SURGERY

DIAGNOSIS AND COMPARATIVE ANALYSIS OF SURGICAL TREATMENT OF PATIENTS WITH LIVER ALVEOCOCCOSIS

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ABSTRACT

Rationale. *Alveococcosis is a rare disease, its diagnosis and treatment depend on surgical techniques, equipment and clinical experience.*
The aim. *To develop a diagnostic algorithm and compare the results of surgical treatment of patients with liver alveococcosis in different periods of time.*
Materials and methods. *At the first stage, we carried out a retrospective analysis (1995–2007) of 33 patients with alveococcosis (a comparison group). At the second stage, a prospective clinical study (2008–2021) was performed on 39 patients (the main group). The number of patients was determined in accordance with the inclusion and exclusion criteria, and the study groups were comparable in age, sex, parasite localization ($p > 0.05$). For the names of operations, the WHO classification of alveococcosis was used.*
Results. *In the main group, there is an increase in the applicability of: enzyme immunoassay; ultrasound and computed tomography; biopsy. Complications decreased by 2.7 times from 54.6 % in the comparison group to 20.6 % in the main group ($\chi^2 = 8.97$; $df = 1$; $p = 0.003$). The average duration of operations, as well as the average volume of blood loss in the comparison group and the main group were, respectively: with atypical resection – 220.4 and 180.2 min ($p = 0.003$), 640.1 and 480.0 ml ($p = 0.005$); with anatomical resection – 296.2 and 247.2 min ($p = 0.002$), 1450.2 and 1150.3 ml ($p = 0.018$); with cytoreductive resection – 230.2 and 200.1 min ($p = 0.004$), 860.3 and 670.4 ml ($p = 0.001$). There were 13 (39 %) cytoreductive resections in the comparison group, and 3 (8 %) in the main group ($\chi^2 = 4.74$; $df = 1$; $p = 0.029$).*
Conclusion. *Timely diagnosis of alveococcosis leads to an increase in the number of radical resections, and modern surgical technologies and equipment can reduce the time of surgery, blood loss and the number of complications.*

Key words: *liver alveococcosis, algorithm for diagnosing liver alveococcosis, minimally invasive surgical interventions, radical liver resections, multi-stage approach to surgical treatment*

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ДИАГНОСТИКА И СРАВНИТЕЛЬНЫЙ АНАЛИЗ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ БОЛЬНЫХ АЛЬВЕОКОККОЗОМ ПЕЧЕНИ

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РЕЗЮМЕ

Обоснование. *Альвеококкоз является редким заболеванием, диагностика и лечение которого зависят от хирургических технологий, оборудования и клинического опыта.*

Цель исследования. *Разработать алгоритм диагностики и сравнить результаты хирургического лечения пациентов альвеококкозом в различные периоды времени.*

Материалы и методы. *На первом этапе проведён ретроспективный анализ (1995–2007 гг.) 33 пациентов с альвеококкозом – группа сравнения. На втором этапе выполнено проспективное клиническое исследование (2008–2021 гг.) 39 пациентов – основная группа. Количество пациентов определялось в соответствии с критериями включения и исключения, а исследуемые группы были сопоставимы по возрасту, полу, локализации паразита ($p > 0,05$). Для названий операций использовалась классификация альвеококкоза Всемирной организации здравоохранения.*

Результаты исследования. *В основной группе отмечается увеличение применяемости иммуноферментного анализа, ультразвукового исследования и компьютерной томографии, биопсии. В 2,7 раза снизилось количество осложнений – с 54,6 % в группе сравнения до 20,6 % в основной группе ($\chi^2 = 8,97$; $df = 1$; $p = 0,003$). Средняя длительность операций, а также средний объём кровопотери в группе сравнения и основной группе составили соответственно: при атипичной резекции – 220,4 и 180,2 мин ($p = 0,003$), 640,1 и 480,0 мл ($p = 0,005$); при анатомической резекции – 296,2 и 247,2 мин ($p = 0,002$), 1450,2 и 1150,3 мл ($p = 0,018$); при циторедуктивной резекции – 230,2 и 200,1 мин ($p = 0,004$), 860,3 и 670,4 мл ($p = 0,001$). В группе сравнения было проведено 13 (39 %) циторедуктивных резекций, а в основной группе – 3 (8 %) ($\chi^2 = 4,74$; $df = 1$; $p = 0,029$).*

