

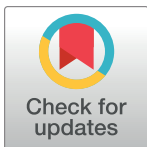
RESEARCH ARTICLE

Standardized approach to the conservative surgery of hepatic cystic echinococcosis: A prospective study

Aymen Trigui¹, Sami Fendri¹, Mohammad Saad Saumtally^{2*}, Amira Akrou¹, Jihen Trabelsi², Rahma Daoud¹, Nozha Toumi³, Salma Ketata⁴, Wael Boujelbene¹, Rafik Mzali¹, Chadli Dziri⁵, Mohamed Ben Amar¹, Salah Boujelben¹

1 University of Sfax, Faculty of Medicine; Department of General and Digestive surgery. Habib Bourguiba Hospital, Sfax, Tunisia, **2** University of Sfax, Faculty of Medicine; Department of Epidemiology. Hédi Chaker Hospital, Sfax, Tunisia, **3** University of Sfax, Faculty of Medicine; Department of Radiology. Habib Bourguiba Hospital, Sfax, Tunisia, **4** University of Sfax, Faculty of Medicine; Department of Anaesthesiology. Habib Bourguiba Hospital, Sfax, Tunisia, **5** University of Tunis, General Surgery; Honoris Medical Simulation Centre director, Tunisia

* saad0991@gmail.com



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Abstract

Objective

Surgery is the mainstay of hepatic cystic echinococcosis (HCE). The conservative surgery of HCE carries a non-negligible risk of recurrence and significant morbidity, dominated by Deep Surgical Site Infections (DSSI). To address these issues, we have improved and standardized this technique, which could reduce complications and achieve better postoperative outcomes.

Patients and methods

We conducted a prospective study from June 2017 to June 2022 involving of patient operated using a standardized open technique for uncomplicated HCE at Habib Bourguiba University Hospital, Sfax, Tunisia. The aim was to obtain results at least similar to radical management in terms of DSSI. Patients with large cystobiliary fistulas or patients with complicated cysts were excluded.

Results

Fifty patients with 106 cysts were operated using the standardized technique comprising of liver mobilization, intraoperative ultrasound, systematic methylene blue injection to detect cystobiliary fistulas and omentoplasty. The median age of the patients was 44 (semi-interquartile range: 16) years. The main symptom described by the patient was pain in 43 cases (86%). An abnormal liver test was found in 20 cases (40%). On imaging studies, the cyst had a median size of 7.4 (3.0) cm. Cyst of the hepatic dome accounted for 38 cases (35.8%) with most cysts being situated in the right hemi-liver. Visual inspection of the cavity and Methylene blue testing allowed for the discovery of 57 cysts (53.7%) that had cystobiliary fistulas that were sutured. Omentoplasty was performed in 77 cysts (72.6%). Postoperatively,

please contact the local ethics committee(Comité de Protection des Personnes adapté à l'Expérimentation Médicale ou Scientifique des Produits Médicaux destinés à la Médecine Humaine) at Rue Firdaous, 3029 Sfax. Email: cppsud.tunisie@gmail.com.

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only 2 cases (1.9%) developed a DSSI in the form of an external bile leak with resolved with conservative management. No case of recurrence was found after a median follow-up of 24 months.

Conclusion

The standardized conservative surgical technique, in selected patients, shows promise in reducing DSSI rates and overall morbidity, and achieve as equally good result as radical management.

Author summary

This study addresses the treatment of hepatic cystic echinococcosis (HCE), a serious health concern in many parts of the world. Surgery has been the mainstay of the management which could be conservative or radical. Conservative surgery has high recurrence rates and complications as opposed to radical surgery. Through a prospective study, we showed that an improved and standardized a surgical technique of the conservative approach could achieve postoperative outcomes as good as the radical management. The standardized approach significantly reduced Deep Surgical Site Infections (DSSI) as well as overall morbidity rates in patients. This was achieved through various adjuncts such as methylene blue test, liver detachment, and omentoplasty.

Introduction

Cystic echinococcosis (CE) is a zoonotic disease that is endemic in certain parts of Eurasia, Africa, Australia, and South America [1] with poses a significant public health problem. Currently, the management of Hepatic Cystic Echinococcosis (HCE) involves various available therapeutic options such as medical, percutaneous, endoscopic, and surgical approach. The goal of treatment is to eradicate the parasite while avoiding complications related to the residual cavity. There are two main surgical approaches to treat HCE: conservative treatment and radical treatment [2].

The most common conservative surgical technique in endemic areas is partial cystectomy (PC) as described by Lagrot in 1957 [3,4]. This technique is simple and quick to perform, requires few resources, and has a low risk of major bleeding. As opposed to the latter technique, radical management which entails liver parenchymal resections with a non-negligible bleeding risk [2,5].

Some of the studies conducted, advocates for radical management citing less operative morbidity and less recurrence [5,6]. Despite these promising results, these studies had certain limitations such as exclusion of complicated cyst cases or multiple cysts and varied in their criteria for selecting patients for radical surgery.

Moreover, the radical technique is more complex and requires a certain level of expertise and/or may be not feasible in cases of liver resections with proximity to major vessels or in cases of multicystic disease. In such cases, PC remains a viable option. The two techniques are not mutually exclusive but rather complementary. Therefore, the idea of improving the PC through standardization arose in order to reduce the significant morbidity associated with this technique. Several technical refinements, such as liver mobilization, intraoperative ultrasound

[7], systematic methylene blue injection to detect cystobiliary fistulas [8] and omentoplasty [9] have been added to the traditional technique to improve postoperative outcomes.

In this study, we present the results of a prospective study of patients undergoing surgery for HCE using the standardized technique.

The primary objective of this study was to compare the results of the standardized technique in terms of specific postoperative morbidity, in particular Deep Surgical Site Infections (DSSI), as compared to radical management.

Patients and methods

Ethics statement

This study was conducted following the Helsinki Declaration. Informed written consent was obtained from each subject. Prior to the start of our study, approval was obtained from the local ethics committee (Comité de Protection des Personnes adapté à l'Expérimentation Médicale ou Scientifique des Produits Médicaux destinés à la Médecine Humaine), under reference "CPP sud numéro 0021/2017." This committee is the sole medical or scientific research centre for human medicine in our institution, the University of Sfax. It is approved by the Ministry of Public Health. All patients who participated in our prospective study signed a written consent form.

