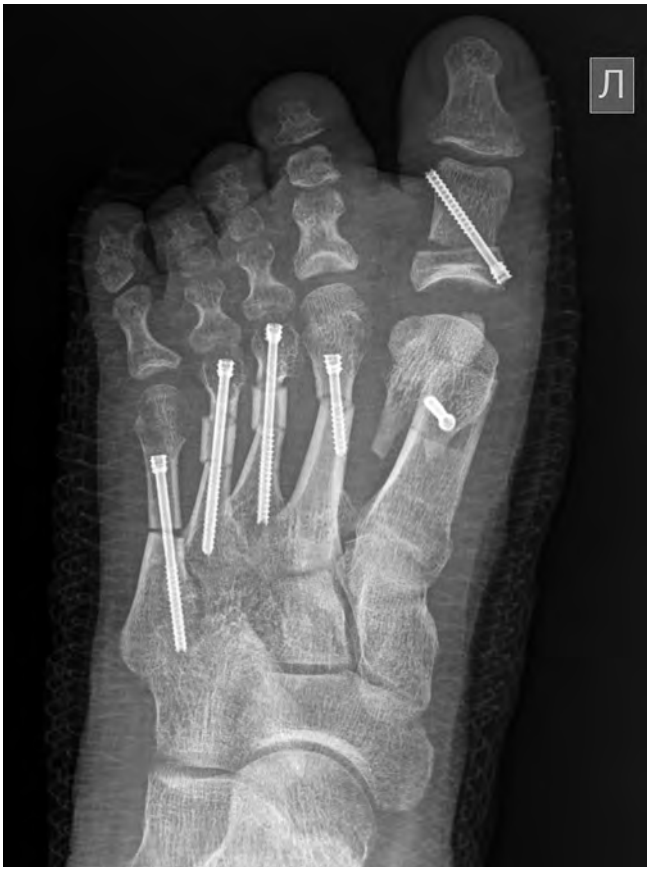

FIG. 10.
Patient S. X-ray of the left foot after the surgery (anteroposterior view)

There were no abnormalities in the postoperative period as well, with restoration of left foot function (Fig. 11–13).

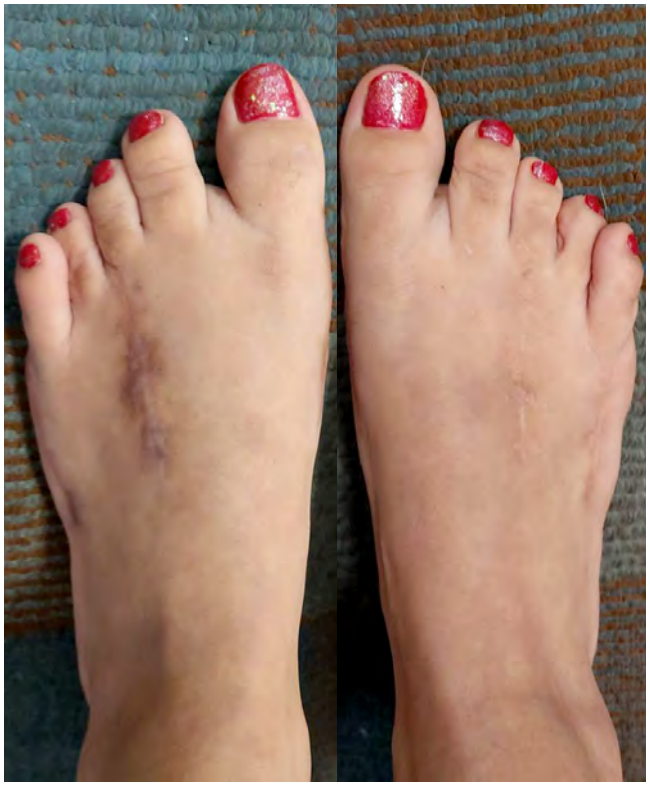

FIG. 11.
Patient S. External view of both feet: right foot – 2 years after the surgery, left foot – 1 year after the surgery (top view)

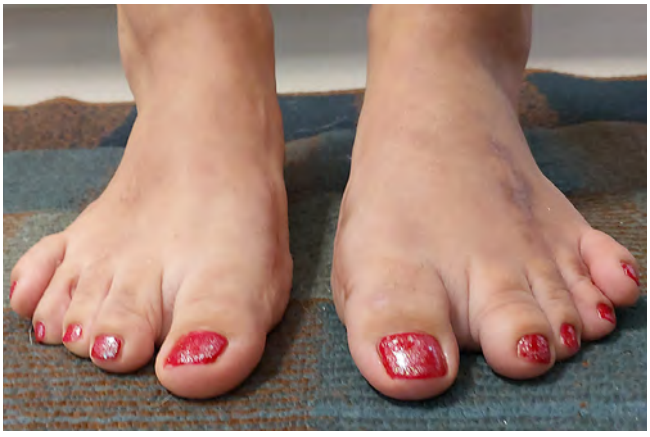

FIG. 12.
Patient S. External view of both feet: right foot – 2 years after the surgery, left foot – 1 year after the surgery (front view)

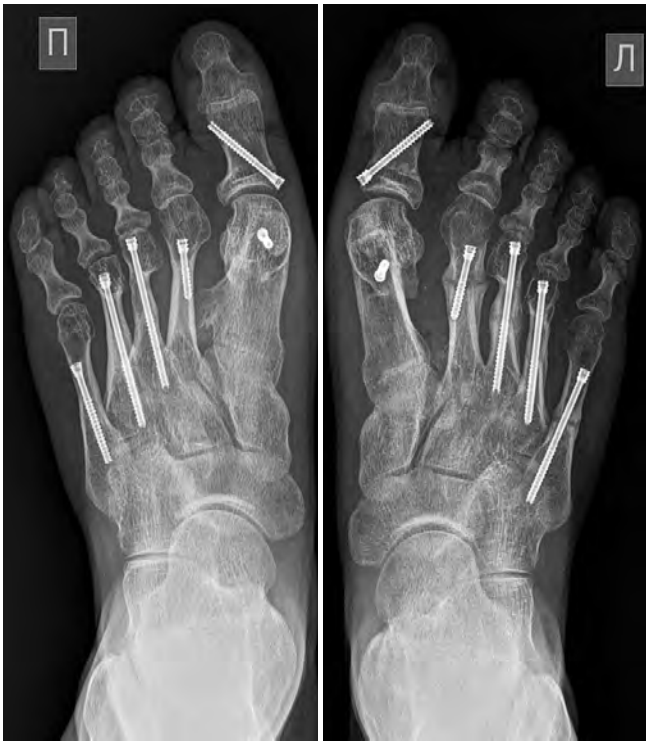

FIG. 13.
Patient S. X-ray of both feet: right foot – 2 years after the surgery, left foot – 1 year after the surgery (anteroposterior view)

RESULTS AND DISCUSSION

Brachymetatarsia is a rare congenital disorder in which there is absolute shortening of one or more metatarsal bones, with an incidence of only 0.05 % in the population [2, 4–6]. Shortening of the IV metatarsal bone is most often observed, and less often of the III metatarsal bone. The peculiarity of this clinical observation is shortening of both metatarsals on both feet, which is even rarer. Another feature was the combination of brachymetatarsia with hallux valgus, of which there are few references [14]. This phenomenon is not an aggravating factor, but increases the volume of surgical intervention. The surgical protocol for the treatment of patients with brachymetatarsia can be accomplished with two groups of techniques, which, without getting into the nuances, can be described as a one-stage increase in metatarsal length using auto-, allo-, or xenografts and fixation with spokes, screws, or plates, or as an increase in metatarsal length over time using EFA. Both of these groups seem to have their own advantages and disadvantages. However, the long period of fixation in EFA, a higher risk of infectious complications in the area of percutaneous elements, and limited mobility of the patient caused by difficulty in selecting and wearing shoes were significant arguments in choosing the treatment method.

CONCLUSION

A complete postoperative recovery of all the functions of both lower extremities, as well as satisfaction with the aesthetic result, allow us to conclude that it is acceptable to use this group of techniques with mandatory preoperative assessment of the necessary shortening and lengthening of the metatarsal bones, based on the parameters of the metatarsal formula of the forefoot deformity (anterior talipes), even in combination with other deformities.

Conflict of interest

The authors of this article declare no conflicts of interest.

Funding

The study was not sponsored. Authors are solely responsible for submitting the final version of the manuscript for printing.

All authors participated in the study conception and design as well as in the writing of the manuscript. The final version of the manuscript was approved by all authors. No research honorarium was paid to the authors.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology

THE CURRENT STATE OF THE ISSUE OF USING CONE BEAM COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF MUSCULOSKELETAL DISEASES

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ABSTRACT

The high incidence rate and wide range of musculoskeletal pathologies determine the improvement of the diagnostic process. Late diagnosis leads to complications, which in turn increase the percentage of disability. Therefore, the search for the most informative method with the least radiation load on the patient remains an urgent problem for radiologists. Cone beam computed tomography (CBCT) is a modern and promising technique that has already found wide application in dentistry and otorhinolaryngology. Among the advantages of CBCT are: three-dimensional image; high spatial resolution; low radiation dose. Thanks to technical improvements in equipment and the introduction of new image processing protocols, it has become possible to expand the indications for conducting the researches, including the researches based on imaging of the upper and lower extremities. Based on the results of a CBCT examinations, we can evaluate: the shape and contour of the bone; solution of continuity of the bone and malposition of bone fragments; the structure of bone tissue and the pathological processes occurring in it (destruction, osteoporosis, osteosclerosis); joint congruence and changes in articular surfaces surrounding soft tissues. Therefore, CBCT can be introduced into the diagnostic process of bones and joints diseases. The use of this technique will find wide application in traumatology and orthopedics (fractures, dislocations, post-traumatic deformities, aseptic necrosis, osteoarthritis), rheumatology (rheumatoid arthritis, polyarthropathy, juvenile arthritis, gout), surgery (osteomyelitis), oncology (benign and malignant bone tumors) both in the adult population and in pediatric practice. This paper presents a review of the literature, which examines the degree of development of the issue of using CBCT and describes study protocols and protocols for processing the obtained images in the diagnosis of musculoskeletal diseases.

Key words: *radiology, cone beam computed tomography, osteoarticular system, musculoskeletal system*

Статья поступила: 29.05.2023
Статья принята: 18.10.2023
Статья опубликована: 05.12.2023

For citation: Sholokhova N.A., Zharkov D.K., Lezhnev D.A., Vasilyev A.Yu., Petrovskaya V.V., Lazarenko E.Yu., Blinov N.N., Sergeeva A.D. The current state of the issue of using cone beam computed tomography in the diagnosis of musculoskeletal diseases. *Acta biomedica scientifica*. 2023; 8(5): 182-191. doi: 10.29413/ABS.2023-8.5.20

СОВРЕМЕННОЕ СОСТОЯНИЕ ВОПРОСА ИСПОЛЬЗОВАНИЯ КОНУСНО-ЛУЧЕВОЙ КОМПЬЮТЕРНОЙ ТОМОГРАФИИ В ДИАГНОСТИКЕ ЗАБОЛЕВАНИЙ ОПОРНО-ДВИГАТЕЛЬНОГО АППАРАТА

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РЕЗЮМЕ

Высокая частота заболеваемости и широкий спектр патологий опорно-двигательного аппарата обуславливают совершенствование диагностического процесса. Поздняя постановка диагноза приводит к возникновению осложнений, что в свою очередь повышает процент инвалидизации. Поэтому поиск наиболее информативного метода с наименьшей радиационной нагрузкой на пациента остаётся актуальной проблемой для радиологов. Конусно-лучевая компьютерная томография (КЛКТ) – современная и перспективная методика, которая уже нашла широкое применение в стоматологии и оториноларингологии. Среди преимуществ КЛКТ можно отметить: объёмное изображение; высокое пространственное разрешение; низкую дозу лучевой нагрузки. Благодаря техническому совершенствованию аппаратуры и появлению новых протоколов обработки изображений появилась возможность расширения показаний к выполнению исследований, в том числе и за счёт съёмки верхних и нижних конечностей. По результатам КЛКТ-исследования можно оценить: форму и контур кости; наличие нарушения целостности кости и положения костных отломков; структуру костной ткани и протекающие в ней патологические процессы (деструкция, остеопороз, остеосклероз); конгруэнтность сустава и изменения суставных поверхностей, окружающих мягкие ткани. Исходя из вышеперечисленного, КЛКТ можно внедрить в диагностический процесс заболеваний костно-суставной системы. Применение данной методики найдёт широкое применение в травматологии и ортопедии (переломы, вывихи, посттравматические деформации, асептические некрозы, остеоартрозы), ревматологии (ревматоидные артриты, полиартропатии, ювенильные артриты, подагра), хирургии (остеомиелиты), онкологии (доброкачественные и злокачественные новообразования костей) как у взрослого населения, так и в педиатрической практике. В данной работе представлен обзор литературы, в которой изучена степень разработанности вопроса применения КЛКТ и описаны протоколы исследования и обработки полученных изображений в диагностике заболеваний опорно-двигательного аппарата.

Ключевые слова: *лучевая диагностика, конусно-лучевая компьютерная томография, костно-суставная система, опорно-двигательный аппарат*

Статья поступила: 29.05.2023
Статья принята: 18.10.2023
Статья опубликована: 05.12.2023

Для цитирования: Шолохова Н.А., Жарков Д.К., Лежнев Д.А., Васильев А.Ю., Петровская В.В., Лазаренко Е.Ю., Блинов Н.Н., Сергеева А.Д. Современное состояние вопроса использования конусно-лучевой компьютерной томографии в диагностике заболеваний опорно-двигательного аппарата. *Acta biomedica scientifica*. 2023; 8(5): 182-191. doi: 10.29413/ABS.2023-8.5.20

RELEVANCE

The incidence of musculo-skeletal system pathology is an urgent problem affecting all age categories of the population. According to statistics, this group of diseases is widespread and occupies a stable 3rd place, second only to respiratory and circulatory diseases [1]. Along with this, high rates of disability remain, ranking 3rd in the structure of primary disability of the population [2]. At this background the necessity of constant search for optimal diagnostic approaches aimed at obtaining comprehensive information with simultaneous reduction of radiation load without loss of informativeness increases.

Radiography is considered the primary and routine method in the diagnosis of musculo-skeletal system diseases in both adults and children mainly due to its easy accessibility and rapidity [3, 4]. Shadow summation, however, can make it difficult to visualize changes in bone, especially when examining complex anatomical structures such as the hand and foot [5]. Multislice computed tomography is a highly informative method that gives a more informative picture of the disease, but is accompanied by a high dose of radiation exposure to the patient [3, 6].

Cone Beam Computed Tomography (CBCT tomography) has already found wide application in dentistry, maxillofacial surgery and otorhinolaryngology [7, 8]. Technical improvements in equipment have resulted in new-generation cone-beam tomographs capable of performing upper and lower extremity studies [8, 9].

THE AIM OF THE STUDY

To analyze the scientific information about the state of Cone Beam Computed Tomography application in diagnostics of musculo-skeletal system diseases.

RESULTS AND DISCUSSION

Cone Beam Computed Tomography (CBCT tomography) is a technique of layer-by-layer diagnostics based on computer reconstruction of the image obtained by circular scanning of an object with a cone-shaped beam of X-rays [10]. CBCT tomography scanners use a collimated X-ray beam in the shape of a cone, as opposed to the narrow fan-shaped beam of multislice computed tomography (MSCT). CBCT tomography has a pulsed radiation pattern, while MSCT is continuous. The obtained data projections are processed and during image reconstruction, the images can be combined into a single object for visualization [11, 12].

The first mention of CBCT tomography is provided by P. Mozzo et al. in 1998. The authors presented in their study a new type of computed tomography and its application in maxillofacial surgery and dentistry [9]. In the Russian literature in 2012 in the work of A.Yu. Vasiliev et al. raised the issue of CBCT tomography application in traumatology for the first time and presented a new generation of CBCT tomograph. The authors outlined the following advantages: high spatial resolution; absence of artefacts from metal structures; rapidity of the examination [7]. At the same time, the possibility of quantifying the level of bone mineralization has been observed for CBCT tomography [13].

The main advantage of CBCT tomography is considered to be its high spatial resolution, which allows obtaining information down to the smallest details of bone architectonics [12]. A special contribution among the domestic scientific literature is highlighted for a number of scientific articles by D.V. Makarova et al. (2014–2017), which demonstrated the possibilities of CBCT tomography in rheumatological practice. For example, in the authors' most recent work, 248 CBCT tomography examinations of hands and feet were analyzed. Variations such as osteoporosis, joint space narrowing, cystic remodelling, erosion, osteolysis, bone proliferation, and soft tissue changes were examined. According to the results of the study, CBCT tomography showed higher informativity than standard radiography, and together with low radiation exposure, CBCT tomography was recommended by the authors as a first-stage diagnostic technique [10].

At the same time, Y. Aurell et al. (2018) also reflected on the use of CBCT tomography in rheumatoid practice. In their study, the authors decided to assess the diagnostic capabilities of CBCT tomography in visualising bone erosions in rheumatoid arthritis and compare it with radiography. Their study included 30 patients with long-standing rheumatoid arthritis. CBCT tomography was able to differentiate bone erosions in all 30 cases, whereas radiography was only able to differentiate bone erosions in 26 cases. The authors pointed out that CBCT tomography has a higher sensitivity to detect erosions than standard radiography and recommend the technique both in initial diagnosis and in further dynamic follow-up [14].

A scientific group headed by M. Posadzy (2018) published a study that demonstrates in detail the capabilities of CBCT tomography in diagnosing the main nosological forms of musculo-skeletal system diseases, such as traumatic changes (fracture, dislocation); tumours and tumour-like bone lesions; osteomyelitis; degenerative changes of joints. They also presented CBCT tomography of joints using contrast agent to study bone and cartilage changes. Following CBCT tomography, osteochondral changes with cystic rearrangement, the presence of intra-articular fragments of different density and proliferative lesions of the synovial membrane were visualized in detail. According to the authors, the results are comparable to magnetic resonance imaging (MRI), and therefore CBCT tomography can serve as an MRI analogue in patients with claustrophobia or other contraindications [12].

Platypodia is a common orthopedic disease characterized by collapse of the arcus pedis longitudinalis

pars medialis with deformity of the foot and talocrural joint [15]. Acquired platypodia in adults includes a wide range of ligament and tendon failures that can lead to curvature of the foot axis and disability [16]. "The gold" diagnostic standard is considered to be radiography of the foot with functional loading. A group of scientists C. de Cesar Netto et al. (2017) studied acquired platypodia in adults and conducted a retrospective study in which 20 patients underwent a CBCT tomography examination with functional loading in a standing position and without loading in a sitting position. In the results obtained, the authors observed high informativeness in both positions, but the studies with functional load had greater diagnostic value. In addition of assessing the platypodia degree, however, CBCT tomography provides a more detailed assessment of the bone and joints of the foot than standard radiography. The authors concluded that, in addition to statistically significant measurements similar to those obtained with traditional radiography, CBCT tomography may also be used to visualize a pattern that demonstrates the severity of bone abnormalities in detail [17].

As a result of its high resolution, CBCT tomography is able to visualise bone tissue changes as clearly as possible, whether it is a lytic lesion forming a cavity or the smallest microfracture. CBCT tomography can be widely used in such areas as traumatology and orthopaedics, rheumatology, surgery, oncology as a result of its diagnostic capabilities. The possibility of performing CBCT tomography examinations with functional loading has also been described and presented as an example for the diagnosis of acquired platypodia in adults [17]. New possibilities in the process of examining the bones and joints of the lower extremities can be achieved by using this technique. Considering the above, the use of CBCT tomography for musculoskeletal system examination becomes relevant both for adults and paediatric patients.

In 2017 in France, C. Borel et al. conducted a clinical trial of the ability of CBCT to diagnose latent navicular bone fractures. Forty-nine patients with clinical manifestations of navicular bone fracture and normal radiographic findings underwent additional CBCT and MRI. In considering the findings, CBCT tomography proved to be a highly informative and more informative diagnostic tool than radiography and was not inferior to MRI; additionally, CBCT is less cost-effective than MRI (Table 1). The authors note that CBCT tomography can act both as an adjunct and as a complete replacement for standard radiography in wrist joint injuries, especially when a navicular fracture is suspected [18].

German scientists J. Neubauer et al. (2018) conducted a retrospective study of CBCT tomography in navicular fractures. They included 102 patients who underwent standard radiography and CBCT tomography. In 2022, independently of this study, a study was published by E. Fitzpatrick et al. in which a meta-analysis of the scientific literature related to the use of CBCT tomography in wrist fractures was conducted. It was aimed to determine the diagnostic accuracy of CBCT tomography in acute wrist joint trauma. CBCT tomography has proven to be a highly informative tool that can replace or supplement radiographs (Table 1) [19, 20]. The British scientists also noted that CBCT tomography gives a more detailed image than MSCT, which improves visualization of the area of interest. They attribute this to the higher spatial resolution, which is 0.4–0.09 mm for CBCT tomography compared to 1–2 mm for MSCT [19].

Elbow joint injury is a high incidence cause of attendance at trauma wards. Standard radiography is quite often insufficient for correct diagnosis and treatment planning [21]. For the purpose of pre-investigation, trauma physicians prescribe MSCT, during which the patient is laid in the "superman" pose with the arm extended in the gentry [22, 23]. In cases of forced immobilization or severe pain in the patient, however, it is necessary to perform atypical patient positioning [23]. A group of German physicians in 2023 submitted a CBC tomograph with a dual robotic radiographic system without gentry, in which it became possible to perform examinations of the elbow joint in both flexed and unbent states without irradiating neighbouring anatomical regions. This work has proved not only high diagnostic value, but also made it possible to perform low-dose studies in people with limited joint motion, which is especially relevant in acute elbow joint trauma (Table 1) [23].

It is essential to assess the osteoregeneration process in order to avoid complications, alongside the detection of bone integrity and fragment position. A group of scientists L.C. Farracho et al. (2020) in an attempt to improve the diagnostic process, analyzed 52 CBCT tomography studies of patients with navicular fracture performed in the 6th week of immobilization and compared them with standard radiography. The Swiss authors considered that CBCT tomography allows trabecular bridge formation and cortical fusion to be traced, unlike radiography, which gives more reliable information on bone consolidation. The high role of CBCT tomography in the diagnosis of both conventional and concealed navicular fractures and a more informative picture of bone fragment displacements were also highlighted. Experts have observed a rather low radiation dose received by the patient [24].

Delayed diagnosis or missed rupture of the navicular ligament may result in the development of post-traumatic osteoarthritis of the wrist [25]. A group of German experts J.E. Dornberger et al. (2021) described CBCT arthrography and demonstrated it in the diagnostic process of navicular ligament rupture. The authors performed a prospective analysis and compared conventional arthrography, MSCT arthrography and CBCT arthrography. The obtained results of CBCT tomography provided full three-dimensional images, the diagnostic value of which is high and not inferior to those of MSCT (Table 1). However, CBCT tomography is accompanied by a low radiation load on the patient (compared to MSCT). As a conclusion, scientists recommend CBCT arthrography as an accurate tool in the diagnosis of navicular ligament rupture [26].

TABLE 1

DIAGNOSTIC ACCURACY INDICATORS OF CBCT TOMOGRAPHY AS PROVIDED IN SCIENTIFIC PUBLICATIONS

Nature of injury and anatomical area		Sensitivity, %	Specificity, %
Borel C. et al. (2017) [18]			
Navicular fracture		100	97
Neubauer J. et al. (2018) [20]			
Navicular fracture		93	96
Fitzpatrick E. et al. (2022) [19]			
Navicular fracture		87.7	99.2
Wrist joint fracture		93.5	99.9
Wrist fracture		90.6	100
Distal radius fracture		90	100
Kunz A.S. et al. (2023) [23]			
Elbow joint	conventional fracture	94–100	94–97
	fracture with articular surface involvement	90–97	97
	multi-fragment fracture	96	95–98
Gibney B. et al. (2019) [27]			
Wrist joint fracture		98.3	100
Dornberger J.E. et al. (2021) [26]			
Scaphalunate ligament rupture		100	95

CBCT tomography is a highly informative technique that provides reliable information about the presence and nature of the injury. According to a number of authors, CBCT tomography has a high diagnostic value in determining musculo-skeletal system diseases of traumatic nature [18–20, 23, 24, 26]. Meanwhile, scientists observe a low dose of radiation exposure received by the patient during the study [23, 24, 26]. It becomes particularly relevant in medical institutions and hospitals specializing in traumatology and orthopaedics. Consideration should also be given to introducing CBCT tomography into the outpatient practice of district trauma centres.

Another important aspect is the active use of CBCT tomography in everyday medical activities. In particular, T. Jacques et al. (2021) analyzed the practical clinical effect of the CBCT tomography integration in the emergency department of radiology, comparing this technique with MSCT in the diagnosis of traumatic changes of the extremities. The authors report not only good visualization and low radiation exposure, but also less time spent on examination and fewer diagnostic procedures. With the introduction of CBCT tomography as an alternative to MSCT, specialists have not only achieved a reduction in radiation dose, but also increased office throughput [27].

Irish scientists B. Gibney et al. (2019) demonstrated their experience of introducing CBCT tomography into everyday medical practice. In their work, they conducted a comparative study of standard radiography and CBCT tomography as part of the diagnostic process in wrist joint bone fractures. In the results obtained, CBCT tomography proved to be a more informative tool, being able to visualize fracture lines not visible on radiography in more than 50 % of cases. They also conducted a diagnostic value analysis, in which the methodology showed high results, and its accuracy reached 99.1 % (Table 1). The authors consider CBCT tomography to be a new diagnostic standard, considering its high resolution and low radiation exposure [28], since wrist joint injuries are widespread and radiographs are not very informative.

To date, osteomyelitis remains an urgent problem in general and paediatric surgery. Inflammatory bone diseases of various etiologies represent 6.5 % of the total structure of musculo-skeletal system diseases [29]. The study by N.A. Sholokhova et al. (2023) addressed the use of CBCT tomography in the examination of children with inflammatory diseases of both specific and nonspecific nature. Clinical cases were presented that demonstrated not only the primary diagnostic potential of CBCT tomography, but also its possibilities in control-dynamic follow-up. The authors have mentioned the high diagnostic informativeness of the technique and the crucial role of CBCT tomography in making the final diagnosis as well as in planning surgical treatment. The publication summarized the radiation doses received by the patients during the course of the examination. For instance, in primary and control-dynamic CBCT tomography examinations, the total radiation dose was 0.13 mSv, which is 10 times less than one MSCT study [30].

The second important advantage of CBCT is the low radiation dose per patient. American authors J.B. Ludlow et al. (2018) used anthropomorphic phantoms simulating wrist, ankle and knee joints. The radiation dose received was 1.3-21.1 μSv for CBCT and 9.1–204 μSv for MSCT. Considering this, it was concluded that the effective dose of CBCT tomography is 90 % lower than that of MSCT [31]. According to other data, the radiation dose of CBCT is 6–19 times lower than that of MSCT. These conclusions were reached by the group of scientists J. Koivisto et al. (2021). These were based on a comparison of MSCT and CBCT tomography doses from an anthropomorphic adult hand phantom study. This resulted in a radiation exposure of 2.0–6.7 μSv for CBCT and 37.4 μSv for MSCT [22].

Musculo-skeletal system impairments can occur in a person in any condition and at any age group. Considering the presence of a number of diseases of the musculo-skeletal system associated with pregnancy, the improvement of radial diagnostic examination is of particular relevance. It is essential to obtain as much information as possible with as little radiation exposure as possible. A. Katlapa et al. (2022) became interested in this issue and conducted an experimental study, where they calculated the received dose of radiation to the fetus during the examination of the elbow and knee joint in each trimester of pregnancy. To do this, scientists used anthropomorphic phantoms simulating the mother's body, arms and legs. Fetal dose was measured at three levels corresponding to each trimester of pregnancy. The results varied: 3.4–6.0 μGy for the knee joint and 2.9–7.7 μGy for the cubitus. The dose received depended on fetal depth and gestational age. Additionally, the scientists conducted supplementary studies: with the use of a protective shield, which reduced the radiation dose by 43 % (knee joint) and 51 % (elbow joint); with turning the body away from the hole in the gentry – as a result, the received dose was reduced by 62 %. In conclusion, the authors concluded that upper and lower extremities diagnosis by CBCT tomography does not carry radiation harm to the foetus [32].

