

Surgical treatment of liver echinococcosis and alveococcosis

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SUMMARY

Parasitic liver zoonoses are endemic to some regions of Russia as well as to Mediterranean countries, Australia, New Zealand, South America, and the Indian subcontinent. However, the available data on the surgical treatment of patients with parasitic liver diseases are often contradictory, and such treatments remain a difficult task today. The effectiveness of surgical treatment was analyzed in 628 patients with echinococcosis and 58 patients with liver alveococcosis managed at the Republican Clinical Hospital during 1998-2018. The most commonly performed surgery for echinococcosis was closed echinococectomy of different types, which was applied in 428 patients. Surgical outcomes were evaluated according to the type of surgery. Although there were no differences in outcomes in the immedi-

ate postoperative period, long-term postoperative outcomes differed with the type of surgery, compelling us to reconsider the surgical methods employed, with a preference for implementing cystectomy with omentoplasty of the residual cavity of the liver. In fact, the best outcomes in terms of recurrence and complications were obtained with minimal but adequate procedures, namely actual echinococectomy without the resection of the residual cavity or liver. Thus procedures with low-traumatic access should be performed in cases with specific indications, such as the presence of easily accessible and well-visualized parasitic cysts.

Keywords: parasitic liver diseases, echinococcosis, alveococcosis, surgical treatment.

INTRODUCTION

Parasitic liver zoonoses (echinococcosis and alveococcosis) are endemic to some regions of Russia as well as to Mediterranean countries, Turkey, North Africa, Australia, New Zealand, South America, the Philippines, North China, and the Indian subcontinent [1]. Notably, the available literature on the surgical treatment of echinococcosis and alveococcosis is mainly based on retrospective studies with large sample sizes compared with prospective studies. However, reported data on the surgical treatment of these diseases are often contradictory, rendering such treatments a difficult task even today because of numerous

reasons. For instance, to date, there has been no universal classification of surgical interventions for patients with parasitic liver zoonoses, and different surgeons refer to the same procedure differently. Moreover, diagnostic measures for liver parasites are inconclusive, particularly in terms of the associated complications, and individual institutions are thus forced to develop their own diagnostic algorithms based on their particular experience. In cases of liver echinococcosis, surgeons have a choice of removing the parasitic cysts alone or performing a more complex surgery to resect the infected liver fragment. Therefore, there is no consensus on the protocol of surgical intervention following the actual echinococectomy, that is, whether it is necessary to resect the residual liver cavity and in what way. Furthermore, there are no clear indications or contraindications for minimally invasive surgeries for the treatment of these zoonoses. Treating recurrent liver echinococcosis is

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rather challenging due to the complex differentiation of the origin of recurrent cysts, which hinders the recommendation of targeted preventive measures against the disease. The need for extended resections in alveococcosis, ways to improve the functional status of the liver before surgery for preventing failure in the near postoperative period, and the requirement of palliative (following partial removal of the “parasitic tumor”) liver resection remain questionable. Although only partly analyzed, results of cadaveric liver transplantations in cases of nonresectable alveococcosis have been reported. Finally, there is no consensus on the problems of postoperative rehabilitation as well as the effectiveness of antiparasitic therapies for reducing the relapse rate of the disease. In this article, we present our experience of the management of patients with parasitic liver cysts.

PATIENTS AND METHODS

Study design

We analyzed the effectiveness of surgical treatment in 628 patients with echinococcosis and 58 patients with liver alveococcosis who were managed at our hospital during 1998-2018 (retrospective study). The study was conducted with effect to the principles of the Declaration of Helsinki and its later amendments. The Ethical Committee of our university approved the study, and all patients provided voluntary signed informed consent for participating in the study.

Statistical analysis

The findings were processed using the Statistica 10.0 statistical package (StatSof Inc, USA). The

normality of the actual data distribution was checked using the Shapiro-Wilk criterion. The groups were described using the median and interquartile interval. Dichotomous adverse peri- or postoperative outcome events were analyzed using a univariate logistic regression model with backwards stepwise elimination and are expressed as odds ratios (OR) and 95% confidence intervals (CI). *P*-value less than 0.05 was considered statistically significant.

Echinococcosis

Of the 628 patients with echinococcosis, 288 (45.9%) were males and 340 (54.1%) were females. The average age of the patients was 58.1 ± 16.3 years (from 14 to 85 years). Table 1 lists the localization of echinococcal cysts in the liver, total number of cases with infected echinococcal cysts, and proportion of patients with recurrent echinococcosis.

