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ORIGINAL ARTICLE

Operative treatment of hepatic hydatid cysts: A single center experience

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KEYWORDS
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Summary *Background:* Hydatid cyst is a zoonotic disease caused by Echinococcus genera. Surgery is needed in most cases. We aimed to describe our center's experience in the surgical management of hepatic hydated cysts (HHC).
Methods: Data was retrospectively collected for patients who underwent operative management for HHC between the years 1994–2014.
Results: Sixty-nine underwent surgical treatment for HHC. Group A included 34 treated with an unroofing procedure, group B included 24 patients who underwent hepatectomy and group C included 11 patients who underwent peri-cystectomy. The median ± (range) age for groups A, B and C were 39.5 (6.5–69), 40 (17–74) and 32 (20–62), respectively ($P > 0.1$). Postoperative complications occurred in 16, 11 and 5 patients in group A, B and C, respectively, as assessed by clavien-dindo classification (CDC). The average CDC was significantly higher in the hepatectomy group as compared to the unroofing group (2.3 vs.1.5, $P = 0.04$). Recurrence was significantly higher after the unroofing procedure as compared to the hepatectomy group ($P = 0.05$).
Conclusion: Surgery remains the mainstay of treatment for HHC, once surgery is pursued, the results are satisfactory.

Abbreviations: HHC, hepatic hydated cyst; CDC, clavien-dindo classification; PAIR, Puncture, Aspiration, Injection of protoscolicidal agent and Re-aspiration; WHO, world health organization.

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1. Introduction

Hydatid cyst of the liver is a chronic, parasitic disease that varies in severity. It is caused by the larva stage of the Echinococcus Granulosus Cestode. The disease can affect animals as well as humans. Although many organs may be affected, the liver is the most commonly affected organ occurring in approximately 5—70% of cases.[1]

Hepatic hydatid cysts (HHC) are either discovered as an incidental finding or when they become symptomatic.[2] The cysts develop when a connective tissue capsule, a peri-cyst, is formed around the parasite to isolate it from the host. The peri-cyst is an important landmark for surgical resection. Several treatment options are available for HHC, including medical, percutaneous or surgical, however, a watchful waiting strategy may be employed in asymptomatic, uncomplicated and small lesions.[3] There is no "best" treatment option strategy for HHC and no head-to head randomized clinical trial has compared the different treatment options. In the past, surgical intervention was the primary approach for patients with HHC.[4] however in recent years medical treatment based on the use anti-parasitic agents is used.[5] Although treatment success is achieved in approximately one third of patients treated medically.[6] percutaneous treatment is often applied in the treatment of HHC patients who are either uncomplicated or are poor surgical candidates and it can be performed either via PAIR (Puncture, Aspiration, Injection of protoscolicidal agent and Re-aspiration) or catheter-assisted endocyst removal with varying success Currently, surgical management is reserved for either complicated cysts (e.g. ruptured cyst, cysts with biliary fistulae, cysts compressing vital structures, cysts with secondary infection or hemorrhage) or for cysts that are not suitable for percutaneous treatment such as cystic echinococcosis World Health Organization (WHO) classification stage CE2 and CE3b.[3,7] The surgical options include unroofing, peri-cystectomy and even hepatectomy.

The aim of this study is to present the experience of our institution in the surgical management of liver hydatid disease over a period exceeding 20 years. Specifically, we aimed to compare the outcomes of the various surgical options (peri-cystectomy, cyst unroofing, and hepatectomy) including cure rate, recurrence rate, morbidity and mortality.

2. Materials and methods

The medical records of all patients who underwent surgical treatment for isolated hepatic echinococcal disease at the Department of Surgery, Hadassah-Hebrew University Medical Center, during a period of over twenty years from January 1994 until December 2014 were retrospectively collected and analyzed. Data collected included demographics, cyst localization and characteristics, surgical treatment, preoperative liver function, general condition of the patients defined by stable vital signs, conscious and comfortable patient, operative time, operative blood loss, blood transfusion amount, morbidity, follow-up periods and the outcome of treated patients. Furthermore, the patients were followed for early post-operative complications including fever defined by temperature of more than 37.6 Celsius; bile leak defined by abnormal fluid accumulation in the abdominal drain with high bilirubin concentration or as diagnosed by cholangiography; pneumonia defined by clinical presentation of respiratory infection (cough, dyspnea, fever) coupled with high white blood count and radiological appearance of consolidation in lungs; surgical site infection defined by abnormal purulent discharge coupled with clinical and laboratory signs of infection; pleural effusion defined by abnormal fluid accumulation in the pleural cavity diagnosed by chest imaging; anaphylaxis defined as a serious life-threatening allergic reaction characterized by itchy rash, throat or tongue swelling, shortness of breath and hypotension and Iatrogenic diaphragmatic injury which in our series diagnosed intra-operatively.