Заключение. *Своевременная диагностика альвеококкоза ведёт к увеличению количества радикальных резекций, а современные хирургические технологии и оборудование позволяют сократить время операции, кровопотерю и количество осложнений.*

Ключевые слова: *альвеококкоз печени, диагностика альвеококкоза печени и его осложнений, малоинвазивные хирургические вмешательства, радикальные резекции печени, многоэтапный подход к оперативному лечению*

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OBJECTIVES

Alveococcosis is characterized by a parasitic lesion of the liver with slow growth, possible spreading and metastasis to other organs and tissues, making it similar to malignant tumor [1–9]. Late detection of the disease reduces the chances of performing radical or conditionally radical liver resections, as well as organ transplantation and patient recovery [10–13]. Moreover, long-term ongoing disease leads to various complications that significantly worsen the patient's condition and reduce the percentage of positive outcome of surgical intervention [14, 15]. The development of both laboratory and imaging diagnostics, as well as surgical technologies, including minimally invasive ones, makes it possible to detect the disease at early stages and increase the possibility of performing radical surgical interventions [16–18]. Minimally invasive surgeries in such cases become very significant, as they allow to manage various complications of parasitic lesions at the early stage(s) with subsequent safe radical surgical interventions, and when this is not possible, they remain the final surgical aids, allowing to alleviate the patient's condition and improve the quality of life. Modern equipment and various hemostatic agents (e. g. coverings) used for liver resection allow to perform surgical intervention faster, with less blood loss, reliable bile stasis and hemostasis, which leads to a decrease in postoperative complications [19–21].

MATERIALS AND METHODS

An open-label prospective retrospective non-randomized controlled single-center study was performed in two stages. At the first stage, a retrospective analysis of 33 medical records of patients with liver alveococcosis for 1995–2007 was performed, who further made up the comparison group. Methods of operative treatment of alveococcosis were developed and improved based on the obtained data. At the second stage of the study, a prospective clinical study involving 39 patients for 2008–2021 included in the main group was performed to evaluate the effectiveness of the proposed methods. The number of patients was determined in accordance with the inclusion and exclusion criteria, and the study groups were comparable in age, sex, parasite localization ($p > 0.05$). The data on patients in both groups are presented in Table 1. The diagnostic methods used in both groups are summarised in Table 2. When performing resection operations in the main group, carbon dioxide laser and spray coagulator were used, as well as hemostatic agents such as wound resorbable coverings. In case of complications and large spread of alveococcosis in the main group a multi-stage approach of surgical treatment was used, aimed at: biliary drainage using X-ray in case of obstructive jaundice; balloon dilatation and bile duct stenting; puncture and necrotic cavity

TABLE 1

DISTRIBUTION OF PATIENTS BY GROUPS

Parameters	Main group	Comparison group	*p* value	Total
Observation period (years)	2008–2021	1995–2007	–	1995–2021
Number of patients, abs. (%)	39 (54.2 %)	33 (45.8 %)	–	72 (100.0 %)
Average age (years), Me [25th; 75th percentiles]	46.1 [38.8; 53.6]	44.3 [37; 51.1]	$p = 0.692$	45.5 [37.8; 53.2]
Sex, abs. (%)				
male	21 (53.8 %)	19 (57.6 %)	$\chi^2 = 0.10$; df = 1; $p = 0.751$	40 (55.6 %)
female	18 (46.3 %)	14 (42.4 %)		32 (44.4 %)
Parasite localization in the liver, abs. (%)				
right lobe	22 (56.4 %)	20 (60.6 %)		42 (58.3 %)
left lobe	10 (25.6 %)	8 (24.2 %)	$\chi^2 = 0.15$; df = 2; $p = 0.927$	18 (25 %)
bilobed	7 (18.0 %)	5 (15.2 %)		12 (16.7 %)

Note. *p* – level of statistical significance.

TABLE 2
DIAGNOSTIC METHODS IN THE COMPARED GROUPS

Diagnostic method	Main group (n = 39)		Comparison group (n = 33)	
	abs.	%	abs.	%
Enzyme immunoassay	31	79.5	10	30.3
Ultrasound investigation	31	79.5	27	81.8
Native computer tomography	29	74.4	8	24.2
Contrast-enhanced computer tomography	25	64.1	4	12.1
Positron-emission tomography	4	10.3	0	0.0
Duplex ultrasound scanning of liver vessels	9	23.1	2	6.1
Needle biopsy	12	30.8	3	9.1
Diagnostic laparoscopy	1	2.6	3	9.1

drainage with ultrasound guidance; portal vein embolization in order to increase the volume of liver parenchyma. We used the 1996 WHO classification of alveococcosis ($P_{x-4}N_{x-1}M_{x-1}$) to name the surgical options, where: P – primary lesion; N – extrahepatic involvement of adjacent organs or tissues; M – distant metastases, as well as the resectability criterion R_{0-2} ($_0$ – radical; $_1$ – conditionally radical; $_2$ – cytoreductive) [22].