There is another advantage of CBCT tomography – fewer significant artefacts from the surgical hardware. It provides significant advantages in monitoring the osteoregeneration process in patients after metallic osteosynthesis (MOS) [5]. This question has been raised by G.M. Osgood et al. who compared radiographs and CBCT tomography images, assessing: cortical bone, trabecular bone, contour of the large metal side plate, thread-to-bone interface, bridging ossification, fracture line and callus formation. Following the results, CBCT tomography outperformed standard radiography in visualizing the bone healing process, providing a more detailed picture of bone callus formation, overlap of the bony trabecula and residual fracture line. Additionally, CBCT tomography made it possible to clearly define the bone-to-screw boundaries, which aids in determining early MOS attenuation. It assumes particular relevance in detecting complications such as nonunion and the occurrence of infection [33].

In their study, a group of German scientists T. Patzer et al. (2022) analyzed the diagnostic accuracy of CBCT tomography using additional iterative algorithms to reduce artefacts from surgical hardware for postoperative assessment after bone grafting. The study included the following criteria: joint screw position (specificity – 98.21 %, sensitivity – 100 %, accuracy – 98.75 %); screw loosening (specificity – 98.53 %, sensitivity – 100 %, accuracy – 98.75 %); implant failure (specificity – 100 %, sensitivity – 100 %, accuracy – 100 %); fragmentary dislocation (specificity – 100 %, sensitivity – 95.83 %, accuracy – 98.75 %); delayed healing/nonunion (specificity – 98.11 %, sensitivity – 96.30 %, accuracy – 97.50 %). Having obtained high rates, CBCT tomography has been shown to be a reliable diagnostic device for postoperative evaluation and detection of complications after MOS placement [34].

In 2021, J. Dartus et al. conducted a retrospective study comparing MSCT and CBCT tomography images obtained during total knee replacement. Their objective was to identify the most informative diagnostic tool that yielded the least amount of metallic artefacts. The analysis was performed for the following anatomical zones: tibial plateau; trochlearis component; posterior condyles; patella. The assessment was carried out us-

ing a Likert response scale by two independent experts. In the results obtained, CBCT tomography provided informative knee prosthesis data by optimizing image quality and using an algorithm to reduce artefacts from surgical hardware. According to the authors, CBCT tomography provides a more detailed picture with few artefacts from the surgical hardware, in contrast to MSCT. It will help the specialist to diagnose emerging complications such as implant loosening in a timely manner [35].

The Italian research group of G. Carrafiello et al. (2012) was the first to describe percutaneous biopsy of the affected bone using CBCT tomography in XperGuide mode. XperGuide has been demonstrated in 17 patients with a technical success rate of 100 %. An adequate specimen for histological examination for definitive diagnosis was obtained in 15 patients; in the remaining 2 patients, the material obtained was insufficient. Scientists analyzed the technique and calculated its diagnostic value – sensitivity 90.91 %, specificity 100 %, accuracy 94.12 % [36].

Meanwhile, Chinese physicians J.F. Liu et al. (2018) described the technique of percutaneous biopsy of the affected bone using flat-panel CBCT tomography and demonstrated its capabilities. Having analyzed the diagnostic value, the authors obtained high values: sensitivity 95.5 %, specificity 83.3 %, accuracy 93.7 %. The technical success rate of percutaneous biopsy using CBCT tomography was 100 %. This study represents the promising potential of CBCT tomography navigation systems in the diagnostic process of bone and joint diseases [37].

Notwithstanding all the advantages described above, the disadvantages of CBCT tomography should also be mentioned. These include high sensitivity to artefacts as a result of motion. Attempting to overcome this problem, a group of American scientists of A. Sisniega et al. (2019) developed a protocol to compensate for dynamic fuzziness in lower extremity examinations based on a three-dimensional "autofocus" algorithm. From the obtained results, the researchers concluded that this protocol is highly effective in eliminating motion artefacts, improving the diagnostic quality of the image [38].

In 2008, in a research study by G.H. Chen et al. presented a method of image reconstruction – Prior Image Constrained Compressed Sensing (PICCS). The distinguishing feature of PICCS concerned that a sparse version of the image is reconstructed instead of the target image. The authors demonstrated the application of the algorithm on the exclusion of dynamic artifacts caused by heartbeat during a CT study [39]. The research team of S. Hatamikia et al. (2023), however, was the first to demonstrate and describe the use of PICCS to suppress metallic artefacts in puncture biopsy using a CBCT tomography machine with a C-arc. The authors observed that this protocol showed high quality of the images obtained, and also due to the CBCT tomography technique, the procedure is accompanied by low radiation exposure [40]. Considering the above, the PICCS reconstruction method may become more relevant in the diagnostic process of musculo-skeletal system disorders with its ability to suppress both dynamic blurring and artefacts from surgical hardware.

CBCT tomography can be fully considered a highly informative low-dose radiotherapy technique. Coupled with the improvement of the hardware equipment itself, there is an active development of image processing and reconstruction protocols. It allows for the levelling of artefacts, which in turn improves image quality. Creation and development of new modes give CBCT tomography an opportunity to open new directions of its application in clinical medicine.

CONCLUSION

CBCT tomography is a modern promising technique that has a number of advantages in the diagnosis of musculo-skeletal system pathology. CBCT tomography examinations can detect the smallest changes in bone architectonics down to microcracks as a result of its high resolution. According to the results, CBCT tomography has a high diagnostic accuracy in detecting diseases, especially bone and joint injuries in the upper and lower extremities. However, CBCT tomography has a low radiation load on the patient, which is especially important in paediatric practice. There are also many image reconstruction protocols and techniques that improve the quality of the images obtained and expand the diagnostic horizon of this technique. Based on the above mentioned, CBCT tomography can be a full-fledged alternative to MSCT in the diagnosis of pathology of the bone and joint system.

Funding

No sources of funding were provided for the study.

Conflict of interest

The authors declare that this study, its topic, subject matter and content do not involve competing interests. Any opinions expressed in the article are those of the authors of the original article.

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Lezhnev D.A. – formulating the study purpose; developing the concept and design of the article; editing the text; approving the final version of the publication – taking responsibility for all aspects of the work, the integrity of all parts of the article and its final version.

Vasiliev A.Yu. – formulating the study purpose; developing the concept and design of the article; editing the text; approving the final version of the article before its submission for publication.

Petrovskaya V.V. – editing the text; approving the final version of the article before its submission for publication.

Lazarenko E.Yu. – editing the article before its submission for publication.

Blinov N.N. – editing the text; approving the final version of the article before its submission for publication.

Sergeyeva A.D. – editing the article before its submission for publication.

The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

SURGICAL TREATMENT OF INTRA-ARTICULAR FRACTURES OF THE PROXIMAL HUMERUS

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ABSTRACT

Background. *The most severe category of fractures of the proximal humerus are intra-articular injuries which are accompanied with humeral head ischemia caused by an injury and aggravated by surgical intervention. Due to frequent disruption of vascularization with subsequent necrosis of the humeral head, there is a need to stimulate reparative osteogenesis in intra-articular injuries to prevent ischemic changes in the humeral head.*

The aim of the study. *To improve the results of surgical treatment of intra-articular fractures of the proximal humerus based on the development of a new osteosynthesis technique using non-free osteomuscular graft.*

Material and methods. *We analyzed the results of treatment of 48 patients with 11-C1 and 11-C2 intra-articular fractures of the proximal humerus, who had hospital treatment at the emergency department of traumatology of the Novosibirsk City Clinical Hospital No. 1 and were subsequently observed on an outpatient basis. An analysis of literature data using search words was carried out in the PubMed and eLibrary databases.*

Results. *According to the data obtained during the study, the functional and radiological results of the patients who were treated using the method of reparative stimulation with a non-free osteomuscular graft from the coracoid process are statistically significantly higher than the results of the control group.*

Conclusion. *Using autoplasty with a non-free osteomuscular graft from the coracoid process improves the results and reduces the risk of developing post-traumatic aseptic necrosis of the humeral head.*

Key words: *intra-articular fracture of the proximal humerus, stimulation of reparative osteogenesis, non-free osteomuscular graft, aseptic necrosis of the proximal humerus*

Received: 18.12.2022
Accepted: 25.09.2023
Published: 05.12.2023

For citation: Prokhorenko V.M., Afanasiev Yu.A. Surgical treatment of intra-articular fractures of the proximal humerus. *Acta biomedica scientifica*. 2023; 8(5): 192-202. doi: 10.29413/ABS.2023-8.5.21

ХИРУРГИЧЕСКОЕ ЛЕЧЕНИЕ ВНУТРИСУСТАВНЫХ ПЕРЕЛОМОВ ПРОКСИМАЛЬНОГО ОТДЕЛА ПЛЕЧЕВОЙ КОСТИ

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РЕЗЮМЕ

Введение. *Наиболее тяжёлой категорией переломов проксимального отдела плечевой кости являются внутрисуставные повреждения, при которых в результате травмы развивается ишемия головки, усугубляемая оперативным вмешательством. В связи с частым нарушением васкуляризации с последующим некрозом головки возникает необходимость стимуляции репаративного остеогенеза при внутрисуставных повреждениях для профилактики ишемических изменений головки плечевой кости.*

Цель исследования. *Улучшить результаты хирургического лечения внутрисуставных переломов проксимального отдела плечевой кости на основе разработки новой методики остеосинтеза с использованием несвободного костно-мышечного трансплантата.*

Материал и методы. *Материалом исследования послужил анализ результатов лечения 48 пациентов с внутрисуставными переломами проксимального отдела плечевой кости категорий 11-С1 и 11-С2, лечившихся стационарно в отделении неотложной травматологии ГБУЗ Новосибирской области «Городская клиническая больница № 1» и в дальнейшем наблюдавшихся амбулаторно. В базах данных электронных информационных ресурсов PubMed, eLibrary проведён анализ литературных данных по поисковым словам.*

Результаты. *Согласно данным, полученным в ходе исследования, функциональные и рентгенологические результаты группы пациентов, оперированных с использованием метода репаративной стимуляции несвободным костно-мышечным трансплантатом из клювовидного отростка лопатки, статистически значимо выше результатов контрольной группы.*

Заключение. *Использование метода аутопластики несвободным костно-мышечным трансплантатом из клювовидного отростка лопатки улучшает результаты и уменьшает риск развития посттравматического асептического некроза головки плечевой кости.*

Ключевые слова: *внутрисуставной перелом проксимального отдела плечевой кости, стимуляция репаративного остеогенеза, несвободный костно-мышечный трансплантат, асептический некроз проксимального эпифиза плечевой кости*

Статья поступила: 18.12.2022
Статья принята: 25.09.2023
Статья опубликована: 05.12.2023

Для цитирования: Прохоренко В.М., Афанасьев Ю.А. Хирургическое лечение внутрисуставных переломов проксимального отдела плечевой кости. *Acta biomedica scientifica*. 2023; 8(5): 192-202. doi: 10.29413/ABS.2023-8.5.21

INTRODUCTION

According to modern domestic literature, fractures of the proximal humerus (PH) comprise from 5 to 15 % of human skeletal bone injuries, and in 15 % of cases they are accompanied by dislocation of the fragments [1]. Fractures of the proximal humerus are most common in the elderly; in young adults, this injury is more common in high-energy traumas such as falls from a height or road traffic accidents [2]. The increasing demands on the quality of life, the increase in the duration of active life, and the improvement of osteosynthesis methods have led to an appropriate expansion of indications for surgical treatment of fractures occurring in this localisation. Concurrent with the increase in surgical activity, there has been an increased interest in studying complications of the results of both surgical and nonsurgical treatments, one of which is humeral head avascular necrosis (HHAN). A complete cessation of the blood supply to the humeral head (AO classification – type C fractures and fracture dislocations, Neer classification – quadrilateral fractures) at the time of injury is the basis for the development of this condition; subsequently, the incidence of HHAN depends not only on the severity of the injury, but also on the traumatic nature of the surgical intervention. The surgical treatment tactics for proximal humerus fractures are represented by three main directions: osteosynthesis with angular stability plates; intramedullary blocking osteosynthesis with various modifications of proximal humeral nails (PHN); shoulder joint endoprosthesis (hemi and total). Alongside the mainstream techniques, there are original author's fixations that have limited prevalence. Transosseous osteosynthesis of PH fractures is not widespread due to technical complexity and the need for constant monitoring of the external fixation apparatus.

The use of PHN intramedullary osteosynthesis in the treatment of intra-articular PH fractures is controversially interpreted in the scientific literature as being associated with a persistent risk of humeral head avascular necrosis, as well as other complications specific to this technique, such as nail head impingement syndrome and migration of non-fixed screws with persisting fragment micromobility. As a consequence of technical difficulties in restoring anatomical relationships in the case of closed repositioning, techniques of "mini-access repositioning with additional stabilisation of the tuberosities" are being introduced [3]. Many studies have focused on primary shoulder arthroplasty procedures as a result of posttraumatic disruption of the blood supply to the fragments, technical difficulties in fracture correction, and a high incidence of complications in the long-term outcome of PH intra-articular fractures. The majority of recent reports are indicating that primary endoprosthesis replacement is usually preferred over arthroplasty in the remote period, as primary surgery is technically easier to perform [4]. As more information becomes available, however, endoprosthesis replacement-specific complications such as recurrent dislocations and aseptic instability of the endoprosthesis replacement components have been reported.

An increasing number of reports describing the unsatisfactory results of shoulder endoprosthesis replacement for proximal humerus fractures have recently appeared. D. Den Hartog et al. in 2010 published the results of a meta-analysis of 33 outcome studies in 1096 patients with three- and four-fragment fractures of the proximal humerus. Patients who underwent endoprosthesis replacement were found to have a worse functional outcome compared to those who did not undergo surgery, with a difference of 10.9 points on a 100-point Constant scale [5]. In a comparative study of the long-term consequences of endoprosthesis replacement, moderate and severe impairment of limb function was noted in up to 30 % of cases [6].

Clinical and experimental data indicate impaired vascularization with subsequent necrosis of the humeral head in 30–100 % of cases after intra-articular fractures [7]; therefore, there is a need to stimulate reparative osteogenesis in intra-articular injuries to achieve fusion and prevent ischaemic changes in the humeral head. The use of free spongy bone autografts from the wing of the iliac bone, which in the bulk of publications are considered exclusively for the replacement of bone defects of the proximal part of the shoulder, is the most widely used when considering this issue. This option of bone grafting is optimal for many parameters, including the absence of immune response, the presence of living osteogenic stromal cells; the disadvantages include prolongation of the surgery time, the emergence of additional infection gates, and patient discomfort. In addition, the lack of a blood supply source to the graft increases the risk of graft lysis.

The most perspective for osteogenesis stimulation appears to be the use of non-free autografts.

In this area of application (shoulder and humerus), the method of non-free bone grafting for the treatment of false joints in the upper third of the humerus draws attention from the available sources [8]. The essence of the method is the formation of an osteomuscular graft (osteomyocutaneous graft), including a fragment of the lower angle of the scapula, which is moved to the reconstruction zone in the upper third of the shoulder. The authors have obtained good to excellent results in the treatment of false joints of the upper third of the humerus through this method. Stimulation of osteogenesis by non-free osteomuscular gratfs (osteomyocutaneous grafts) in intra-articular pathology has been studied for the hip joint region, for which predominantly good results have also been noted, including in the treatment of avascular necrosis of the femoral head. The use of a non-free osteomuscular graft (osteomyocutaneous graft) from the clavicular process of the scapula on the feeding pedicle of the short head of the biceps brachii muscle is mainly used in the correction of shoulder joint instability (Latarger surgery); the study of the long-term consequences of this method revealed the main regularities of bone block remodelling and resorption.

THE AIM OF THE STUDY

To improve the results of surgical treatment of intra-articular fractures of the proximal humerus by means of the development of the osteosynthesis technique using a non-free osteomuscular graft (osteomyocutaneous graft).

MATERIALS AND METHODS

We analyzed the results of treatment of 48 patients with 11-C1 and 11-C2 intra-articular fractures of the proximal humerus, who had hospital treatment at the emergency department of traumatology of the Novosibirsk City Clinical Hospital No. 1 and were subsequently observed on an outpatient basis.

Inclusion criteria for the study group were the following parameters: male or female patients aged 20 to 80 years inclusive with diagnosed AO/ASIF (Association for Osteosynthesis/Association for the Study of Internal Fixation) type C (C1–C2) fractures of the proximal humerus in need of surgical treatment. Patients with extra-articular PH fractures (types A and B) and fracture dislocations (type C3); patients not tolerant or not agreeing to surgical treatment were not included in the study.

Two groups were formed out of the total number of patients: control or comparison group – 25 patients who underwent surgery using traditional methods (osteomuscular graft osteosynthesis with an angular stability plate or intramedullary blocked osteosynthesis with proximal humeral pins); study group – 23 patients whose treatment was additionally based on the method of transplantation of a non-free osteomuscular graft (osteomyocutaneous graft) from the clavicular process of the scapula into the fracture zone. The mean age of the patients was 65 years for the study group and 67 years for the comparison group; all patients were underwent surgery within 7–10 days after the injury, except for 2 patients in the study group who underwent transplantation of the clavicle fragment 6–8 weeks after the injury as a consequence of primary osteosynthesis failure. Both groups of patients were examined in the preoperative and postoperative periods using clinical (anamnesis, complaints, local status), X-ray (radiographs of the shoulder joint in 2 or 3 projections) methods and multi-layer spiral computed tomography (X-ray dynamics of changes in the fracture zone and bone structure of the humeral head were studied). In the long-term period, histological examination of intraoperative biopsy specimens was selectively performed to determine the severity of posttraumatic ischemic impairment of the humeral head bone tissue. Functional outcomes of surgical treatment were assessed using the American Shoulder and Elbow Surgeons' (ASES) scale. The obtained data were assessed in three main areas: presence and severity of pain syndrome (PS) index of the ASES scale, in points); range of shoulder joint motion (flexion, abduction, external and internal rotation); patient satisfaction with the ability to use the affected limb for household activities (ADL) index of the ASES scale, in points), and X-ray expression of signs of postischemic impairment of the PC head. The degree of aseptic necrosis of the head was assessed using the ARCO (Association Research Circulation Osseous) scale. Functional and X-ray changes in patients were observed over the period 2015–2022.

The conduct of the study was approved by the ethical committee of the Novosibirsk City Clinical Hospital No. 1 and the Biomedical Ethics Committee of the Novosibirsk Research Institute of Traumatology and Orthopedics n. a. Ya.L. Tsivyan (No. 42/19 dated November 11, 2019; No. 001/23 dated January 17, 2023).

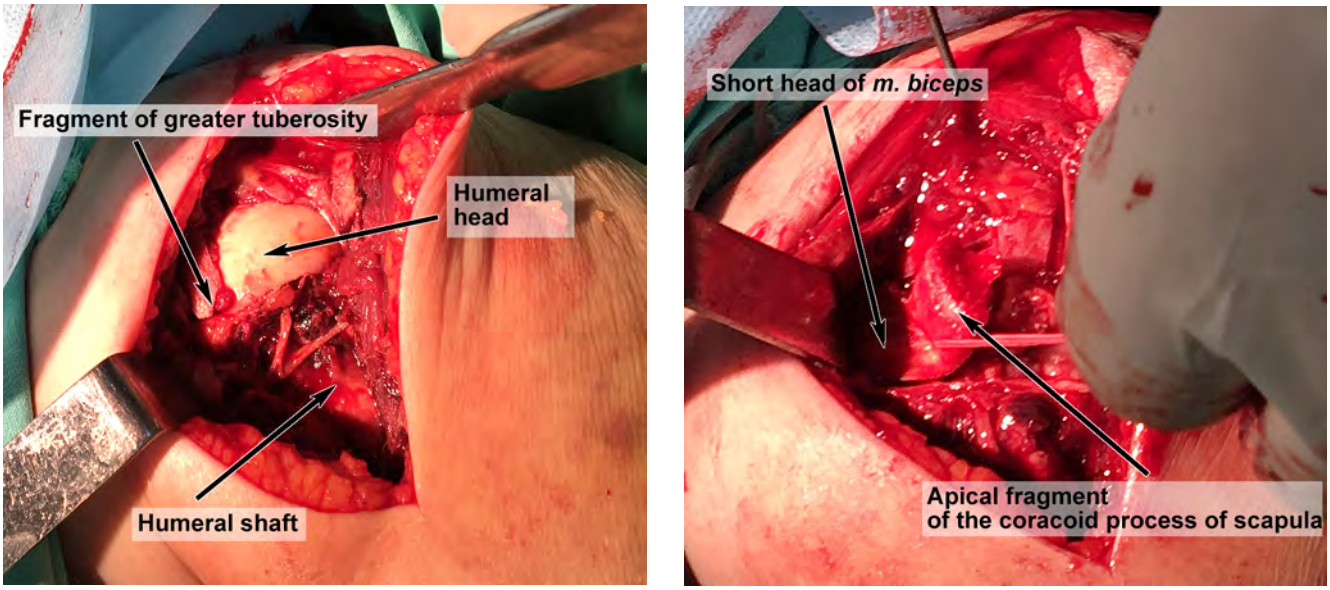
The course of the surgery

The main stages of the surgery are schematically shown in Figure 1.

a ***b*** ***c*** ***d***

FIG. 1.

*Revision of the fracture zone (**a**); reposition of fragments (**b**); taking and carrying into the fracture zone a graft from the coracoid process on the muscle-tendon pedicle of the short head of the biceps muscle (**c**); bone osteosynthesis with an LCP plate (**d**)*



a *b*

FIG. 2.
*Revision of the fracture zone (**a**); carrying into the fracture zone a graft from the coracoid process on the muscle-tendon pedicle of the short head of the biceps muscle (**b**)*

Surgical intervention was performed in the supine position using general and conduction anaesthesia of the upper extremity. From the anterior deltoideopectoral access, the fracture zone was isolated layer by layer, and after revision of the fragments and rotator cuff tendons, gentle repositioning of the fragments with minimal periosteum separation was performed (Fig. 2a). After conventional osteosynthesis with the LCP proximal humeral plate, the clavicular process of the scapula and the tendon of the short head of the biceps brachii and the coracoacromial ligament attached to it were subfascially isolated. The coracoacromial ligament was partially incised according to the length of the graft; after performing a 1–1.5 cm long osteotomy of the coracoid process of the scapula, the short head of the biceps brachii muscle was mobilised.

The osteomuscular graft formed in this way was guided into the fracture zone under the fragment of the small tuberosity of the humerus using a ligature (Fig. 2b) with its ends brought to the outer part of the greater tuberosity, which provides additional fixation of the greater tuberosity (Fig. 3a, b).

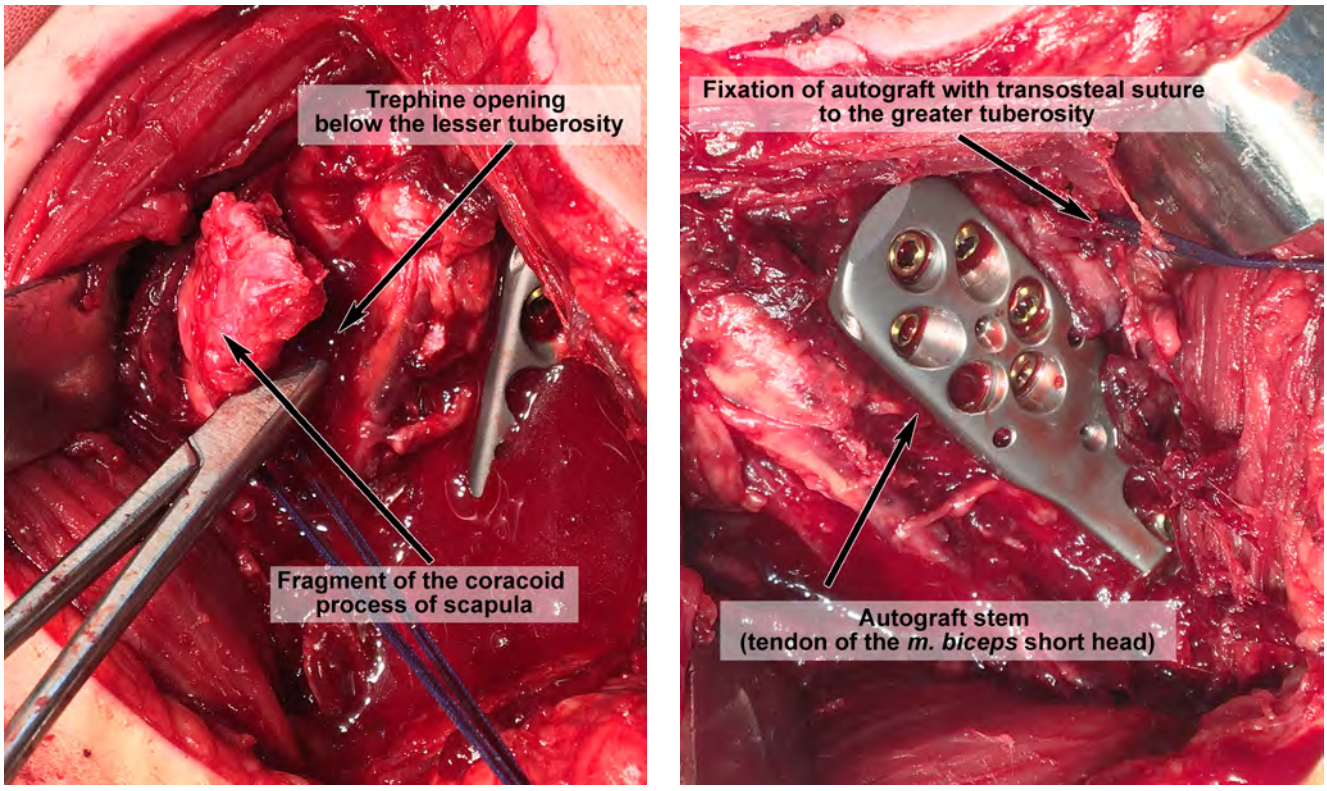
After being tested, the wound was sutured layer by layer, and immobilization was performed with a many-tailed bandage. Postoperative follow-up was typical for all patients in both groups: active elbow joint development from day 2; passive non-aggressive shoulder joint development standing and lying down after suture removal (day 9–10). Active shoulder joint development was allowed after 6 weeks from the time of surgery, from day 8–10 postoperatively. Treatment outcomes were assessed using the ASES scale at 6 to 12 months (1 month to 5 years) after surgery.

RESULTS AND DISCUSSION

The outcomes of patients' treatment with intra-articular fractures of the proximal humerus were assessed at two stages – immediate and long-term. Treatment outcomes at the time of hospital discharge and after 12 weeks from the date of surgery were considered to be the closest. Functional and X-ray results 18–24 months after surgery were considered as long-term outcomes. According to the data obtained in the course of the study, the functional results of the patient group who underwent surgery using the method of reparative stimulation with a non-free osteomuscular graft (osteomyocutaneous graft) from the clavicular process of the scapula were statistically significantly higher than those of the control group (Table 1).

Statistical data processing

Sample distributions of continuous measures of age, height, weight, postoperative examination time, PS and ADL according to the ASES scale, abduction, flexion, internal and external rotation were examined to ensure compliance with the law of normal distribution using the Shapiro – Wilk test; equality of variance in the compared groups was examined using the Fisher test. Most of the distributions were found to be abnormal and heteroscedastic, and therefore comparisons were made using the nonparametric Mann – Whitney U-test. The pseudo-median (PM) of the differences in values and the standardised difference in mean (SDM) were calculated to assess the magnitude of the difference between the groups. Continuous indices were described as median [first quartile; third quartile]



а *б*

FIG. 3.

*Positioning of a non-free graft downwards from the small humerus tuberosity (**a**); insertion of the graft with the withdrawal of guide ligatures on the greater tuberosity (**b**)*

(M [Q1; Q3]), mean ± standard deviation (M ± SD), minimum and maximum values (min–max).