All patients included in this study were treated surgically. Inclusion criteria were according to the world health organization (WHO) and included large liver cysts (>5 cm) with multiple daughter cysts; single liver cysts (>5 cm), cyst that were located superficially that pose the risk to rupture spontaneously or as a result of trauma; viable cysts with signs of active infection; cysts communicating with the biliary tree, cysts that cause local pressure to adjacent organs and complicated cysts (such as bleeding into the cyst or rupture).[3,6] Exclusion criteria included patients who refused surgery, pregnant woman, patient with concomitant severe cardio-pulmonary diseases. In addition, surgery is contra-indicated in patients with cysts that are difficult to access, inviable cysts, either partly or totally calcified cysts, and in patients with small cysts.

Patients were divided into three groups, according to the surgical procedure that was performed, including unroofing procedure, hepatectomy and peri-cystectomy (which is removal of the cyst as a whole without opening it, by dissecting through the peri-cystic layer, (the outer inactive part of the hydatid cyst that is composed of host liver tissue)).

All patients with signs of an active cyst received Albendazole pre-operatively for 3—4 weeks (at a dose of 10 mg/kg) and subsequently for 4 weeks after the operation. Broad spectrum antibiotics were administered peri-operatively in all cases. The study was approved by the hospital IRB committee.

2.1. Surgical approach selection

The decision regarding the type of the surgery was individualized according to each case and according to the hepato-biliary surgeon who performed the surgery. Generally, the unified criteria used to choose the surgical intervention type was based on cyst location, cyst depth and cyst proximity to vascular and biliary organs. Laparoscopic peri-cystectomy was performed for single peripheral lesion more than 5 cm not involving the biliary structures. Unroofing was utilized for peripheral multiple structures with proximity to biliary and vascular structures. For deep lesions affecting one lobe which were very close or connected to a vascular structure, hepatectomy was performed. Overall each individual decision regarding the type of surgery was chosen so as to prevent recurrence and minimize complications.

2.2. Statistical analysis

All analysis was performed using Excel 2003 (Microsoft, Redmond, WA, United States). Continuous variables were expressed as median + range. The comparison of two independent groups was performed using Student's *t*-test. All tests applied were two-tailed. Categorical variables (gender, general condition and pre-operative liver function) was performed via Chi square test. *P* value of 0.05 or less was considered statistically significant.

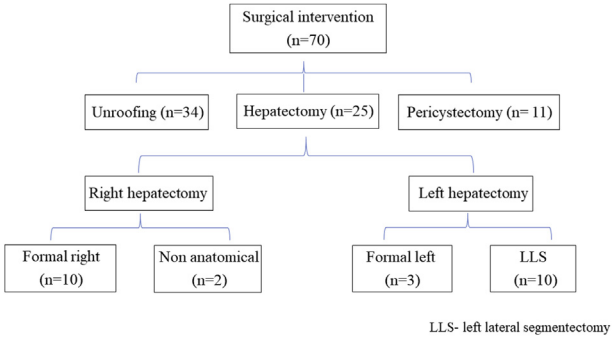

Figure 1 Demonstrating the flow chart of our cohort.

3. Results

3.1. Demographics

Overall, 69 patients underwent surgical treatment for HHC at the Hadassah Hebrew University Medical Center between 1994 and 2014. Fig. 1 demonstrating the distribution of our patient's cohort. Group A included 34 patients who were treated by unroofing procedure. Group B included 24 patients who underwent hepatectomy and group C included 11 patients who underwent peri-cystectomy. The median (range) age for groups A, B and C were 39.5 (6.5—69), 40 (17—74) and 32 (20—62), respectively ($P > 0.1$). Forty-four percent, 32% and 27% in groups A, B and C were males, respectively ($P = 0.4$). Baseline demographics, operative details and cyst characteristics are shown in Table 1.

