

## **Surgical intervention for Liver Hydatid Disease; Review**

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### **Abstract:**

In this article we review the current management modalities of LHC with particular emphasis on risk, benefit and safety profile and also emphasize the diagnosis method and classification of the LHC. Conducted a detailed search among electronic databases: MEDLINE, EMBASE, and Google scholar, searching in literature for articles related to surgical intervention for Liver Hydatid Disease. Studies were included as publication up to 2017, September with English language and human subject. Keywords used in search strategies were as following: "Liver Hydatid", "surgery", "surgical intervention". LHC is a complex and dynamic illness with a progressing phase when the cysts expand, followed by an involution procedure throughout which the parasite is gradually dying off leaving a solidified, frequently calcified cyst or a scar. Each successive active cyst stage carries its own risks for severe and even lethal complications. For complex diseases, no "one size fits all" method is to be adopted and a stage-specific and resource-specific approach would be deemed essential. The majority of released researches conclude that radical surgical treatment is a far better option than conservative treatment. Omentoplasty related to conservative surgical treatment is effective in preventing postoperative problems. Further studies are needed to evaluate reoccurrence rates following laparoscopic surgery for liver HC.

## Introduction:

Hydatid disease is an important parasitic ailment that affects primarily the liver in 75% of cases[1]. Most cases in humans are caused by *Echinococcus granulosus* or *Echinococcus multilocularis*, which account for cystic and alveolar echinococcosis, respectively [1]. The worldwide annual incidence of cystic echinococcosis is 1–200 per 100 000[1]. Dogs and other canids are the definitive hosts for the adult tapeworm, whereas ungulates (typically sheep) act as intermediate hosts by ingesting shed eggs [1]. Humans living in proximity to definitive and intermediate hosts can become accidental intermediate hosts by the same mechanism. Hydatid disease is endemic in many sheep- and cattle-raising parts of the world, namely Mediterranean countries, the Middle East, Eastern Europe and South America.

The management of hydatid cysts of the liver is controversial. Therapeutic options can be broadly divided into 3 categories: medical treatment, conservative surgery and radical surgery. Medical therapy, using the antihelminthic agents albendazole or mebendazole, has been recommended for asymptomatic and uncomplicated cysts smaller than 5 cm [2]. Conservative surgical options include external drainage and unroofing procedures in addition to various types of residual cavity management strategies. Radical surgical options include formal liver resection and complete pericystectomy.

The disease has a world-wide distribution. It is endemic in the Mediterranean and Baltic areas, Middle and Far East, South America and South Africa. Sheep-rearing European regions and central North America are also affected. *E. granulosus* producing unilocular hydatid disease (cystic echinococcosis - CE) is cosmopolitan whereas *E. multilocularis* producing alveolar

hydatid disease (alveolar echinococcosis - AE) is limited to restricted areas of the northern hemisphere. Although less common, AE poses a far more serious problem due to the infiltrative nature of its cysts and its greater ability to metastasise; it has to be regarded as a malignant disease carrying a mortality of up to 90% in untreated cases. Unless otherwise stated in text we refer to *E. granulosus* and CE.

In this article we review the current management modalities of LHC with particular emphasis on risk, benefit and safety profile and also emphasize the diagnosis method and classification of the LHC.

### **Methodology:**

Conducted a detailed search among electronic databases: MEDLINE, EMBASE, and Google scholar, searching in literature for articles related to surgical intervention for Liver Hydatid Disease. Studies were included as publication up to 2017, September with English language and human subject. Keywords used in search strategies were as following: “Liver Hydatid”, “surgery”, “surgical intervention”. Furthermore, references list of each included study were scanned for more relevant articles to be included and support our review.

### **Discussion:**

- **Diagnostic approach**

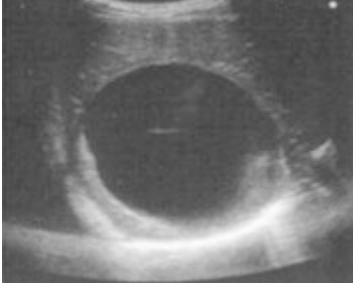



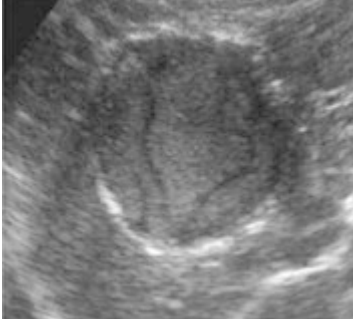
Although most patients may be asymptomatic for years or have nonspecific symptoms, about one third of the patients with LHCs may present with pressure effects or complications. The pressure effect of the cyst can produce symptoms of obstructive jaundice and abdominal pain. The common complications are infection and rupture in to the biliary tree while intraperitoneal rupture, intrathoracic rupture, internal rupture, rupture into viscera, rupture into vascular system and external compression leading to portal hypertension are rare[3],[4].