Study design

Our study focuses on patients who underwent conservative surgery (PC) for HCE at the Department of General Surgery of the Habib Bourguiba University Hospital in Sfax. The prospective cohort, consists of patients who underwent surgery using the standardized technique from June 2017 to June 2022. This trial was registered with [PACTR.org](https://www.pactr.org): PACTR202312729770861.

We included in our study all patients who were operated for HCE in an emergent or elective setting by laparotomy. We excluded patients who had cysts complicated with a large cystobiliary fistula revealed by acute cholangitis or acute pancreatitis or presence of cyst debris in the common bile duct on preoperative imaging which could manifest itself through a common bile duct dilation or direct visualization of obstacle in the common bile duct.

We distinguish 2 types of cysts: cysts with overt, large CBF and cysts presenting occult fistulas. Management differs for these 2 types. For large and peripheral cysts, radical resection is preferred. However, cysts with close proximity to major veins and biliary structures, internal trans-fistulary drainage or cystobiliary disconnection (Perdromo technique) is performed since simple suturing of the fistula within the pericyst is not effective. Thus, only patients with occult fistulas were included, to get a homogeneous population and minimize selection bias.

Surgical procedure for the standardized technique

All patients were operated by laparotomy by 2 designated surgeons. We opted for a right subcostal incision for anterior single cysts, sometimes extended to the left for HCE of the left lobe, or a Makuuchi incision in case of multiple hepatic hydatid lesions and/or posterior HCE. Liver mobilization is performed by cutting the round ligament and the falciform ligament 1 cm from the surface of the liver. Mobilization of the liver through sectioning of the right or left triangular ligament is only performed to expose a cyst located in the posterior superior region, particularly on the dome or segment II. These manoeuvres allow better exposure to the cyst and may allow easier inspection of the cyst wall. The extent of this mobilization is adjusted

according to the location and relationships of the HCE. Visual and manual exploration of the cysts is carried out through inspection and palpation.

Intraoperative ultrasound is performed using a convex probe with a frequency range of 3 to 5 MHz. The pericyst is carefully examined, and vascular and biliary relationships, wall thickness, presence of calcifications, and the presence of exocysts are noted which are the primary source of recurrence [7].

The peritoneal cavity is protected by using laparotomy sponges soaked in 20% hypertonic saline solution. In case of CE1 and CE3a detected on intraoperative ultrasound, the cyst is carefully punctured with a 15G needle and the liquid is initially, slowly aspirated using a number of 50 cc syringes using a 3-way valve. Deflating the cyst helps to decrease the intracystic pressure and prevent accidental spillage when incising the cyst. In case of mastic contents (CE4 or CE3b), a 10 mm trocar without the mandrel is carefully inserted in the cyst wall and it is used to suck the mastic and lumpy contents which often cause blockages in suction systems. For multivesicular cysts such as in CE2 cysts, cyst aspiration is often unsuccessful because of the multiple daughter cysts. Therefore, the 10 mm trocar is used to aspirate cyst contents.

Once the intracystic pressure decreases and cyst becomes flaccid, a 2 cm incision is carefully performed on the pericyst. The cyst content is fully aspirated, and the cyst cavity is generously irrigated with normal saline, aspirating and replenishing the solution 2 to 3 times to thoroughly dilute any remaining protoscoleces. The cavity is then swabbed with gauze dipped in 20% hypertonic saline solution and the swab is left in the cavity for 10 minutes. Direct washing with hypertonic saline solution is not done to prevent sclerosing cholangitis.

The cyst incision is widened to better assess the cavity and a visual exploration of the residual cavity is carried out to detect any bile leakage or visible cystobiliary fistula. The inner wall is gently scraped using a curette to remove membranous debris. Any visible CBFs detected during the visual exploration of the cavity are sutured using Vicryl 2/0.

A systematic cholecystectomy is performed, and a transcystic catheter is inserted for the Methylene Blue Test (MBT) to detect occult cysto-biliary fistulas. The dye is administered at low pressure and any leakage of the dye in the cyst cavity would be considered as cystobiliary fistulas (CBF) [8]. These are then sutured using Vicryl 2/0. Then, clamping the main bile duct during dye injection enables the identification of additional CBF and serves as a leakage test for the previously sutured fistula. The sutures that showed leakage of methylene blue are reinforced, and as well as any additional occult cystobiliary fistulas detected during this methylene blue test. The integrity of the sutures is checked by performing a methylene blue test with and without manual clamping of the common bile duct.

After the leakage tests are negative or in the absence of any CBFs, the cavity is thoroughly washed with hypertonic saline. The protruding part of the pericyst is then resected, preventing any live protoscoleces from leaking outside the cavity.

In case of a non-yielding and rigid pericyst intralamellar pericystectomy is performed to give a supple cavity wall. The greater omentum is partly detached from the transverse colon and the greater omentum is affixed to the residual cavity for omentoplasty, if possible, using a 2/0 Vicryl suture [9]. A passive drainage is inserted in the residual cavity through a stab incision in the right flank in all cases.

Patient follow-up

As part of the protocol of study, food was allowed on post-operative day 1 with early mobilization and administration of oral albendazole, 400 mg twice daily. The drain was usually removed on post-operative day 5 before discharge unless a complication is detected.

After discharge from the hospital, the patients are followed up in the outpatient clinic of the surgical department. The latter takes care of perioperative albendazole treatment and follow-up for relapses. To detect recurrences early—depending on the location of the cyst—ultrasound or CT or MRI investigations are regularly performed.

Definition of outcomes of the study

The main complication of conservative surgery of HCE which are:

- External Biliary Fistula: We considered any clear bile drainage from the abdominal drain, regardless of the timing, duration, or quantity, as a postoperative biliary fistula [10].
- Cavity infection: Defined as the occurrence of an infection in the residual cavity with or without the presence of drainage.

These aforementioned complications were grouped under the term "Deep Surgical Site Infection" (DSSI) [11]. Cavity infections result from bile accumulation by means of a CBF. External bile leakage shares the same cause. Therefore, the rationale behind grouping these complications together is that they both stem from the common cause. The primary outcome of our study was the occurrence of DSSI in the population which was main specific complication of the conservative surgery. Postoperative morbidity was assessed using the Clavien-Dindo classification [12].

The secondary outcomes were the overall morbidity, mortality and disease recurrence. Morbidity was defined as the occurrence of one or more complications during hospitalization or within the 30 days following the surgery and mortality was defined as is defined as death occurring within 30 days following the surgery or during the same hospitalization, regardless of its duration. Recurrent hepatic hydatid disease refers to the emergence of new active cysts following surgery.

