

ORIGINAL ARTICLE

Radical versus conservative surgical management for liver hydatid cysts: A single-center prospective cohort study

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Abstract

Background and Aim: We prospectively compared the clinical outcomes of radical and conservative surgical procedures for primary liver hydatid cysts, additionally radical surgical procedures with and without the two-month administration of albendazole after the operation were compared.

Methods: Overall, 90 patients undergoing open surgical treatment for liver hydatid cysts were divided into three surgical groups: first group, patients who underwent radical surgery (pericystectomy) followed by albendazole treatment for 2 months following the operation group; second group, patients who underwent radical surgery(pericystectomy) without receiving albendazole after surgery group; third group, patients, who underwent conservative surgery (partial cystectomy) with albendazole treatment after surgery. The clinical outcomes and rate of recurrence were analyzed in follow-up period.

Results: The mean surgery duration in the Radical groups was significantly longer in comparison to the Conservative surgery + Albendazole group. (212.0 and 202.5 min vs. 173.2 min; $p < 0.05$). Blood loss in the Radical groups was significantly higher in comparison to the Conservative surgery + Albendazole group (218.3 and 174.6 ml vs. 67.2 ml; $p < 0.05$). However, postoperative complication rate in the Radical group was significantly lower in comparison to Conservative surgery + Albendazole group (13.3% [$n = 4$] and 6.7% [$n = 2$] vs. 36% [$n = 11$]; $p < 0.05$). The postoperative hospital stay in both Radical groups was significantly lower in comparison to the Conservative surgery + Albendazole group (7.9 and 7.4 days vs. 11.3 days; $p < 0.05$).

Conclusion: In comparison to conservative surgery, radical surgery is a preferable treatment modality for patients with active liver hydatid cysts. Postoperative albendazole treatment is preferable, regardless of the type of surgical procedure.

Introduction

Echinococcosis (hydatid cyst disease) is a parasitic disease that has a cosmopolitan distribution and which represents a major public health problem in endemic countries.¹ Despite its benign outcome, management of the disease presents a dilemma for surgical clinics because of the high complication and recurrence rates, which lead to prolonged hospitalization.² The liver (liver hydatid cyst; LHC) is the organ most frequently affected by echinococcosis.³ Currently, there are several treatment modalities for active LHC (minimally invasive treatment, conservative surgical treatment, and radical surgical treatment), which are selected according to the number of cysts, stage, size, and location.³ Because of the limited efficacy of systemic chemotherapy alone and minimally invasive treatment, the surgical treatment has been

accepted as the gold standard for the management of LHC.⁴ Radical surgical management (complete removal of all layers of LHC including fibrous capsule), despite being more aggressive surgery in comparison to conservative surgery (evacuating cyst content, leaving residual cavity with fibrous capsule), has been proposed as the most effective technique with the lowest rate of recurrence after surgery.² On the other hand, in Kazakhstan, albendazole as a subsequent therapy after surgery, is not covered by governmental insurance, and not all patients receive albendazole after surgery because of the cost of the drug. Thus, we prospectively compared the clinical outcomes of radical and conservative surgical procedures for LHC, additionally radical surgical procedures with and without the administration of albendazole for two months after the operation were compared.

TABLE 1 The preoperative characteristics of the patients

	Radical + Alb (n = 30) Medium (min–max)	Radical – noAlb (n = 30) Medium (min–max)	Conservative + Alb (n = 30) Medium (min–max)	p-value
Age	35.2 (18–66)	36.6 (17–66)	35.8 (16–70)	Ns
Sex (m/f)	(10/20)	(9/21)	(20/10)	Ns
Body mass index	23.1 (17.2–31.4)	23.3 (17.9–29.7)	24.5 (16.9–29.0)	ns
Number of cysts	1.52 (1–4)	1.17 (1–2)	2.17 (1–12)	ns
Size (cm)	10.3 (6.0–25.0)	9.9 (6.0–16.0)	9.9 (5.8–19.0)	ns
Right lobe	16 (53.4%)	22 (64%)	20 (66.6%)	ns
Left lobe	7 (23.3%)	4 (18%)	4 (13.4%)	ns
Bilobar location	7 (23.3%)	4 (18%)	6 (20%)	ns
≤ 2 segments	21 (70%)	25 (83.3%)	24 (80%)	ns
≥ 3 segments	9 (30%)	5 (16.7%)	6 (20%)	ns
Hydatid serology	12/18	9/21	7/23	ns