The results of routine laboratory blood work are nonspecific. LHCs may be reflected in an elevated bilirubin or alkaline phosphatase level. Leukocytosis may suggest infection of the cyst. Eosinophilia is present in 25% of all persons who are infected, while hypogammaglobinemia is present in 30%. Almost every serodiagnostic technique has been evaluated for echinococcosis, with variable results. The indirect hemagglutination test and the enzyme-linked immunosorbent assay (ELISA) have a sensitivity of 90% overall and are the initial screening tests of choice. Immunodiffusion and immunoelectrophoresis demonstrate antibodies to antigen 5 and provide specific confirmation of reactivity.

The advent of ultrasonography (USG) has represented a breakthrough in the diagnosis, treatment and follow-up of patients with LHCs. USG based classification of LHCs, their correlation with individual cyst stages, natural history and treatment induced involution process have been extensively studied[5]. WHO informal working group on Echinococcus (IWGE) classification (Table 1) of LHCs has important consequences on treatment decision making and is widely accepted.

**Table 1.** Ultrasonography classification of echinococcal cyst [7].

| WHO IWGE 2001 | Image | Description | Stage |
|---------------|-------|-------------|-------|
|---------------|-------|-------------|-------|

|      |   |   |             |
|------|---|---|-------------|
| CE1  |    | Unilocular,<br>anechoic cyst with<br>double line sign                                       | Activ       |
| CE2  |    | Multiseptate honey<br>comb cyst   |             |
| CE3a |   | Cyst with detached<br>membrane  | Transitiona |
| CE3b |  | Cyst with daughter<br>cysts in solid matrix   |             |
| CE4  |  | Cyst with<br>heterogenous<br>hypoechoic /<br>hyperechoic<br>contents. No<br>daughter cysts. | Inactiv     |

|     |   |                           |  |
|-----|---|---------------------------|--|
| CE5 |  | Solid plus calcified wall |  |
|-----|---|---------------------------|--|

Computed tomography (CT) is indicated in cases in which USG fails due to patient-related difficulties (e.g. obesity, excessive intestinal gas, abdominal wall deformities and previous surgery) or disease complications. CT has a high sensitivity and specificity for LHCs. Intravenous administration of contrast material is not necessary unless complications are suspected, especially infection and communication with the biliary tree[6]. In patients with suspicion of intrabiliary rupture and/or obstruction of biliary passages based on clinical, biochemical or radiologic findings, a preoperative endoscopic retrograde cholangiography (ERCP) establishes cystobiliary communication and provides a therapeutic option in majority of patients.

- **Treatment modalities currently in use**

### **Surgery**

Until three decades ago, surgery was the only treatment option available for LHCs, applicable over the entire spectrum of the disease[8]. Despite refinement in surgical techniques, there is considerable controversy as to what is the most effective technique, the role of cyst aspiration and external drainage, hepatic resection, management of the residual cavity, cyst recurrence after surgery, and high rates of complications and mortality related to reoperation in recurrent disease[9]. An immediate cure is claimed for surgical treatment of liver cysts, but even with radical procedures, this is far from being achieved, with morbidity, mortality, and relapse rates of

32%, 8%, and 20%, respectively[10]. However in patients with complicated cysts (rupture, cysto-biliary fistulas, compression of vital organs and vessels, hemorrhage, secondary bacterial infection), surgery maintains its place as the treatment of choice. In uncomplicated cysts, surgery is increasingly being replaced with other treatment options depending on the stage of the cyst. This is, however, not based on appropriate comparative prospective clinical trials with long-term follow-up.

