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*

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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*

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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).

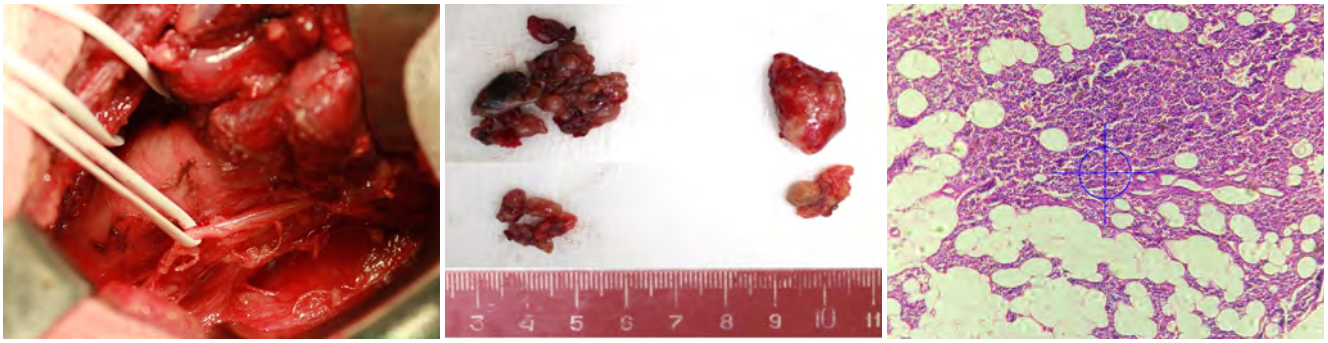
QOL was assessed by using the SF-36 (Short Form 36) questionnaire [8]. The calculation of indicators was performed using 8 scales according to the methodology of V.M. Amirjanov et al. [9]. The indicators of physical and mental health components were calculated according to the Evidence Company's manual – "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

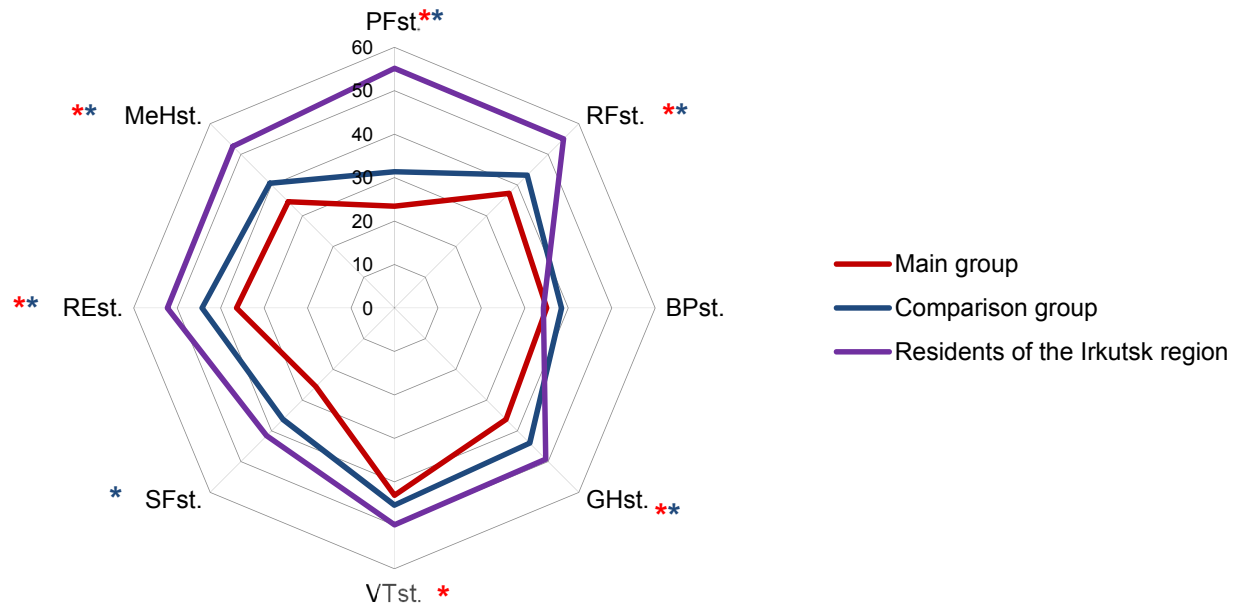


FIG. 3.