Statistical study

IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA) was used for data entry and for all statistical analyses. Frequencies were calculated for qualitative variables, while the median (semi-interquartile range (SIR)) was computed for quantitative variables. For overall morbidity and nonspecific morbidity, the analysis was done per patient. For specific complications and cyst recurrence, the unit of study was the cyst. Therefore, for patients with two or more cysts, each cyst was considered independent.

We hypothesized that the standardized technique should achieve results which are at least good as the radical management. The sample size of 99 cysts for a single arm was calculated to give 95% power for detecting a statistically significant difference in terms of DSSI (with alpha-value 0.05), based on a previous meta-analysis [13] comparing DSSI rates in conservative surgery (14.6%) versus radical surgery (5.1%). We hoped to achieve DSSI rates using the standardised technique at least similar to the radical treatment in this single arm trial.

Results

A flowchart of the eligibility criteria is presented in Fig 1. Following the exclusion of 18 cysts, 106 cysts were included in our study (50 patients) who underwent surgery for one or more cystic echinococcosis of the liver between July 2013 and June 2022.

The Table 1 and Table 2 resumes the data of the participants in terms of demographic parameters, clinical examination data, laboratory findings, and imaging data.

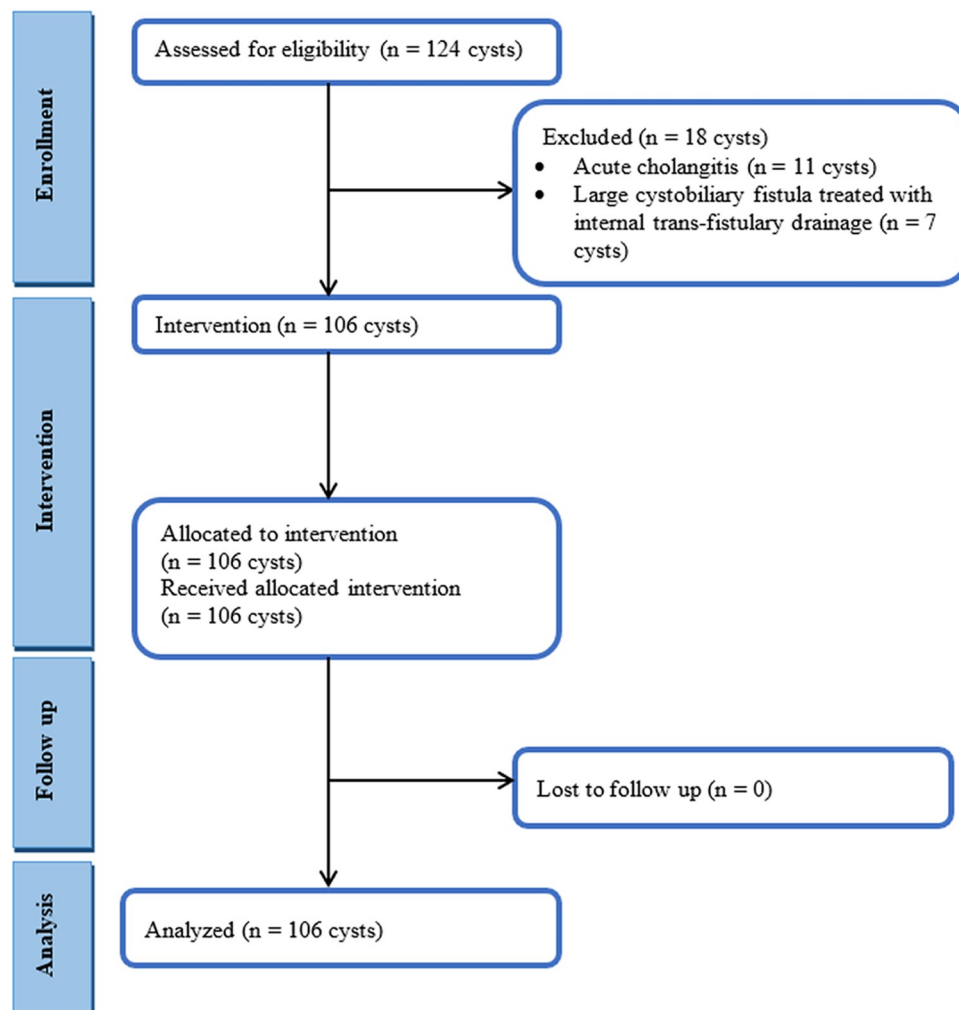


Fig 1. Flow diagram of the inclusion and exclusion criteria.

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Operative findings

Operative findings showed that most cysts were exophytic with a protruding dome and with clear cyst contents as showed by the Table 3.

In the study population, the Makuuchi J incision was the most commonly performed accounting for 60.0%. followed by the right subcostal incision in 14 cases (28.0%). The rest of the participants had bilateral subcostal incision and median incision depending in the cyst localisation, 39 patients (78.0%) underwent liver mobilization to improve exposure of posterior cysts.

Occult cystobiliary fistulas

The MBT was performed in all patients in the population.

A total of 122 cystobiliary fistulas (CBF) were identified and sutured. Among the 48 cysts that were complicated by occult FKB (i.e. not evident on initial examination), the preoperative injection of methylene blue (MBT) during surgery allowed the detection of 106 additional CBF. Moreover, clamping of the common bile duct was performed, leading to the

Table 1. Preoperative parameters of the patients in both groups.