Binary consolidation and elevation indices were described as number of events and incidence (*n*, %) with construction of 95 % confidence interval (95% CI) using Wilson's formula. Risk difference (RD) and odds ratio (OR) with 95% CI were calculated to assess the difference between groups. The number of patients and frequency (degree – *n* (%)) were calculated for the degrees of HHAN categorical indicators. Binary and categorical indicators were compared by two-tailed Fisher's exact test. Correction of multiple comparison error by the Benjamini – Hochberg criterion was performed during the comparison of degrees in categorical indices (Table 1).

The statistical hypotheses were tested at a critical significance level of $p = 0.05$, i. e., differences were considered statistically significant at $p < 0.05$.

All statistical calculations were performed in the Rstudio software (version 2022.07.2 + 576, 2022-09-06, USA) in the R language (version 4.1.3, Austria). The results of statistical calculations are summarized in Table 1.

The distribution of HHAN degrees in the comparison and study groups differed statistically significantly ($p = 0.010$), namely, for the 0th degree (absence) – in 12 (48 %) and 20 (87 %) patients, respectively ($p = 0.018$); for the 4th degree – in 10 (40 %) and 2 (8.7 %) patients, respectively ($p = 0.028$). There were no differences in the 3rd HHAN degree ($p = 0.610$) (Fig. 4).

PS in the comparison and study groups was within 45 [35; 50] and 45 [45; 50] units, respectively, with a statistically significantly higher ($p = 0.024$) average of 5 points in the study group (Fig. 5).

The range of active motion in the comparison and study groups was within comparable limits: in the comparison group, it was lower on average by 5–10 units (degrees) ($p = 0.483$–0.532) (Fig. 6).

The ADL and total ASES score indices in the comparison and study groups were within comparable limits, but the minimum score in the study group was statistically significantly greater ($p = 0.877$ and $p = 0.535$, respectively), by an average of 7 (ADL) and 12 units (ASES total score).

Consequently, the manifestations of posttraumatic aseptic necrosis of the humerus proximal epiphysis of the 4th degree were reduced 4-fold. A single application of the osteosynthesis technique with a non-free osteomuscular graft (osteomyocutaneous graft) from the clavicular process of the scapula in a case of an unconsolidated intra-articular fracture of the humeral head more than 6 weeks old did not lead to a positive result, con-

TABLE 1

COMPARATIVE TREATMENT RESULTS OF PATIENTS IN THE CONTROL GROUP AND THE STUDY GROUP

Indicators	Comparison group (*n* = 25)	Study group (*n* = 23)	Difference assessment	*p*
Age, M [Q1; Q3] (min–max)	67 [55; 70] (33–77)	65 [62; 76] (46–81)	PM: 4 [–3; 9] SMD: 0.43	0.296
Postoperative examination, M [Q1; Q3] (min–max)	48 [24; 48] (12–68)	18 [11; 24] (6–36)	PM: 24 [12; 36] SMD: 1.52	< 0.001*
Consolidation, *n* (%) [95%CI]	23 (92 %) [75 %; 98 %]	23 (100 %) [86 %; 100 %]	RD: 8 % [3 %; 19 %]	0.491
HHAN, degree	0th degree – 12 (48 %) 3rd degree – 3 (12 %) 4th degree – 10 (40 %)	0th degree – 20 (87 %) 3rd degree – 1 (4.3 %) 4th degree – 2 (8.7 %)		Overall comparison *p* = 0.010* Category: *p*; correction *p* 0th: 0.006*; 0.018* 3rd: 0.610; 0.610 4th: 0.019*; 0.028*
PS, M [Q1; Q3] (min–max)	45 [35; 50] (5–50)	45 [45; 50] (35–50)	PM: 5 [0; 10] SMD: 0.83	0.017*
ADL, M [Q1; Q3] (min–max)	37 [22; 45] (12–50)	33 [29.5; 42] (22–50)	PM: 0 [–6; 10] SMD: 0.18	0.877
ASES total, M [Q1; Q3] (min–max)	80 [62; 88] (27–100)	80 [77; 88.5] (68–95)	PM: 4 [–5; 16] SMD: 0.54	0.535

Note. * – statistically significant differences.

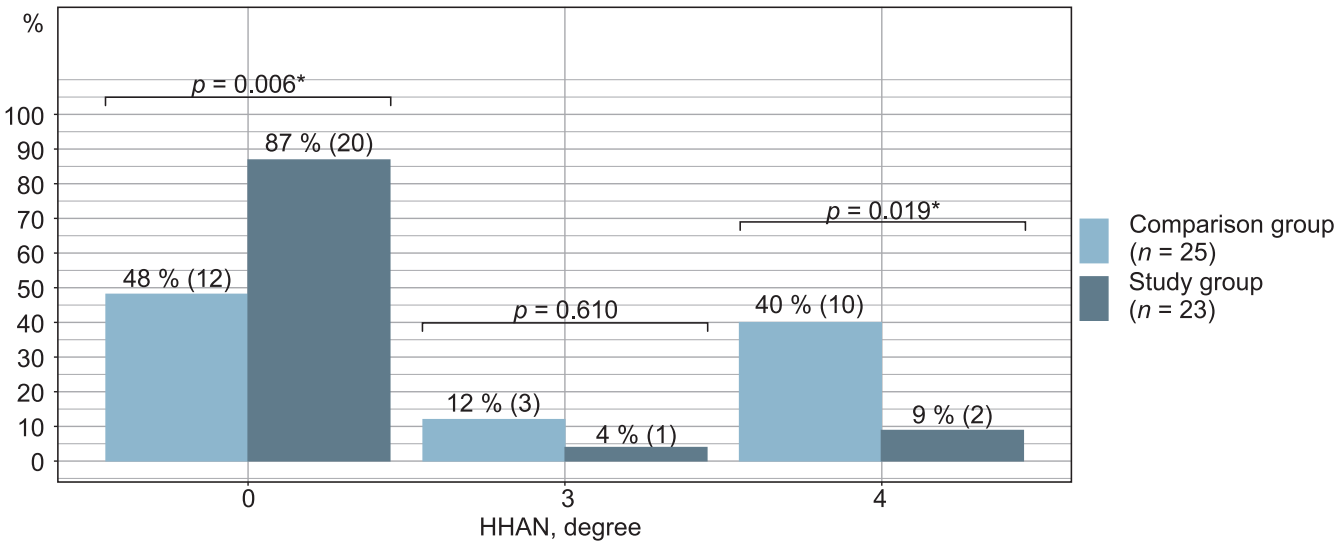


FIG. 4.

Degree distribution of humeral head aseptic necrosis development by groups

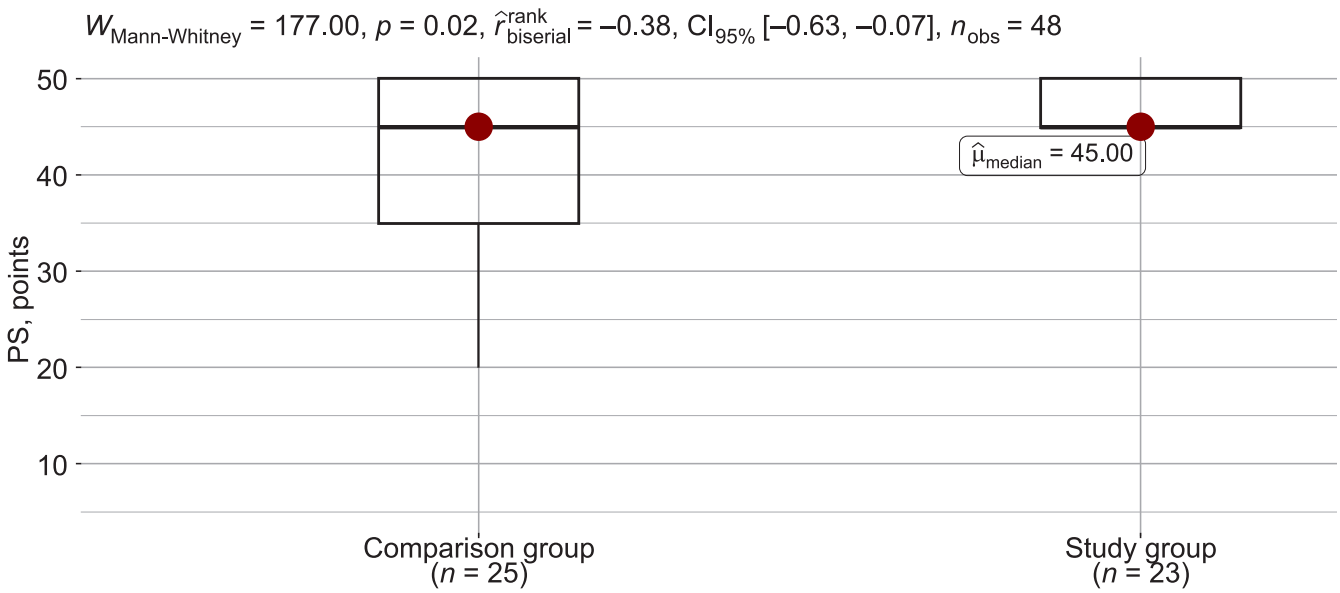


FIG. 5.
Distribution of degrees of pain syndrome (PS index) severity by groups

solidation was not obtained. An assessment of the pain syndrome in the rehabilitation period (6–12 months after surgical treatment) and in the long-term period (more than 1 year) reveals a decrease in the intensity of postoperative pain, mainly as a result of good consolidation of the fracture and a decrease in post-ischaemic bone tissue impairment.

Following the end of the rehabilitation period and restoration of the range of motion in the shoulder joint, in addition to the reduction of pain syndrome, the patients in the study group also experienced a significant reduction or disappearance of pain at night.

Based on the results of the study, a patent for invention "Method of treatment of intra-articular fractures of the proximal humerus" (No. 2740851; priority of invention from June 30, 2020) was obtained.

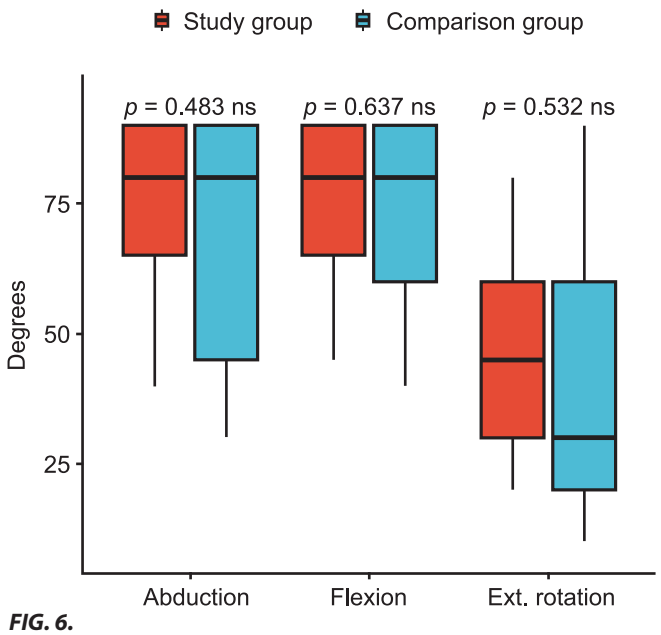


FIG. 6.
Ratio of the active shoulder joint motion volume in the study group and the comparison group

Clinical case No. 1

Patient G., 57 years old, underwent surgery in February 2020 (Fig. 7a, b). The intra-articular nature of the fracture was confirmed intraoperatively, and coracoid transposition was performed (Fig. 7c). At examination after 7.5 months – full range of motion, no pain syndrome, household and partly sports activities without difficulties. Bone structure of the humeral head is radiographically without signs of ischaemia (Fig. 7d). The treatment outcome is excellent.

Clinical case No. 2

Patient D., 74 years old, underwent surgery in early August 2020. Fracture consolidation occurred after 2 months; after 7 months – full range of motion, household activities of the hand do not cause pain and discomfort. No signs of aseptic necrosis were radiologically observed (Fig. 8). The treatment outcome is excellent.

Clinical case No. 3

Patient S., 72 years old. Primary osteosynthesis was performed in September 2019, and secondary displacement of the fragments was observed 2 months later (Fig. 9a). Revision in early December 2019 revealed aseptic necrosis of the head with massive lysis, intraoperatively the remaining part of the head up to 1.5 cm

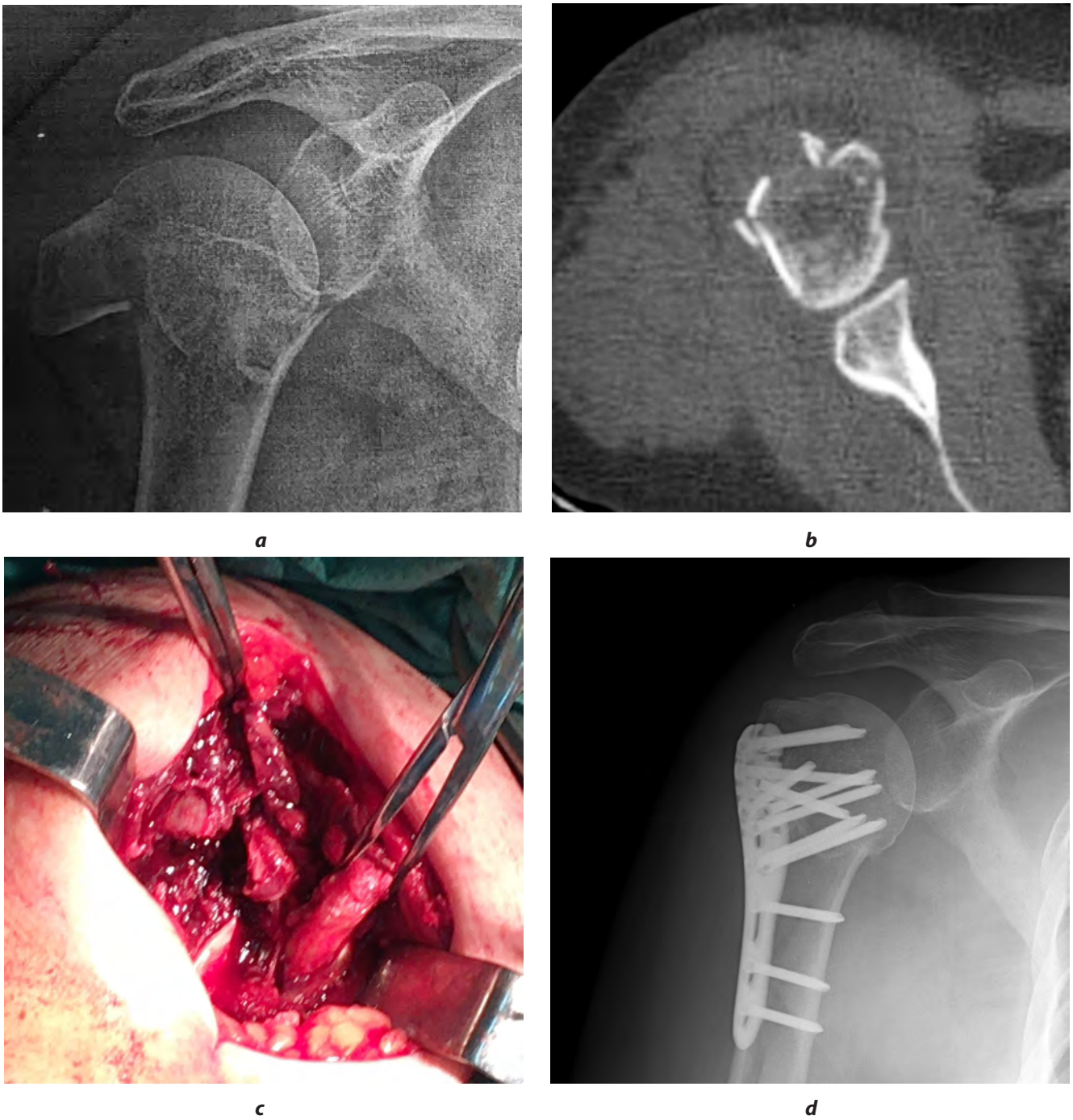


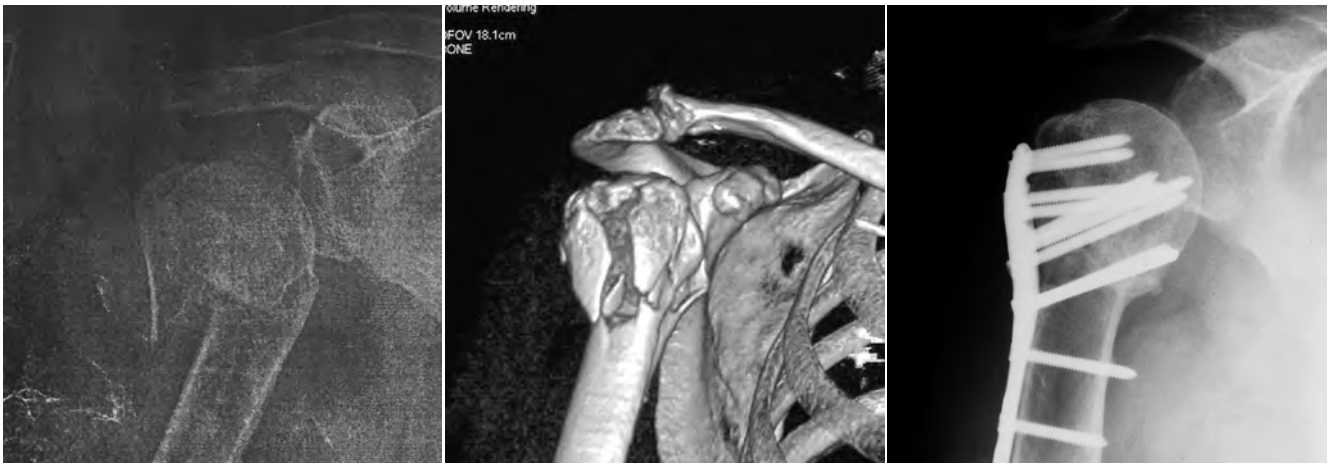
FIG. 7.

Patient G. ***a*** *– X-ray of the shoulder joint before the surgery;* ***b*** *– multi-layer spiral CT before the surgery;* ***c*** *– intraoperative photo of mobilization of a non-free autograft;* ***d*** *– control X-ray of the shoulder joint 7.5 months after the surgery*

of subchondral bone (Fig. 9b). An extramedullary re-osteosynthesis with LCP plate and non-free bone grafting with a graft from the coracoid process was performed. At the follow-up examination 3 months after revision intervention, no fusion was noted (Fig. 9c). At 6 months after removal of the constructs, intraoperative signs of a false joint and ongoing lysis of the head. Intraoperative biopsy confirmed aseptic necrosis of the humeral head.

CONCLUSION

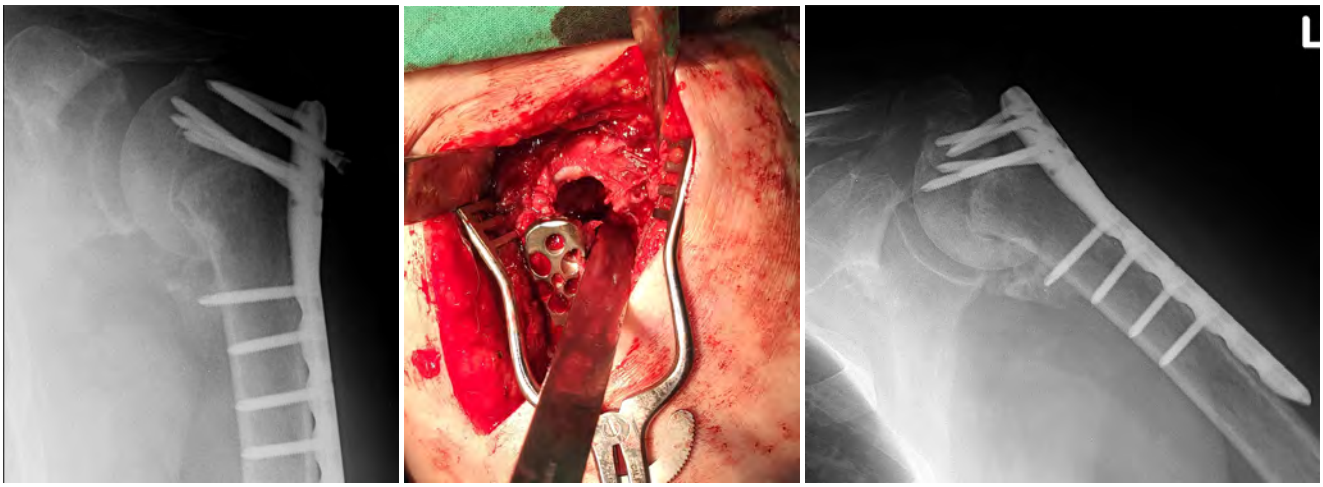
The use of autoplasty with a non-free osteomuscular graft (osteocutaneous graft) from the clavicular process of the scapula in the treatment of "fresh" intra-articular fractures of the proximal humerus reduces the risk of posttraumatic aseptic necrosis of the humeral head, provides predominantly excellent and good results with primary stable osteosynthesis.



а *б* *в*

FIG. 8.

Patient D. ***a*** *– X-ray before the surgery;* ***b*** *– 3D reconstruction of the fracture zone according to multi-layer spiral CT;* ***c*** *– control X-ray of the consolidated fracture 7 months after the surgery y*



а *б* *в*

FIG. 9.

Patient S. ***a*** *– control X-ray 8 weeks after primary osteosynthesis;* ***b*** *– intraoperative photograph of the humeral head lysis;* ***c*** *– control X-ray of an unconsolidated fracture 6 months after re-osteosynthesis*

Conflict of interest

The authors of this article declare no conflicts of interest.

Funding

The study was conducted without sponsorship.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology

SURGICAL TREATMENT OF MASSIVE ROTATOR CUFF TEARS (LITERATURE REVIEW)

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ABSTRACT

The prevalence of rotator cuff tears according to the literature ranges from 20 to 40 %, and this injury occurs more often in people over 60 years of age. Massive rotator cuff tears account for 10–40 % of all rotator cuff tears. Massive rotator cuff tears are considered to be tears with a diastasis of more than 5 cm or tears involving two or more tendons. With such injuries, the kinematics of the shoulder joint changes: proximal subluxation of the humeral head and arthropathy of the shoulder joint occur, which subsequently causes pseudoparalysis. The main clinical manifestations are pain and dysfunction of the shoulder joint. Patients may experience a loss of active range of motion in the shoulder joint while maintaining passive range of motion. There is currently no unified approach to the choosing the tactics for surgical treatment. The most common options include partial rotator cuff repair, subacromial balloon plasty, replacement of tendon defects with allografts and autografts, proximal shoulder joint capsule plasty, muscle-tendon transfers, and shoulder joint arthroplasty. However, according to the literature data, the frequency of re-ruptures after surgery ranges from 11 to 94 %. Despite the large number of methods for the treatment of massive rotator cuff tears, there are no clear algorithms for managing patients and choosing one or another surgical tactics. In addition, there is a high percentage of unsatisfactory outcomes of treatment. Taking all of these factors into account, the problem of improving the treatment of patients with massive rotator cuff tears remains relevant and timely.

Key words: *rotator cuff, surgical treatment, massive tears, supraspinatus tendon, shoulder joint*

Received: 02.06.2023
Accepted: 23.10.2023
Published: 05.12.2023

For citation: Menshova D.V. Surgical treatment of massive rotator cuff tears (literature review). *Acta biomedica scientifica*. 2023; 8(5): 203-210. doi: 10.29413/ABS.2023-8.5.22

ХИРУРГИЧЕСКОЕ ЛЕЧЕНИЕ МАССИВНЫХ РАЗРЫВОВ ВРАЩАТЕЛЬНОЙ МАНЖЕТЫ ПЛЕЧА (ОБЗОР ЛИТЕРАТУРЫ)

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РЕЗЮМЕ

Встречаемость разрывов вращательной манжеты плеча, по данным литературы, составляет от 20 до 40 %, и чаще данное повреждение выявляется у лиц старше 60 лет. Доля массивных разрывов вращательной манжеты плеча составляет от 10 до 40 % от всех разрывов. Массивными разрывами вращательной манжеты плеча принято считать разрывы с диастазом более 5 см или разрывы двух и более сухожилий. При таких разрывах изменяется кинематика плечевого сустава, а именно происходит проксимальный подвывих головки плечевой кости, артропатия плечевого сустава, что в дальнейшем приводит к псевдопараличу. Основные клинические проявления – это болевой синдром и нарушение функции плечевого сустава. У пациентов может наблюдаться потеря активного диапазона движений в плечевом суставе при сохранении пассивных движений. Единый подход к выбору хирургического лечения пациентов на сегодняшний день отсутствует. Самыми распространёнными вариантами можно считать частичное восстановление вращательной манжеты плеча, субакромиальную баллонопластику, замещение дефектов сухожилий аллотрансплантатами и аутотрансплантатами, пластику проксимальной капсулы плечевого сустава, мышечно-сухожильные трансферы и эндопротезирование плечевого сустава. Однако, по данным литературы, частота повторных разрывов после хирургического вмешательства составляет от 11 до 94 %. Несмотря на большое количество методов лечения массивных разрывов вращательной манжеты плеча, отсутствуют чёткие алгоритмы ведения пациентов и выбора той или иной хирургической тактики. Кроме того, сохраняется высокий процент неудовлетворительных исходов лечения. Учитывая всё вышесказанное, проблема совершенствования лечения таких пациентов остаётся актуальной и своевременной.

Ключевые слова: *вращательная манжета, хирургическое лечение, массивные разрывы, сухожилие надостной мышцы, плечевой сустав*

Статья поступила: 02.06.2023
Статья принята: 23.10.2023
Статья опубликована: 05.12.2023

Для цитирования: Меньшова Д.В. Хирургическое лечение массивных разрывов вращательной манжеты плеча (обзор литературы). *Acta biomedica scientifica*. 2023; 8(5): 203-210. doi: 10.29413/ABS.2023-8.5.22

INTRODUCTION

The incidence of rotator cuff ruptures, according to the literature, ranges from 20 % to 40 %; this pathology is more common in people over 60 years of age [1, 2]. The proportion of massive ruptures of the rotator cuff ranges from 10 to 40 % of all ruptures [3, 4]. There is currently no uniform approach in defining massive ruptures of the cuff. Massive rupture, according to the literature, is an injury of two or more tendons or a rupture with a diastasis of more than 5 cm [5, 6]. The main clinical manifestations in such injuries are pain syndrome and impaired function of the shoulder joint. Patients may experience loss of active range of motion in the shoulder joint while passive motion is preserved. These ruptures change the kinematics of the shoulder joint, namely proximal subluxation of the humeral head, arthropathy of the shoulder joint, which subsequently leads to pseudoparalysis [7]. Pseudoparalysis in massive ruptures of the rotator cuff is considered to be the presence of active abduction and flexion of less than 90° with full passive range of motion in the absence of neurological impairment [8]. There is currently no unified approach to the choice of surgical treatment. The most common options can be considered: partial rotator cuff restoration; subacromial balloon angioplasty, proximal rotator cuff plasty, musculotendinous transfers; and shoulder endoprosthetics. However, according to the literature, the incidence of recurrent ruptures after surgery ranges from 11 % to 94 % [9, 10].

THE AIM OF THE STUDY

To analyze the literature data of foreign and domestic authors and provide an overview of modern concepts of surgical treatment of massive ruptures of the rotator cuff.

MATERIALS AND METHODS

A literature search of foreign and domestic authors was performed using PubMed and eLibrary using the following keywords: "rotator cuff", "surgical treatment", "massive ruptures", "tendon of the supraspinous muscle", "shoulder joint" and their English-language counterparts. Publications between 2004 and 2023 were analyzed.