We developed and applied a tactical diagnostic algorithm that considers all necessary variables (symptoms, anamnesis, place of residence since the disease is endemic, and laboratory and instrumental methods of research) for the diagnosis of the disease and its complications. Among the laboratory studies, we paid special attention to enzyme immunoassays (EIAs) and used ultrasound as the most common diagnostic technique to accurately determine the nature and location of parasites in the liver; we only relied upon computer tomography for differential diagnoses in difficult cases. All patients were treated surgically, and the surgical procedure was selected based on our developed classification of surgical interventions implemented for liver echinococcosis.

Table 1 - Localization of echinococcal cysts in the liver (including infected and recurrent cysts).

Localization	Total number of cases with echinococcal cysts <i>n</i> (%)	Radical surgery treatment <i>n</i> (%)
Right lobe	382 (60.8)	29 (7.6)
Left lobe	96 (15.3)	11 (11.5)
Bilobate	66 (10.5)	11 (11.5)
Liver + abdominal cavity	19 (3.1)	6 (9.1)
Liver + spleen	10 (1.6)	2 (10.5)
Liver + retroperitoneum	9 (1.4)	2 (20)
Recurrent hydatid liver cysts	46 (7.3)	13 (28.3)
Total	628 (100)	13 (28.3)

Classification of surgical procedures for echinococcosis of the liver:

1. LIVER RESECTION
 - 1.1. Resection of the liver without opening the cyst
 - 2.2. Echinococectomy with atypical resection of nonfunctional liver tissue
2. IMPERFORATE ECHINOCOCCECTOMY
 - 2.1. Complete removal of the cyst (without opening it) together with its fibrous capsule
 - 2.2. Total pericystectomy: complete removal of the fibrous capsule after opening and removal of the cyst and its contents
 - 2.3. Partial pericystectomy with liquidation of the residual cavity by either of the following:
 - Capitonage and invagination of the residual cavity
 - Tamponade by the omentum
 - Aplatizata (abdominal) of the residual cavity
3. OPEN ECHINOCOCCECTOMY
 - 3.1. Marsupialization of the residual cavity
 - 3.2. Partial peri-cystectomy with external drainage of the residual cavity
4. MINIMALLY INVASIVE ECHINOCOCCECTOMY
 - 4.1. Puncture draining the puncture, aspiration, injection, and re-aspiration (PAIR) method
 - 4.2. Laparoscopy
 - 4.3. Mini-laparotomy

Table 2 presents various surgical interventions implemented in our patients. During all open interventions, the residual cavities in the liver were treated with ethanol and glycerin and CO₂ laser and antimicrobial photodynamic therapies were applied to the inner cyst walls for sterilization. During the PAIR method, the cavities were washed with a hypertonic solution of sodium chloride as an antiparasitic treatment.

Alveococcosis

Of the 58 patients with liver alveococcosis, 37 were males and 21 were females. Most patients were young or middle-aged individuals (35±3.6 years). The right liver lobe was affected in 33 (56%) patients, the left liver lobe in 17 (29%) patients, and both lobes in 8 (14%) patients. For alveococcosis diagnosis, we used the same

methods as those used for liver echinococcosis diagnose, but we relied to a greater extent on computer tomography and magnetic resonance imaging; we used positional emission tomography in 3 cases. Surgical procedures were selected based on

Table 2 - Types and number of surgical interventions for echinococcosis of the liver.

Type of surgery	Number n (%)
<i>Liver resection</i>	
Resection of the liver without lancing the cyst	28 (4.5)
Echinococectomy with atypical resection of nonfunctional liver tissue.	68 (10.8)
<i>Closed echinococectomy</i>	
Capitonage and invagination of the residual cavity	71 (11.3)
Tamponade of the residual cavity with omentum	56 (8.9)
Aplatiza (abdominization) of the residual cavity	238 (37.9)
Perfect echinococectomy	63 (10.0)
Open (Partial pericystectomy with external drainage of the residual cavity)	56 (8.9)
<i>Minimally invasive echinococectomy</i>	
Puncture draining (PAIR method)	19 (3.1)
Laparoscopic	17 (2.7)
Mini-laparotomy	12 (1.9)
Total	628 (100)

PAIR: puncture, aspiration, injection, and re-aspiration.

Table 3 - Types and number of surgical interventions for echinococcosis of the liver.

Type of surgery	Number of surgeries (n = 58)
<i>Radical, n=36</i>	
<i>Anatomical resections, n=20</i>	
Right hemihepatectomy	12
Left hemihepatectomy	8
<i>Atypical resections, n=14</i>	
Trisegmentectomy	6
Bisegmentectomy	6
Segmentectomy	2
Liver transplantation, n=2	2
<i>Palliative, n=22</i>	
"Morcellation"	4
Cavernotomy with external drainage	6
Biliary surgery	12

surgical benefits, depending on the prevalence of parasitic liver disease and its complications. Table 3 presents different techniques used for treating alveococcosis.