The obtained data was processed using statistical software packages Microsoft Excel (Microsoft Corp., USA) and Statistica 12 (StatSoft Inc., USA). Qualitative variables were described by absolute numbers and relative frequencies (%). Conformity to normal distribution of quantitative data was assessed using the Shapiro – Wilk test. Group variables were presented as median and interquartile range, Me [25%; 75%]. The Mann – Whitney U test was used for intergroup comparison. The χ^2 test was determined to compare categorical variables; the Yates correction was used in cases where tables contained small frequencies ($n < 5$). The Fisher angular transformation (φ-transformation) was used to compare the percentages. Differences were considered statistically significant at $p < 0.05$. The conjugate table method was used to express the results and efficacy of the intervention.

The study was based on the principles established by the International Committee of Medical Journal Editors (ICMJE) and the Universal Declaration on Bioethics and Human Rights.

RESULTS AND DISCUSSION

Table 2 shows that there is a higher number of procedures performed in the main group, except for laparoscopy, which is due to the progressive development and introduction of diagnostic equipment in different periods of time. In addition to quantitative differences, we also noted a qualitative difference associated with more sensitive expert-class diagnostic equipment. Based on all studies, we developed and implemented an algorithm for differential diagnosis of liver alveococcosis, presented in Figure 1.

As a result of analyzing the quantitative ratio of the liver surgeries performed, we did not obtain a statistically significant difference in the compared groups when performing atypical and anatomical resections, although significant differences in absolute numbers are visible: 9 (main group) versus 4 (comparison group) – right lobe, 4 versus 1 respectively – left lobe. Examples of atypical and anatomical resections are shown in Figures 2–5. Extended resections, as shown in Figures 6–8, were performed only in the main group, and therefore the comparison was not possible. However, we obtained a statistically significant difference by evaluating the number of cytoreductive resections performed, of which there were significantly more in the comparison group: 3 (main group) versus 10 (comparison group) – right lobe, 0 versus 3 respectively – left lobe ($\chi^2 = 4.74$; df = 1; $p = 0.029$*). The surgical interventions are summarized in Table 3.