PARTIAL RESTORATION OF MASSIVE RUPTURES OF THE ROTATOR CUFF

The technique of partial restoration in massive ruptures of the rotator cuff was first proposed by S.S. Burkhart in 1994. This method involved restoration of most of the damaged tendons to partially restore shoulder function. S.S. Burkhart et al. performed partial restoration of rotator cuff in 14 patients. Patients after surgical treatment were observed to have an improvement in active abduction from 91° to 150°. Functional outcome according to The University of California – Los Angeles Shoulder Scale (UCLA) improved from 10 points preoperatively, to 28 points after surgical treatment [11]. Partial restoration was originally proposed as open surgery, but advances in minimally invasive technology have made it possible to perform this surgery arthroscopically. This treatment is indicated in patients with massive rupture of the supraspinous muscle tendon and repairable ruptures of the infraspinous and subscapularis tendons [12]. According to the literature, the incidence of recurrent rupture after partial restoration is high at 48.9 % [13]. Good functional results are believed to be short-term and dependent on adjunctive treatments such as subacromial decompression, sanatization, bursectomy, tenotomy or biceps tenodesis [14]. However, O. Galasso et al. in their study demonstrated an improvement in functional performance after partial rotator cuff reconstruction from 39.1 ± 8.4 to 76.3 ± 9.7. 87.4 % of patients were satisfied with the results of treatment [15]. J.D. Hallock et al. found that 4.5 years after partial cuff restoration, revision interventions were required in 5.2 % of patients, with 87 % not requiring reoperative interventions [16]. M.S. Shon et al. reported that after 2 years of follow-up, 50 % of patients showed no improvement after partial reconstruction with decreasing ASES (American Shoulder and Elbow Surgeons) scores [17]. S.J. Kim et al. published the results of 27 patients who underwent partial restoration of the rotator cuff. The mean preoperative rupture size was 42.1 mm and the mean postoperative defect size was 12.0 mm. Functional UCLA outcome improved from 10.5 preoperatively to 25.9 postoperatively [18]. N.D. Iagulli et al. compared partial restoration of rotator cuff versus complete restoration for massive ruptures. The follow-up period was 24 months. The assessment was performed using the UCLA scale. No significant differences were observed in the two groups [19]. M. Moser et al. in their study which compared partial versus full cuff restoration noted that external rotation was significantly better with full restoration. However, the severity of pain and functional outcome were not statistically significant [20].

Consequently, partial restoration of the rotator cuff results in improved functional outcomes and reduced pain in the short term and is suitable for the treatment of patients with low functional needs [21].

BIODEGRADABLE SUBACROMIAL SPACER

An option for surgical treatment of massive ruptures of the rotator cuff is arthroscopic placement of a biodegradable subacromial spacer. The essence of surgical treatment is the introduction of a balloon spacer into the subacromial space, which is subsequently filled with physiologic solution. This device is designed to increase the acromiohumeral interval, lower the humeral head, and thereby eliminate secondary subluxation. The average lifespan of this device is 6–12 months, followed by device degradation [21]. V. Senekovic et al. conducted a prospective study of 20 patients who had been implanted with a biodegrad-

able spacer. The follow-up period was 5 years. Functional improvement was observed in 84.6 % of cases. E. Gervasi et al. suggested in their study that it is not necessary to perform subacromial decompression before balloon positioning. Other authors, however, argue that subacromial decompression should be performed in order to rule out other sources of pain, as well as to select an appropriate balloon size. Some studies have also found that spacer insertion is not indicated for ruptures of the subscapularis tendon, as there is a high risk of balloon migration. In other studies, satisfactory results were obtained when reconstruction of the subscapularis muscle tendon and spacer insertion were performed [21–23]. M. Holschen et al. performed rotator cuff sanation in 11 patients, and 12 patients underwent joint sanation with subacromial spacer insertion. The follow-up period was 23 months. Statistically significant improvement ($p < 0.001$) was observed in the group with spacer insertion. There is doubtful about the results of this study since no randomisation is available [24]. J. Deranlot et al. have assessed the results of arthroscopic balloon plasty in 37 patients. The mean follow-up was 32.8 months. Patients had a significant increase in the range of movements compared to the preoperative period. Active flexion increased from 130° to 160°, active abduction increased from 100° to 160°, and external rotation increased from 30° to 45°. In the presence of good functional results, however, a decrease in the acromiohumeral interval from 8.2 mm preoperatively to 6.2 cm at final follow-up was radiologically observed [25]. M.A. Malahias et al. conducted a comparable study of 32 patients. The first group underwent partial restoration of rotator cuff combined with subacromial spacer insertion. The second group underwent only partial restoration of the rotator cuff. All patients experienced improved functional outcomes and pain reduction after 12 months, but no statistically significant differences were found between the two groups [26].

Arthroscopic insertion of a biodegradable spacer is a minimally invasive procedure in the treatment of patients with massive ruptures of the rotator cuff. This surgical technique results in reduced pain, improved functional outcomes. This procedure, however, is suitable for elderly patients with low physical activity, as it does not eliminate the cause, namely the rotator cuff rupture itself. And the implant "survival" period ranges from 6 to 12 months.

REPLACEMENT OF TENDON DEFECTS WITH GRAFTS

Allograft replacement of the tendon defect is another treatment option for massive ruptures of the rotator cuff. Xenografts are used as allografts. M.H. Metcalf et al. first reported the use of xenotransplants for the treatment of massive ruptures of the cuff. Twelve patients were involved in the study. The follow-up period was 2 years. Complete graft engraftment was observed in 11 patients according to magnetic resonance imaging (MRI) data. Complete resorption of the graft was observed in one patient. No infectious complications were observed. The functional UCLA outcome increased from 9.9 to 19.9 points, but shoulder joint function remained below normal [27]. S.P. Badhe et al. conducted a prospective study of 10 patients with massive ruptures of the rotator cuff who underwent xenograft replacement of the defect. All patients experienced a significant reduction in pain as well as an increase in range of motion. According to ultrasound findings, graft destruction was observed in two patients [28].

Dermal allografts are also used to replace defects. W.Z. Burkhead et al. used a cell-free dermal collagen matrix to restore massive ruptures in 17 patients. The mean follow-up period was 24 months. Mean UCLA scale scores improved from 9.06 to 26.12 points. Unsatisfactory treatment results were observed in 3 patients [29]. J.L. Bond et al. performed arthroscopic implantation of cell-free dermal collagen matrix in 16 patients with non-restorable rotator cuff ruptures. The mean follow-up period was 26.7 months. 15 out of 16 patients were satisfied with the treatment. The average UCLA scale score increased from 18.4 to 30.4 points. According to MRI data, complete graft engraftment was observed in 13 patients [30]. A.K. Gupta et al. have followed 24 patients with a mean follow-up of 36 months. There were improvements in ASES scale scores from 66.6 to 88.7 during the follow-up period. Visual analogue scale (VAS) scores decreased significantly over the follow-up period, from 5.4 to 0.9 points. A statistically significant improvement in active abduction and active flexion at the shoulder joint was observed [31]. P.J. Denard et al. analyzed 59 patients who underwent plasty with cell-free dermal collagen matrix. The follow-up period was 1 year. Functional outcome was assessed using the ASES scale. Flexion improved from 130° to 158° postoperatively. Pain was assessed using the VAS. Pain syndrome decreased from 5.8 to 1.7 points. The acromiohumeral interval increased from 6.6 to 7.6 mm, but decreased again to 6.7 mm 2 weeks after surgery. 70 % of patients were satisfied with the treatment. Based on postoperative MRIs, 45 % of cases had complete graft engraftment and 74.6 % of cases were considered successful. Revision surgeries were performed in 18.6 % of cases, of which 7 patients underwent reverse endoprosthesis [32]. S. Lee et al. noted a decrease in the acromiohumeral interval as a sign of dermal graft failure [33]. In 2012 T. Mihata et al. proposed and described the technique of arthroscopic reconstruction of the upper rotator cuff using an autograft of the fasciae latae muscle. The essence of this method was fixation of the proximal edge of the autograft to the articular process of the scapula rather than to the retracted tendon stumps. The other end of the graft was fixed to the tuberculum majus humeri. This technique improves the correction of proximal subluxation of the head of the humerus (caput humeri) and the prevention of shoulder arthropathy. T. Mihata et al. conducted a study of 24 patients who underwent reconstruction of the upper part of the rotator cuff with an autograft of the fasciae latae muscle. The follow-up period was 2 years. 83.3 % of patients experienced good functional outcomes, namely abduction and external

rotation. The acromiohumeral increased from 4.6 mm preoperatively to 8.7 mm postoperatively [34, 35]. R.W. Jordan et al. performed a systematic review of the literature of reconstruction in upper part of the rotator cuff of the fasciae latae muscle and cell-free dermal collagen matrix. 9 studies were included in the review. Five studies reported grafting with the fasciae latae muscle, and four studies focused mainly around a cell-free dermal collagen matrix. The average follow-up time ranged from 10.9 to 42.4 months. The results were assessed using X-ray techniques. The incidence of dermal matrix failure ranged from 5.5 to 55 %, and fasciae latae muscle failure ranged from 4.2 to 36.1 % [36]. Y.S. Kim et al. published a method of plasty of the proximal rotator cuff with the long head of the biceps tendon. The essence of this surgical intervention is to move the long head of the biceps tendon to the tuberculum majus humeri, which helps to increase the acromiohumeral interval. The preference of this "all-inside" technique is that it is technically less demanding and the use of autograft reduces infectious risks [37, 38].

N.N. Chirkov in 2019 proposed a new method of arthroscopic restoration of the supraspinatus tendon integrity with the autotendon of the long peroneal muscle. The method involves fixation of a tendon autograft, which is passed through the soft tissues of the retracted tendons and fixed with spud legs on a tuberculum majus humeri [39]. N.N. Chirkov et al. published a study comparing partial restoration of the rotator cuff with autotendinous reconstruction of the long peroneal muscle. A total of 58 individuals participated in the study. The patients were divided into two groups. The first group was 30 patients who underwent partial restoration of the rotator cuff. The second group was 28 patients who underwent rotator cuff reconstruction according to the previously described method. The results were evaluated on the scales of VAS, UCLA, ASES, CS (Constant Shoulder Score). Patients in the second group had better functional outcomes. Good and excellent results in the second group of patients were observed in 53.6 % of cases, while in the first group the figure was 26.7 %. Revision surgeries were required in 4 patients, two of whom underwent reverse prosthesis because of advanced osteoarthritis. No complications were observed in both groups [40].

The replacement of rotator cuff tendon defects with both autografts and allografts is currently receiving much attention. Patients have good functional outcomes and pain reduction, but there remains a high rate of graft failure.

MUSCULOTENDINOUS TRANSFERS

If the articular cartilage of the humeral head is preserved, musculotendinous transfers represent one of the surgical options. The most common is the transfer of the latissimus dorsi tendon. In 1998, C. Gerber was the first to suggest and perform latissimus dorsi tendon transposition to the head of the humerus in massive ruptures of the rotator cuff. The essence of surgical treatment was to change the force vector and lower the head of the humerus. In their study, C. Gerber et al. reported 74 % of good and excellent clinical outcomes with a follow-up period of 10 years [41]. S. Namdari et al. conducted a systematic literature review between 1992 and 2010 to determine the outcomes of latissimus dorsi tendon transposition. Ten studies were analysed, with a mean follow-up of 45.5 months. Functional scores improved from 45.9 to 73.2 points. There was an improvement in flexion from 101.9 to 130.7° postoperatively. The overall reported complication incidence was 9.5 %; these included infectious complications, neuropathy, ruptures of transferred tendons, haematomas, and wound disruption [42].

The main factors contributing to a better outcome after latissimus dorsi tendon transposition are preserved or reconstructable sublumbar tendon, absence of deltoid muscle dysfunction, preservation of passive movements in the shoulder joint, and absence of signs of severe osteoarthritis [43]. Researchers believe that irreparable damage to the tendon of the subscapularis muscle is an absolute contraindication to latissimus dorsi tendon transposition, as the centring effect of the rotator cuff muscles is lost [44, 45]. In 2003 E. Gervasi et al. proposed arthroscopic-assisted latissimus dorsi tendon transposition. This technique is minimally invasive, as a result, the risks of traumatization of the acromiohumeral muscle and iatrogenic damage to the neurovascular bundle are reduced. Reducing the risk of injury to the acromiohumeral muscle contributes to the preservation of muscle strength and earlier rehabilitation of patients [46].

S.Y. Dokolin et al. proposed a new method of arthroscopic-assisted latissimus dorsi tendon transposition. Features of the technique include the placement of an additional suprapectoral arthroscopic port, which is necessary to sever the tendon at the crest of the humerus. The tendon of the latissimus dorsi is also augmented with an allograft from the iliotibial tract. Next, the formed graft is passed between the acromiohumeral muscle and teres minor muscle and fixed on the head of the humerus using spud legs. This method reduces the risks of damage to the neurovascular bundle and also reduces the likelihood of postoperative graft detachments [47].

N.V. Zagorodny et al. proposed the technique of double tendon transposition as a method of treatment of non-restorable, massive ruptures of the rotator cuff. Surgical treatment was performed arthroscopically with additional access in the subaxillary region. The essence of this surgery was to excise the tendons of the latissimus dorsi and greater teres muscles from their attachment site and transpose them with fixation to the tuberculum majus humeri. Surgical treatment is performed in an arthroscopically assisted manner with additional access to the subaxillary region to mobilize the latissimus dorsi and teres major muscle. Five patients were underwent surgery using this technique. The follow-up period was 5 ± 1 month. Significant improvement in functional outcomes was observed after surgical treatment. Flexion ranged from 140 to 170° and abduction from 140 to 176°. On the UCLA scale, the mean score changed from 12 to 22.5. Good to satisfactory outcomes were reported in all five patients [48].

Muscle-tendon transfers can be considered the technique of choice for young and active patients. The risk of iatrogenic damage to the neurovascular bundle when excising the tendon from the crest of the humerus remains high, however, as well as the risks of graft detachment both after primary transposition and after revision intervention.

REVERSE SHOULDER REPLACEMENT

Another treatment option for massive ruptures of the rotator cuff is reverse shoulder replacement. Common indications for endoprosthesis are pain and "pseudoparalysis" of the rotator cuff that develops from massive ruptures of the rotator cuff. According to the authors, endoprosthesis is not suitable for the treatment of young and active patients, since there are functional limitations of the shoulder joint, as well as rapid wear of the endoprosthesis, respectively, there is a high probability of upcoming repeated revision surgical interventions [49]. According to the literature, there is a significant reduction in pain syndrome after reverse endoprosthesis, but there is a limitation of flexion to 117–121°. The incidence of complications after this surgery is 33–50 %. Repeated revision interventions comprise 8.3–9.0 %. The most frequent complications include periprosthetic infections (0–6 %), endoprosthesis instability and dislocation (0–30 %), and periprosthetic fractures (1–2 %). Considering the high risk of complications, caution should be exercised when performing reverse replacement arthroplasty in young, active patients [50].

CONCLUSION

The analysis of literature data revealed advantages and disadvantages of existing operative methods of treatment of patients with massive ruptures of the rotator cuff. A high percentage of unsatisfactory treatment outcomes remains regardless of the large number of surgical techniques proposed. No clear algorithms for the choice of a particular surgical tactic are available. Having taken all the above into account, it becomes clear that the problem of improving the treatment of such patients currently remains urgent and requires additional efforts to solve.

Conflict of interest

The author of this article declares that there is no conflict of interest.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

SURGERY

SHORT-TERM AND LONG-TERM RESULTS OF BIMAMMARY BYPASS SURGERY IN PATIENTS WITH MULTIVESSEL CORONARY DISEASE AND TYPE 2 DIABETES MELLITUS AFTER PROPENSITY SCORE MATCHING

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ABSTRACT

Background. *Among patients who have undergone coronary artery bypass surgery (CABG), the proportion of people with diabetes mellitus (DM) is about 40 %. To date, the problem of choosing the optimal method of surgical myocardial revascularization, which can provide the best result in this cohort, remains completely unresolved.*
The aim of the study. *To assess the in-hospital and long-term results of bimammary and traditional bypass surgery in patients with type 2 diabetes mellitus.*
Methods. *From September 2018 to December 2021, 176 CABG surgeries were performed in patients with coronary heart disease (CHD) and type 2 diabetes at the Federal Center for Cardiovascular Surgery (Krasnoyarsk). Group 1 (n = 45) included patients who underwent myocardial revascularization using two mammary arteries; group 2 (n = 131) included patients who underwent myocardial revascularization using traditional technique. After propensity score matching, 45 patients were selected into each group, comparable by basic preoperative characteristics.*
Results. *In group 1, cardiopulmonary bypass surgeries were performed in 23 (51.1 %) patients (group 1CPB), off-pump surgeries – in 22 (58.2 %) (group 1OP); in group 2, all patients underwent cardiopulmonary bypass surgeries. Hospital mortality was recorded in group 2 in 1 (2.2 %) case. Deep sternal infection developed in 1 (4.5 %) patient in group 1OP. Long-term survival in group 2 was 85.3 %, in group 1CPB – 83.3 % (p = 0.689), in group 1OP – 84.2 % (p = 0.739). 84.2 % of patients in group 2 and 100 % in groups 1CPB and 1OP had no cardiovascular events (p = 0.144 and p = 0.145, respectively).*
Conclusion. *Bimammary bypass surgery in patients with type 2 diabetes is a safe and effective method of surgical treatment of coronary artery disease in both short- and long-term period and may be the operation of choice in patients with multivessel disease. There were no differences in patient survival up to 45 months; bimammary revascularization was associated with 100 % absence of cardiac mortality.*

Key words: *coronary bypass surgery, bimammary bypass surgery, diabetes mellitus, deep sternal infection*

Received: 04.05.2023
Accepted: 31.10.2023
Published: 05.12.2023

For citation: Muradov A.G., Grinshtein Yu.I., Drobot D.B., Miller A.Yu., Sakovich V.A. Short-term and long-term results of bimammary bypass surgery in patients with multivessel coronary disease and type 2 diabetes mellitus after propensity score matching. *Acta biomedica scientifica*. 2023; 8(5): 211-224. doi: 10.29413/ABS.2023-8.5.23

БЛИЖАЙШИЕ И ОТДАЛЁННЫЕ РЕЗУЛЬТАТЫ БИМАММАРНОГО ШУНТИРОВАНИЯ У ПАЦИЕНТОВ С МНОГОСОСУДИСТЫМ КОРОНАРНЫМ ПОРАЖЕНИЕМ И САХАРНЫМ ДИАБЕТОМ 2-ГО ТИПА ПОСЛЕ ПСЕВДОРАНДОМИЗАЦИИ

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РЕЗЮМЕ

Обоснование. *Среди пациентов, перенёсших операцию коронарного шунтирования (КШ), доля лиц с сахарным диабетом (СД) составляет около 40 %. На сегодняшний день вопрос о выборе оптимального метода хирургической реваскуляризации миокарда, который обеспечит лучший результат у данной когорты, остаётся до конца нерешённым.*

Цель исследования. *Оценить госпитальные и отдалённые результаты бимаммарного и традиционного шунтирования у пациентов с сахарным диабетом 2-го типа.*

Методы. *С сентября 2018 г. по декабрь 2021 г. в ФГБУ «Федеральный центр сердечно-сосудистой хирургии» Минздрава России (г. Красноярск) проведено 176 операций КШ у пациентов с ишемической болезнью сердца (ИБС) и СД 2-го типа. Группа 1 (n = 45) состояла из пациентов, которым для реваскуляризации миокарда использовали две маммарные артерии; группа 2 (n = 131) – из пациентов, у которых реваскуляризация миокарда проводилась с использованием традиционной методики. После псевдорандомизации в каждую группу отобрано по 45 пациентов, сопоставимых по основным предоперационным характеристикам.*

Результаты. *В группе 1 операции в условиях искусственного кровообращения выполнены 23 (51,1 %) пациентам (1ИК), в условиях работающего сердца – 22 (58,2 %) (1РС); в группе 2 все операции проведены в условиях ИК. Госпитальная летальность зарегистрирована в группе 2 у 1 (2,2 %) пациента. Глубокая стернальная инфекция развилась у 1 (4,5 %) пациента в группе 1РС. Выживаемость в отдалённом периоде в группе 2 составила 85,3 %, в группе 1ИК – 83,3 % (p = 0,689), в группе 1РС – 84,2 % (p = 0,739). Свобода от кардиоваскулярных событий составила 84,2 % в группе 2 и по 100 % в группах 1ИК и 1РС (p = 0,144 и p = 0,145 соответственно).*

Заключение. *Бимаммарное шунтирование у пациентов с СД 2-го типа – безопасный и эффективный метод хирургического лечения ИБС как в ближайшем, так и в отдалённом периоде; может быть операцией выбора у пациентов с многососудистым поражением. В период до 45 месяцев не выявлено различий в выживаемости пациентов; бимаммарная реваскуляризации ассоциировалась с 100%-й свободой от кардиальной смертности.*

Ключевые слова: *коронарное шунтирование, бимаммарное шунтирование, сахарный диабет, глубокая стернальная инфекция*

Для цитирования: Мурадов А.Г., Гринштейн Ю.И., Дробот Д.Б., Миллер А.Ю., Сакович В.А. Ближайшие и отдалённые результаты бимаммарного шунтирования у пациентов с многососудистым коронарным поражением и сахарным диабетом 2-го типа после псевдорандомизации. *Acta biomedica scientifica*. 2023; 8(5): 211-224. doi: 10.29413/ABS.2023-8.5.23

Статья поступила: 04.05.2023
Статья принята: 31.10.2023
Статья опубликована: 05.12.2023

INTRODUCTION

For many decades, coronary heart disease (CHD) has been the leading cause of death and disability among all cardiovascular diseases [1]. Although there have been advances in modern interventional cardiology associated with the use of the latest generation of drug-eluting stents, surgical myocardial revascularization in patients with complex multivessel coronary artery (CA) lesions is the preferential method of treatment, including patients with diabetes mellitus (DM) [2].

Coronary artery bypass grafting (CABG) is the most widely performed cardiac surgery worldwide, with isolated CABG procedures comprising more than half of all cardiac surgeries [3]. The modern level of coronary surgery allows performing operations with hospital mortality not exceeding 2–3 % [3]. The excellent long-term results obtained using the left internal thoracic artery (ITA) for revascularization of the anterior descending artery and the great saphenous vein for other target CAs, compared with the use of venous grafts alone, prompted the possibility of using the right ITA as well. The results of bimammary CABG surgery in numerous studies have demonstrated comparable hospital outcomes and better long-term results as opposed to the traditional bypass technique in patients with multivessel coronary lesions [4, 5]. Notwithstanding these encouraging results, this technique has not been widely used in the daily practice of cardiac surgeons since it requires high precision for the formation of coronary anastomoses and the associated increase in the duration of surgery, duration of the cardiopulmonary bypass (CPB), concerns about bleeding and severe sternal infectious complications as a result of decreased vascularisation of the sternum, especially in high surgical risk patients (diabetes mellitus, overweight, old age, chronic obstructive pulmonary disease (COPD)).

Among patients undergoing surgical myocardial revascularization, the proportion of patients with DM is about 40 % [6]. The question remains unresolved as to the optimal choice of the method of surgical intervention that can provide the best outcome for this category of patients. The presence of concomitant DM is associated with a risk of postoperative complications and poorer long-term survival after CABG. One of the main problems preventing the widespread implementation of bimammary bypass surgery in patients with DM remains the high risk of deep sternal infection as a result of the development of metabolic and severe microcirculatory disorders. The harvesting of only one left ITA can reduce the blood supply to half of the sternum by up to 90 %, while harvesting both ITAs can lead to devascularization of the entire sternum and prevent sternotomy wound healing [7]. As a result, the problem of CHD and DM comorbidity in patients requiring surgical myocardial revascularization is highly relevant. In view of the above-mentioned, it is necessary to evaluate the efficacy of bimammary CABG technique in comparison with the traditional technique of myocardial revascularization in order to reveal the advantages of surgical treatment by means of decreasing the surgery time considering the reduction of the number of formed anastomoses, decreasing sternal infectious complications, mortality and decreasing major cerebrovascular events in patients with multivessel CA lesions and concomitant DM.

THE AIM OF THE STUDY

Analysis of the immediate and long-term results of bimammary and traditional coronary bypass surgery in patients with multivessel coronary lesions and concomitant diabetes mellitus.

METHODS

The analysis of the results of CHD surgical treatment in 176 patients with multivessel coronary lesions and compensated type 2 DM, who underwent isolated CABG in the period from 2018 to 2021 in the cardiac surgery department No. 1 of the Federal Center for Cardiovascular Surgery (Krasnoyarsk) was performed. Indications for CABG were in compliance with the 2018 ESC/EACTS (European Society of Cardiology/European Association for Cardio-Thoracic Surgery) guidelines for myocardial revascularisation. The study was performed as a retrospective, prospective, single-center, controlled study. The retrospective part of the study is represented by hospital outcomes and the prospective part is represented by long-term outcomes. Two groups of patients were formed: group 1 (n = 45) (study group) included patients who underwent myocardial revascularisation using both ITAs; group 2 (n = 131) (control group) included patients who underwent revascularisation using the traditional method of coronary artery bypass surgery (TCABG), namely, by anastomosis between the left ITA and the anterior descending artery; the other affected CAs were bypassed using the great saphenous vein. All patients underwent complete revascularisation according to the SYNTAX study criteria, including the 2018 ESC/EACTS guidelines for myocardial revascularisation: revascularisation of epicardial vessels with a diameter of at least 1.5 mm and lumen stenosis in the lesion area of 50 % or more. In diffuse CA atherosclerosis, the distal anastomosis was sought to be formed in the least altered area. The study was conducted in accordance with the standards of good clinical practice and the principles of the World Medical Association Declaration of Helsinki. The study protocol was approved by the bioethical committee of the Federal Center for Cardiovascular Surgery (Krasnoyarsk) (minutes No. 3 dated July 06, 2021). Inclusion criteria: patients aged 35 to 80 years with angina pectoris of functional class II and higher (according to the criteria of the Canadian Cardiovascular Society (CCS) with concomitant type 2 DM and having haemodynamically significant lesions of 2 or more CA or isolated lesion of the left coronary artery trunk more than 50 %. Exclusion criteria: age of patients older than 80 years; concomitant cardiac or aortic pathology requiring one-stage surgical correction; single-vessel lesion suitable for CA stenting; previous cardiac

surgery. The primary endpoints of the study were hospital mortality and mortality in the remote postoperative period; mortality from cardiac causes in the remote period; myocardial infarction (MI); acute cerebrovascular accident (ACVA) in the early and remote postoperative periods; deep sternal infection during hospitalization; repeat revascularization in the remote period; freedom from major cardiovascular events (death from cardiac causes + freedom from MI + freedom from ACVA + freedom from repeat revascularization). Secondary endpoints of the study were the clinic of recurrent angina pectoris. The main preoperative clinical indicators are summarised in Table 1.

The groups were comparable in terms of age ($p = 0.295$), gender ($p = 0.561$), and body mass index ($p = 0.856$). No differences were found for comorbidities: arterial hypertension ($p = 0.432$), chronic kidney disease (glomerular filtration rate less than 60 mL/min/1.73m^2; $p = 0.130$), COPD ($p = 0.662$); the groups were similar in nicotine addiction in patients ($p = 0.07$). The functional class of angina pectoris was assessed according to the CCS classification. Most patients from both groups had functional class III angina pectoris. In group 1, the prevalence of heart failure was mainly of functional class III (57.8 %), in group 2 – of functional class II (51.1 %) according to the classification of the New York Heart Association (NYHA).

The groups were comparable in terms of haemodynamically significant (stenosis greater than 60 %) lesions in the brachiocephalic artery system (BCA) ($p = 0.513$); the number of patients with severe calcinosis of the ascending aorta was statistically significantly higher in the bimammary CABG group ($p = 0.001$); the groups were identical in terms of the number of haemodynamically significant CA lesions ($p = 0.629$). Echocardiography (EchoCG) findings revealed no differences between groups in left ventricular contractile function ($p = 0.266$). According to the EuroScore II postoperative complications risk scale, the risk of adverse outcome was statistically significantly higher in group 1 ($p = 0.016$).