■ RESULTS

We performed 96 liver resections in patients with echinococcosis. In terms of short-term postoperative complications, 9 patients suffered from hepatic bleeding, of whom 6 were treated conservatively and 3 required re-laparotomies, and 7 developed bile leakage, of whom 5 resolved spontaneously with observational management and 2 required active surgical tactics (1 re-laparotomy due to bile peritonitis and 1 bile plug elimination via puncture drainage under ultrasound control). In addition, 14 of the 96 cases developed liver failure that lead to 2 deaths. In terms of long-term complications, only 1 patient among those who underwent liver resection suffered a disease relapse, which was associated with an extensive radical surgery to eliminate *Echinococcus scolex* (removal of the entire parasitic cyst, without leaving a residual cavity).

The most commonly performed surgery for echinococcosis was closed echinococectomy of different types, which was applied in 428 patients. Although there were no differences in outcomes in the immediate postoperative period, long-term postoperative outcomes differed with the type of surgery, compelling us to reconsider the surgical methods employed, with a preference for implementing cystectomy with aplatization of the residual cavity of the liver. In fact, an ideal echinococectomy would not be analogous to liver resection, which is based on the principle of radical surgery, and the resection of the residual liver cavity following echinococectomy is therefore worth considering. The number of relapses were similar with all surgical techniques (aplatization, capitonnage, and omentopexy), although those who underwent omentopexy or capitonnage showed a higher rate of infections with suppuration of the residual cavity [2,3]. In addition, we performed ultrasound examinations of all patients postoperatively, but differentiating residual hollow liver lesions from recurrent echinococcal cysts was difficult. Consequently, we reoperated 4 patients suspected of having recurrent echinococcosis and only found empty lesions, which we then closed

via aplatization. Many authors consider the results of EIAs reliable for diagnosing echinococcosis and employ instrumental methods to clarify the location and nature of parasitic cysts. In contrast, we found that 63% of all cases showed positive EIA results, suggesting that positivity is associated with the developmental stage of the parasite or other unknown causes.

■ DISCUSSION

Conventionally, liver surgeries for echinococcosis have relied upon 2 approaches: radical removal of cysts within the anatomical structure of the liver and “practical” resection with direct removal of cysts and parasites.

To date, only 2 meta-analyses have compared the radical and “practical” liver resection approaches to treat echinococcosis. Pang et al conducted an analysis of 19 clinical studies from 10 countries including 1853 patients who underwent radical resections and 2274 patients who underwent cyst excisions and found that the risk of postoperative complications (biliary fistula and relapse) was significantly lower in the group that underwent radical surgery, the operative time was longer in the same group, and mortality rate and hospital stay duration were similar between the 2 groups [4].

Some studies have reported that radical liver surgery is more effective for echinococcosis and alveococcosis than other techniques [5-7]; however, these studies were retrospective and non-randomized.

In a comparative retrospective study including 242 patients, Aydin et al showed significantly higher relapse rates in patients who underwent sparing surgery [8]. Similarly, in a retrospective study including 54 patients, Abdelraouf et al showed significantly higher relapse rates in patients undergoing surgeries [9].

In a study including 454 patients (214 undergoing sparing surgery with external drainage, compatibility, or balto plate and 240 undergoing radical surgery), the recurrence rate was significantly higher in the group undergoing organ-preserving cystectomy [10].

Only 1 randomized study has compared outcomes of radical and organ-preserving surgeries in 32 patients and found that “practical” resections led to significantly higher early recurrence

rates and a higher complication rate than radical surgeries [11]. However, sparing and “practical” surgeries are technically easier and safer than radical liver resection to treat echinococcosis [12].

Different methods have been used to prevent postoperative complications due to the presence of a residual cavity following the removal of an echinococcal cyst (omentoplasty, introflection, capitonage, external drainage, or synthetic fibrin). In prospective study, Sokouti et al compared outcomes of 3 groups of patients (cyst removal, cyst aspiration with antiseptic filling and re-aspiration, and additional omentoplasty) and found that the group that underwent omentoplasty developed no infectious complications or relapses and experienced shorter hospital stay durations [13].

A comparative retrospective study including 304 patients demonstrated that external drainage led to a significantly higher complication rate (infection of the residual cavity and formation of the biliary fistulae) than omentoplasty or capitonage [14].

In another comparative study by Menten et al, omentoplasty led to fewer complications and shorter hospital stay durations than introflection [15].