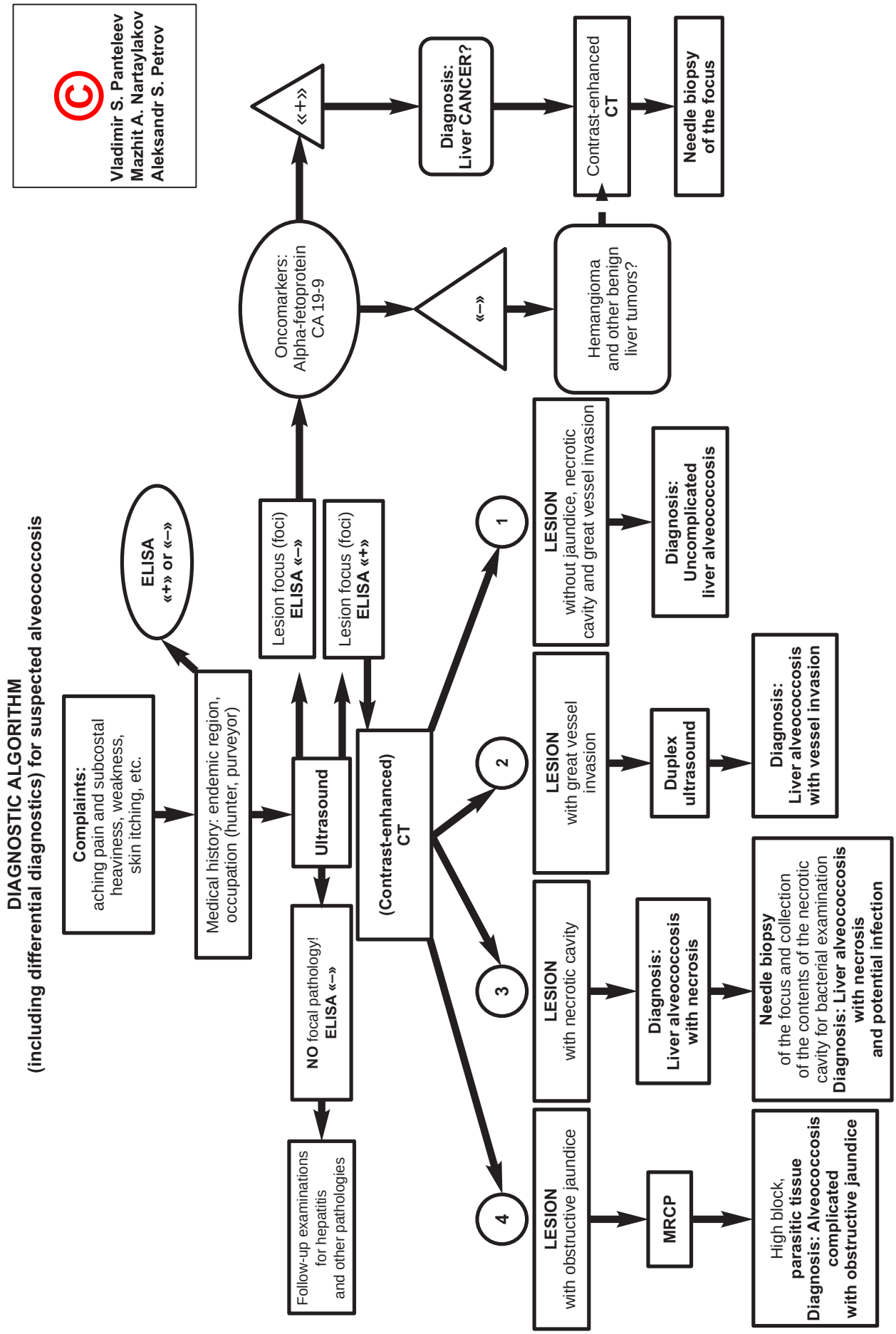

FIG. 1.
Diagnostic algorithm (including differential diagnostics) for suspected alveococcosis

FIG. 2.
Atypical liver resection: gross specimen of "alveolar echinococcus tumor"

FIG. 3.
Atypical liver resection: alveococcus gross specimen with necrotic cavity and suppuration

TABLE 3
VARIANTS OF SURGICAL INTERVENTIONS IN GROUPS

Surgical intervention	Main group (n = 39) 100%		Comparison group (n = 33) 100%		p value	
	right lobe	left lobe	right lobe	left lobe	right lobe	left lobe
$P_1N_0M_0(R_{0-1})$ – atypical resection	6 (15 %)	5 (13 %)	6 (18 %)	4 (13 %)	$\chi^2 = 0.1$; df = 1; $p = 0.751$	$\chi^2 = 0.07$; df = 1; $p = 0.789$*
$P_{1-2}N_{0-1}M_0(R_{0-1})$ – anatomic resection	9 (23 %)	4 (10 %)	4 (12 %)	1 (3 %)	$\chi^2 = 0.8$; df = 1; $p = 0.370$*	$\chi^2 = 0.54$; df = 1; $p = 0.461$*
$P_{1-3}N_{0-1}M_0(R_{0-1})$ – extended resection	4 (10 %)	1 (3 %)	0 (0 %)	0 (0 %)	–	–
$P_{3-4}N_{0-1}M_{0-1}(R_{1-2})$ – cytoreductive resection	3 (8 %)	0 (0 %)	10 (30 %)	3 (9 %)	$\chi^2 = 4.74$; df = 1; $p = 0.029$*	–
Total	22 (56 %)	10 (26 %)	20 (60 %)	8 (25 %)	$\chi^2 = 0.13$; df = 1; $p = 0.719$	$\chi^2 = 0.02$; df = 1; $p = 0.891$
$P_{3-4}N_{0-1}M_0$ – liver transplant	3 (8 %)		0 (0 %)		–	
$P_{3-4}N_{0-1}M_{0-1}$ – palliative	4 (10 %)		5 (15 %)		$\chi^2 = 0.39$; df = 1; $p = 0.532$*	

Note. * – the Yates' correction was used in the comparison between groups; p values corresponding to statistically significant differences between groups are marked in bold.