In an attempt to minimise systematic errors, which could lead to misinterpretation of the results, and to maximise equivalence of the two groups with each other, a computer-generated equating of the groups was performed by adjusting the raw data using the pseudorandomization method. This statistical method allowed the formation of a study control group with minimal variation in baseline parameters coded into the various intervening factors (confounders) that were included in the propensity score matching model ("Propensity Score Matching"). The following parameters that may have influenced the outcomes of surgical interventions were used to minimize variation in preoperative data: age; sex; body mass index; smoking; chronic kidney disease (glomerular filtration rate less than 60 ml/min/1.73 m^2); COPD; lower limb atherosclerosis; hypertension; left ventricular ejection fraction; myocardial infarction; and history of percutaneous coronary interventions. The Nearest Neighbor Matching method with a calibre value of 0.85 was used, with no prior discarding of unsuitable patients in the groups, with a given 1:1 ratio of the groups to be searched. RStudio software (version 2022.02.0, build 443, USA) was used to perform propensity score matching. After performing propensity score matching, both groups were equalized according to baseline characteristics, selecting 45 patients in each group. The groups were comparable in terms of baseline characteristics (Table 1). The majority of patients in both groups had insulin-independent DM. The groups were predominantly male patients ($p = 0.460$), most of them were elderly (over 60 years) ($p = 0.571$), obese (body mass index over 30) ($p = 0.997$), good left ventricular contractile function (ejection fraction over 50 %) ($p = 0.405$). There were 4 (8.9 %) patients in group 1 with left ventricular ejection fraction less than 40 % and 2 (2.2 %) patients in group 2. In both groups, according to the results of preoperative coronary angiography, patients with multiple (more than two) CA lesions predominated. Calcinosis of the ascending aorta was statistically significantly more common in patients from the bimammary CABG group (group 1) ($p = 0.007$); accordingly, the risk of surgical complications was statistically significantly higher in this group ($p = 0.012$).

The criteria for selection of the bimammary CABG technique was the surgeon's preference based on experience with this technique, as well as the absence of an adequate quality VSM (vena saphena magna) conduit. The use of bimammary CABG in patients with DM was considered individually, with such criteria as patient's age, body mass index, and severity of concomitant pathology being considered.

The criteria for choosing OP CABG (Off-Pump Coronary Artery Bypass Graft) were: the surgeon's experience in conducting bimammary multivessel CABG; hemodynamically significant BCA lesion; severe calcinosis of the ascending aorta.

Most patients were monitored for bypass patency following completion of the main stage of surgery. Ultrasound flowmetry (Medistim Mira Q, Norway) using transducers of different diameters was used to assess the bypass patency functioning; the volume velocity of blood flow through the shunt (Q) (the norm is at least 15–20 ml/min) and pulse index (Pi) (not more than 5) were estimated.

All surgeries were performed using the ITA skeletonization technique, and no other arterial conduits were used for revascularization of the affected CAs. The technique of bimammary CABG was used in two modifications: *"in situ"* – each ITA was excised distally before bifurcation and an anastomosis with the affected CA was formed; composite bypass surgery – the right ITA after mobilization was excised proximally to its branching from the right subclavian artery and distally to its branching and sewn into the left ITA (Y-graft). The use of the composite-sequential bypass surgery technique allowed to form more than 2 distal anastomoses, thereby enabling the surgeon to perform complete myocardial revascularization in patients with 3 or more CA lesions. The choice of bimammary CABG method was determined based on the number of target arteries and lesion topography. More details describing the technical aspects of surgical myocardial revascularization using both ITAs can be found in our previous publications [4]. TCABG was performed using the left ITA, separated

TABLE 1
PREOPERATIVE CLINICAL CHARACTERISTICS OF PATIENTS

Parameters	Before propensity score matching			After propensity score matching		
	Group 1 (*n* = 45)	Group 2 (*n* = 131)	*p*	Group 1 (*n* = 45)	Group 2 (*n* = 45)	*p*
IDDM, *n* (%)	11 (24.4 %)	21 (16 %)	–	11 (24.4 %)	8 (17.8 %)	–
NIDDM, *n* (%)	34 (75.5 %)	110 (84 %)	–	34 (75.5 %)	37 (82.2 %)	–
Glycated hemoglobin level						
M ± SD	7.5 ± 0.37	7.5 ± 0.41		7.5 ± 0.37	7.6 ± 0.43	
Me [Q1; Q3]	7.5 [7.4; 7.7]	7.5 [7.4; 8.0]	0.762	7.5 [7.4; 7.7]	7.5 [7.5; 8,0]	0.568
6–8.4 %, *n* (%)	44 (97.8 %)	129 (98.5 %)		44 (97.8 %)	43 (95.6 %)	
8.5–10 %, *n* (%)	1 (2.2 %)	2 (1.5 %)		1 (2.2 %)	2 (4.4 %)	
Age, years						
M ± SD	62.3 ± 7.1	63.3 ± 6.8		62.3 ± 7.1	63.3 ± 4.3	
Me [Q1; Q3]	62 [60.2; 64.5]	64 [62.1; 64.5]		62 [60.2; 64.5]	64 [61.2; 65]	
45–59 years, *n* (%)	9 (20.0 %)	24 (18.3 %)	0.295	9 (20.0 %)	8 (17.8 %)	0.571
60–74 years, *n* (%)	33 (73.3 %)	97 (74.0 %)		33 (73.3 %)	35 (77.8 %)	
> 74 years, *n* (%)	3 (6.7 %)	10 (7.6 %)		3 (6.7 %)	2 (4.4 %)	
Male, *n* (%)	33 (73.3 %)	90 (68.7 %)	0.561	33 (73.3 %)	36 (80 %)	0.460
BMI, kg/m^2						
M ± SD	31.3 ± 5.4	31.1 ± 4.8	0.856	31.3 ± 5.4	31.2 ± 4.4	0.997
Me [Q1; Q3]	32 [27.5; 35.2]	32 [28.1; 34.7]		32 [27.5; 35.2]	32 [28.7; 34]	
Persistent smoking, *n* (%)	10 (22.2 %)	15 (11.5 %)	0.075	10 (22.2 %)	10 (22.2 %)	0.998
Arterial hypertension, *n* (%)	44 (97.8 %)	130 (99.2 %)	0.432	44 (97.8 %)	45 (100 %)	0.328
Chronic kidney disease (GFR < 60 ml/min/1,73 m^2), *n* (%)	22 (48.9 %)	81.6 (61.8 %)	0.130	22 (48.9 %)	13 (73.3 %)	0.051
COPD, *n* (%)	2 (4.4 %)	4 (3.05 %)	0.662	2 (4.4 %)	2 (4.4 %)	0.990
Obesity (BMI > 30), *n* (%)	29 (64.4 %)	81 (64.4 %)	0.757	29 (64.4 %)	26 (57.8 %)	0.522
Angina pectoris according to CCS, *n* (%)						
functional class II	11 (24.4 %)	50 (38.2 %)	–	11 (24.4 %)	22 (48.9)	–
functional class III	31 (68.9 %)	62 (47.3 %)	–	31 (68.9 %)	15 (33.3)	–
functional class IV	3 (6.7 %)	10 (7.6 %)	–	3 (6.7 %)	4 (8.9)	–

TABLE 1 (*continued*)

Heart failure according to NYHA, *n* (%)						
functional class II	19 (42.2 %)	67 (51.1 %)	–	19 (42.2 %)	25 (55.6 %)	–
functional class III	26 (57.8 %)	60 (45.8 %)	–	26 (57.8 %)	20 (44.4 %)	–
BCA atherosclerosis (more than 60 %), *n* (%)	8 (17.8 %)	18 (13.7 %)	0.513	8 (17.8 %)	5 (11.1 %)	0.374
Calcification of the aorta, *n* (%)	11 (24.4 %)	2 (1.5 %)	0.001	11 (24.4 %)	2 (4.4 %)	0.007
Number of CA lesions, M ± SD	2.8 ± 0.6	2.7 ± 0.5	0.629	2.8 ± 0.6	2.8 ± 0.6	0.970
2 CA, *n* (%)	14 (31.1 %)	39 (29.8 %)	–	14 (31.1 %)	12 (26.7 %)	–
3 CA, *n* (%)	25 (55.6 %)	85 (64.9 %)	–	25 (55.6 %)	30 (66.7 %)	–
4 CA, *n* (%)	6 (13.3 %)	5 (3.82 %)	–	6 (13.3 %)	2 (4.44 %)	–
5 CA, *n* (%)	–	2 (1.53 %)	–	–	1 (2.22 %)	–
Left ventricular ejection fraction, %						
M ± SD	51.3 ± 7.6	52.8 ± 9.2		51.3 ± 7.6	52.3 ± 7.2	
Me [Q1; Q3]	52 [49; 53.5]	54 [49; 54.3]		52 [49; 53.5]	54 [50.1; 54.4]	
< 40 %, *n* (%)	4 (8.9 %)	11 (8.4 %)	0.266	4 (8.9 %)	2 (4.4 %)	0.405
40–49 %, *n* (%)	10 (22.2 %)	28 (21.4 %)		10 (22.2 %)	10 (22.2 %)	
> 50 %, *n* (%)	31 (68.9 %)	92 (70.2 %)		31 (68.9 %)	33 (73.3 %)	
EuroSCORE II assessment						
M ± SD	2.9 ± 1.7	3.2 ± 9.7	0.016	2.9 ± 1.7	4.7 ± 16.4	0.012
Me [Q1; Q3]	2.6 [2.5; 3.5]	2.1 [1.5; 4.8]		2.6 [2.5; 3.5]	2.1 [0.2; 9.6]	

Note. IDDM – insulin-dependent diabetes mellitus; NIDDM – non insulin dependent diabetes mellitus; GFR – glomerular filtration rate.

by a skeletonization technique for bypass surgery of the anterior descending artery and a VSM (vena saphena magna) conduit for revascularization of the remaining target CAs. Autovenous conduits were harvested in an open manner using the skeletonization technique.

The RStudio program (version 2022.02.0, build 443, USA) was used for statistical analysis. To identify the type of mean values distribution of the studied indicators, the Shapiro – Wilk test was performed between the groups. No normal distribution of the mean was revealed for each of the indicators; thereby further non-parametric statistics were used. The Wilcoxon-rank sum test was used to analyze continuous variables of independent groups, categorical variables were assessed using the Pearson's χ^2 test. 0.05 was chosen as the reference value of the statistical significance level of *p*. The data are presented in the table in two versions: the mean value together with the standard deviation value and the median value together with the 25 and 75 % quartile values. The values of the categorical variables are also presented by discrete values as the absolute number of patients and their percentage of the total number of patients in the group. Survival and cardiovascular events in the long-term period were analyzed using the Kaplan – Meier method. $p < 0.05$ was considered to indicate statistical significance for the primary outcome.

HOSPITAL OUTCOMES

According to the results of this study, in group 1, 23 (51.1 %) surgeries were performed in CPB (group 1CPB) and 22 (49.9 %) surgeries were performed in OP (group 1OP).

Further comparative analysis was performed between group 2 and groups 1CPB and 1OP. The main postoperative results are summarized in Table 2.

Group 2 was comparable to groups 1CPB and 1OP in terms of the total duration of surgery (p = 0.431 and p = 0.142, respectively); we saw no intergroup differences in the number of distal anastomoses formed either (p = 0.263 and p = 0.901, respectively). Although no proximal anastomoses were formed when performing the bimammary CABG technique, aortic occlusion time and CPB duration were statistically significantly higher than in group 2 (p = 0.05 and p = 0.05, respectively). The rationale for this is that bimammary cardiac revascularisation and sequential anastomosis techniques require the surgeon to be very precise in shunt formation and, consequently, the duration of the surgical procedure. In group 1CPB, extubation of patients in the intensive care unit (ICU) occurred later than in group 2 (p = 0.022), but was comparable in duration to group 1OP (p = 0.114). Drainage losses during the first day in the ICU were comparable between the groups (p = 0.214 and p = 0.243, respectively). Diagnostic coronary artery bypass grafting in the early postoperative period was performed in group 1CPB in 1 (4.3 %) patient, in group 2 – in 1 (2.2 %) patient (p = 0.645) due to ischemic changes recorded on the electrocardiogram (ECG) and EchoCG. In group 1CPB, the bypass patency was intact; in group 2, a kink of the autovenous bypass to the right CA with stenosis of the conduit lumen up to 80 % was revealed, and a resternotomy was performed as an emergency procedure to correct the kink. According to EchoCG data, no statistically significant difference was found between group 2 and groups 1CPB and 1OP in left ventricular contractility before hospital discharge (p = 0.932 and p = 0.241, respectively). Following the results of flowmetric study in both subgroups of bimammary CABG, the volumetric blood flow velocity (Q) was statistically significantly higher than in the traditional CABG group (p < 0.001 and p < 0.001, respectively), but the indices were within the reference values in all groups; the pulse index (Pi) was comparable between group 2 and groups 1PCB and 1OP (p = 0.474 and p = 0.526, respectively), the mean indices were within the normal range.

Analyses of major hospital complications are summarised in Figure 1. Hospital mortality was only 1 (2.2 %) case in group 2 (p = 0.491 and p = 0.503, respectively) and

TABLE 2
INTRAOPERATIVE AND HOSPITAL OUTCOMES

Parameters	Group 1CPB (n = 23)	p	Group 2 (n = 45)	p	Group 1OP (n = 22)
Duration of CPB, min					
Me [Q1; Q3]	78 [67; 99.7]	0.05	78 [74.4; 89.1]	–	–
M ± SD	83.3 ± 37.8		81.7 ± 24.4		–
Duration of aortic occlusion, min					
Me [Q1; Q3]	58 [45; 67.9]	0.05	48 [44.8; 53]	–	–
M ± SD	56.4 ± 26.4		48.9 ± 13.6		–
Duration of surgery, min					
Me [Q1; Q3]	220 [201; 229]	0.431	201 [200; 222]	0.142	189 [178; 211]
M ± SD	215 ± 32.9		211 ± 36.5		194 ± 37.2
Number of distal anastomoses					
Me [Q1; Q3]	2.9 ± 0.6	0.263	2.7 ± 0.5	0.901	2.7 ± 0.6
M ± SD	3 [2.6; 3.1]		3 [2.5; 2.8]		3 [2.4; 3]
2 anastomoses, n (%)	6 (26.1 %)	–	15 (33.3 %)	–	8 (36.4 %)
3 anastomoses, n (%)	14 (60.9 %)	–	29 (64.4 %)	–	12 (54.5 %)
4 anastomoses, n (%)	3 (13 %)	–	1 (2.2 %)	–	2 (9.1 %)

TABLE 2 (*continued*)

ALV (artificial lung ventilation) duration, h					
Me [Q1; Q3]	7 [6.2; 8.5]	0.022	9 [8.4; 11.5]	0.114	7 [6.7; 9.7]
M ± SD	9.9 ± 5.1		9.9 ± 5.1		8.2 ± 3.3
Blood loss, ml					
Me [Q1; Q3]	250 [193; 397]	0.214	300 [287; 385]	0.243	200 [187; 333]
M ± SD	295 ± 236		336 ± 163		260 ± 164
Stay in ICU, days					
Me [Q1; Q3]	2 [2.05; 3.1]	0.756	2 [1.8; 3.8]	0.375	2 [1.8; 2.6]
M ± SD	2.6 ± 1.2		2.8 ± 3.5		2.2 ± 0.8
Inpatient stay, days					
Me [Q1; Q3]	11 [8.9; 18.7]	0.932	11 [9.9; 17.3]	0.214	10 [9.1; 16.3]
M ± SD	10 ± 11.2		13.6 ± 12.3		12.7 ± 8.1
Coronary bypass angiography, *n* (%)	1 (4.3)	0.645	1 (2.2)	–	–
Left ventricular ejection fraction, %					
Me [Q1; Q3]	53 [50.4; 54.6]	0.932	53 [49.8; 55.9]	0.241	51 [46.2; 53.3]
M ± SD	52.5 ± 4.9		52.8 ± 10.2		49.8 ± 8
Flowmetry parameters					
Q, ml/min					
Me [Q1; Q3]	72 [64.2; 77.3]	< 0.001	47 [42.5; 56.5]	< 0.001	60.5 [56.1; 70.2]
M ± SD	70.7 ± 11.2		49.5 ± 11		63.1 ± 12
Pi					
Me [Q1; Q3]	1.9 [1.3; 3.7]	0.474	3 [2.5; 3.2]	0.526	2.1 [1.9; 2.5]
M ± SD	2.5 ± 2.8		2.9 ± 0.7		2.2 ± 0.6

was associated with the development of acute mesenteric thrombosis. Acute perioperative myocardial infarction was observed only in group 2 in 2 (4.4 %) patients ($p = 0.322$ and $p = 0.334$). The first case was associated with impaired patency of the autovenous conduit, and the second case was associated with ischaemic changes observed during ECG at the initial stage of surgery as a result of the severity of the coronary lesion. Acute cerebrovascular accident resulted in postoperative complications in only 1 (4.5 %) patient in the 1OP group ($p = 0.307$). An initially severe lesion of the carotid arteries appeared to be the probable cause. Bleeding requiring resternotomy developed in 1 (4.3 %) case in group 1CPB and 3 (6.7 %) patients in group 2 ($p = 0.714$), with no active bleeding sources identified in either case; none of the cases in group 1OP had this complication ($p = 0.236$). Group 2 and groups 1CPB and 1OP were comparable in the development of superficial wound infection ($p = 0.231$ and $p = 0.227$, respectively). Severe mediastinitis developed in 1 (4.5 %) case in group 1OP ($p = 0.328$) – in a patient with insulin-dependent type 2 DM.

LONG-TERM RESULTS

The median duration of follow-up was 30.8 months (range from 14 to 45 months). 86.7 % of the total number of patients were examined in the long-term period. We were unable to follow-up 4 (8.9 %) patients from group 2, 5 (21.7 %) patients from group 1CPB and 3 (13.6 %) patients from group 1OP. Kaplan – Meier survival curves demonstrated 1-year, 2-year, and 3-year survival rates for all-cause mortality: 100 %, 88.9 %, and 83.3 %, respectively, in group 1CPB; 100 %, 84.2 %, and 84.2 %, respectively, in group 1OP; 95.1 %, 92.7 %, and 85.3 %, respectively, in group 2. A Kaplan – Meyer survival curve analysis of survival estimates revealed no statistically significant advantage in overall survival between the 1CPB and 2 ($p = 0.689$) and 1OP and 2 ($p = 0.739$) groups

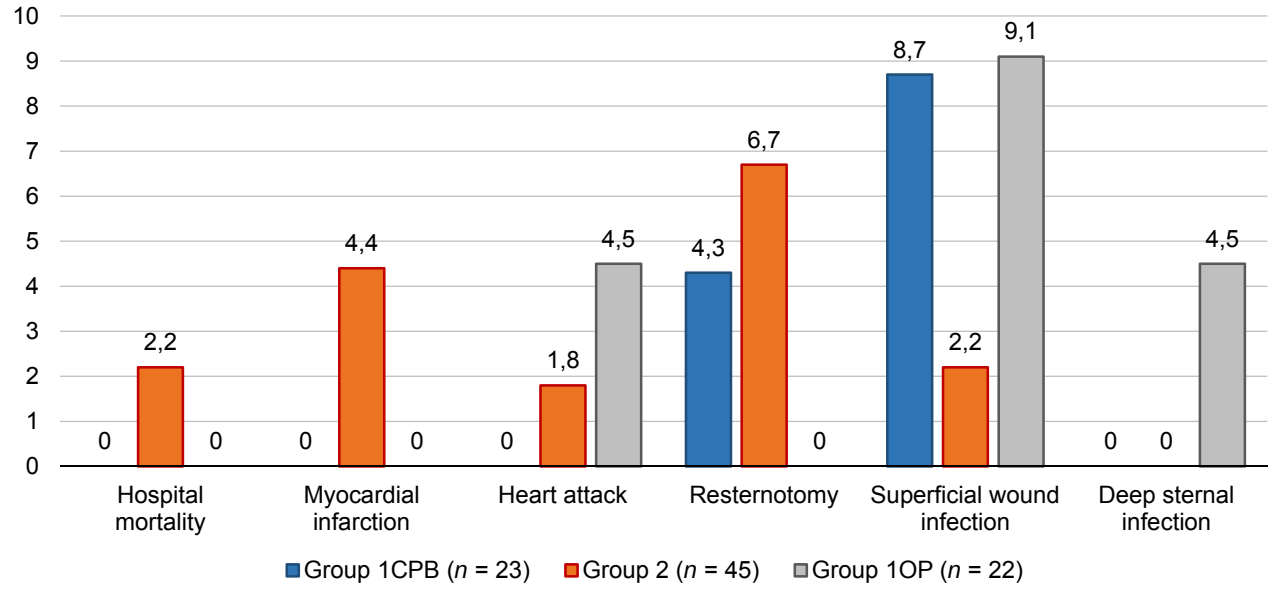

FIG. 1.
Complications in the postoperative period

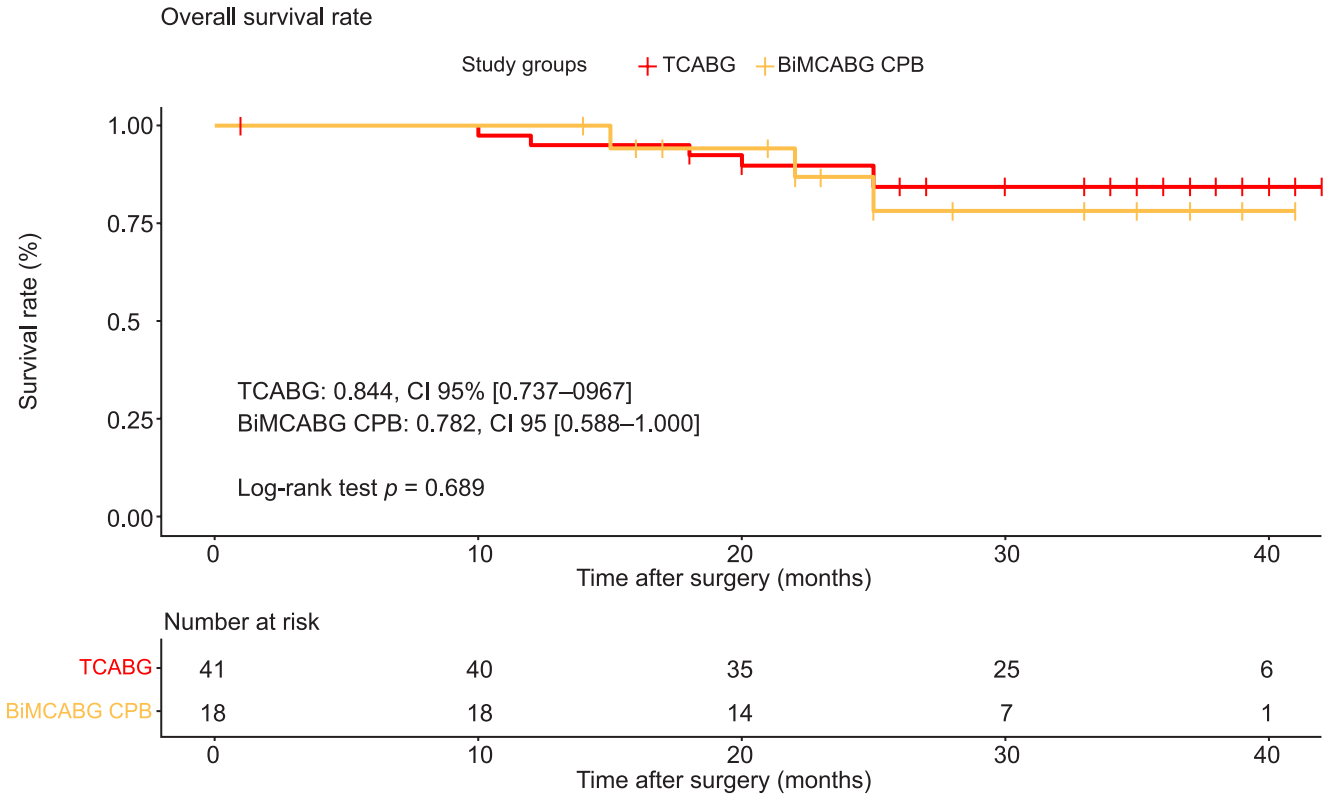

FIG. 2.
Kaplan – Meier all-cause survival curves between group 1CPB (cardiopulmonary bypass surgeries) and group 2

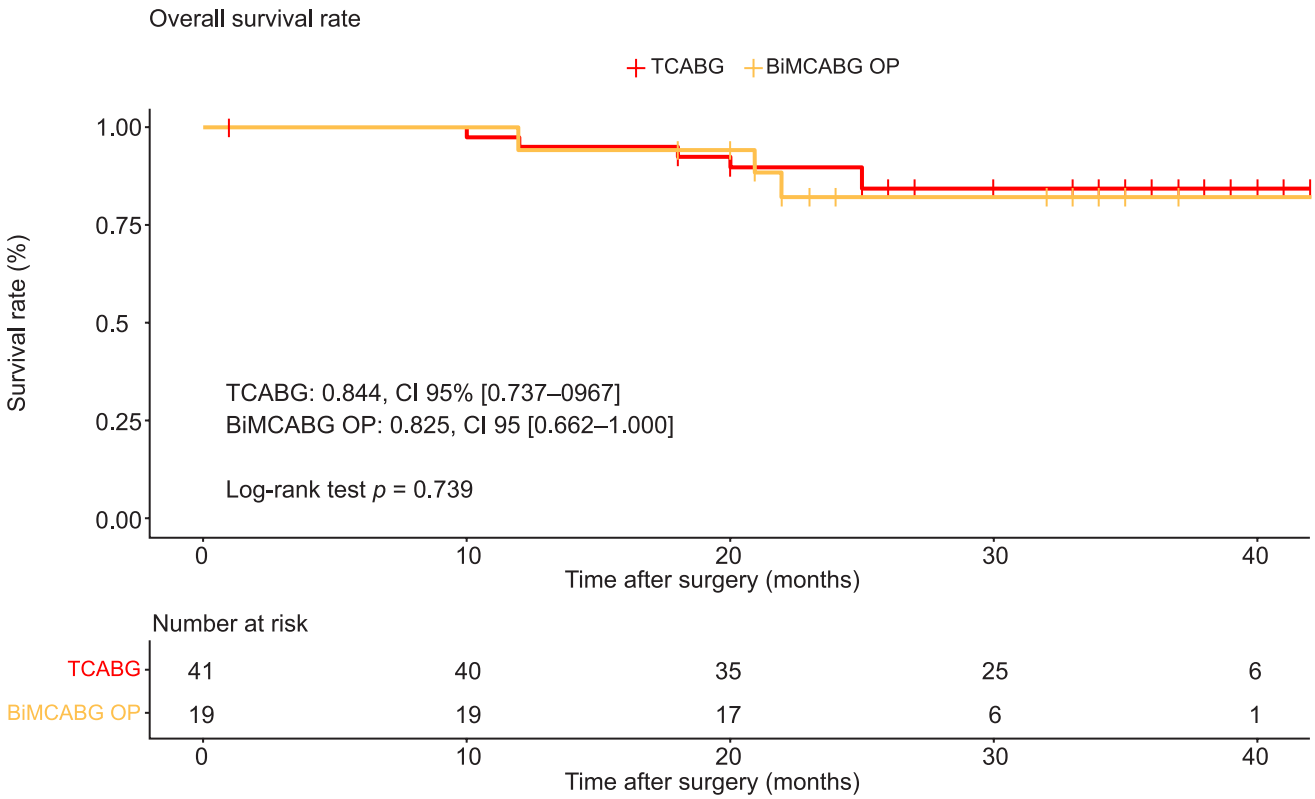

FIG. 3.

Kaplan – Meier all-cause survival curves between group 1OP (off-pump surgeries) and group 2

(Fig. 2, 3). But it is important to note that in the bimammary CABG groups, freedom from cardiac mortality was 100 %, while in group 2, in 50 % of cases (3 patients), mortality was associated with the development of acute myocardial infarction, in other cases with complications of COVID-19. In group 1CPB, in 1 case patient died from complications of oncological disease, in 2 cases – from complications of COVID-19. In group 1OP, one patient died from complications of oncological disease, the second patient died from complications of COVID-19, and the third patient died from an accident.