Vagianos et al studied the effectiveness of the combined use of orthoplasty and echinococectomy (cystectomy and drainage) but noted no advantages of such a combination [16]. Reportedly, omentoplasty is associated with fewer complications than external drainage [17-19].

The use of fibrin glue in radical liver resection [20] and “practical” surgeries [21] may not be advantageous in terms of postoperative complication rate.

In the present study, 46 (7.3%) patients developed recurrent echinococcosis and required repeated surgical interventions. We used open echinococectomy only during the initial two years of the study period. After analyzing the initial outcomes, we avoided the technique due to high associated trauma and poor patients’ quality of life. One-way analysis revealed a relationship between the duration of hospitalization and open surgery (OR 30, $p=0.01$).

We performed 3 types of minimally invasive echinococectomies in 48 patients (Table 2). Based on our experience of laparoscopic echinococectomies, we still cannot conclude that this approach

provides significant advantages. Of the 17 patients who underwent laparoscopic echinococectomy in our study, 3 developed bile outflow from the residual liver cavity, 2 of whom required another laparotomy to resolve the problem. Moreover, although we carefully selected patients for this type of surgery (on the basis of the presence of small single-chamber cysts), the rate of complications suggests a need for the application of more rigorous indications. We diagnosed serious long-term complications in the form of echinococcal cysts in the abdominal cavity of 3 of the 17 patients. This is due to the dissemination of parasites into the free abdominal cavity during laparoscopic manipulation, suggesting the need for improving the technique.

We used the PAIR method with cyst drainage in 19 patients with echinococcal cysts of types I and II (without daughter vesicles or complications). Using this method strictly according to the indications, we successfully treated 11 (57.9%) patients. The remaining 8 patients underwent subsequent treatments (laparotomy, including mini-laparotomy, and closed cystectomy with apposition of the cyst walls) due to persistent parasites in the cavities, which were not efficiently eliminated with the hyperosmotic sodium chloride solution for reasons that are unclear to us.

During our 20-year experience in treating liver alveococcosis, we have noted that recent cases have been diagnosed during earlier stages owing to advances in medical science and technology, increasing the proportion of radically operable patients. We performed radical resections with the complete removal of the parasitic “tumors” from the liver. At the very beginning of the implementation of these surgeries, we experienced 2 lethal outcomes from liver failure in the short-term postoperative period, which we believe were due to the large volumes of organs resected. Nowadays, patients with large parasitic lesions undergo endovascular embolization of the lobular branch of the portal vein from the lesion to redistribute blood flow to the healthy lobe of the liver before undergoing radical resections. This allows the remaining liver to achieve hypertrophy within 20-25 days, thus maintaining its proper function following the extensive resection. Two of the 58 patients underwent successful cadaveric liver transplantations with favorable outcomes.

Palliative surgery is mostly performed in cases with bile drainage and obstructive jaundice developing as a result of the compression and/or germination of the draining ducts by the parasitic "tumors" (OR 8,7, $p=0,01$). Such patients undergo a minimally invasive surgery via the antegrade drainage of bile ducts under radiographic control, with the installation of external, at first, and external-internal drainage systems subsequently. Six patients underwent external drainage (3 with infected cavity contents that required urgent intervention).

Summing up the results of the analysis of our experience, the diagnosis of liver parasitic diseases has progressed through the development and implementation of new techniques that have allowed for the early detection and prediction of complications. The best results for the treatment of echinococcosis were obtained with minimal but adequate surgeries-echinococectomy without the resection of the residual cavity or liver. As noted, resection of the residual cavity and parenchymal organs leads to severe and even fatal complications. Thus, low-traumatic approaches (laparoscopy, mini-laparotomy, and the PAIR method) should be used based on strict indications, such as when parasitic cysts are easily accessible and well-visualized, to minimize the risk of intra-abdominal dissemination of parasites. Over the years, the outcomes of our patients with liver alveococcosis have improved as new surgical methods, preoperative preparations, and postoperative managements are being implemented. Particular attention should be paid to the preliminary embolization of the portal vein branches before the main resection of the affected liver lobe to allow the remaining organ to maintain its functional reserve and to reduce the risk of postoperative insufficiency. A radical solution by organ transplantation seems promising for patients with alveococcosis.

Conflicts of interest: None.