3.2. Post-operative complications, length of hospitalization and follow-up

Post-operative complications were classified according to the Clavien-Dindo classification (CDC).[8] graded between 1 and 5. In the unroofing group there were 16 complications, including eight patients with fever (grade 1 CDC), four patients had anemia (grade 1 CDC), one patient had a collection that was drained via computed tomography guidance (grade 3 CDC), 2 patients had bile leak (one of whom was treated with ERCP) (grade 3 CDC) and 1 patient had anaphylaxis with hypotension who required vasopressor therapy with noradrenaline (grade 4 CDC). In the hepatectomy group, eleven complications were documented, as three patients developed fever (grade 1 CDC), one patient had a surgical site infection (grade 2 CDC), one patient had anemia (grade 1 CDC), one patient developed a pleural

Table 1 baselines characteristics.

	Unroofing (group A)	Hepatectomy (group B)	Peri-cystectomy (group C)	P value
Age (years), median (range)	39.5 (6.5—69)	40 (17—74)	32 (20—62)	>0.1
Male (%)	44	29	27	0.4
Maximal cyst size (cm), median (range)	7.5 (0.5—15)	9 (1—20)	8 (4—20)	1.1 for A vs. C 0.02 for A vs. B 0.3 for B vs. C
Average number of cysts	1.9	1.4	1.27	>0.14
Normal pre-operative liver function (%)	73	54	91	0.001 for A vs. C 0.005 for A vs. B 0.001 for B vs. C
Good general condition (%)	97	92	100	>0.15
Operative hours, median (range)	4 (2—10.5)	5.75 (3—9)	5.5 (2—7.5)	0.12 for A vs. C 0.01 for A vs. B 0.3 for B vs. C
Average operative blood loss (units)	0.2	0.75	0	>0.12
Average blood unit transfusion (n)	0.24	0.7	0	>0.17

effusion necessitating pleural paracentesis (grade 3 CDC), one patient had a skin rash that was treated conservatively (grade 2 CDC), one patient had a fluid collection that was drained under the CT guidance (grade 3 CDC), two patients suffered from a bile leak treated with ERCP (grade 3) and one patient died (grade 5 CDC). While in the peri-cystectomy group, five complications were reported, including three patients with fever (grade 1 CDC), one patient with pneumonia (grade 2 CDC) and one patient had iatrogenic diaphragmatic injury (grade 3 CDC) (Table 2). Moreover, the median (range) length of hospitalization in groups A, B and C was 12 (3–35), 11 (3–70) and 11 (5–19) days, respectively ($P > 0.05$). Moreover, the median length of hospitalization of right and left hepatectomy was 12 (3–70) and 10 (5–31), respectively ($P = 0.1$). The follow-up period in group A and group A were 32.4 and 2.9 months, respectively, while in group C, all patient were lost follow-up after the surgery.

3.3. Hepatic hydatid cyst recurrence

Unroofing surgical intervention was the only factor connected to HHC recurrence as cyst recurrence occurred in 6 patients (18%) those who underwent unroofing as compared to 1 patient (4%) in the hepatectomy group ($P = 0.05$), while we couldn't know about the recurrence rate among the peri-cystectomy group given that all patients in this group were lost follow-up following the surgery. The patient in the hepatectomy group who experienced recurrence was treated by partial hepatectomy, while in the unroofing group, 4 patients were treated by partial hepatectomy and the other two patients were followed-up by radiological imaging studies.

There was a trend for higher recurrence rates with increasing cyst size, as HHC size of 7 cm or greater showed cyst recurrence after surgical management, while no HHC recurrence when the size of the cyst was less than 7 cm ($P = 0.08$) (Fig. 2). Moreover, there was no difference in HHC recurrence among all groups whether medical therapy with albendazole was administered pre-operatively, post-operatively or pre- and post-operatively ($P = 0.5$).