In groups 1CPB and 1OP, the freedom from myocardial infarctions in the long-term period was 100 %, while in group 2 it was 97.6 % (p = 0.683 and p = 0.683, respectively): in 1 patient, myocardial infarction developed against the background of occlusion of the autovenous bypass to the right coronary artery basin.

Freedom from acute cerebral complications in group 2 was 97.6 %: in 1 patient the long-term postoperative period was complicated by the development of acute cerebral circulatory disturbance of ischaemic type. No such complications were observed in the 1PCB and 1OP groups (p = 0.547 and p = 0.500, respectively).

Freedom from repeated revascularization in the group 2 was 97.6 %, in groups 1CPB and 1OP – 100 % (p = 0.564 and p = 0.645, respectively). In group 2, bypass dysfunction was revealed in 2 patients. An occlusion of the conduit from the midline was revealed in one case, however, a conservative medical therapy as a result of the depleted distal native channel beyond the anastomosis site was recommended. The second patient required stenting of the right CA as a consequence of recurrence of angina pectoris, the CBA revealed occlusion of the autovenous bypass to the proximal posterior interventricular artery.

The patency of the left and right ITA for up to 45 months in all groups was 100 %, the patency of venous bypass was lower and was 96.1 %.

Absence from recurrent angina pectoris was observed in 94.1 % of cases in group 2, in 100 % and 87.5 % in groups 1CPB and 1OP (p = 0.450 and p = 0.208), respectively. The results of multi-layer spiral computed tomography of CA in group 1OP revealed no impairment of bypass patency; the probable cause of recurrent angina was associated with the progression of atherosclerosis in the native coronary bed. Both cases in group 2 were caused by dysfunction of the autovenous bypass.

Freedom from cardiovascular events (MACCE, major adverse cardiac and cerebrovascular event) (death from cardiac causes + freedom from MI + freedom from ACVA + freedom from repeat revascularization) in groups using two ITAs was 100 %, in group 2 – 84.2 %, but no statistically significant difference was obtained (p = 0.144 and p = 0.145).

In assessing the functional classes of heart failure (according to NYHA) during the long-term period in the patients who underwent surgery, we did not see statistically significant differences in the intergroup study (p = 0.429 and p = 484, respectively), but in the intragroup analysis, when comparing the preoperative data and the results in the long-term period, there was a statistically

significant decrease in the functional classes of heart failure in each of the groups: in group 1CPB $p < 0.005$; in group 1OP $p < 0.001$; in group 2 $p < 0.001$.

DISCUSSION

The number of DM patients undergoing CABG is steadily increasing worldwide. A higher propensity for progression of multifocal atherosclerosis, a higher incidence of extensive peripheral and visceral arterial lesions, and a higher risk of perioperative mortality are also associated with the type 2 DM existence. It is currently very important to optimize clinical outcomes in patients with concomitant DM undergoing CABG.

The use of the skeletonization technique of both ITAs in this study did not increase the incidence of both superficial wound infection ($p = 0.23$ and $p = 0.22$) and deep sternal complications ($p = 0.47$ and $p = 0.42$). It may safely be used for myocardial revascularization in patients with multivessel coronary lesions and type 2 DM. This view is shared by a number of authors. In the study by U. Benedetto et al. it was demonstrated that the number of sternal complications does not increase when both ITAs are harvested by the skeletonization technique and is comparable with the use of the left ITA through the preservation of collateral blood flow in the sternum (odds ratio (OR) – 1.00; 95% confidence interval (95% CI): 0,65–1,53) [8]. Also no difference in the incidence of deep sternal infection in patients with bimammary and conventional bypass surgery was obtained in the study conducted by D.J. LaPar et al. (0.4 % vs. 0.2 %; $p = 0.48$) [9]. In contrast, in a study by Japanese colleagues, the incidence of deep sternal infection in patients with type 2 DM was higher in the group that used the bimammary CABG technique (2.7 % vs. 1.2 %; $p > 0.05$), with no information about the method of ITA harvesting being reported in the study [10]. A review article covering the literature between 1970 and 2017 advised that deep sternal infection is a multifactorial problem and the use of ITA skeletonization technique does not affect the development of infectious complications [11]. The ART (The Arterial Revascularization Trial), the only randomized multicentre study to date, assessed the results of surgery using bimammary and traditional CABG technique: about 50 % of patients had DM, and more than 40 % of all surgeries were performed without CPB [12]. The study results revealed that hospital mortality was comparable between groups (relative risk (RR), 0.96 (0.79–1.17); $p = 0.9$), but the incidence of sternal reconstruction was higher in patients where both ITAs were used (OR = 2.91; 95% CI: 1.42–5.95; $p = 0.002$). However, the study does not emphasise the techniques of conduit isolation. The authors suggest that an individualized approach is needed to apply the bimammary CABG technique in patients with DM. A contraindication to the harvesting of both ITAs, according to the authors, is insulin-dependent DM, especially in overweight female patients. Relative contraindications include age over 70 years. Despite the ongoing debate about the role of ITA skeletonization in preventing sternal infection, most authors believe that this technique remains the main one in the prevention of infectious complications, including this technique being the main one in the latest recommendations for myocardial revascularisation.

Major hospital outcomes were comparable between the study groups: hospital mortality was only observed in group 2 in 1 (2.2 %) patient ($p = 0.49$ and $p = 0.50$, respectively): the patient died of acute intestinal ischaemia. Acute perioperative myocardial infarction also developed in 2 patients of group 2 (4.4 %) ($p = 0.32$ and $p = 0.33$, respectively): in one case it was associated with kinking of the autovenous bypass, in the second case – with the initial severe coronary lesion, multiple CA stenting, pronounced calcinosis in the arterial walls complicating the formation of anastomoses. Acute cerebrovascular accident was observed in one case (4.5 %) in the 1OP group ($p = 0.31$ and $p = 0.30$, respectively).

These results were similar to ours in the study of L. Di Bacco et al., which included 268 patients with CHD and concomitant DM, of whom half of the patients were underwent surgery using bimammary CABG technique. No statistically significant difference was observed between groups for hospital mortality ($p = 0.89$), acute perioperative myocardial infarction ($p = 0.86$), neurological complications ($p = 0.98$), and resternotomies for acute bleeding ($p = 0.32$). The authors of the study have come to the conclusion that the use of bimammary CABG technique does not worsen hospital outcomes in patients with CHD and concomitant DM and may be the operation of choice in this cohort of patients [13]. Alternately, in a study by A.M. Calafiore et al. the use of one ITA versus the use of two ITAs was associated with statistically significantly higher hospital mortality from all cardiac causes ($p = 0.015$) [14]. In the work of D. Pevni et al. hospital mortality was similar in both groups (2.6 % and 3.0 %; $p = 0.113$), but in the bimammary CABG group there was an increase in the incidence of heart attack in the early postoperative period (4.87 % vs. 2.13 %; $p = 0.003$), despite the fact that the «no touch aorta» technique was used [15].

According to the results of this study, the groups were comparable in terms of the number of distal anastomoses formed: in group 2 – 2.7 ± 0.5, in group 1CPB – 2.9 ± 0.6 ($p = 0.26$), in group 1OP – 2.7 ± 0.6 ($p = 0.90$). A non-significant statistical difference was obtained in the duration of CPB and aortic cross-clamping time ($p = 0.05$); this difference can be associated with the high precision of bimamar myocardial revascularisation and the technique of distal anastomosis formation. Extubation of patients in the group 2 occurred later than in group 1CPB ($p = 0.02$), but no difference in clinical picture between the groups was observed. In the study by B. Gansera et al. [16], the mean number of distal anastomoses formed using both ITAs was higher than ours, but in an intergroup comparison of the number of distal anastomoses formed, the studies were comparable (3.3 ± 0.8 vs. 3.2 ± 0.9, respectively; $p = 0.921$), which is consistent with our results. In the study by A. Iribarne et al. including 430 patients with CHD and concomitant DM who underwent surgical myocardial

revascularisation (217 TCABG and 213 bimammary CABG), no group difference was obtained in the number of affected CAs and the number of distal anastomoses performed ($p < 0.503$). The groups were similar in terms of CPB duration ($p = 0.177$), however, aortic cross-clamping time was statistically significantly higher in the bimammary CABG group ($p < 0.001$), which is similar to our results, except that patients were extubated earlier in the group using both ITAs ($p = 0.049$) [17].

The consistency of the bypasses was analyzed by means of a flowmetric study. Flowmetry results of the formed bypasses revealed a statistically significant difference between groups 2 and CPB, as well as 1OP in linear blood flow velocity (Q) at the formed bypass ($p < 0.001$ and $p < 0.001$, respectively). Linear blood flow velocity was higher in the bimammary CABG groups, but the groups were completely comparable in terms of pulse index (Pi) ($p = 0.47$ and $p = 0.52$, respectively). The results of the study revealed that, despite the difference in linear blood flow velocity, this hydrodynamic parameter was within the reference limits in all groups. Statistically significant difference in Q parameter can be associated with the fact that in the bimammary CABG group in most cases composite and composite-sequential bypass surgery technique was used, and comparable intergroup results in Pi parameter can be explained by the fact that in all patients revascularisation was performed with hemodynamically significant lesions in CA with a satisfactory distal bed behind the lesion. In case of composite and composite-sequential bypass surgery, hydrodynamic parameters in bypasses with rhomboidal anastomoses were statistically significantly higher than in parallel anastomosis technique, which is associated with higher pulse blood flow velocity along the conduits through the anastomosis area and lower probability of bypass deformation in this area [18]. In the study by D. Glineur et al. the 7-year results of bimammary bypass surgery depending on the bypass configuration were assessed; no statistically significant difference in long-term survival in patients was revealed ($p = 0.3$), but the composite bypass technique was associated with a lower incidence of cardiovascular events ($p = 0.01$) and repeat revascularisations ($p = 0.009$) [19]. Concurrently, the results of the PREVENT IV study demonstrated that the use of composite-sequential technology was associated with poorer bypass patency and consequently worse clinical outcomes compared with the use of linear bypasses (OR = 1.24; 95% CI: 1.03–1.48) [20].

The long-term patient survival in this study (median follow-up, 30.8 months) was comparable between the bimammary and traditional CABG groups ($p = 0.689$ and $p = 0.739$, respectively), which correlates with the results of other studies. In a study by A. Iribarne et al. the survival rate of patients in the long–term period (median follow-up was 9.5 years) after bimammary bypass surgery was statistically significantly higher (OR = 0.75; 95% CI: 0.57–0.98; $p < 0.034$) [17]. At the opposite end of the spectrum, in the study performed by B. Gansera et al. revealed no difference in survival between the groups: 5-, 10-, and 14-year survival rates were 93.4 %, 76.6 %, and 67.5 % in the bimammary bypass surgery group and 89.5 %, 81.5 %, and 32.8 % in the traditional CABG group ($p = 0.288$), respectively [16]. Cardiac-related mortality was 30.8 % in the TCABG group and 30.0 % in the bimamar CABG group. Analyzing them by causes of mortality in this study, we revealed that in the TCABG group, 50 % of mortality was associated with the development of myocardial infarctions, whereas in the bimammary bypass surgery subgroups, patient mortality was not associated with cardiac pathology. An important point to be mentioned is that in the aforementioned studies, the follow-up period was longer than in our work. The survival advantage in patients after bimammary CABG is observed after 7 years of follow-up, as reported by a number of researchers [21]. A shorter follow-up period in the long-term period may have been the reason for the lack of differences in our study.

Analysis of the MACCE development incidence in the long-term postoperative period revealed no advantages of one surgical technique over the other, despite the fact that, indeed, these complications were absent in the bimammary CABG groups. Freedom from MACCE in the group 2 was 84.2 %, in groups 1CPB and 1OP – 100 % ($p = 0.144$ and $p = 0.145$, respectively). Similar results were obtained in a recent publication that assessed the impact of multiple arterial bypass surgery versus traditional CABG in a retrospective analysis of 10-year outcomes in patients with DM from the ART study. In a cohort of DM patients, the incidence of MACCE was actually higher in the TCABG group (35.4 %) (28.9 %; OR = 0.80; 95% CI: 0.61–1.03), but the subgroup interaction effect was not significant ($p = 0.93$); even adjustment for potentially distorting factors had little effect on the results: the adjusted OR for MACCE was 0.80 (95% CI: 0.61–1.05; $p = 0.93$) [22]. Conversely, the study by L. Di Bacco et al. revealed that the use of arterial conduits provides significantly better results compared to traditional revascularization in terms of freedom from major cardiac and cerebrovascular events (77 ± 6.0 % vs. 53 ± 5.8 %, respectively; $p < 0.001$) [13].

This study demonstrated that the use of the bimammary bypass surgery technique in patients with multivessel CA lesions and type 2 DM is comparable to the in-hospital and mid-term outcomes of traditional myocardial revascularization techniques. The use of bimammary CABG in off-pump surgeries should be considered as an operation of choice in patients with significant lesions of brachiocephalic and visceral arteries, in patients with low contractile function of the left ventricular myocardium. The ITAs skeletonization technique did not increase the number of infectious complications in the surgical area, and comparable results were obtained with the group where a single ITA was used, which may indicate the high efficiency and safety of this conduit harvesting technique. Considering the fact that the simultaneous use of both ITAs did not increase the number of hospital complications, we believe that the use of this strategy to revascularize myocardium in patients with type 2 DM should be considered on an individual basis, with the consideration of such factors as the severity of the underlying and concomitant disease, age, sex, and body mass index of the patient.

In the long-term period, no statistically significant difference was observed between the groups in terms of mortality and cerebrovascular events, but the use of bimammary myocardial revascularization technique was associated with 100 % freedom from cerebrovascular events and cardiac mortality in this study.

Study limitations

A limitation of the study is its single-centre nature, the small sample of patients and the fact that surgeries were performed by multiple surgeons. This study is retrospective and does not have the same power as prospective randomized multicentre studies with large patient sample.

CONCLUSION

Bimammary bypass surgery may be a suitable option for surgical myocardial revascularization for patients with type 2 DM either in CPB or OP cases. Bimammary CABG in off-pump surgeries should be considered as the surgery of choice in patients with hemodynamically significant lesions of the brachiocephalic and visceral arteries. No differences in overall survival were observed during the period from 14 to 45 months in the groups of bimammary and traditional coronary bypass surgery in patients with type 2 diabetes mellitus; in the groups using two ITAs for myocardial revascularization, cardiac cause of death was not revealed in any of the cases, which may indicate the high efficacy of this technique of CHD surgical treatment. The use of the bimammary myocardial revascularization technique was associated with complete freedom from major cardiovascular complications. Further analyses of longer-term outcomes will be required to assess the efficacy of bimammary coronary bypass surgery in patients with type 2 DM.

Conflict of interest

The authors of this article declare no conflicts of interest.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

QUALITY OF LIFE OF PATIENTS WITH SINGLE- AND MULTIGLAND PARATHYROID DISEASE IN SPORADIC PRIMARY HYPERPARATHYROIDISM BEFORE AND AFTER SURGICAL TREATMENT

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ABSTRACT

Background. *In 15–25 % of cases, the cause of primary hyperparathyroidism (PHPT) is multigland parathyroid disease. The complexity of clinical and laboratory prognosis, low efficiency of imaging methods, inaccurate assessment of the radicality of the surgery are the components of the problem of this variant of the disease. Quality of life (QOL) is an important criterion for the effectiveness of surgical treatment. A study of the QOL in patients with multigland parathyroid disease in PHPT has not been previously conducted in our country.*

The aim of the study. *To assess the quality of life of patients with single- and multigland parathyroid disease in sporadic primary hyperparathyroidism before and after parathyroidectomy (PTE).*

Methods. *As part of a prospective observational study, the quality of life of 64 patients with PHPT before and after PTE was assessed using SF-36 (Short Form 36) questionnaire: main group (n = 13) – patients with multigland parathyroid disease; comparison group (n = 51) – patients with single-gland parathyroid disease. The quality of life indicators of the patients were compared with those in a sample of the Irkutsk region population similar in gender and age.*

Results. *Before performing PTE, the quality of life of patients with PHPT was lower than that of the Irkutsk region population. The greatest decrease in both health components was registered in the main group. In 90 % of patients, the quality of life improved after PTE, while in the main group changes were established 1 year after the surgery, in the comparison group – 6 months after the surgery. Transient complications (laryngeal paresis) and disease outcomes (hypocalcemia, hypoparathyroidism) did not interfere with the improvement of quality of life in both groups. When persistence was detected, no significant improvement in QOL was established.*

Conclusion. *The quality of life of patients with PHPT is significantly reduced. PTE improves the QOL of these patients, and only persistence of the disease does not allow this to be achieved. Therefore, surgical tactics aimed at reducing the frequency of persistence will achieve a decent quality of life in the majority of patients with multigland parathyroid disease in PHPT.*

Key words: *multigland parathyroid disease, primary hyperparathyroidism, parathyroidectomy, quality of life*

For citation: Ilyicheva E.A., Bersenev G.A., Roy T.A. Quality of life of patients with single- and multigland parathyroid disease in sporadic primary hyperparathyroidism before and after surgical treatment. *Acta biomedica scientifica*. 2023; 8(5): 225-234. doi: 10.29413/ABS.2023-8.5.24

Received: 30.05.2023
Accepted: 07.11.2023
Published: 05.12.2023

КАЧЕСТВО ЖИЗНИ ПАЦИЕНТОВ С СОЛИТАРНЫМ И МНОЖЕСТВЕННЫМ ПОРАЖЕНИЕМ ОКОЛОЩИТОВИДНЫХ ЖЕЛЁЗ ПРИ СПОРАДИЧЕСКОМ ПЕРВИЧНОМ ГИПЕРПАРАТИРЕОЗЕ ДО И ПОСЛЕ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ

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РЕЗЮМЕ

Обоснование. *Причиной первичного гиперпаратиреоза (ПГПТ) в 15–25 % случаев является множественное поражение околощитовидных желёз (ОЩЖ). Сложность клинико-лабораторного прогнозирования, низкая эффективность методов визуализации, неточная оценка радикальности операции – составляющие проблемы данного варианта заболевания. Оценка качества жизни (КЖ) – важный критерий эффективности оперативного лечения. Исследование КЖ пациентов с множественным поражением ОЩЖ при ПГПТ ранее в нашей стране не проводилось.*

Цель исследования. *Оценить качество жизни пациентов с солитарным и множественным поражением околощитовидных желёз при спорадическом первичном гиперпаратиреозе до и после паратиреоидэктомии (ПТЭ).*

Методы. *В рамках проспективного наблюдательного исследования оценено КЖ 64 пациентов с ПГПТ до и после ПТЭ методом анкетирования с использованием опросника SF-36 (Short Form 36): основная группа (n = 13) – множественное поражение ОЩЖ; группа сравнения (n = 51) – солитарное. Показатели КЖ больных сравнивали с аналогичными в сопоставимой по полу и возрасту выборке населения Иркутской области.*

Результаты. *До выполнения ПТЭ КЖ больных с ПГПТ было ниже показателей жителей региона. Наибольшее снижение обоих компонентов здоровья было в основной группе. У 90 % больных КЖ после ПТЭ улучшилось, при этом в основной группе изменения установлены спустя 1 год после операции, в группе сравнения – через полгода. Транзиторные осложнения (парез гортани) и исходы заболевания (гипокальциемия, гипопаратиреоз) не мешали улучшению КЖ в обоих группах. При выявленной персистенции значимого улучшения КЖ не установлено.*

Заключение. *КЖ больных ПГПТ значительно снижено. ПТЭ улучшает качество жизни этих пациентов, и лишь персистенция заболевания не позволяет этого достичь. Поэтому хирургическая тактика, направленная на снижение частоты персистенции, позволит добиться приличного качества жизни у большинства пациентов с множественным поражением ОЩЖ при ПГПТ.*

Ключевые слова: *множественное поражение околощитовидных желёз, первичный гиперпаратиреоз, паратиреоидэктомия, качество жизни*

Статья поступила: 30.05.2023
Статья принята: 07.11.2023
Статья опубликована: 05.12.2023

Для цитирования: Ильичева Е.А., Берсенев Г.А., Рой Т.А. Качество жизни пациентов с солитарным и множественным поражением околощитовидных желёз при спорадическом первичном гиперпаратиреозе до и после хирургического лечения. *Acta biomedica scientifica*. 2023; 8(5): 225-234. doi: 10.29413/ABS.2023-8.5.24

INTRODUCTION

Primary hyperparathyroidism (PHPT) currently ranks 3rd in the structure of endocrinological diseases [1]. Data from the Russian register of patients with PHPT demonstrates that its incidence is 1.3 cases per 100,000 population, with the symptomatic form being diagnosed in the majority of cases (67.1 %) at initial treatment [2].

The etiological basis of the disease is autonomous production of parathyroid hormone (PTH) by sporadic adenoma (80–90 % of cases – solitary perithyroid gland (PTG) lesion) or hyperplasia of two or more glands (15–25 % of cases – multiple PTG lesions) [3]. The clinical picture of PHPT is diverse and includes *bony* (generalized muscle weakness, fatigue; bone pain; skeletal deformity; low-traumatic, long-healing fractures; formation of false joints; loosening and loss of teeth), *visceral* (nephrolithiasis with recurrent attacks of renal colic; arterial hypertension; heart rhythm disorders, fat and carbohydrate metabolism disorders) and non-specific (fatigue; weakness; arterial hypertension; heart rhythm disorders; fat and carbohydrate metabolism disorders); recurrent attacks of renal colic; arterial hypertension; heart rhythm disorders, disorders of fat and carbohydrate metabolism) and *nonspecific* (fatigue; weakness; moderate depression; neurocognitive disorders; indefinite abdominal pain; constipation) manifestations [4].

The only radical method of treatment is surgery [5]. The world standard of treatment for solitary PTG lesions is selective parathyroidectomy (PTE), which involves the excision of only one affected gland based on preoperative imaging data [6]. The new draft clinical guidelines governing the diagnosis and management of PHPT in adult patients indicate that multiple PTG lesions are associated with reduced efficacy of all imaging modalities and require bilateral neck revision with detection of all glands and removal of abnormal glands [7]. Lack of clinical and laboratory criteria, reduced diagnostic efficiency of ultrasound and scintigraphy, inability to assess the radicality of surgery by intraoperative monitoring of intact parathyroid hormone are the basis for the problems of treatment of multiple PTG lesions in PHPT [1, 3, 7].

Considering the late diagnosis of hyperparathyroidism in symptomatic form with a vivid clinical picture, the study of the quality of life (QOL) in these patients with assessment of the dynamics after surgical treatment would be appropriate. QOL relies on the subjective perception of a person's state of health, which includes the aggregate characteristic of physical and psychological functioning. QOL assessment is an important criterion for the effectiveness of surgical treatment. According to the eLibrary information system, no study of QOL in patients with sporadic PHPT with multiple PTG lesions has been performed in our country.

THE AIM OF THE STUDY

To assess the quality of life in patients with solitary and multiple perithyroid lesions in sporadic primary hyperparathyroidism before and after surgical treatment.

MATERIALS AND METHODS

A prospective, continuous cohort study of 100 patients who underwent surgical treatment for primary, secondary and tertiary hyperparathyroidism during 2019–2021 was conducted. Inclusion criterion: diagnosis of PHPT. Exclusion criteria: diagnosis of secondary or tertiary hyperparathyroidism; suspicion of hereditary nature of PHPT; presence of absolute contraindications to surgical treatment (acute cardiovascular pathology); decompensation of chronic diseases.

64 patients were included in the study. Main group – PHPT patients with multiple PTG lesions (n = 13); comparison group – PHPT patients with solitary PTG lesions (n = 51). In the main group, the median age of patients was 60 (56–66) years; 12 (92 %) were female. In the comparison group, the median age of patients was 61 (56–67) years; 44 (86 %) were female. The symptomatic form of the disease was revealed in 11 (84.6 %) patients of the main group and in 46 (90.1 %) patients of the comparison group. Hypercalcaemic variant was observed in 9 (69.2 %) patients in the main group and in 40 (78.4 %) in the comparison group.

If more than one abnormal PTG was excised or if persistence was detected after removal of at least one pathologically altered PTG, multiple PTG lesions were considered to be criteria for PHPT.

The structure of surgical interventions made in surveyed patients is summarised in Table 1. A total of 64 PTG surgeries were performed, including 1 case in combination with thyroid surgery in the volume of thyroidectomy (TE).

Table 1 demonstrates that the extent of surgery ranged from selective to subtotal PTE: double (47 %) prevailed in the main group and selective (80 %) in the comparison group (Fig. 1, 2).

Figure 1 demonstrates a clinical observation of multiple PTG lesions: bilateral neck revision with subtotal PTE in a patient from the main group.

Figure 2 summarises a clinical observation of a solitary PTG lesion: unilateral neck revision and selective PTE in a patient from the comparison group.

In the postoperative period, PHPT persistence was observed in 4 (6.25 %) patients in the main group. Transient hypocalcaemia was revealed in 15 (23.4 %) patients (2 in the main group, 13 in the comparison group), and transient hypoparathyroidism in 20 (31.25 %) patients (4 in the main group, 15 in the comparison group). Within the study cohort, reversible postoperative laryngeal paresis was diagnosed in 5 (7.8 %) patients (1 in the main group, 4 in the comparison group).

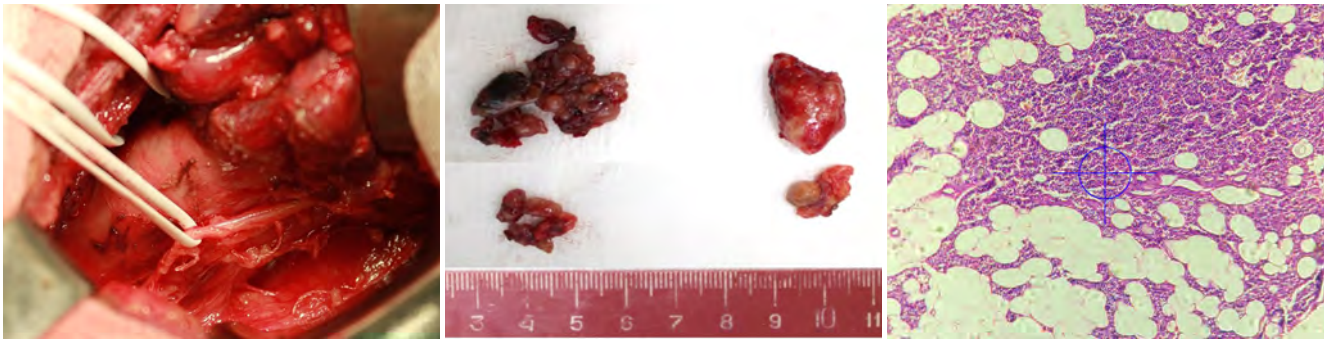
QOL was assessed by using the SF-36 (Short Form 36) questionnaire [8]. The calculation of indicators was performed using 8 scales according to the methodology of V.M. Amirjanov et al. [9]. The indicators of physical and mental health components were calculated according to the Evidence Company's manual – "Clinical and Pharmacological Studies" [10].