■ REFERENCES

- [1] Conraths F.J., Probst C., Possenti A., et al. Potential risk factors associated with human alveolar echinococcosis: Systematic review and meta-analysis. *PLoS Negl. Trop. Dis.* 11, e0005801, 2017.
- [2] Panteleyev V.S. Analysis of early and distant results of various options for eliminating the residential liver cavity following echinococectomy. *Creat. Surg. Onc.* 8, 203-207, 2018.
- [3] Zolotukhin K.N., Krüger P., Samorodov A.V. Low level of antithrombin III as a warning sign for developing thrombotic complications in surgical patients. *Creat. Surg. Onc.* 8, 52-56, 2018.
- [4] Pang Q., Jing H., Man Z., Wang Y., Yang S., Li Z. Radical versus conservative surgical treatment of liver hydatid cysts: a meta-analysis. *Front. Med.* 12, 350-359, 2018.
- [5] Berrada S., Essadki B., Zerouali N.O. Hydatid cyst of the liver. Treatment by resection of the cyst wall. Our experience apropos of a series of 495 cases. *Ann. Chir.* 47, 510-512, 1993.
- [6] Alfieri S., Doglietto G.B., Pacelli F., et al. Radical surgery for liver hydatid disease: A study of 89 consecutive patients. *Hepatogastroenterology* 44, 496-500, 1997.
- [7] Alonso O.C., Moreno E.G., Loinaz C.S., et al. Results of 22 years of experience in radical surgical treatment of hepatic hydatid cysts. *Hepatogastroenterology* 48, 235-243, 2001.
- [8] Aydin U., Yazici P., Onen Z., et al. The optimal treatment of hydatid cyst of the liver: radical surgery with a significant reduced risk of recurrence. *Turk. J. Gastroenterol.* 19, 33-39, 2008.
- [9] Abdelraouf A., El-Aal A.A., Shoeib, E.Y., et al. Clinical and serological outcomes with different surgical approaches for human hepatic hydatidosis. *Rev. Soc. Bras. Med. Trop.* 48, 587-93, 2015.
- [10] Tagliacozzo S., Miccini M., Amore Bonapasta S., Gregori M., Tocchi A. Surgical treatment of hydatid disease of the liver: 25 years of experience. *Am. J. Surg.* 201, 797-804, 2011.
- [11] Yüksel O., Akyürek N., Sahin T., Salman B., Azili C., Bostanci H. Efficacy of radical surgery in preventing early local recurrence and cavity-related complications in hydatid liver disease. *J. Gastrointest. Surg.* 12, 483-489, 2008.
- [12] Ozaslan E., Bayraktar Y. Endoscopic therapy in the management of hepatobiliary hydatid disease. *J. Clin. Gastroenterol.* 35, 160-174, 2002.
- [13] Sokouti M., Sadeghi R., Pashazadeh S., Abadi H., Sokouti M., Rezaei-Hachesu P. A systematic review and meta-analysis on the treatment of liver hydatid cyst: Comparing laparoscopic and open surgeries. *Arab. J. Gastroenterol.* 18, 127-135, 2017.
- [14] Zaouche A., Haouet K., Jouini M., El Hachaichi A., Dziri C. Management of liver hydatid cysts with a large biliocystic fistula: multicenter retrospective study. Tunisian Surgical Association. *World J. Surg.* 25, 28-39, 2001.
- [15] Mentis A., Yüzer Y., Ozbil O., Coker A., Ilter T., Musoğlu A. Omentoplasty versus introflexion for hydatid liver cysts. *J. R. Coll. Surg. Edinb.* 38, 82-85, 1993.
- [16] Vagianos C.E., Karavias D.D., Kakkos S.K., Vagenas C.A., Androulakis J.A. Conservative surgery in the treatment of hepatic hydatidosis. *Eur. J. Surg.* 161, 415-420, 1995.
- [17] Dziri C., Haouet K., Fingerhut A. Treatment of hy-

datid cyst of the liver: where is the evidence? *World J. Surg.* 28, 731-736, 2004.

[18] Utkan N.Z., Cantürk N.Z., Gönüllü N., Yildirim C., Dülger M. Surgical treatment of hydatid disease of the liver: omentoplasty or capitonnage versus tube drainage. *Hepatogastroenterology* 48, 203-207, 2001.

[19] Mousavi S.R., Khoshnevis J., Kharazm P. Surgical treatment of hydatid cyst of the liver: drainage versus omentoplasty. *Ann. Hepatol.* 4, 272-274, 2005.

[20] Cois A., Iasiello G., Nardello O., Mattana A., Uccheddu A., Cagetti M. Human fibrin glue in the treatment of residual parenchymal surface after total pericystectomy for hepatic echinococcus. *Ann. Ital. Chir.* 68, 701-706, 1997.

[21] Hofstetter C., Segovia E., Vara-Thorbeck R. Treatment of uncomplicated hydatid cyst of the liver by closed marsupialization and fibrin glue obliteration. *World J. Surg.* 28, 173-178, 2004.