FIG. 4.
Right anatomic liver resection: gross specimen of resected organ with gallbladder and alveococcus

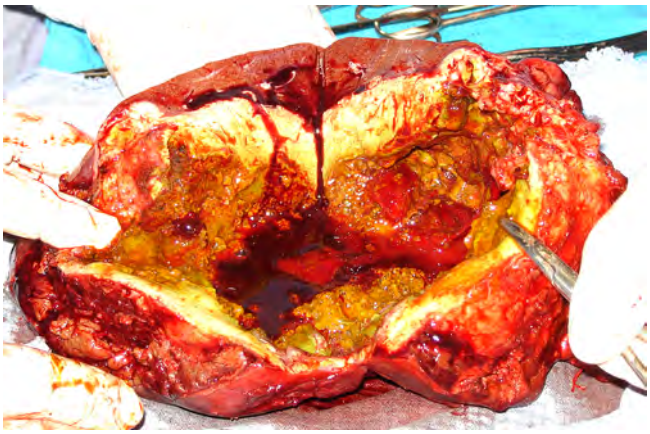

FIG. 5.
Right anatomic liver resection: gross specimen of "alveolar echinococcus tumor" with necrotic cavity

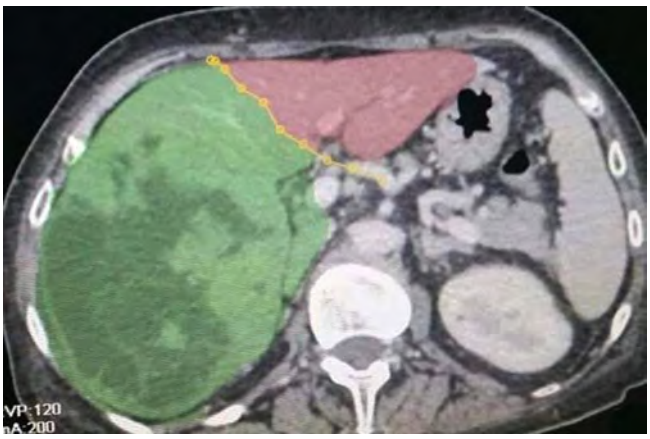

FIG. 6.
Computed tomography of the liver: the area of alveococcus lesion is marked in green

FIG. 7.
Right extended hemihepatectomy: gross specimen of a resected organ with gallbladder and alveococcus

FIG. 8.
Formed hepaticojejunal anastomosis after extended hemihepatectomy (fragment of the surgery)

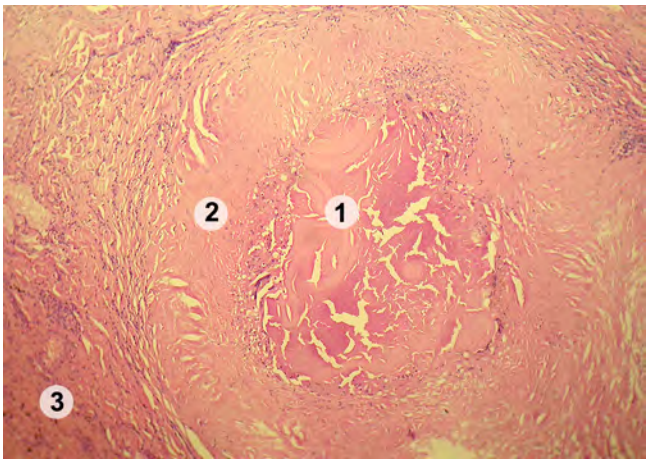

FIG. 9.
Alveococcosis of the liver: **1** *– daughter vesicles in the center of the parent bladder;* **2** *– parent cuticular membrane;* **3** *– fibrous membrane (productive inflammation)*

TABLE 4

AVERAGE DURATION AND AVERAGE VOLUME BLOOD LOSS IN RESECTABLE SURGERIES, ME [25 %; 75 %]

Parameters	Main group (n = 39)	Comparison group (n = 33)	p
Average surgery duration (min)			
Atypical resection	180.2 (132.5; 227.7)	220.4 (156.8; 284.0)	$p = 0.003$
Anatomic resection	247.2 (183.9; 385.8)	296.2 (233.9; 359.3)	$p = 0.002$
Extended resection	310.3 (273.7; 346.9)	0	–
Cytoreductive resection	200.1 (158.0; 242.3)	230.2 (187.8; 274.1)	$p = 0.004$
Average blood loss volume (ml)			
Atypical resection	480.0 (240.2; 720.5)	640.1 (409.8; 870.4)	$p = 0.005$
Anatomic resection	1150.3 (640.1; 1660.2)	1450.2 (909.8; 1990.5)	$p = 0.018$
Extended resection	1930.3 (1109.8; 2750.5)	0	–
Cytoreductive resection	670.4 (480.0; 860.8)	860.3 (590.1; 1130.6)	$p < 0.001$