An initial questionnaire was conducted to all patients 1 day before surgical treatment. Secondary questionnaire

TABLE 1

STRUCTURE OF SURGICAL INTERVENTIONS PERFORMED IN THE SURVEYED PATIENTS AND RESULTS OF MORPHOLOGICAL EXAMINATION OF PARATHYROID GLANDS

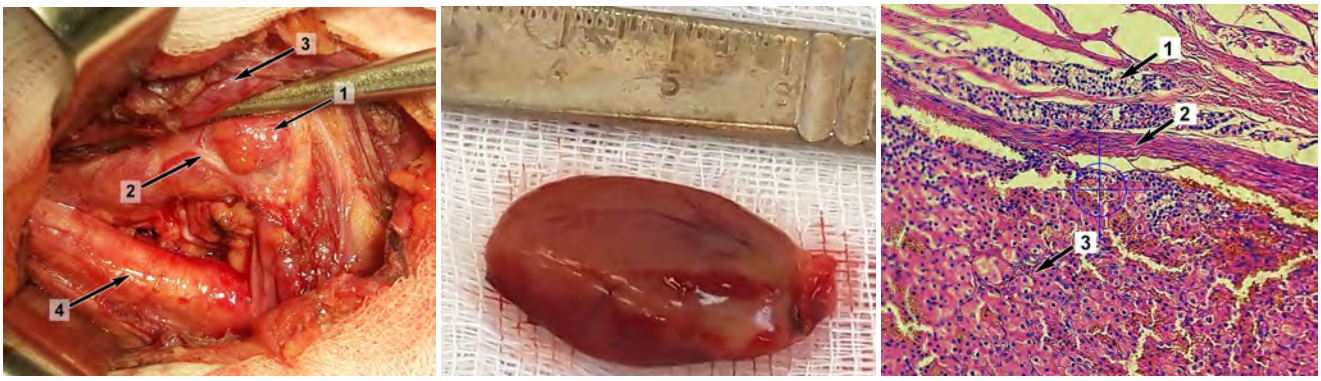
Scope of surgery		Main group (*n* = 13)	Comparison group (*n* = 51)
Unilateral neck revision	selective PTE	2 (15 %)	41 (80 %)
	dual PTE	1 (9 %)	8 (15 %)
Bilateral neck revision	dual PTE	5 (38 %)	–
	subtotal PTE	5 (38 %)	1 (2.5 %)
	selective PTE + TE	–	1 (2.5 %)
Histological conclusion			
PTG adenoma		–	51 (100 %)
PTG hyperplasia		12 (92.3 %)	–
Combinations of PTG adenoma and hyperplasia		1 (7.7 %)	–



a ***б*** ***c***

FIG. 1.

Clinical case of multigland parathyroid disease: bilateral neck revision with subtotal parathyroidectomy in a patient from the main group. ***a*** *– intraoperative photograph: bilateral neck revision – both recurrent laryngeal nerves are taken on holders;* ***b*** *– macroscopic specimens;* ***c*** *– microphotograph: histological picture of all removed parathyroid glands is identical and is represented by diffuse hyperplasia*



a ***b*** ***c***

FIG. 2.

Clinical case of single-gland parathyroid disease: unilateral neck revision and selective left lower parathyroidectomy in a patient from the comparison group. ***a*** *– intraoperative photo:* **1** *– adenoma of the left lower parathyroid gland;* **2** *– left recurrent laryngeal nerve;* **3** *– left lobe of the parathyroid gland;* **4** *– left neurovascular bundle of the neck.* ***b*** *– macroscopic specimen of an adenoma of the left lower parathyroid gland.* ***c*** *– microphotograph of an adenoma of the left lower parathyroid gland:* **1** *– an islet of unchanged parathyroid tissue;* **2** *– connective tissue capsule;* **3** *– parenchyma of a parathyroid gland adenoma*

was conducted in 4 patients up to 6 months, 16 patients up to 1 year, and 44 patients 1 year after surgery.

The results of standardised indicators are summarised as a score (0–100) using 8 scales, where the highest score corresponded to a higher QOL: Physical Functioning (PFst.); Role-Physical Functioning (RPst.); Bodily Pain (BPst.); General Health (GHst.); Vitality (VTst.), Social Functioning (SFst.); Role-Emotional (REst.); Mental Health (MeHst.).

After the scale, two indicators are formed – the physical (PHst.) and psychological (MHst.) components of health.

The QOL indicators of patients were compared with those of the Irkutsk region population [11]. In order to obtain a gender and age comparable sample, individuals with an age limit of 50–70 years were selected from the database. In order to determine the percentage equivalent of QOL before and after surgery in the studied groups, the obtained values of physical and psychological health component indicators were compared with similar indicators in the population of the Irkutsk region [12].

Statistical analysis of data was performed using Statistica 10.0 software package (StatSoft Inc., USA; license No. AXAR402G263414FA-V). Continuous data are presented as median with lower and upper quartiles, categorical data are presented as number of observations and frequency as percentages with lower and upper limits of 95 % confidence interval (95% CI). The determination of the statistical significance of differences for continuous data (p) in the compared samples was carried out according to the Mann – Whitney test (U) and Wilcoxon test (W), for categorical data – according to Pearson's (χ^2) test, Fisher's exact test. Differences were considered statistically significant at $p < 0.05$.

All patients signed informed consent to participate in the study. The work was carried out in accordance with the research work plan of the Irkutsk Scientific Centre of Surgery and Traumatology No. 063 "Biomedical technologies for the prevention and treatment of organ failure in reconstructive and restorative surgery" (due dates 2013–2021). The study was approved by the Biomedical Ethics Committee of Irkutsk Scientific Centre of Surgery and Traumatology (minutes No. 9 dated November 9, 2012).

RESULTS

Quality of life indicators of patients before surgery

Figure 3 represents standardised QOL indices of the patients from the main group and the comparison group before surgical treatment in comparison with similar indices of a comparable sample of Irkutsk region residents by sex and age.

Figure 3 reveals that preoperative QOL of PHPT patients was statistically significantly lower than that of comparable sex- and age-matched residents of the Irkutsk region for all indicators, except for BPst. (pain intensity) and SFst. (social functioning) in the main group and BPst. (pain intensity) in the comparison group.

Figure 4 presents the physical and psychological components of health of the patients of the main

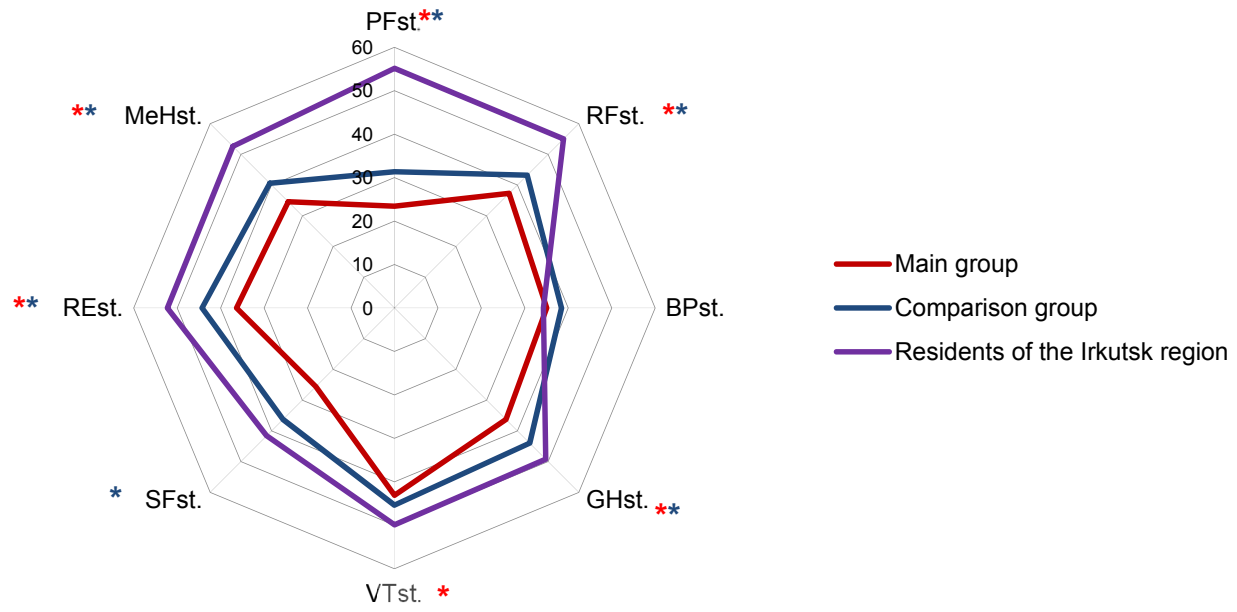


FIG. 3.

*Standardized indicators of quality of life of patients of the main and comparison groups before surgical treatment as compared with indicators of a sample of the Irkutsk region residents similar in gender and age. Statistically significant differences with a sample of the Irkutsk region residents similar in gender and age ($p_U < 0.05$): * – of the main group; * – of the comparison group*

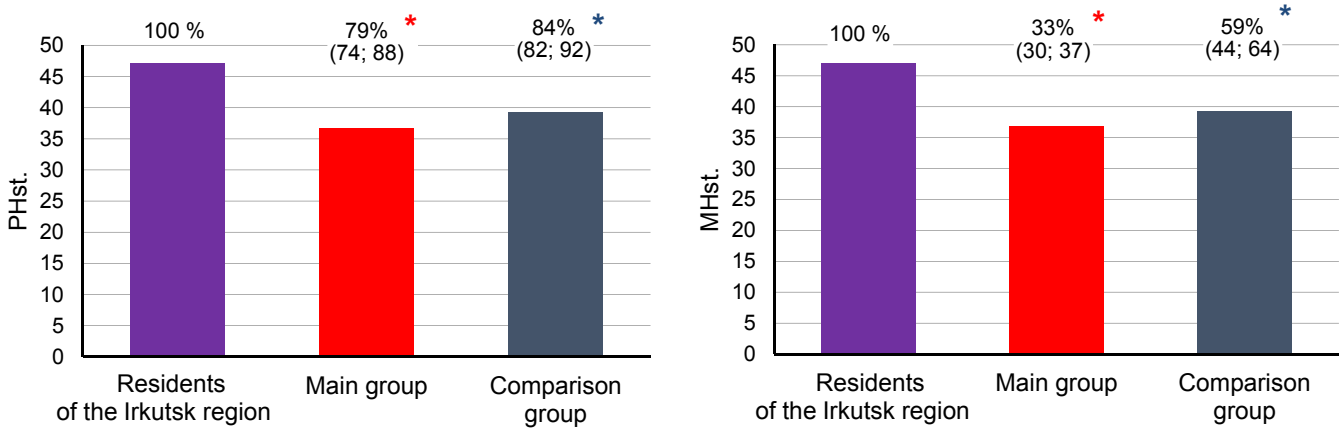


FIG. 4.

*Physical and psychological health components of patients of the main and comparison groups before surgical treatment as compared with indicators of a sample of the Irkutsk region residents similar in gender and age. Statistically significant differences with a sample of the Irkutsk region residents similar in gender and age ($p_U < 0.05$): * – of the main group; * – of the comparison group*

group and the comparison group before surgical treatment in comparison with the indicators of a comparable sample of Irkutsk region residents by sex and age.

As indicated in Figure 4, the physical component of health (PHst.) was statistically significantly lower and was of the same value of the regional residents (100 %): 79 (74; 88) % in the main group and 84 (82; 92) % in the comparison group ($p_U < 0.05$). The psychological component of health (MHst.) was also statistically significantly lower than the population indicator (100 %): 33 (30; 37) % in the main group and 59 (44; 64) % in the comparison group ($p_U < 0.05$). Comparison of QOL indicators revealed that patients in the main group had 6 % and 44 % lower physical and psychological components of health, respectively, than in the comparison group ($p_U < 0.05$).

In summary, the QOL of hyperparathyroidism patients before surgical treatment was statistically significantly lower than in a comparable sample of Irkutsk region residents by sex and age. The most significant decrease in preoperative QOL was found in the group of patients with multiple PTG lesions in PHPT.

The analysis of QOL changes after surgical treatment has revealed that improvement was found in 58 (90 %) of the surveyed patients, impairment in some scales of the questionnaire – in 6 (10 %).

Patterns of improvement in patients' quality of life after surgery

Figure 5 demonstrates the physical and psychological components of health of the patients of the main group and the comparison group at different questionnaire periods after surgical treatment.

Figure 5 demonstrates that surgical treatment of PHPT statistically significantly improved the physical and psychological components of health compared with preoperative ones, with the comparison group showing improvement at 6 months after surgery and the main group at 1 year.

Figure 6 demonstrates the physical and psychological health components of the patients in the main and comparison groups after surgery, depending by outcome and complications.

As indicated in Figure 6, despite the identified complications, the health components of the patients in the main and comparison groups statistically significantly improved when remission of the disease was achieved, except for the lack of improvement in the psychological component in the main group when laryngeal paresis was diagnosed. Disease persistence is the outcome of surgical treatment in which no statistically significant differences in health components were found compared to preoperative values.

Figure 7 represents the physical and psychological health components of the patients from the main and comparison groups after surgery in comparison with the indicators of a comparable sample of Irkutsk region residents by sex and age.

Figure 7 indicates that the physical component of health (PHst.) in patients after surgery was from the similar index of the residents of the region (100 %): 95 (92; 95) % in the main group, 102 (89; 103) % in the comparison group ($p_U > 0.95$). The psychological component of health (MNst.) in patients after surgery comprised from the population indicator (100 %): 101 (96; 102) % in the main group ($p_U > 0.95$), 121 (117; 123) % – in the comparison group ($p_U < 0.05$).

Therefore, disease persistence is an outcome with no statistically significant improvement in QOL after surgery as a result of PHPT. The presence of transient complications does not prevent improvement in postoperative QOL when disease remission is achieved.

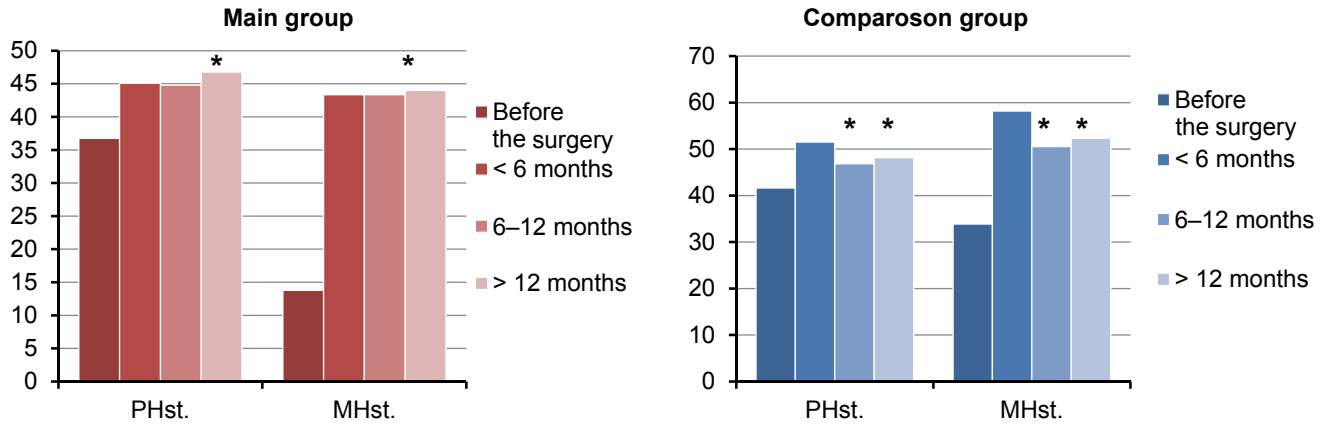


FIG. 5.

*Physical and psychological health components of patients of the main and comparison groups at different periods of questioning after the surgery. Statistically significant differences in indicators before and after surgery: * – $p_W < 0.05$*

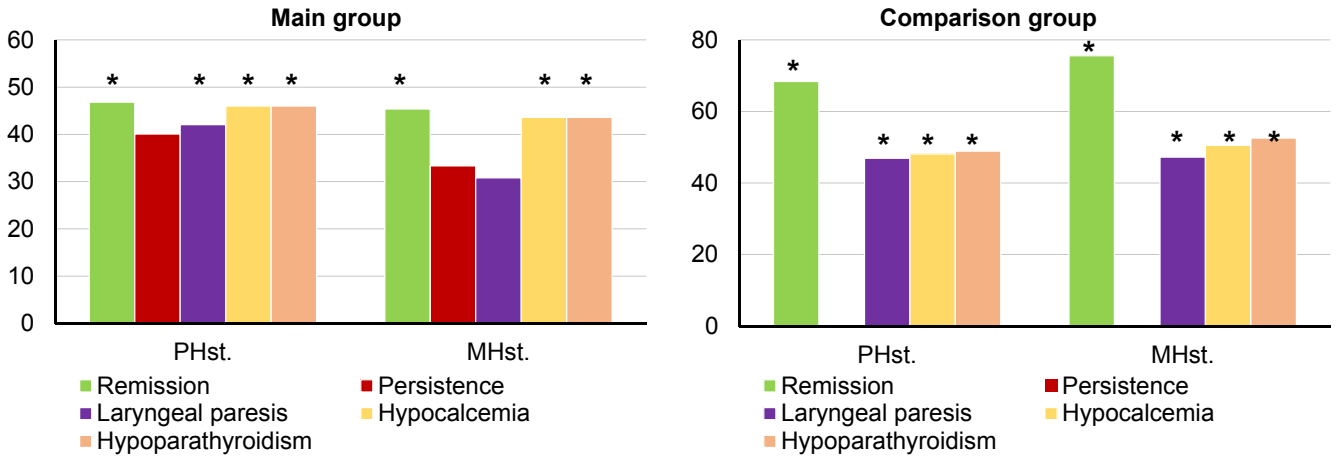


FIG. 6.

*Physical and psychological health components of patients of the main and comparison groups after the surgery, depending on the outcome and complications. Statistically significant differences in indicators before and after surgery: * – $p_W < 0.05$*

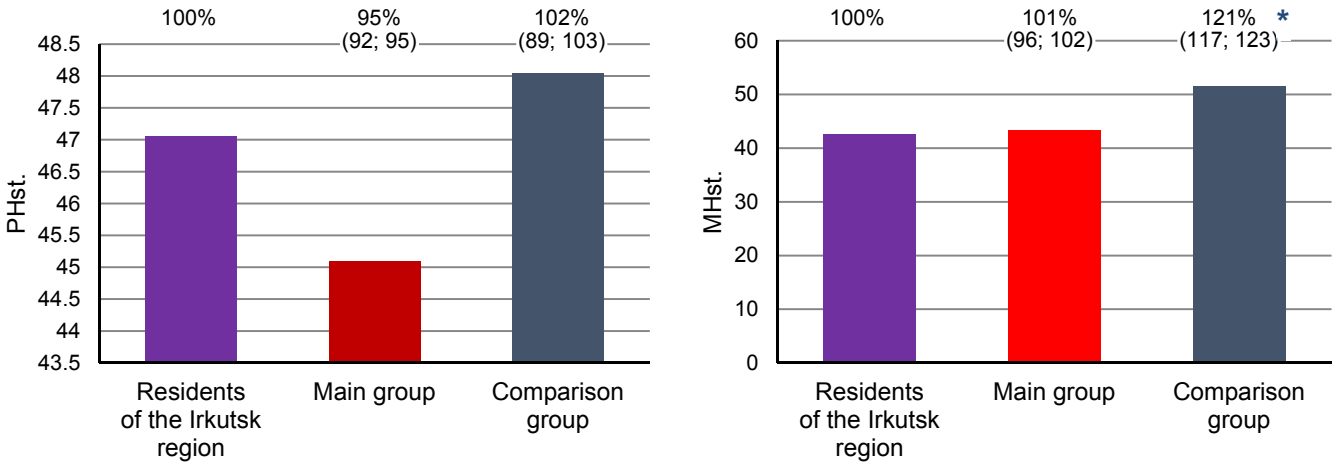


FIG. 7.

*Physical and psychological health components of patients of the main and comparison groups after the surgery as compared with indicators of a sample of the Irkutsk region residents similar in gender and age: * – statistically significant differences between the comparison group and a sample of the Irkutsk region residents similar in gender and age ($p_U < 0,05$)*

Patterns of impairment in patients' quality of life after surgery

QOL impairment according to some scales after surgery was found in 6 surveyed patients: in 1 out of 13 in the main group, in 5 out of 51 in the comparison group.

Comparison group patients were questioned up to six months after surgery and had postoperative transient hypocalcaemia. No statistically significant changes in VTst. (vitality), BPst. (pain intensity), and MeHst. (mental health) scales ($p_U > 0.05$) were revealed as compared to preoperative ones.

Comparative analysis revealed that QOL impairment was found in 4 of 15 patients with hypocalcaemia and in 2 of 49 patients with normal blood calcium levels ($p_{\chi 2} < 0.05$). In comparison group patients with transient hypocalcaemia, the T-criterion values at the lumbar vertebrae by osteodensitometry were: –2.5 (–2.9; –2.5) for QOL improvement and –3.15 (–3.0; –3.9) for QOL impairment ($p < 0.05$; Mann – Whitney criterion) (Fig. 8).

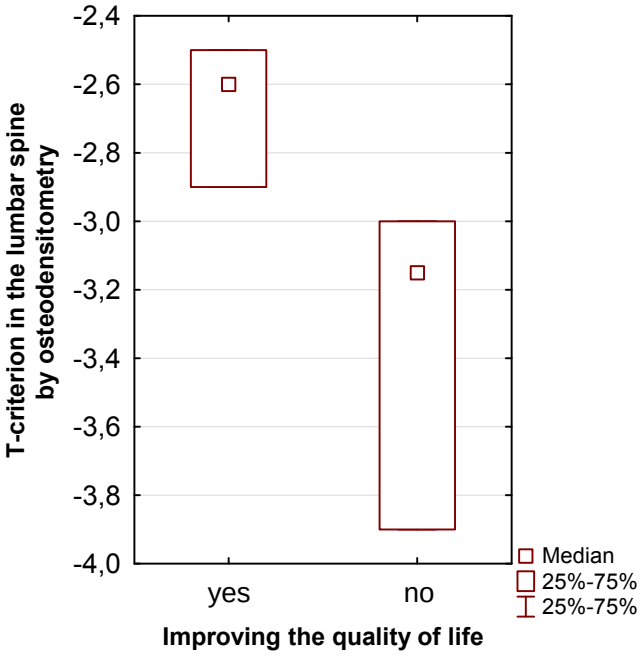


FIG. 8.

Dependence of improvement/deterioration of the quality of life on the T-score in the lumbar spine based on osteodensitometry results in patients of the comparison group with transient hypocalcemia

Two patients with QOL impairment were questionnaired more than a year after surgery: 1 patient in the main group, 1 in the comparison group.

Five months after undergoing unilateral revision of the neck, left upper PTE, a patient in the main group was diagnosed with persistence of the disease caused by multiple PTG lesions and false-positive intraoperative monitoring of intact PTH. Since the clinic functioned as a covid hospital, a second intervention was performed only 2 years after the primary one in the scope of bilateral neck revision, double inferior bilateral PTE with achievement of remission of the disease.

In the comparison group, QOL impairment was observed in 1 patient in whom PTG surgery was combined with thyroidectomy. The latter was performed as a case of diffuse toxic goiter complicated by thyrotoxic heart with paroxysmal form of atrial fibrillation without postoperative complications.

DISCUSSION

This prospective study has assessed the quality of life of a limited sample of patients with PHPT preoperatively in comparison with the regional population and at different time points postoperatively using the SF-36 general questionnaire. The sample included patients with solitary adenoma and with multiple PTG lesions in sporadic PHPT.

These findings revealed a decrease in both the general physical and psychological components of health in PHPT patients before surgery compared to those of comparable sex- and age-matched residents of the region. We first revealed that the greatest reduction in quality of life indicators was observed in patients with multiple PTG lesions compared to solitary lesions.

Evidence from the literature reveals that surgical treatment improves the quality of life of patients with PHPT regardless of the extent of surgical intervention [13–16]. It has been previously reported that PHPT patients have improved quality of life scores at 3 and 12 months after PTE [17].

The quality of life of PHPT patients was found to improve up to 1 year after surgery for solitary PTG lesions and after 1 year for multiple lesions. Disease persistence is the outcome of surgical treatment in which there was a statistically insignificant improvement in the physical and mental health components compared to preoperative values. Transient complications did not interfere with the improvement of QOL scores while achieving remission of hyperparathyroidism.

Postoperative impairment of quality of life was found in 10 % of patients. In patients up to 6 months after surgical treatment of solitary PTG lesions in PHPT, the impairment of quality of life indicators was associated with postoperative hypocalcaemia associated with severe osteoporosis and hungry bone syndrome.

CONCLUSION

QOL of PHPT patients is significantly reduced with the worst indicators in multiple PTG lesions. Surgical treatment, despite transient complications, does not prevent improvement in quality of life indicators, provided remission of the disease is achieved. Only persistence of the disease prevents statistically significant improvement in quality of life. Consequently, surgical tactics aimed at reducing the incidence of persistence will achieve a de-

cent quality of life in most patients with multiple PTG lesions in PHPT.

Funding

The study and publication of the article are carried out in accordance with the plan of research work (R&D) of Irkutsk Scientific Centre of Surgery and Traumatology No. 063 "Biomedical technologies for the prevention and treatment of organ failure in reconstructive and restorative surgery" (due dates 2013–2021) and R&D "Personalized approach to the prevention and correction of multiple organ dysfunction in the treatment of surgical diseases" (due dates 2013–2021).), as well as R&D "Personalized approach to the prevention and correction of multi-organ dysfunction in the treatment of surgical diseases" (due dates 2022–2026).

Conflict of interest

The authors declare no apparent and potential conflicts of interest related to the publication of the present article.

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The article was published as part of the All-Russian Research and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology.

EXPERIMENTAL RESEARCHES

RESTORATION OF X-RAY BONE DENSITY WHEN REPLACING CORTICAL PLATE DEFECTS WITH A TISSUE-ENGINEERED CONSTRUCT IN THE EXPERIMENT

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ABSTRACT

Over the past decade, in global practice, the frequency of using high-resolution multi-layer spiral computed tomography (MSCT) for assessing the state of cancellous and cortical bone tissue has significantly increased. Using high-resolution MSCT makes it possible to assess X-ray bone density at various times after replacement of cortical plate defects with osteoplastic materials.

The aim of the research. *To study the restoration of cortical bone density in the area of osteoplasty using tissue-engineered construct in the experiment.*

Materials and methods. *In an in vivo experiment on New Zeland White (NZW) rabbits, perforation defects of cortical bone were formed in the femoral diaphysis. Three study groups were set up: group 1 – without bone defect replacement; group 2 – with bone defect replacement with deproteinized cancellous bone; group 3 – with bone defect replacement with tissue-engineered construct based on deproteinized cancellous bone with stromal vascular fraction of adipose tissue. Follow-up periods were 2, 4 and 6 weeks after the surgery. The X-ray density of cortical bone tissue was measured in Hounsfield units (HU). Fragments of deproteinized human cancellous bone were used alone and in combination with the stromal vascular fraction of NZW rabbit adipose tissue as a bone-replacing material for bone defect replacement.*

Results. *Cortical plate density the in the area of the defect in the group 3 by the week 6 is on average 1.3 times lower than that of the intact cortical plate and corresponds to D1 according to Misch classification. Cortical plate density in the area of the defect on the side of medullary canal by the week 6 in the group 3 corresponds to D1 according to Misch classification and is equal to 1351.25 ± 221.18 HU (1052; 1805), which is 1.5 times higher than in group 2 (D2 according to Misch classification; $p < 0.05$). The obtained results indicate an earlier restoration of X-ray bone density when using a tissue-engineered construct (group 3) compared to the same indicators in groups 1 and 2.*

Key words: *X-ray density, tissue-engineered construct, MSCT, stromal vascular fraction of adipose tissue, bone defect, deproteinized cancellous bone*

Received: 11.09.2023
Accepted: 05.10.2023
Published: 05.12.2023

For citation: Anastasieva E.A., Cherdantseva L.A., Medvedchikov A.E., Lukinov V.L., Kirilova I.A. Restoration of X-ray bone density when replacing cortical plate defects with a tissue-engineered construct in the experiment. *Acta biomedica scientifica*. 2023; 8(5): 235-243. doi: 10.29413/ABS.2023-8.5.25

ВОССТАНОВЛЕНИЕ РЕНТГЕНОВСКОЙ ПЛОТНОСТИ КОСТИ ПРИ ЗАМЕЩЕНИИ ДЕФЕКТОВ КОРТИКАЛЬНОЙ ПЛАСТИНЫ ТКАНЕИНЖЕНЕРНОЙ КОНСТРУКЦИЕЙ В ЭКСПЕРИМЕНТЕ

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РЕЗЮМЕ

За последнее десятилетие в общемировой практике для оценки состояния губчатой и кортикальной кости значительно возросла частота применения мультиспиральной компьютерной томографии (МСКТ) с высоким разрешением, позволяющим оценивать рентгеновскую плотность кости в различные сроки после замещения дефектов кортикальной пластины остеопластическими материалами.