Material and methods

The present study was approved by the ethics committee of Syzganov's National Scientific Center of Surgery on January 2017 (protocol number 2). Research was carried out in accordance with the conditions of the Declaration of Helsinki (Research Registry number: research registry5568). In addition, this study has been reported in line with Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) criteria.⁵ In total, 90 patients who underwent surgical treatment for LHC in our hospital by an open procedure were enrolled in this study from January 2017 to August 2019. Patients of 18–70 years of age with active primary LHC (size: >5 cm) without extrahepatic localization and without previous treatment were eligible to participate in this study. Written informed consent was obtained from each participant before surgery. Preoperatively, chest X-ray, computed tomography (CT), and ultrasound of the abdominal cavity (US) were performed to determine the size, number, location, and stage of LHC. LHC was classified according to the World Health Organization Informal Working Group on Echinococcosis (WHO-IWGE) classification.⁶ The following exclusion criteria were applied: a history of previous surgical or drug

treatment; extrahepatic localization; cyst size <5 cm (treated with albendazole without surgery) and no active cysts (CE4 or CE5). The patients were prospectively divided into three groups in a 1:1:1 ratio.

Overall, 90 patients undergoing open surgical treatment for LHC were divided into three surgical groups: s: first group, patients who underwent radical surgery (pericystectomy: complete removal of the cyst with fibrous capsule) followed by albendazole treatment for 2 months following the operation (Radical + Alb) group; second group, patients who underwent radical surgery (pericystectomy) without receiving albendazole after surgery (Radical – noAlb) group; third group, patients, who underwent conservative surgery (partial cystectomy; evacuating cyst content, leaving residual cavity with fibrous capsule) with albendazole treatment after surgery (Conservative + Alb). The clinical outcomes and rate of recurrence were analyzed in the follow-up period.

Surgical technique

Partial cystectomy. We performed laparotomy for all cases in this study. After observing all of the rules of anti-parasiticity and

TABLE 2 The surgical outcomes and the postoperative complications

	Radical + Alb (n = 30)	Radical – noAlb (n = 30)	Conservative + Alb (n = 30)	p-value
Operation time (min)	212 (120–540)	202.5 (150–420)	173.2 (85–560)	p < 0.05
Blood loss (ml)	218.3 (50–1500)	174.6 (40–600)	67.2 (30–150)	p < 0.05
Complications:	4 (13.3%)	2 (6.7%)	11 (36.6%)	p < 0.05
Biliary complications	2	0	1	ns
Intra-abdominal abscess	0	1	2	ns
Pleural effusion	1	2	8	p < 0.05
Clavien Dindo surgical complications				
Grade 1	3	2	9	p < 0.05
Grade 2	2	3	8	p < 0.05
Grade 3a	1	0	2	ns
Grade 3b, 4 and 5	0	0	0	–
Hospital stay (days)	7.9 (5–20)	7.4 (5–18)	11.3 (7–26)	p < 0.05
Recurrence rate	0	1	1	ns

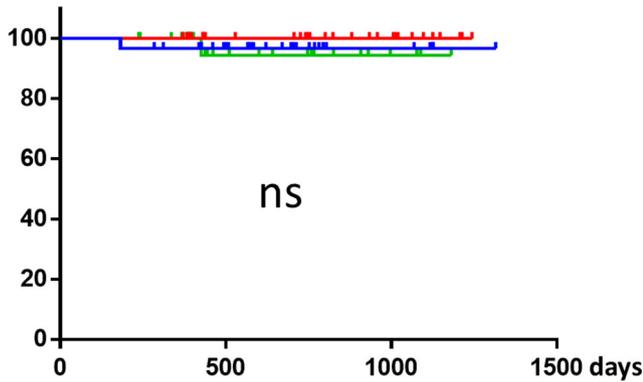


FIGURE 1 Patient recurrence-free survival after surgery. — Radical - noAlb; — Radical + Alb; — Conservative + Alb