*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*

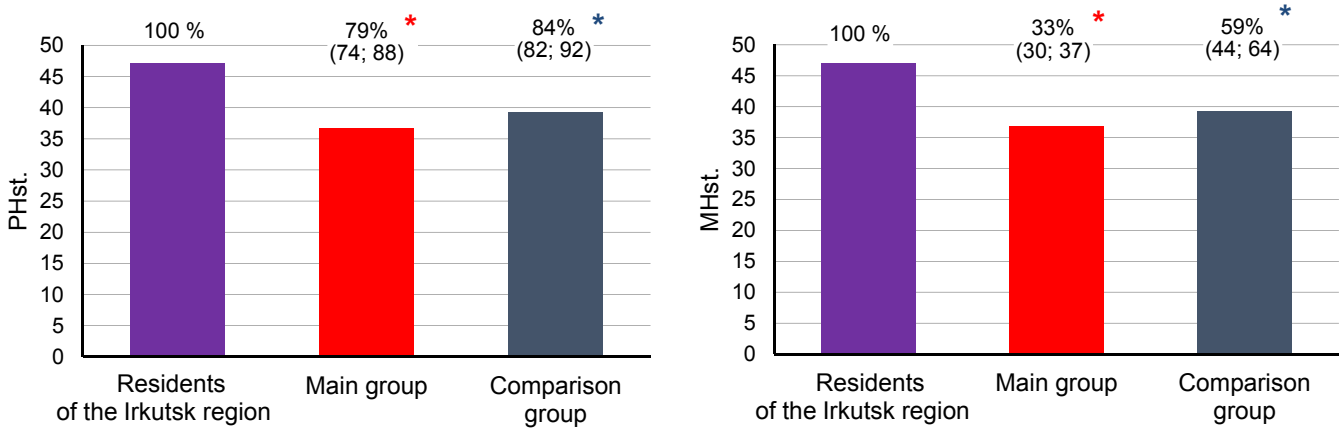


FIG. 4.

*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.

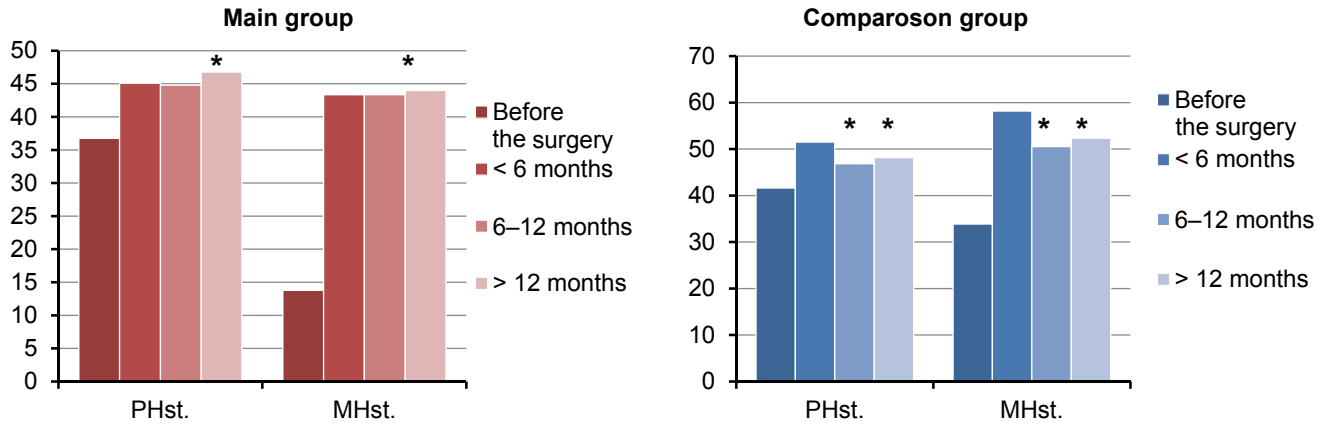


FIG. 5.