Цель исследования. *Изучить восстановление плотности кортикальной кости в области остеопластики тканеинженерной конструкцией в эксперименте.*

Материалы и методы. *В эксперименте in vivo на кроликах линии New Zeland White (NZW) в диафизарной части бедренной кости сформированы перфорационные дефекты кортикальной пластины. Сформированы три группы исследования: 1-я группа – без заполнения дефекта; 2-я группа – с заполнением дефекта депротеинизированной губчатой костью; 3-я группа – с заполнением тканеинженерной конструкцией на основе депротеинизированной губчатой кости с стромально-васкулярной фракцией жировой ткани. Сроки наблюдения составили 2, 4 и 6 недель после операции. Плотность кортикальной пластины измеряли в единицах Хаунсфилда (HU). В качестве костно-замещающего материала для заполнения костных дефектов использовали фрагменты депротеинизированной губчатой кости человека изолированно и в сочетании со стромально-васкулярной фракцией жировой ткани кролика линии NZW.*

Результаты. *Плотность кортикальной пластины в области дефекта в 3-й группе к 6-й неделе в среднем в 1,3 раза ниже аналогичного показателя интактной кортикальной пластины и при этом соответствует D1 по классификации Misch. Плотность кортикальной пластины в области дефекта со стороны костномозгового канала к 6-й неделе в 3-й группе соответствует D1 по Misch и составляет 1351,25 ± 221,18 HU (1052; 1805), что в 1,5 раза выше, чем во 2-й группе (D2 по Misch; $p < 0,05$). Полученные результаты свидетельствуют о более раннем восстановлении рентгеновской плотности костной ткани при использовании тканеинженерной конструкции (3-я группа) по сравнению с показателями 1-й и 2-й групп.*

Ключевые слова: *рентгеновская плотность, тканеинженерная конструкция, МСКТ, стромально-васкулярная фракция жировой ткани, костный дефект, депротеинизированная губчатая кость*

Для цитирования: Анастасиева Е.А., Черданцева Л.А., Медведчиков А.Е., Лукинов В.Л., Кирилова И.А. Восстановление рентгеновской плотности кости при замещении дефектов кортикальной пластины тканеинженерной конструкцией в эксперименте. *Acta biomedica scientifica*. 2023; 8(5): 235-243. doi:10.29413/ABS.2023-8.5.25

Статья поступила: 11.09.2023
Статья принята: 05.10.2023
Статья опубликована: 05.12.2023

INTRODUCTION

In replacing bone tissue defects, in case of restrictions associated with the use of autografts, practical specialists (orthopaedic traumatologists, maxillofacial surgeons and others) prefer materials made of allogeneic and xenogeneic bone since they are widely available and have distinctive properties [1, 2]. This is why the development of new materials and tissue-engineered constructions (TECs) for bone tissue repair is a promising area of activity [2–4]. To assess the changes in X-ray density of bone tissue when using TEC from allogenic bone tissue, the main method of investigation is morphological. However, it has limitations with regard to "vital" macro- and microscopic assessment of bone tissue [1].

Over the last decade, the frequency of high-resolution MSCT application for the assessment of cancellous and cortical bone tissue has increased significantly in the global practice [1, 5, 6]. Multi-spiral computed tomography (MSCT) method together with specialised software allows not only quantitative assessment of bone density, but also obtaining a spatial image with the possibility of 3D-modelling [1]. The ability to visualise changes in X-ray density of bone tissue and assess bone and surrounding soft tissue allows for a 'vital' bone assessment. Therefore, it is relevant to study these parameters at different times after bone defects replacement by obtaining the necessary number of tissue contrast gradations [7–9].

THE AIM OF THE STUDY

To study the restoration of cortical bone density in the area of osteoplasty using tissue-engineered construct in the experiment.

MATERIALS AND METHODS

The study was performed on 24 sexually mature male rabbits of the New Zealand White (NZW) line weighing 2500-2800 g. The animals had a veterinary quality certificate of health status and were kept under identical standard drinking and feeding conditions (GOST R ISO 10993-2-2009). Fragments of deproteinized cancellous bone of human isolated and in combination with stromal vascular fraction of adipose tissue of rabbit NZW line were used as bone replacement material for filling bone defects.

According to the current standards, 3 perforation defects of the cortical bone were formed in the diaphyseal part of the femur of both hind legs of each animal under general combined anaesthesia in sterile conditions using sterile surgical instruments. Three study groups were formed:

- Group 1 – perforation defect of the cortical plate in sections of the diaphysis of the femur without replacement;
- Group 2 – perforation defect of the cortical bone plate in sections of femur diaphysis being filled with fragments of deproteinized cancellous bone (DPCB);
- Group 3 – perforation defect of the cortical bone plate in sections of the femoral shaft with being filled with tissue-engineered construction based on deproteinized cancellous bone with stromal vascular fraction (SVF) of adipose tissue (Patent US10512659B2).

Animals were removed from the experiment by overdose of ether anesthesia at 2, 4, and 6 weeks after surgery.

X-ray density of compact bone in the osteoplasty area at all follow-up periods was assessed by MSCT with an Aquilion Prime 2018 tomograph (Toshiba, Sapon Medical Systems, Japan). Sagittal slices of the bone regenerate area were processed in the multiplanar reconstruction mode (MPR, multiplanar reconstruction); slice parameters – 120 kV, 50 mA, Bone filter, slice thickness 0.5 mm. During the MSCT examination of the distal tibia of rabbits, the bone density from the medullary canal and periosteum sides, as well as the intact cortical plate density, were assessed. Cortical plate density was measured in Hounsfield units (HU, Hounsfield unit). Using the K-Pacs v. 1.6.0 software package designed for work with DICOM, ROI (Region of Interest) tool, the cortical plate density was measured by statistical evaluation of averaged values for each study group in three areas: the 1st corresponded to the area of bone defect on the periosteum side; the 2nd – to the area on the medullary canal side; the 3rd – to the area of intact cortical plate. According to the HU values, bone tissue was classified according to Misch [10].

Descriptive statistics of continuous defect measures were calculated as median [first quartile; third quartile] (M [Q1; Q3]), mean ± standard deviation (MEAN ± SD), minimum and maximum value (min-max). The nonparametric Wilcoxon test was used to compare the parameters of the defect areas with those of the intact cortical plate; differences at $p < 0.05$ were considered statistically significant. Statistical calculations were performed in the RStudio IDE (version 2022.07.2, build 576; RStudio PBC, USA) in the R language (version 4.1.3, https://www.R-project.org; Austria).

RESULTS

In the 1st study group 2 weeks after surgery, bone defects with signs of poorly expressed filling with bone tissue corresponding to the D4 type according to Misch classification were detected (Table 1).

At the same time, the mean X-ray density of bone in the area of bone defect on the medullary canal side was 27 ± 6.32 HU (14; 40) and on the periosteum side was 202.92 ± 65.35 HU (66; 296). In the area of intact bone plate, X-ray bone density measured 1880.88 ± 475.65 HU (1258; 3200) and was greater compared to other areas of measurement ($p < 0.001$).

At 4 weeks after surgery, the X-ray density of the bone tissue was found to correspond to the Misch D3 values

TABLE 1

BONE DENSITY INDICES ACCORDING TO MSCT DATA IN THE 1ST STUDY GROUP (BONE DEFECT WITHOUT REPLACEMENT)

Parameter name	Follow-up period		
	2 weeks **M [Q1; Q3]** **MEAN ± SD** **(min–max)**	**4 weeks** **M [Q1; Q3]** **MEAN ± SD** **(min–max)**	**6 weeks** **M [Q1; Q3]** **MEAN ± SD** **(min–max)**
	Areas (measurement points)		
on the side of the medullary canal (area 1), HU	26.5 [24.75; 29.25] 27 ± 6.32 (14–40)	14 [2.97; 27] 15.18 ± 17.21 (–12–47)	29 [–46.25; 81.25] 30.5 ± 78.01 (–84–197)
on the periosteum side (area 2), HU	225 [155; 253.25] 202.92 ± 65.35 (66–296)	907 [628; 983] 824.92 ± 252.64 (349–1242)	1302.5 [696; 1459] 1103.25 ± 440.15 (421–1678)
Intact cortical plate (area 3), HU	**1792 [1417.5; 2083]** **1850.88 ± 475.65** **(1258–3200)**	**2182.5 [2073.5; 2444]** **2220.33 ± 311.95** **(1508–2850)**	**2184.5 [2069; 2252]** **2178.67 ± 268.51** **(1726–2791)**
According to Misch (area 1 / area 2 / area 3)	4 / 4 / **1**	4 / 3 / **1**	4 / 2 / **1**
	Comparison of measurement points*(p)*		
area 1 – area 2	$p < 0.001$*	$p < 0.001$*	$p < 0.001$*
area 1 – area 3	$p < 0.001$*	$p < 0.001$*	$p < 0.001$*
area 2 – area 3	$p < 0.001$*	$p < 0.001$*	$p < 0.001$*

Note. * – statistically significant differences ($p < 0.05$).

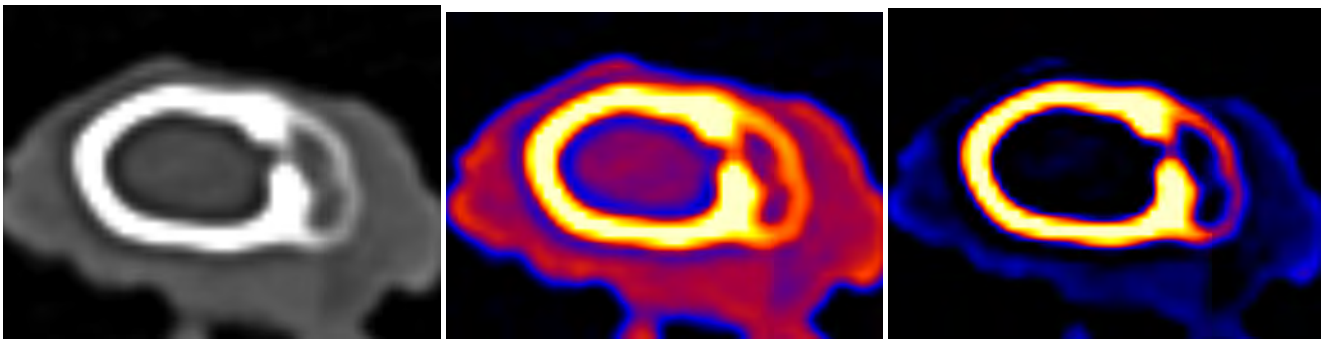

FIG. 1.

MSCT data at week 6 in the group 1 without bone defect replacement (processed in K-Pacs software v. 1.6.0, magnification ×10)

in the defect zone on the periosteum side and to the D4 values on the medullary canal side. Herewith, the mean X-ray density value on the medullary canal side (15.18 ± 17.21 HU (–12; 47)) was not significantly different from that noted at the previous study period. The X-ray density value for the defect area from the periosteal side was

824.92 ± 252.64 HU (349; 1242), which was 4.1 fold higher than the one obtained after 2 weeks.

After 6 weeks, bone density corresponded to D2 in the area of the bone defect from the periosteum side

TABLE 2

BONE DENSITY INDICES ACCORDING TO MSCT DATA IN THE 2ND STUDY GROUP (BONE DEFECT WITH DEPROTEINIZED CANCELLOUS BONE REPLACEMENT)

Parameter name	Follow-up period		
	2 weeks (*n* = 8) M [Q1; Q3] MEAN ± SD (min–max)	**4 weeks (*n* = 8) M [Q1; Q3] MEAN ± SD (min–max)**	**6 weeks (*n* = 8) M [Q1; Q3] MEAN ± SD (min–max)**
	Areas (measurement points)		
on the side of the medullary canal (area 1), HU	580.5 [492; 639.25] 575.25 ± 130.04 (383–759)	519.5 [352.5; 660] 529 ± 244.42 (195–958)	777 [683.5; 1032.5] 874.38 ± 283.51 (575–1336)
on the periosteum side (area 2), HU	406.5 [37.25; 601] 322.38 ± 370.1 (–188–727)	1399 [1368; 1409.75] 1388.75 ± 32.73 (1329–1430)	1490.5 [1351.75; 1609.5] 1426.25 ± 326.81 (742–1774)
Intact cortical plate (area 3), HU	**1749.5 [1678; 1870.25] 1826.25 ± 255.89 (1558–2344)**	**2143.5 [2094; 2339.75] 2183.5 ± 226.68 (1770–2462)**	**2269 [2078; 2672.5] 2329.12 ± 414.44 (1659–2852)**
According to Misch (area 1 / area 2 / area 3)	3 / 3 / **1**	3 / 2 / **1**	2 / 1 / **1**
	Comparison of measurement points(*p*)		
area 1 – area 2	*p* = 0.195	*p* = 0.008*	*p* = 0.008*
area 1 – area 3	*p* = 0.012*	*p* = 0.008*	*p* = 0.008*
area 2 – area 3	*p* = 0.012*	*p* = 0.008*	*p* = 0.008*

Note. * – statistically significant differences ($p < 0.05$)

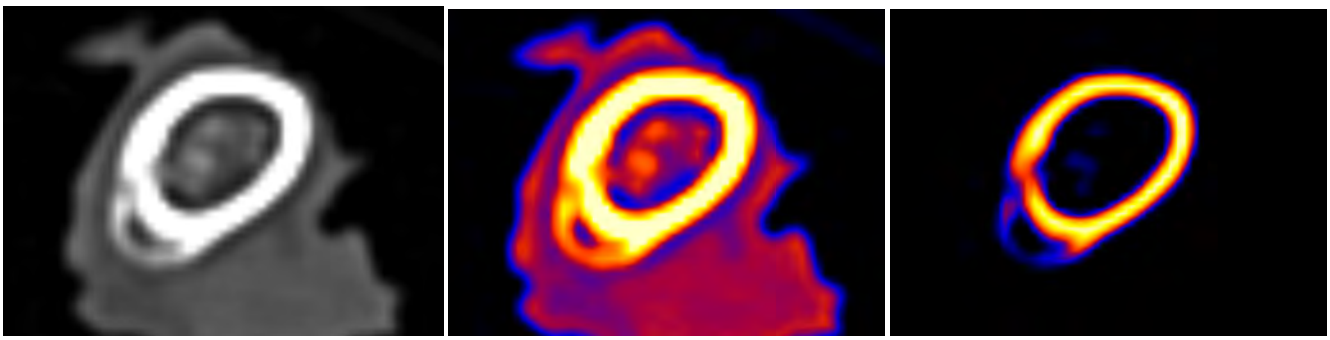

FIG. 2.

MSCT data at week 6 in the group 2 with bone defect replacement by deproteinized cancellous bone (processed by K-Pacs v. 1.6.0 software, magnification ×10)

and D4 from the medullary canal side. As the follow-up period extended, a 1.3-fold increase in the X-ray density of bone in the defect area from the periosteum side and a slight increase from the medullary canal side were noted (Fig. 1). The density of the intact bone plate measured as 2178.67 ± 268.51 HU (1726; 2791) and had differ-

TABLE 3

BONE DENSITY INDICES ACCORDING TO MSCT DATA IN THE 3RD STUDY GROUP (BONE DEFECT WITH REPLACEMENT BY DEPROTEINIZED CANCELLOUS BONE WITH STROMAL VASCULAR FRACTION OF ADIPOSE TISSUE)

Parameter name	Follow-up period		
	2 weeks (*n* = 8) M [Q1; Q3] MEAN ± SD (min–max)	4 weeks (*n* = 8) M [Q1; Q3] MEAN ± SD (min–max)	6 weeks (*n* = 8) M [Q1; Q3] MEAN ± SD (min–max)
	Areas (measurement points)		
on the side of the medullary canal (area 1), HU	560 [480.5; 664.25] 572.38 ± 178.07 (322–834)	1028 [897.5; 1204.25] 1043.62 ± 194.32 (789–1271)	1363 [1235; 1391.25] 1351.25 ± 221.18 (1052–1805)
on the periosteum side (area 2), HU	435.5 [347.25; 467] 413.38 ± 145.55 (158–649)	1260 [1220; 1393.5] 1294.12 ± 110.38 (1149–1442)	1330.5 [1294.75; 1383.25] 1360.75 ± 120.82 (1235–1580)
Intact cortical plate (area 3), HU	**1437 [1412.75; 1701.25] 1613.38 ± 344.39 (1353–2172)**	**2303 [2155; 2542] 2341.12 ± 213.97 (2113–2622)**	**1773 [1669; 1847.25] 1773.62 ± 149.36 (1548–1992)**
According to Misch (area 1 / area 2 / area 3)	3 / 3 / **1**	2 / 2 / **1**	1 / 1 / **1**
	Comparison of measurement points (*p*)		
area 1 – area 2	*p* = 0.148	*p* = 0.039*	*p* = 0.547
area 1 – area 3	*p* = 0.012*	*p* = 0.021*	*p* = 0.045*
area 2 – area 3	*p* = 0.012*	*p* = 0.021*	*p* = 0.023*

Note. * – statistically significant differences ($p < 0.05$)

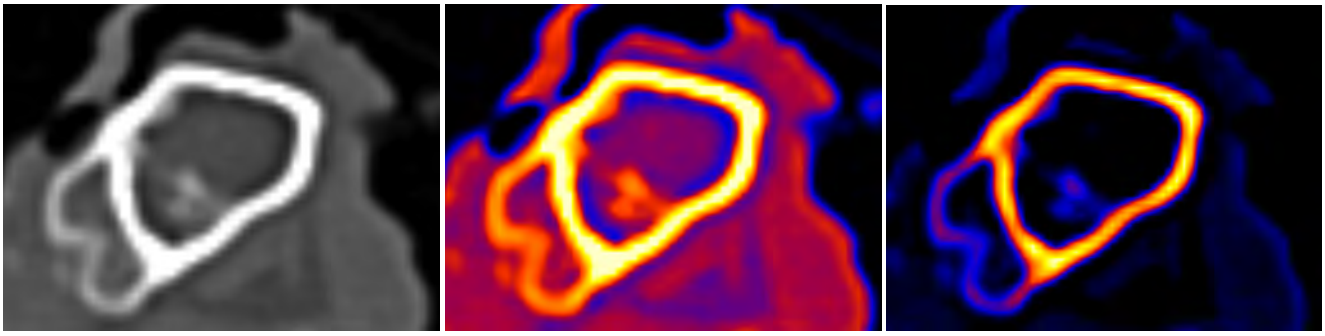

FIG. 3.

MSCT data at week 6 in the group 3 with bone defect replacement using tissue-engineered construction based on deproteinized cancellous bone with autologous stromal-vascular fraction as cellular material (processed by K-Pacs v. 1.6.0 software, magnification ×10)

ences with respect to the rest of the measurement areas ($p < 0.001$). The dynamics of X-ray bone density indices in the studied areas of the bone defect in group 1, demonstrates a gradual increase and approaching to the intact bone density indices.

The X-ray density of bone on both the periosteal and medullary canal sides was consistent with D3 in the 2nd study group 2 weeks after surgery (Table 2).

After 4 weeks, an increase in bone density indices was observed in all areas of measurement. After 6 weeks, X-ray density in the defect filling areas along the medullary canal side corresponded to the D3–D2 type and increased 1.6-fold from week 4 to week 6 (Table 2; Fig. 2). For the area of defect replacement from the periosteum side, a slight increase in X-ray density was observed from week 4 to week 6 of the study.

In the 3rd group 2 weeks after surgery, the X-ray density of bone in the area of bone defect replacement corresponded to the D3 type and the indices in the 2nd group during the similar study period. The mean bone density from the medullary canal side measured as 572.38 ± 178.07 HU (322; 834) and from the periosteum side as 413.38 ± 145.55 HU (158; 649) (Table 3).

At 4 weeks after surgery, X-ray density of the bone corresponded to D2 in the defect filling area on both the periosteal side (1294.12 ± 110.38 HU (1149; 1442)) and the medullary canal side (1043.62 ± 194.32 HU (789; 1271)). Besides, an increase in these indices was observed compared to the indices after 2 weeks by 3.1 and 1.8 times, respectively (Table 3). In the area of intact cortical bone plate, the mean X-ray density was slightly lower as compared to the indices at other follow-up periods and corresponded to the D1 type. This may be caused by the individual bone density characteristics of the selected line of animals. The difference between the values of the studied parameters in the area of bone defect replacement and the X-ray bone density of the intact cortical plate area was statistically significant ($p = 0.021$).

After 6 weeks, X-ray bone density in the area of bone defect replacement (Fig. 3) corresponded to D1 with evenly distributed compact and cancellous bone substance. The mean X-ray bone density indices in the area of TEC bone defect filling were: from the periosteum side, 1360.75 ± 120.82 HU (1235; 1580), and from the medullary canal side, 1351.25 ± 221.18 HU (1052; 1805) (Table 3). There was a 3.3-fold and 2.3-fold increase in these indices from week 2 to week 6, respectively.

The X-ray density indices of the intact cortical bone plate after 6 weeks measured as 1773.62 ± 149.36 HU (1548; 1992), corresponded to D1 (Table 3; Fig. 3), and were not significantly different from the X-ray bone density indices in the defect replacement area from the medullary canal side and the periosteum side ($p = 0.045$ and $p = 0.023$, respectively). This may indicate an earlier recovery of X-ray bone density in the defect replacement area if TEC is applied.

DISCUSSION OF RESULTS

According to the literature, three main factors influence the rate of bone remodelling and regeneration. The first factor – replacement of the bone defect with bone-replacement material – reduces the time of bone regeneration in the defect area. If bone-replacement material obtained from the head of the human femur bone was used, according to the MSCT findings, the rearrangement of the implanted material was already observed by the day 45 [1, 11]. However, these findings have not been confirmed morphologically.

The second factor having an influence on the rate of bone tissue regeneration may be the proregenerative effect of periosteum, which has a pronounced osteogenic potential induced by cellular elements [12].

The third factor affecting the rate of bone repair is the presence of cellular elements in the bone replacement material or tissue-engineered construction [6, 7, 12].

According to the conducted study, the variability of values of radiological density of intact cortical plate in rabbits of NZW line was revealed, which corresponds to the data of literature describing the variability of values of X-ray density of intact cortical plate ranging from 1080 ± 439 to 2890.0 ± 63.1 HU [8, 9, 13, 14].

As the follow-up period increased in all groups, the indices of X-ray bone density in the area of bone defect replacement both on the side of the medullary canal and on the side of the periosteum approached the indices of X-ray bone density of the intact cortical plate.

In group 3 at week 6 of the study, X-ray bone density in the defect replacement area corresponded to type D1 – thick compact bone. Meanwhile, the X-ray bone density index in the area of bone defect replacement from the medullary canal side was 1351.25 ± 221.18 HU (1052; 1805) and was 1.5 times higher than in the group 2, where the X-ray bone density index remained comparable to that of D2–D3 ($p < 0.05$).

CONCLUSION

Replacement of the perforation defect of the cortical plate density of the rabbit femur with tissue-engineered construction made of deproteinized cancellous bone in combination with stromal vascular fraction of adipose tissue leads to faster restoration of bone density in comparison with the unfilled defect and isolated use of deproteinized cancellous bone, as evidenced by the indices of radiological bone density at MSCT examination.

Ethical review

Extract No. 016/23 from the minutes of the meeting of the local Ethics Committee of the Novosibirsk Research Institute of Traumatology and Orthopedics named after Ya.L. Tsivyan No. 006/23 dated 31.07.2023.

Conflict of interest

The authors of this article report the absence of obvious and potential conflict of interests related to the publication of materials.

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The article was published as part of the All-Russian Scientific and Practical Conference with international participation, dedicated to the 25th anniversary of the Irkutsk Scientific Centre of Surgery and Traumatology

ERRATUM

ERRATUM: SUMIN A.N., VAKHRUSHEV A.K., SHCHEGLOVA A.V. CLINICAL SYMPTOMS AND ECG DATA IN WOMEN WITH ACUTE CORONARY SYNDROME. ACTA BIOMEDICA SCIENTIFICA. 2023; 8(3): 70-80. DOI: 10.29413/ABS.2023-8.3.7

ERRATUM: СУМИН А.Н., ВАХРУШЕВ А.К., ЩЕГЛОВА А.В. ОСОБЕННОСТИ КЛИНИЧЕСКОЙ СИМПТОМАТИКИ И ДАННЫХ ЭКГ У ЖЕНЩИН С ОСТРЫМ КОРОНАРНЫМ СИНДРОМОМ. ACTA BIOMEDICA SCIENTIFICA. 2023; 8(3): 70-80. DOI: 10.29413/ABS.2023-8.3.7

We hereby inform the readers that in the article “Clinical symptoms and ECG data in women with acute coronary syndrome” (Sumin A.N., Vakhrushev A.K., Shcheglova A.V) published in Vol. 8, No. 3 (2023) of the journal “Acta biomedica scientifica” (pp. 70–80; doi: 10.29413/ABS.2023-8.3.7), at the request of the authors of the article, changes have been made to the “Funding” section.

Funding

The results were obtained with the support of the Russian Federation represented by the Ministry of Science and Higher Education of the Russian Federation within the framework of the Agreement on the provision of grants from the federal budget in the form of subsidies dated September 30, 2022 No. 075-15-2022-1202, a comprehensive scientific and technical program of the full innovation cycle “Development and implementation of a set of technologies in the areas of exploration and production of solid minerals, industrial safety, bioremediation, creation of new deep processing products from coal raw materials while consistently reducing the environmental burden on the environment and risks to the lives of the population” (approved by Order of the Government of the Russian Federation dated May 11, 2022 No. 1144-p).

ERRATUM: SUMIN A.N., SHCHEGLOVA A.V., ANICHKOVA M.I., FEDOROVA D.N., SHABALINA K.A. CLINICAL AND PSYCHOLOGICAL CORRELATIONS WITH TYPE D PERSONALITY IN PATIENTS WITH CHRONIC CORONARY SYNDROME. ACTA BIOMEDICA SCIENTIFICA. 2023; 8(4): 126-135. DOI: 10.29413/ABS.2023-8.4.14

ERRATUM: СУМИН А.Н., ЩЕГЛОВА А.В., АНЬЧКОВА М.И., ФЕДОРОВА Д.Н., ШАБАЛИНА К.А. КЛИНИКО-ПСИХОЛОГИЧЕСКИЕ КОРРЕЛЯЦИИ ПРИ ТИПЕ ЛИЧНОСТИ Д У БОЛЬНЫХ ХРОНИЧЕСКИМ КОРОНАРНЫМ СИНДРОМОМ. ACTA BIOMEDICA SCIENTIFICA. 2023; 8(4): 126-135. DOI: 10.29413/ABS.2023-8.4.14

We hereby inform the readers that in the article “Clinical and psychological correlations with type D personality in patients with chronic coronary syndrome” (Sumin A.N., Shcheglova A.V., Anichkova M.I., Fedorova D.N., Shabalina K.A.), published in Vol. 8, No. 4 (2023) of the journal “Acta biomedica scientifica” (pp. 126–135; doi: 10.29413/ABS.2023-8.4.14), at the request of the authors of the article, changes have been made to the “Funding” section.

Funding

The results were obtained with the support of the Russian Federation represented by the Ministry of Science and Higher Education of the Russian Federation within the framework of the Agreement on the provision of grants from the federal budget in the form of subsidies dated September 30, 2022 No. 075-15-2022-1202, a comprehensive scientific and technical program of the full innovation cycle “Development and implementation of a set of technologies in the areas of exploration and production of solid minerals, industrial safety, bioremediation, creation of new deep processing products from coal raw materials while consistently reducing the environmental burden on the environment and risks to the lives of the population” (approved by Order of the Government of the Russian Federation dated May 11, 2022 No. 1144-p).

A4 format (60x84/8). Commissioned: November 21, 2023.
Signed for publication: November 29, 2023, publication date: December 05, 2023.
Press sheets: 30,75; conventional printed sheets: 28,6; published sheets: 26,3. Order: 038-23.

Prepared by the editorial and publishing department of Irkutsk Scientific Centre of Surgery and Traumatology.
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