aparasiticity during surgery to prevent contamination due to parasitic liquid, the cyst was punctured, and its contents were aspirated. The residual cavity of the cyst was treated with boiling saline (+100°C) for 10 min and povidone iodine with an exposure time of 5 min (three times). Thereafter, the removal of the parasitic chitinous membrane was performed. The residual cavity was left open in all cases. At least one control drainage tube was inserted into the abdominal cavity.

Total pericystectomy. After observing all of the rules of anti-parasiticity and aparasiticity during surgery to prevent contamination due to parasitic liquid, the complete removal of all layers of the cyst including fibrous capsule was performed, with or without puncture of the cyst (depending on size of the cysts). During the detachment of the fibrous capsule from the liver parenchyma through the pericystic layer, to prevent biliary complications after surgery, all vessel structures connecting with the cyst were precisely ligated or clipped. At least one control drainage tube was inserted into abdominal cavity.

Follow-up. In the follow-up period, the patients underwent hematological liver function tests and serological tests. US examinations were performed at 1, 3, 6 months and CT examinations were performed at 1 and 2 years after surgery, respectively.

Statistical analysis. The GraphPad Prism 6 software program (GraphPad Software, San-Diego, California, USA) was used for all statistical analyses. The results are reported as the mean \pm SD. Differences between groups were tested for significance by the chi-squared test. Comparisons of groups were performed with a two-way ANOVA test. Recurrence-free survival between groups was analyzed by a log-rank (Mantel-Cox) test. *P*-values of <0.05 were considered to indicate statistical significance.

Results

The preoperative characteristics of the patients in all treatment groups are summarized in Table 1. There were no significant differences among the groups in age, sex, body mass index, serology test results, cyst number, cyst size, or localization of LHC.

The operative and postoperative characteristics are shown in Table 2. The mean duration of surgery in the Radical groups was significantly longer in comparison to the Conservative+Alb group. (212.0 and 202.5 min vs. 173.2 min; $p < 0.05$). Blood loss in the Radical groups was significantly higher than that in the Conservative + Alb group (218.3 and 174.6 ml vs. 67.2 ml; $p < 0.05$). However, the rate of postoperative complications in the Radical groups was significantly lower in comparison to the Conservative + Alb group (13.3% [$n = 4$] and 6.7% [$n = 2$] vs. 36% [$n = 11$]; $p < 0.05$). The rate of postoperative pleural effusion in the Conservative + Alb group was significantly higher in comparison to the Radical groups ($p < 0.05$). Two patients in the Radical + Alb group and one patient in the Conservative + Alb group presented bile leakage from control drainage, which resolved spontaneously within 1 week without additional treatment; the difference was not statistically significant. Intra-abdominal abscess occurred in two patients in the Conservative + Alb group and 1 patient in the Radical - noAlb group; the difference was not statistically significant. All patients with abscess underwent additional percutaneous drainage placement under US guidance with antibiotic treatment. The Conservative + Alb group showed a significantly higher rate of Clavien-Dindo⁷ grade 1 and 2 complications in comparison to the Radical groups ($p < 0.05$), mostly due to the incidence of postoperative pleural effusion. No patients required relaparotomy and there was no postoperative mortality in any of the groups. The postoperative hospital stay in both Radical groups was significantly shorter in comparison to the Conservative + Alb group (7.9 and 7.4 days vs. 11.3 days; $p < 0.05$).

At the time of writing this report, the mean follow-up period was 23 ± 9 months (range 8.1–43.9 months). Recurrence-free survival after surgery is shown in Figure 1. In the postoperative period, disease recurrence was seen in two patients (one patient in the Radical - noAlb group and one patient in the Conservative + Alb group). However, the differences among the three groups did not differ to a statistically significant extent.