4. Discussion

Echinococcosis is an endemic disease in many parts of the world but is not considered to be endemic to Israel. To the best of our knowledge, this is the largest study of surgical treatment of HHC in Israel. In this study we reviewed the characteristics of patients treated surgically for HHC. Overall, all patients underwent surgical intervention as indicated for HHC. There was no difference in cyst number among the different surgical groups.

In this study, the decision regarding the type of surgery was based mainly on surgeon preference according to cyst location, depth and proximity to vital organs. Peri-cystectomy was attempted in all patients when technically feasible (single peripheral cyst). In some cases, specifically when the cyst was too deep, there were multiple cysts, or there was proximity to vital organs, unroofing of the cyst or hepatectomy was chosen to minimize complications. Our institution has our own criteria for operation and standardization of treatment. We prefer unroofing as the first line procedure for most of HHC. Similarly to our approach, still, many prefer performing unroofing\partial cystectomy, as the procedure is simpler and easier to perform.[9] However, one of the main disadvantages of conservative surgery such as unroofing is a higher recurrence rate.[10] Similarly, the recurrence rate in our study was higher in the unroofing surgical intervention group. Thirty-four patients in our study underwent unroofing, and of them 18% had recurrence of HHC. Most patients with recurrent HHC were surgically treated by partial hepatectomy to eliminate the subsequent risk of recurrence. Earlier study by Yuskel et al reported that more radical hepatic surgery diminish early recurrence of HHC.[11]

Another potential limitation of unroofing is the occurrence of anaphylaxis, as this can be a catastrophic side effect and necessitates careful planning to avoid intra-abdominal spillage of the cyst contents into the peritoneal

Table 2 Post-operative complications.

Procedure	Unroofing (group A)	Hepatectomy (Group B)	Peri-cystectomy (Group C)	P value
Fever	8	3	3	>0.1
Anemia	4	1	0	0.1
Bile leak	2	2	0	>0.1
Collection	1	1	0	>0.2
Pneumonia	0	0	1	0.03 for A vs. C 0.07 for B vs. C
Iatrogenic diaphragmatic injury	0	0	1	0.03 for A vs. C 0.07 for B vs. C
Surgical site infection	0	1	0	>0.1
Pleural effusion	0	1	0	>0.1
Anaphylaxis	1	0	0	>0.2
Average CDC grade[a]	1.5	2.3	1.6	0.04 for A vs. B 0.4 for A vs. C
Total	**16**	**11**	**5**	

[a] CDC: clavien-dindo classification.