TABLE 5

COMPLICATIONS, RECURRENT SURGERIES, MORTALITY IN IMMEDIATE POSTOPERATIVE PERIOD

Complications	Main group (n = 39) 100 %	Comparison group (n = 33) 100 %	Total (n = 72) 100 %
Liver stump bleeding / *relaparotomy*	2 (5.1 %) / 1 (2.6 %)	4(12.1 %) / 2(6 %)	6 (8.3 %) / 3 (4.2 %)
	$\chi^2 = 0.41$; df = 1; $p_1 = 0.521$*		
	$\chi^2 = 0.02$; df = 1; $p_2 = 0.882$*		
Liver stump bile leakage / *relaparotomy / ultrasound-guided puncture*	2 (5.1 %) / 0 / 1 (2.6 %)	5 (15.2 %) / 2 (6 %) / 0	7 (9.7 %) / 2 (2.8 %) / 1 (1.4 %)
	$\chi^2 = 1.10$; df = 1; $p_1 = 0.302$*		
Intra-abdominal abscess(s) / *relaparotomy / US-guided puncture*	1 (2.6 %) / 0 / 1 (2.6 %)	2 (6 %) / 1 (3 %) / 1 (3 %)	3 (4.2 %) / 1 (1.4 %) / 1 (1.4 %)
	$\chi^2 = 0.02$; df = 1; $p_1 = 0.882$*		
	$\chi^2 = 0.36$; df = 1; $p_3 = 0.549$*		
Portal vein thrombosis	1 (2.6 %)	0	1 (1.4 %)
	–		
Pneumothorax / *puncture* / *puncture* + *pleural drainage*	1 (2.6 %) / 1 (2.6 %) / 0	1 (3 %) / 1 (3 %) / 1 (3 %)	2 (2.8 %) / 2 (2.8 %) / 1 (1.4 %)
	$\chi^2 = 0.36$; df = 1; $p_1 = 0.549$*		
	$\chi^2 = 0.36$; df = 1; $p_3 = 0.549$*		
Liver failure	1 (2.6 %)	5 (15.2 %)	6 (8.3 %)
	$\chi^2 = 2.24$; df = 1; $p = 0.134$*		
Mortality	0	1 (3 %)	1 (1.4 %)
	–		
Total	8(20.6 %)	18 (546 %)	26 (36.1 %)
	$\chi^2 = 8.97$; df = 1; $p = 0.003$		

Note. US – ultrasound; * – the Yates' correction was used in the comparison between groups; p values corresponding to statistically significant differences between groups are marked in bold.

During histological examination of the material, there were occasional difficulties in differential diagnosis with malignant tumor of the liver. A typical picture of liver alveococcus and its growth are shown in Figure 9.

When comparing the surgery duration and blood loss during resectable surgical interventions, we obtained a statistically significant difference in all variants of liver resections, which is presented in Table 4.

We analyzed and compared all complications encountered in the immediate postoperative period and the surgical interventions performed to manage them. The complications identified and presented in terms of their characteristics when comparing the study groups had no statistically significant difference when compared individually. However, when combined, we obtained a significant difference between the groups in terms of the number of all complications and surgical interventions performed for their management: 8 (20.6 %) in the main group versus 18 (54.6 %) in the comparison group ($\chi^2 = 8.97$; df = 1; $p = 0.003$), as presented in Table 5.

CONCLUSION

Our long-term clinical experience of surgical treatment allowed us to develop and introduce into practice an algorithm of differential diagnostics in case of suspected liver alveococcosis, the application of which allows early detection of the disease, as well as its various complications. Comparative analysis showed differences in comparable groups, which in some indicators have a significant difference, which is primarily due to modern diagnostic capabilities and technical surgery support. Early detection of the disease allows to perform radical or conditionally radical surgery aimed at removing the «parasitic tumor», which leads to recovery or to a significant reduction in the subsequent possible manifestations of liver alveococcosis. Minimally invasive surgical interventions have a twofold significance: firstly, as a preparatory stage for radical surgery; secondly, as a definitive surgical intervention when resection surgery is not possible, which significantly improves the quality of life.

Conflict of interest

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

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