N = 50 patients		N (%)
Characteristics		
Age (median, SIR)		44 (16)
Gender	Male	17 (34.0)
	Female	33 (66.0)
Origin	rural	44 (88.0)
	urban	6 (12.0)
Recurrence of HCE at admission		4 (8.0)
Recurrence of PCE at admission		4 (8.0)
ASA Score	ASA 1	42 (84.0)
	ASA 2	5 (10.0)
	ASA 3	3 (6.0)
Physical examination		
Incidental discovery		7 (4.8)
Abdominal pain		43 (86.0)
Nausea and emesis		15 (30.0)
Jaundice		1 (2.0)
Palpable abdominal mass		5 (10.0)
Abdominal tenderness		28 (56.0)
Hepatomegaly		4 (8.0)
Laboratory findings		
Leucocytosis		11 (22.0)
Hypereosinophilia		15 (31.3)
CRP	> 6 mg/l	18 (38.3)
Elevated ALT or AST		6 (12.5)
Cholestasis		18 (40.9)
Hyperbilirubinemia, Total bilirubin >25μmol/l		2 (4.0)
Abnormal Liver Function Test		20 (40.0)
Hemostasis tests	Normal	44 (88.0)
Serologic test	positive	37 (86.0)

SIR: semi-interquartile range, HCE: Hepatic Cystic Echinococcosis, PCE: Pulmonary Cystic Echinococcosis, CRP: C Reactive Protein, AST: aspartate aminotransferase, ALT: alanine aminotransferase

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identification of 16 more CBF in 15 cysts. The median diameter of the fistula was 1.1 mm. We also found that cysts CBFs were larger (mean diameters of 6.1 ± 0.6 cm without CBFs vs 8.0 ± 0.5 cm with CBFs), $p = 0.024$.

At the end of these explorations, a total of 57 cysts complicated by cystobiliary fistulas (CBF) were discovered, accounting for 53.7% of cases.

Management of the residual cavity

Omentoplasty was performed almost systematically whenever possible. A total of 77 cysts (72.6%) and capitonnage was performed in only 2 cysts (1.9%). A passive drainage was inserted in 101 cysts (95.3%).

Analysis of the primary end-point: DSSI

We obtained a DSSI rate of 1.9% in our cohort which is at least better than DSSI rates of 5.1% as defined in our aims. These were 2 cysts that developed an external bile fistula in the

Table 2. Preoperative characteristics the cysts in both groups.

N = 106 cysts		N (%)
Imaging findings		
Number of cysts	Solitary	28 (54.9)
	2 cysts	11 (21.6)
	Multiple cysts	12 (23.5)
Cyst size in cm	(median, SIR)	7.4 (3.0)
Calcifications		14 (13.2)
Visible laminated layer		25 (23.6)
Heterogeneous mass		34 (32.1)
Daughter cysts		40 (37.7)
Exocysts		15 (14.2)
WHO-IWGE classification	CE 1	25 (23.6)
	CE 2	21 (19.8)
	CE 3a	22 (20.8)
	CE 3b	21 (19.8)
	CE 4	18 (17.0)
Cyst localisation	segment I	1 (0.9)
	segment II	19 (17.9)
	segment III	20 (18.9)
	segment IV	18 (17.0)
	segment V	14 (13.2)
	segment VI	17 (16.0)
	segment VII	23 (21.7)
	segment VIII	19 (17.9)
	Left hemiliver	31 (29.2)
	Right hemiliver	78 (73.6)
Hepatic dome		38 (35.8)
Suspected complicated cyst		57 (53.8)
Biliary compression		22 (20.8)
Vascular compression		46 (43.4)

SIR: semi-interquartile range, WHO-IWGE: World Health Organization—Informal Working Groups on Echinococcosis

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Table 3. Intraoperative characteristics of the cysts in both groups.

	N (%)
Type of cyst	
Exophytic cyst	101 (95.3)
Intrahepatic cyst	5 (4.7)
Characteristics of the pericyst	
Supple pericyst	82 (77.4)
Hard pericyst	24 (22.6)
Cyst contents	
Clear	94 (88.7)
Bile stained	10 (9.4)
Purulent	4 (3.8)
Gelatinous	34 (32.1)

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postoperative period. In response to the fistula occurrence, intravenous antibiotic therapy with cefotaxime and metronidazole was initiated. No persistent fistulas beyond 30 days were found, and none of these patients required sphincterotomy or additional surgery. These bile leak appears on post-operative day 2 in both cases. The patients were started on antibiotic course of intravenous cefotaxime and metronidazole upon detection of the fistula. The average output of the fistula was 106 ml/day and it stopped being productive after a mean duration of 25 days. No need for sphincterotomy or surgery was required for these patients. Both patients had a hospital stay of 14 days.

No patients developed injury to bile ducts as a result of hypertonic saline use during the sterilization of the cyst.

Secondary outcomes

We report an overall morbidity of 10% in the 50 patients studied with 3 patients having medical complications and 2 patients having the abovementioned DSSI. The median length of stay was 5.0 days with extremes of 1 day to 14 days.

The median follow-up duration for the patients was 24 months and no recurrence were detected on successive exams and imaging studies.

Discussion

The standardized technique as described above demonstrates effective surgical management of cystic echinococcosis of the liver with low rates of complications, particularly DSSI (1.9%) which is at least as good as radical surgery. Moreover, our study also found an overall morbidity rate of 10% and no recurrence in the follow-up period. This could be attributed to the new improved techniques with adjuncts such as methylene blue test to detect occult CBF.

According to literature, several cohort studies a controlled randomized trial, and 3 meta-analyses [13–15] comparing the two mentioned techniques were found. These authors concluded that radical treatment is superior to conservative surgery in terms of Surgical Site Infections, overall morbidity, bile duct fistulas, and recurrence.

However, it should be noted that these studies excluded cysts classified as "difficult" or complicated cysts. Radical surgery was chosen based on the cyst's location. For instance, Ramia et al. [16] excluded cysts operated on in an emergency context. Others, such as Mohkam et al. [17] and Secchi et al. [18], selected patients with cysts smaller than 10 cm. Yuksel et al. [19] and Motie et al. [20] excluded cysts complicated by large fistulas, cysts with intimate relationships with vessels, and intraparenchymal cysts. Moreover, a significant part of these comparative studies was conducted in specialized centers [21], indicating the presence of major selection biases in most of these studies. Due to these biases, the World Health Organization still advocates for conservative surgery as the method of choice in endemic areas [22].

Without doubt, radical treatment has shown promising results, but it may not be applicable in all cases, such as in cases of multiple cysts. Therefore, radical treatment and conservative treatment are not opposing techniques but rather complementary. Conservative surgery still plays an important role in endemic areas. It is crucial to try and improve its short and long-term outcomes through the standardization of surgical techniques.

The morbidity associated with conservative surgery for Hepatic Cystic Echinococcosis remains high despite many advances. Standardizing the conservative surgical technique could be the solution to reduce the rate of postoperative complications. It may also lead to a decrease in specific morbidity, which is the main factor to consider. Short-term complications of conservative treatment include residual cavity infection and external biliary fistula [19]. These

complications are the most frequent specific complications in conservative surgery, with a frequency ranging from 8.4% to 20.5% [8,23–26].