*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: * – $p_W < 0.05$*

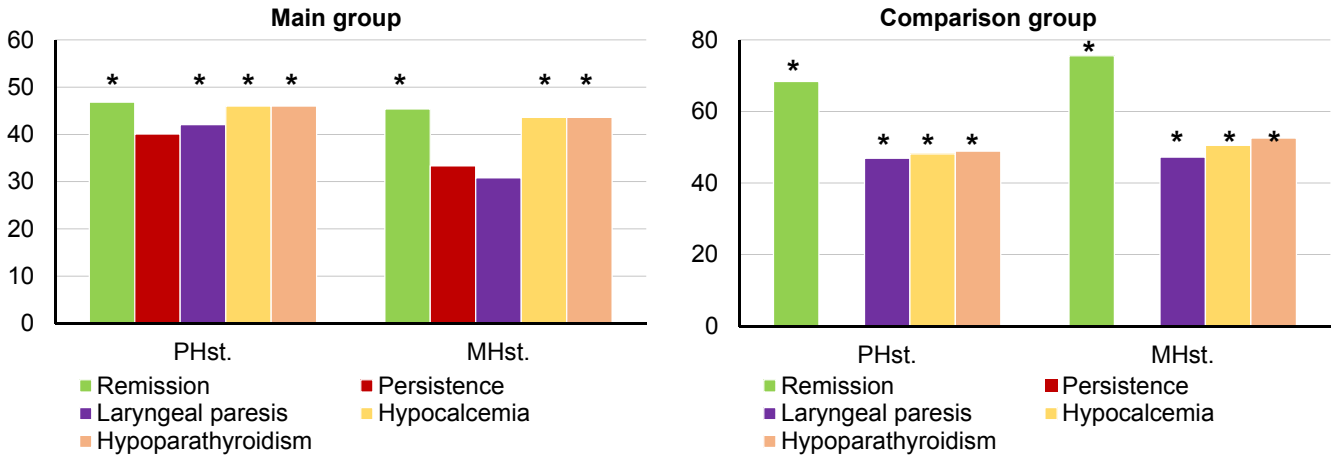


FIG. 6.

*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: * – $p_W < 0.05$*

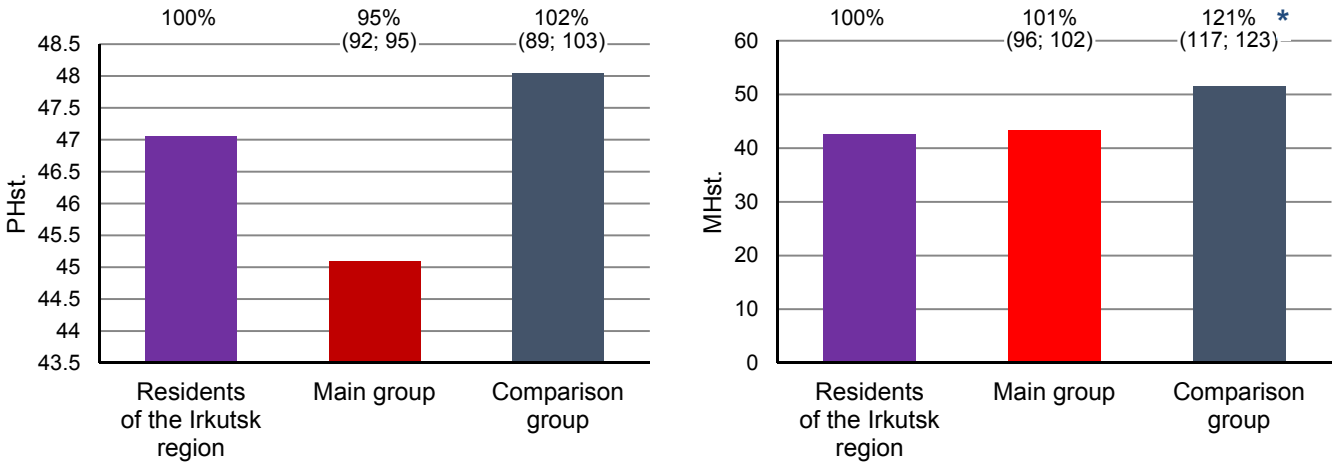


FIG. 7.

*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).

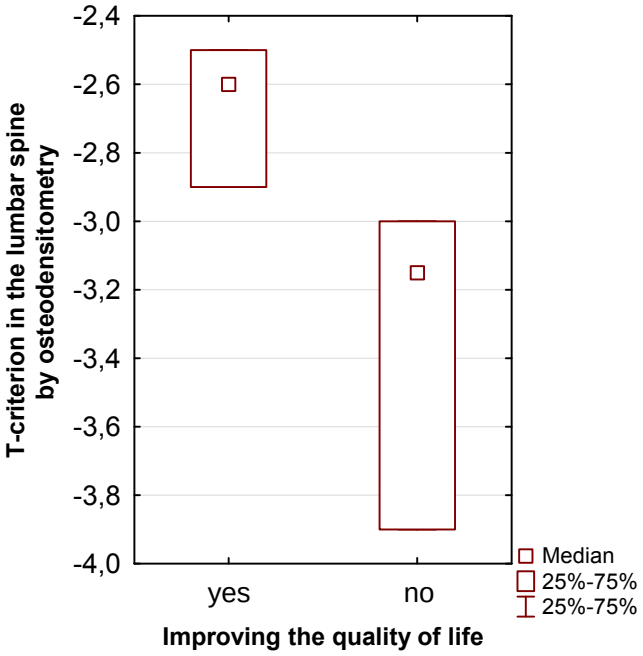


FIG. 8.

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.

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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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