Discussion

Kazakhstan is highly endemic country for hydatid cyst disease. Both *Echinococcus granulosus* and *Echinococcus multilocularis* are widely distributed in the country.⁸ Despite advances in surgical techniques and the use of chemotherapy, recurrence remains a major problem in the management of hydatid disease.^{9–12} The optimal approach to LHC treatment is still challenging. Despite improvements in surgical methods, there is substantial controversy as to which method is the most effective for treatment.^{13,14} Some authors are inclined to believe that radical surgery is more effective than conservative surgery, since conservative surgery has higher rates of complications.^{15–17} Moreover, many authors consider radical surgery reduces the recurrence rate to 0–4.6%, which implies the superiority of radical surgery, since non-radical surgical treatment methods (external drainage, marsupialization, and omentoplasty) are associated with a recurrence rate of 25.0–30.4%.^{15,18} Other authors have suggested that conservative surgical approaches, such as partial cystectomy is less invasive and complex in comparison to radical surgery.^{14,19} Even though the risk of associated morbidity may be higher after conservative surgery due to the presence of the residual cavity, which can

increase the postoperative hospital stay and cost effectiveness.^{14,15} Moreover, it has been reported that leaving a residual cavity after conservative surgery increases the incidence of early local recurrence of the disease.¹⁵ In our study, to achieve a more precise understanding of the real benefit of radical surgery in comparison to conservative surgery, we only included patients undergoing primary treatment for active LHC. We excluded patients with a history of previous surgical or drug treatments and those with extrahepatic localization, which can also affect the potential for relapse-free survival.

In our study, the operation time and blood loss were significantly higher in the Radical surgery groups in comparison to the Conservative surgery group. Furthermore, the complication rate and postoperative hospital stay were significantly lower in the radical groups. Even though radical surgery is a more aggressive management modality, the recovery time of patients was reduced, which contributed to early discharge from the hospital. Although, the economic benefit after radical surgery would be lower. We hypothesize that the higher rates of reactive pleural effusion and hyperthermia without signs of infection in the Conservative group were probably due to a residual cavity with remaining within the fibrous capsule, which prolonged the postoperative hospital stay.

There are alternative treatment modalities, including percutaneous minimally invasive methods, such as the PAIR (Puncture, Aspiration, Injection of protoscolicidal agent, and Reaspiration) technique and laparoscopic approaches for LHC.¹³ The PAIR technique is an effective procedure for LHC, but strongly depends on size, location, and stage according to WHO-IWGE classification for LHC. The advantages of a laparoscopic approach in comparison to open surgery are a shorter hospital stay, a lower incidence of wound infection, and less postoperative pain.^{10,11,13} However, the usefulness of this procedure is still limited due to difficulty in accessing cysts in certain locations, as well as the number and size of cysts, which increase the difficulty of aspirating cysts with viscous contents and increase the risk of intraoperative cyst content spillage.^{10,11,13}

We performed a prospective study to compare radical and conservative surgical methods with and without subsequent albendazole treatment. In Kazakhstan, albendazole is not covered by insurance and patients have to buy albendazole themselves. Consequently, not all patients can receive albendazole after surgery because of the cost of the drug. Thus, our second goal was to compare radical surgical management with and without subsequent albendazole treatment. The Radical + Alb group had no recurrence, while the Radical – noAlb and Conservative + Alb groups each had one case of recurrence; however, this difference was not statistically significant.

The present study was associated with some limitations. The follow-up period after surgery was relatively short. Some authors recommend that a follow-up period of up to 10 years is required to evaluate recurrence.¹⁹ Thus, a longer follow-up period is necessary to clarify whether radical surgery without subsequent albendazole therapy is effective and comparable or not. The analysis of the surgical approach to LHC is important and we intend to determine the most appropriate surgical approach and evaluate complications based on a long follow-up period.

In conclusion, radical surgery is a preferable treatment modality in patients with active LHC of >5 cm in size in comparison to conservative surgery. Postoperative albendazole treatment is preferable regardless of the type of surgery.

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