In the literature, several studies have focused on evaluating risk factors for Surgical Site Infections. These risk factors include communication with the bile ducts, thick pericyst and posterior cyst location.

Specific complications, especially DSSI, share a common denominator: bile leakage at the residual cavity postoperatively. Postoperative bile leakage is caused by cysto-biliary communication [19,23,27]. This allows us to regroup all these specific complications under the single term of DSSI since they share the same pathogenesis. DSSI represents a significant turning point in the management of Hepatic Cystic Echinococcosis. It transforms a simple and easily treatable parasitic cyst into a hepatobiliary pathology. Biliary fistula is a frequent complication, present in 37% of cases [28] and accounting for 60% of HCE complications [29].

Various predictive factors for occult cysto-biliary fistulas (CBF) have been identified in the literature. These include factors such as cyst size [30–32], thick pericyst [33], and elevated levels of liver enzymes and total bilirubin [34,35]. These risk factors are also often associated with a higher incidence of postoperative bile leak. Larger cysts often present with more extensive cyst walls and irregular internal surfaces, making it challenging for surgeons to detect and address all potential fistulas. Hence, there is a need for improvement and standardization in the management of HCE to effectively treat these CBF.

Biliary fistulas can be latent, occluded by the hydatid membrane, or patent. They can be identified during surgery or manifest postoperatively as an external biliary fistula or purulent retention [3,36]. Occult cysto-biliary fistulas are usually asymptomatic. The sensitivity of radiological examinations for detecting these fistulas varies widely among studies [29]. Frikha et al. [37] demonstrated the limitations of abdominal ultrasound and CT scan in detecting cysto-biliary fistulas. This makes their preoperative diagnosis challenging, highlighting the importance of intraoperative exploration.

Except in cases where the cyst content is stained with bile and there is a visible fistula at the bottom of the residual cavity, the intraoperative diagnosis remains difficult. The internal surface of the residual cavity is generally irregular and the pericyst is often thick, concealing small fistula orifices. Moreover, it is not always easy to explore the entire cavity (hepatic dome, intra-hepatic cyst).

In 2011, Kayaalp et al. [8] conducted a comparative study aimed at studying the impact of intraoperative search for occult cysto-biliary fistulas on the DSSI rate. This study concluded that searching for and suturing cysto-biliary fistulas could reduce the postoperative bile leakage rate (8.8% vs. 27.7%; $p = 0.03$), which supports our findings. However, in this study, the search for fistulas was done with normal saline, which might miss small fistulas, possibly explaining the morbidity rate of 8.8%. Thus, neglecting silent occult cysto-biliary fistulas, especially the smallest ones (infra-millimetric) that can only be visualized through meticulous MBT testing, could be the cause of higher morbidity.

Methylene blue testing (MBT) appears to be the best examination for detecting occult cysto-biliary fistulas. In the literature, the technique of MBT was not well-defined (method of methylene blue injection, with or without clamping the main bile duct, leak test after suturing the fistula). MBT test in our study allowed us to detect a significant number of CBF in 53.7% of cysts.

Some authors postulate that the posterior liver segments are more prone to developing postoperative deep infections after conservative surgery [25,38,39]. This could be explained by several mechanisms such as the negative pressure exerted by the diaphragm, which would reverse the bile flow or having a suspended non-declining cavity [40]. For cysts located in the hepatic dome, the sectioning of the falciform, coronary and triangular ligaments allow for liver

Table 4. DSSI rates in the medical literature.

	Study period	Country	Type	DSSI
Monographie tunisienne [26]	2016–2021	Tunisia	Observational Retrospective	8.4%
Al Saeedi et al. [24]	-	Many	Meta-analysis	14.7%
Baraket et al. [23]	2001–2011	Tunisia	Observational Retrospective	16.6%
Kayaalp et al. [8]	1975–2007	Argentina	Observational Retrospective	20.5%
Our study	2017–2022	Tunisia	Prospective	1.9%

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mobilization to expose the cyst properly. This manoeuvre initially creates a dependent residual cavity, especially when involving the posterior liver segments, reducing the DSSI rates. Moreover, liver release better protects the peritoneal cavity with scolical-soaked gauzes. Thus, a cyst rupture could be easily controlled, preventing peritoneal cavity contamination by spillage, which is a source of recurrence, especially for posterior segments [41].

Several authors have demonstrated that a thick pericyst is a risk factor for the occurrence of deep surgical site infections [39]. Various technical measures have been employed to reduce complications related to the residual cavity, such as capitonnage, omentoplasty, or simple drainage. Among the studies that have addressed this question, only the study by Manterola et al. [42] showed that capitonnage resulted in less morbidity than omentoplasty. Two other randomized controlled trials [11,43] demonstrated the superiority of omentoplasty in reducing deep infections. The meta-analysis by Dziri et al. [9] showed a protective effect of omentoplasty compared to simple drainage of the cavity. Indeed, in our study, 67.2% of the cysts in the population underwent omentoplasty, contributing to reducing the DSSI rates.

As a result, conservative surgery still has a place in the therapeutic arsenal. The standardized technique, as we have described it, seems to yield better postoperative results. This standardization was achieved by considering various measures and techniques described in the literature. The absence of recurrence in the population may be attributed to the ameliorated techniques with systematic intraoperative ultrasound that is performed to detect all exogenous vesicles. Precautions taken, such as deflating the cysts before opening, during cyst puncture also contributes to decreasing recurrence.

The DSSI rate reported in the literature for conservative surgery, ranges from 8.4% to 20.5%, as presented in Table 4. The improvement in the specific morbidity rate in patients operated after the standardization of the technique is showed compared to the literature data.

The variability in the reported rates of complications could be attributed to the different definitions of external biliary fistula used by various authors. The criteria for defining a biliary fistula varied among studies, leading to differences in the interpretation and classification of postoperative bile leakages. Some authors considered any postoperative bile leakage through the drainage as a biliary fistula. Others defined a temporary bile leak as any bile leakage occurring within the first ten days after surgery and they considered it a biliary fistula if the bile leak persisted beyond the tenth day postoperatively.

The results of radical treatment (Table 5) reported in the literature show a low rate of overall morbidity ranging from 11% to 39%, as well as low rates of specific complications, ranging from 0% to 11% [14,18–20,26,44,45] and low rate of recurrence. However, these results were obtained at the cost of a longer operative duration. Comparing our results to those in the literature, we find that the rate of specific complications in the population treated with the standardized technique was at least as low as the radical treatment.