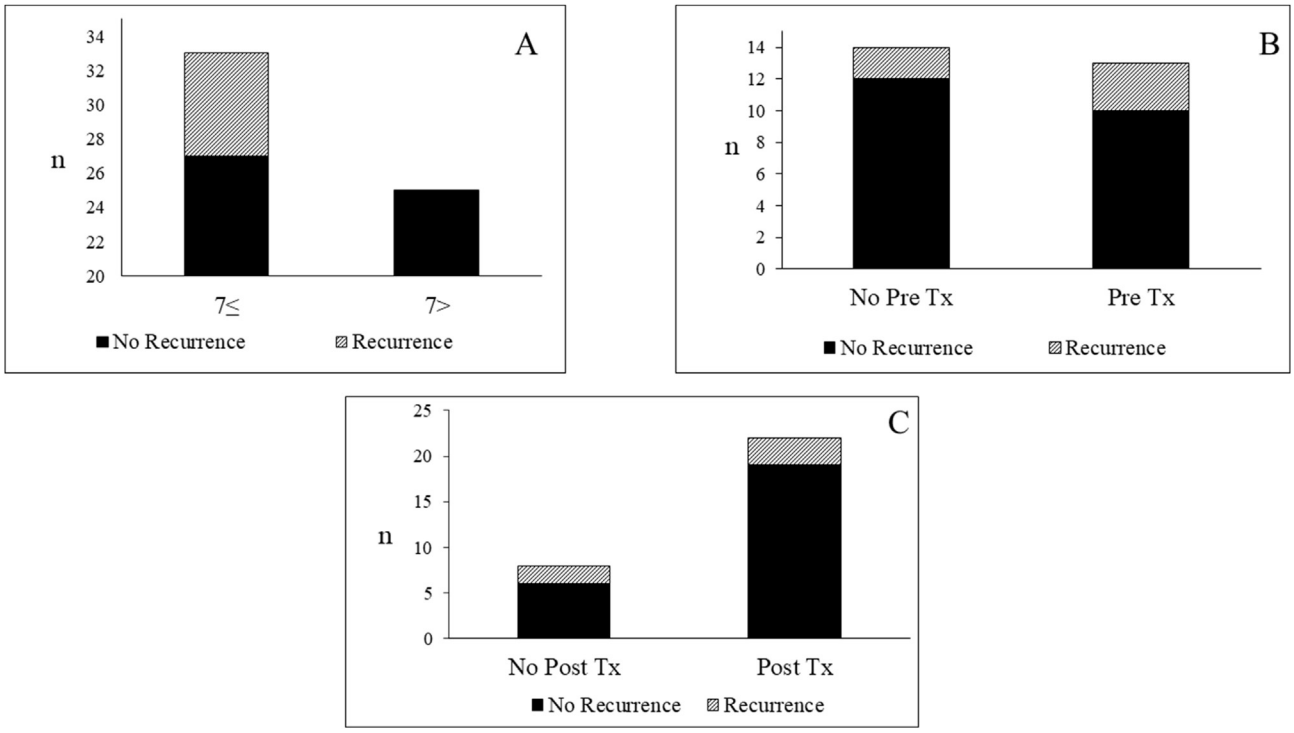

Figure 2 Demonstrating a trend for cyst recurrence at cyst size of ≥7 cm.

cavity.[12] In our study, one patient (2.9%) developed anaphylaxis in the unroofing group which resolved with immediate therapy with vasopressors and steroids while no episode occurred in the other groups. Previous studies have shown an increased morbidity of HHC treated with radical surgical intervention such as hepatectomy which indirectly lengthens hospital stay.[13] In our study there was no significant difference in length of hospitalization among the different surgical groups, moreover, right hepatectomy was associated with longer hospital stay as compared to left hepatectomy, although the difference was not statistically significant ($P = 0.1$). Recent studies showed that pre-and post-operative administration of medical anti-parasitic agents reduced the risk of anaphylactoid reactions and prevented recurrence.[14] However, in our study, pre-, +/− post-operative medical treatment with albendazole did not impact the recurrence rate, thus questioning the necessity for anti-parasitic management in the perioperative timeframe. This observation needs further validation by performing prospective randomized trials.

Overall, the complication rate among all patients who underwent unroofing was 47%, with most having fever and anemia. In the peri-cystectomy group, the complication rate was 45.5% of which half were mild fever and the complication rate in the hepatectomy group was 46% with one case of post-surgical mortality. Notably, most complications in the hepatectomy group necessitated endoscopic and radiological treatment. The complication rate as estimated by Clavien-Dindo classification was significantly higher in the hepatectomy group as compared to the unroofing group ($P = 0.04$). The complication rate in our study was slightly higher than that reported in the literature, however, the mortality rate of 1.4% was within the range or lower than that reported.[15] Moreover, in the unroofing and peri-cystectomy groups, most of the post-operative complications were mild consisting of fever and anemia. As we showed in this retrospective cohort, major morbidity is not common in surgical management of HHC as it would be expected for a benign disease. Furthermore, mortality was rare which shows that even in non-endemic area, the surgical results for HHC are satisfactory.

The present study had several limitations. Firstly, it was a retrospective study, thereby increasing the risk of data collection bias and, secondly that the study was performed in a single center. Second, patients in the peri-cystectomy were lost follow-up after the surgery, thus we couldn't assess the recurrence rate in this group. Nonetheless, this is the largest study regarding surgical management of HHC originating in Israel. In conclusion, hydatid cyst disease in Israel is infrequent. Surgical intervention is undoubtedly reasonable with regards to morbidity, recurrence, and mortality.

Author contribution

Abed Khalaileh contributed to the concept and design of the study. All authors contributed to data collection and analysis. Abed Khalaileh, Gad Marom and Tawfik Khoury contributed to data interpretation and statistical analysis. Abed Khalaileh, Gad Marom and Tawfik Khoury wrote the final version of the manuscript. All authors approved the final version to be published.

Conflict of interest

The authors declare no conflict of interest regarding this manuscript.

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