Table 5. Results of radical management reported in literature.

Study	Study period	Country	Type	Overall morbidity	Specific morbidity	Recurrence
Akbulut et al. [46]	2004–2009	Turkey	Retrospective	16.6%	11.1%	0
Yuksel et al. [19]	2001–2005	Turkey	Prospective	0	0	0
Secchi et al. [18]	1975–2007	Argentina	Retrospective	39%	-	1.3%
Motie et al. [20]	1993–2003	India	Retrospective	19%	6.2%	1.5%
Tagliacozzo et al. [47]	1980–2005	Italy	Retrospective	16.2%	4.6%	1.2%
Baimakhanov et al. [5]	2017–2019	Kazakhstan	Prospective	13.3%	-	0
Pang et al. [14]	2016	China	Meta-analysis	18.4%	-	2%
Farhat et al. [44]	2000–2019	Tunisia	Retrospective	11.0%	7.7%	2.8%
Dziri et al. [13]	2018	Tunisia	Meta-analysis	19.2%	5.1%	1.7%
Monographie tunisienne [26]	2006–2021	Tunisia	Retrospective	14.9%	11.2%	1.0%
Our study	2017–2022	Tunisia	Prospective	13.7%	3.7%	0

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The standardized technique involves performing a cholecystectomy and cannulation of the cystic duct. These procedures are not without associated complications, such as bile duct injury or vascular injury during dissection. Moreover, performing intraoperative ultrasound requires specific skills and prior knowledge, such as understanding the functioning and settings of the ultrasound equipment. These factors, combined with the cost of the ultrasound device, may pose challenges to the widespread implementation of the standardized technique.

Limits of our study

Our study has certain biases. The results of our study still remain hypothetical given the methodology adopted. To validate our conclusions, further comparative studies are necessary such as a prospective study comparing the standardised technique to the known partial cystectomy. Given the promising results of our study, a controlled randomized trial comparing radical surgery to the standardized technique could be conducted.

Conclusion

Conservative surgery holds a significant place in the management of hepatic echinococcosis. However, the major drawback of conservative surgery is the high morbidity and recurrence rate. We studied a prospective cohort undergoing a standardized surgical technique for the conservative management and achieved results at least similar to radical management in terms of DSSI.

Several factors contributed to the success of the standardized technique in terms of DSSI. Liver mobilization by sectioning its attachments resulted in a more declivous residual cavity and improved exposure of posterior and upper segments. The use of methylene blue test before and after clamping detected occult CBF and allowed for adequate suturing, which could decrease specific complications. Finally, omentoplasty could reduce the DSSI rate. All these protective factors showed a statistically significant relationship with the occurrence of DSSI. By standardizing conservative surgery, it might be possible to achieve a specific morbidity rate similar to that of radical surgery while avoiding the morbidity associated with liver resection.

Author Contributions

Conceptualization: Aymen Trigui, Rafik Mzali.

Data curation: Mohammad Saad Saumtally, Amira Akrou, Rahma Daoud, Wael Boujelbene.

Formal analysis: Aymen Trigui, Mohammad Saad Saumtally, Jihen Trabelsi.

Investigation: Aymen Trigui, Sami Fendri, Nozha Toumi, Salma Ketata.

Methodology: Aymen Trigui, Jihen Trabelsi.

Project administration: Aymen Trigui, Sami Fendri, Salah Boujelben.

Resources: Wael Boujelbene.

Software: Mohammad Saad Saumtally, Amira Akrou, Rahma Daoud, Wael Boujelbene.

Supervision: Rafik Mzali, Chadli Dziri, Salah Boujelben.

Validation: Chadli Dziri, Mohamed Ben Amar, Salah Boujelben.

Writing – original draft: Sami Fendri, Amira Akrou, Rahma Daoud, Nozha Toumi, Salma Ketata.

Writing – review & editing: Aymen Trigui, Chadli Dziri, Mohamed Ben Amar, Salah Boujelben.

References

1. Eckert J, Gemmell MA, Meslin FX, Pawlowski ZS, Organization WH. WHO/OIE manual on echinococcosis in humans and animals: a public health problem of global concern. World Organisation for Animal Health; 2001.
2. Dziri C, Haouet K, Fingerhut A. Treatment of hydatid cyst of the liver: Where is the evidence? World Journal of Surgery. 2004 Aug; 28(8):731–6. <https://doi.org/10.1007/s00268-004-7516-z> PMID: 15457348
3. Benkabbou A, Majbar MA, Souadka A, El Malki HO, Settaf A. Traitement chirurgical des kystes hydatiques du foie. EMC—Techniques chirurgicales—Appareil digestif. 2020; 37(1):1–14.
4. Smego RA, Sebanego P. Treatment options for hepatic cystic echinococcosis. International Journal of Infectious Diseases. 2005; 9(2):69–76. <https://doi.org/10.1016/j.ijid.2004.08.001> PMID: 15708321
5. Baimakhanov Z, Kaniyev S, Serikuly E, Doskhanov M, Askeyev B, Baiguissova D, et al. Radical versus conservative surgical management for liver hydatid cysts: A single-center prospective cohort study. JGH Open. 2021 Oct; 5(10):1179–82. <https://doi.org/10.1002/jgh3.12649> PMID: 34622005
6. Deo KB, Kumar R, Tiwari G, Kumar H, Verma GR, Singh H. Surgical management of hepatic hydatid cysts—conservative versus radical surgery. HPB. 2020 Oct 1; 22(10):1457–62. <https://doi.org/10.1016/j.hpb.2020.03.003> PMID: 32229090
7. Trigui A, Toumi N, Fendri S, Saumtally MS, Zribi I, Akrou, et al. Cystic Echinococcosis of the Liver: Correlation Between Intra-Operative Ultrasound and Pre-Operative Imaging. Surgical Infections. 2024 Mar 13 [cited 2024 Apr 1]; Available from: <https://www.liebertpub.com/doi/10.1089/sur.2023.335> PMID: 38483340
8. Kayaalp C, Aydin C, Olmez A, Isik S, Yilmaz S. Leakage tests reduce the frequency of biliary fistulas following hydatid liver cyst surgery. Clinics. 2011 Jan; 66(3):421–4. <https://doi.org/10.1590/s1807-59322011000300010> PMID: 21552666
9. Dziri C, Dougaz W, Khalfallah M, Samaali I, Nouira R, Fingerhut A, et al. Omentoplasty decreases deep organ space surgical site infection compared with external tube drainage after conservative surgery for hepatic cystic echinococcosis: Meta-analysis with a meta-regression. Journal of Visceral Surgery. 2022 Apr 1; 159(2):89–97. <https://doi.org/10.1016/j.jvisc.2021.03.009> PMID: 33771491
10. Skroubis G, Vagianos C, Polydorou A, Tzoracoleftherakis E, Androulakis J. Significance of bile leaks complicating conservative surgery for liver hydatidosis. World Journal of Surgery. 2002 Jun; 26(6):704–8. <https://doi.org/10.1007/s00268-002-6259-y> PMID: 12053223
11. Dziri C, Paquet JC, Hay JM, Fingerhut A, Msika S, Zeitoun G, et al. Omentoplasty in the prevention of deep abdominal complications after surgery for hydatid disease of the liver: a multicenter, prospective, randomized trial. Journal of the American College of Surgeons. 1999 Mar 1; 188(3):281–9.
12. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Annals of surgery. 2009 Aug; 250(2):187–96. <https://doi.org/10.1097/SLA.0b013e3181b13ca2> PMID: 19638912

13. Dziri C, Dougaz W, Samaali I, Khalfallah M, Jerraya M, Mzabi R, et al. Radical surgery decreases overall morbidity and recurrence compared with conservative surgery for liver cystic echinococcosis: systematic review with meta-analysis. *Annals of Laparoscopic and Endoscopic Surgery*. 2019; 4(2):92–92.
14. Pang Q, Jin H, Man Z, Wang Y, Yang S, Li Z, et al. Radical versus conservative surgical treatment of liver hydatid cysts: a meta-analysis. *Frontiers of Medicine*. 2018 Jun 1; 12(3):350–9. <https://doi.org/10.1007/s11684-017-0559-y> PMID: 29170917
15. He YB, Yao G, Tuxun T, Bai L, Li T, Zhao JM, et al. Efficacy of radical and conservative surgery for hepatic cystic echinococcosis: a meta-analysis.
16. Ramia JM, Ruiz-Gomez F, Plaza RD Ia, Veguillas P, Quiñones J, García-Parreño J. Ambispective comparative study of two surgical strategies for liver hydatidosis. *World Journal of Gastroenterology: WJG*. 2012; 18(6):546. <https://doi.org/10.3748/wjg.v18.i6.546> PMID: 22363121
17. Mohkam K, Belkhir L, Wallon M, Darnis B, Peyron F, Ducerf C, et al. Surgical management of liver hydatid disease: Subadventitial cystectomy versus resection of the protruding dome. *World Journal of Surgery*. 2014 Aug; 38(8):2113–21. <https://doi.org/10.1007/s00268-014-2509-z> PMID: 24969045
18. Secchi MA, Pettinari R, Mercapide C, Bracco R, Castilla C, Cassone E, et al. Surgical management of liver hydatidosis: a multicentre series of 1412 patients. *Liver International*. 2010 Jan; 30(1):85–93. <https://doi.org/10.1111/j.1478-3231.2009.02116.x> PMID: 19747191
19. Yüksel O, Akyürek N, Şahin T, Salman B, Azili C, Bostanci H. Efficacy of radical surgery in preventing early local recurrence and cavity-related complications in hydatid liver disease. *Journal of Gastrointestinal Surgery*. 2008 Mar 5; 12(3):483–9. <https://doi.org/10.1007/s11605-007-0301-1> PMID: 17917786
20. Motie MR, Ghaemi M, Aliakbarian M, Saremi E. Study of the Radical vs. Conservative Surgical Treatment of the Hepatic Hydatid Cyst: A 10-Year Experience. *Indian J Surg*. 2010 Dec; 72(6):448–52. <https://doi.org/10.1007/s12262-010-0163-8> PMID: 22131653
21. El Malki HO, Souadka A, Benkabbou A, Mohsine R, Ifrine L, Abouqal R, et al. Radical versus conservative surgical treatment of liver hydatid cysts. *The British journal of surgery*. 2014 May; 101(6):669–75. <https://doi.org/10.1002/bjs.9408> PMID: 24843869
22. Brunetti E, Kern P, Angèle D, Panel W, E Brunetti PK Vuitton DA. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. *Acta Trop*. 2010 Apr; 114(1):1–16. <https://doi.org/10.1016/j.actatropica.2009.11.001> PMID: 19931502
23. Baraket O, Moussa M, Ayed K, Kort B, Bouchoucha S. Predictive factors of morbidity after surgical treatment of hydatid cyst of the liver. *Arab Journal of Gastroenterology*. 2014 Sep; 15(3–4):119–22. <https://doi.org/10.1016/j.ajg.2014.05.004> PMID: 25596975
24. Al-Saeedi M, Ramouz A, Khajeh E, El Rafidi A, Ghamarnejad O, Shafiei S, et al. Endocystectomy as a conservative surgical treatment for hepatic cystic echinococcosis: A systematic review with single-arm metaanalysis. *PLoS Neglected Tropical Diseases*. 2021 May 1; 15(5).
25. Ghannouchi M, Rodayna H, Ben Khalifa M, Nacef K, Boudokhan M. Postoperative morbidity risk factors after conservative surgery of hydatid cyst of the liver: a retrospective study of 151 hydatid cysts of the liver. *BMC Surgery*. 2022 Mar 30; 22(1):120. <https://doi.org/10.1186/s12893-022-01570-7> PMID: 35351087
26. Dougaz MW, Trigui A. Monographie de l'Association Tunisienne de Chirurgie: Echinococcose Kystique du Foie. Rapport présenté au 43ème Congrès National de Chirurgie. 2022.
27. Daradkeh S, El-Muhtaseb H, Farah G, Sroujeh AS, Abu-Khalaf M. Predictors of morbidity and mortality in the surgical management of hydatid cyst of the liver. *Langenbeck's Archives of Surgery*. 2007; 392(1):35–9. <https://doi.org/10.1007/s00423-006-0064-2> PMID: 17021792
28. Hassan BAA. The identification of risk factors that predict occult cystobiliary communication in liver hydatid cysts. *Iraqi Journal of Medical Sciences*. 2017; 15(3):71–7.
29. Ramia JM, Figueras J, De La Plaza R, García-Parreño J. Cysto-biliary communication in liver hydatidosis. *Langenbeck's Archives of Surgery*. 2012; 397(6):881–7. <https://doi.org/10.1007/s00423-012-0926-8> PMID: 22374106
30. El Nakeeb A, Salem A, El Sorogy M, Mahdy Y, Abd Ellatif M, Moneer A, et al. Cystobiliary communication in hepatic hydatid cyst: predictors and outcome. *Turk J Gastroenterol*. 2017 Mar 3; 28(2):125–30. <https://doi.org/10.5152/tjg.2017.17553> PMID: 28119271
31. Dezfouli SA, Rafidi AE, Aminizadeh E, Ramouz A, Al-Saeedi M, Khajeh E, et al. Risk factors and management of biliary leakage after Endocystectomy for hepatic cystic echinococcosis. *PLOS Neglected Tropical Diseases*. 2023 Oct 31; 17(10):e0011724. <https://doi.org/10.1371/journal.pntd.0011724> PMID: 37906617
32. Unalp HR, Baydar B, Kamer E, Yilmaz Y, Issever H, Tarcan E. Asymptomatic occult cysto-biliary communication without bile into cavity of the liver hydatid cyst: a pitfall in conservative surgery. *International*

- journal of surgery (London, England). 2009 Aug; 7(4):387–91. <https://doi.org/10.1016/j.jisu.2009.06.012> PMID: 19573629
33. Malki HOE, Mejdoubi YE, Souadka A, Mohsine R, Ifrine L, Abouqal R, et al. Predictive model of biliocystic communication in liver hydatid cysts using classification and regression tree analysis. *BMC Surgery*. 2010; 10:16. <https://doi.org/10.1186/1471-2482-10-16> PMID: 20398342
 34. Demircan O, Baymus M, Seydaoglu G, Akinoglu A, Sakman G. Occult cystobiliary communication presenting as postoperative biliary leakage after hydatid liver surgery: Are there significant preoperative clinical predictors? *Can J Surg*. 2006 Jun; 49(3):177–84. PMID: 16749978
 35. Atli M, Kama NA, Yuksek YN, Doganay M, Gozalan U, Kologlu M, et al. Intrahepatic Rupture of a Hepatic Hydatid Cyst: Associated Clinical Factors and Proper Management. *Arch Surg*. 2001 Nov 1; 136(11):1249–55. <https://doi.org/10.1001/archsurg.136.11.1249> PMID: 11695968
 36. Noomen F, Mahmoudi A, Fodha Md, Boudokhane M, Hamdi A, Fodha M. Traitement chirurgical des kystes hydatiques du foie. *EMC—Techniques chirurgicales—Appareil digestif*. 2013 May; 8(2):1–18.
 37. Frikha F, Trigui A, Rejab H, Toumi N, Fendri S, Jemal A, et al. Correlation of radiological findings with surgical findings in hepatic hydatid disease. A prospective study of 79 cases. *Ann Ital Chir*. 2018; 89:309–14.
 38. Kayaalp C, Bzeizi K, Demirbag AE, Akoglu M. Biliary complications after hydatid liver surgery: Incidence and risk factors. *Journal of Gastrointestinal Surgery*. 2002; 6(5):706–12. [https://doi.org/10.1016/s1091-255x\(02\)00046-x](https://doi.org/10.1016/s1091-255x(02)00046-x) PMID: 12399060
 39. El Malki HO, El Mejdoubi Y, Souadka A, Mohsine R, Ifrine L, Abouqal R, et al. Predictive Factors of Deep Abdominal Complications after Operation for Hydatid Cyst of the Liver: 15 Years of Experience with 672 Patients. *Journal of the American College of Surgeons*. 2008 Apr; 206(4):629–37. <https://doi.org/10.1016/j.jamcollsurg.2007.11.012> PMID: 18387467
 40. Paquet JC, Dziri C, Hay JM, Fingerhut A, Zeitoun G, Suc B, et al. Prevention of deep abdominal complications with omentoplasty on the raw surface after hepatic resection. *The American Journal of Surgery*. 2000 Feb; 179(2):103–9.
 41. Jerraya H, Khalfallah M, Osman SB, Nouira R, Dziri C. Predictive factors of recurrence after surgical treatment for liver hydatid cyst. *Surgical Endoscopy*. 2015 Jan; 29(1):86–93. <https://doi.org/10.1007/s00464-014-3637-0> PMID: 24962861
 42. Manterola C, Roa JC, Urrutia S, MINCIR Group. Treatment of the residual cavity during hepatic hydatidosis surgery: a cohort study of capitonnage vs. omentoplasty. *Surg Today*. 2013 Dec; 43(12):1412–8.
 43. Wani AA, Rashid A, Laharwal AR, Kakroo SM, Abbas M, Chalkoo MA. External tube drainage or omentoplasty in the management of residual hepatic hydatid cyst cavity: a prospective randomized controlled study. *Ger Med Sci*. 2013 Jul 29; 11:Doc11. <https://doi.org/10.3205/000179> PMID: 23904825
 44. Farhat W, Ammar H, Rguez A, Harrabi F, Said MA, Ghabry L, et al. Radical versus conservative surgical treatment of liver hydatid cysts: A paired comparison analysis. *American Journal of Surgery*. 2022; 224(1):190–5. <https://doi.org/10.1016/j.amjsurg.2021.12.014> PMID: 34949334
 45. Yucel Y, Seker A, Eser I, Ozgonul A, Terzi A, Gozeneli O, et al. Surgical treatment of hepatic hydatid cysts: A retrospective analysis of 425 patients. *Annali Italiani di Chirurgia*. 2015; 86(5):437–41. PMID: 26568422
 46. Akbulut S, Senol A, Sezgin A, Cakabay B, Dursun M, Satici O. Radical vs conservative surgery for hydatid liver cysts: Experience from single center. *World Journal of Gastroenterology: WJG*. 2010 Feb 28; 16(8):953. <https://doi.org/10.3748/wjg.v16.i8.953> PMID: 20180233
 47. Tagliacozzo S, Miccini M, Bonapasta SA, Gregori M, Tocchi A. Surgical treatment of hydatid disease of the liver: 25 years of experience. *The American Journal of Surgery*. 2011 Jun 1; 201(6):797–804. <https://doi.org/10.1016/j.amjsurg.2010.02.011> PMID: 20832053