### **Surgical procedures**

These may be conservative or radical. Conservative procedures aim at sterilization and evacuation of cyst content, including the hydatid membrane (hydatidectomy), and partial removal of the cyst. The evacuation and hydatidectomy consist of puncture of cyst and aspiration of part of the content to permit introduction of scolicedal agent and total aspiration thereafter. The risks are anaphylactic shock, chemical cholangitis, if the cyst communicates with the biliary tree, and spillage of the cyst contents and secondary hydatidosis. Relapse rates of up to 20% are reported after surgery of LHCs[11]. After partial removal of the cyst, a residual cavity remains, bearing the risk of secondary bacterial infection and abscess formation. Radical procedures aim at complete removal of the cyst with or without hepatic resection. Radical procedures bear greater intraoperative risks, with less postoperative complications and relapses.

Laparoscopic management of LHCs has gained ground despite the initial exaggerated fear of complications such as anaphlaxis. Various techniques such as total pericystectomy, puncture and aspiration of contents followed by marsupialization, unroofing and drainage, unroofing and omentoplasty, and omentoplasty using helical fasteners have been described[12]. One of the problems faced in laparoscopic treatment of liver hydatid cysts is the difficulty in evacuating the

particulate contents of the cyst, the daughter cysts, and laminated membrane. Bickel et al initially advocated the use of a large transparent beveled cannula[13].Saglam described a perforator-grinder-aspirator apparatus designed specifically for the evacuation of hydatid cysts[14]. Palanivelu developed the “Palanivelu Hydatid System” (PHS) consisting of a complex system of fenestrated trocar and cannulas to avoid peritoneal spillage. PHS not only prevents any spillage of hydatid fluid but also assists complete evacuation of the cyst content and allows intracystic magnified visualization for cyst-biliary communication.

### **Adjunctive treatment**

There is some evidence for the following adjunctive measures to play a useful role.

#### 1)Prevention of secondary CE and relapses

a)Albendazole – starting 1 week before surgery and continuing to up to 3 months after surgery.

There is no uniform recommendation and the efficacy is not known[16].

b) Surgical field protection with pads soaked with scolicial agents.

#### 2) Prevention of cholangitis

a) If de-roofing is performed, a search for cystobiliary-fistulae is mandatory. Bile-stained fluid content, raised levels of bilirubin in the aspirated fluid and spillage of contrast on anterograde cholangiography are all indicative of cystobiliary communication.

b) Strictly avoiding injection of scolicial solution into cysts that communicate with the biliary tree (cysto-biliary fistulas)[17].



### 3) Management of the residual cavity

a) Ideally, cysts are completely removed to avoid residual cavities. This prevents suppuration, reduces the risk of biliary fistulas, and achieves faster healing and shorter hospital stay[15].

b) When hydatidectomy or partial or subtotal cystectomy is performed, the residual cavities are managed by simple drainage with suction and filling with epiploon (omentoplasty) to reduce the risk of complications[15].

### **Risk, benefit, and safety profile**

The principal advantage of cyst resection is the immediate cure of the disease. For hepatic cysts, the more radical the intervention, the higher the intraoperative risk and the lower the frequency of relapse, and vice versa in the more conservative approach[15].

### **Percutaneous treatment**

Percutaneous treatment of LHCs introduced in the mid-1980s has become an attractive alternative to surgery and medical management. The first percutaneous treatment used was to puncture the cyst, aspirate cyst fluid, inject a scolicidal agent (e.g., hypertonic saline, 95% ethanol, albendazole or betadine), and re-aspirate the cyst content (PAIR). Khuroo and others found PAIR under ultrasonography or tomograph guidance, combined with periinterventional benzimidazole derivatives to be as effective as open surgical drainage with fewer complications and less cost[18]. Yagci et al from Turkey reported a single-center experience comparing surgery, laparoscopic surgery, and percutaneous treatments in 355 patients of LHCs over a period of 10 years and concluded that PAIR is an effective and safe option[19]. Giorgio and others and Kabaalioglu and others reported repeated failures of PAIR in multivesiculated cysts (CE2 and

CE3B)[20]. These findings prompted most clinicians to use PAIR exclusively for unilocular cysts, with or without detached endocysts.

### **Other percutaneous techniques**

These are generally reserved for cysts that are difficult to drain or tend to relapse after PAIR (multivesiculated cysts or cysts with predominantly solid content and daughter cysts). Percutaneous evacuation (PEVAC), modified catheterization technique (MoCaT), and dilatable multi-function trocar (DMFT) are some of the devices used for aspiration of the “solid” content of the LHCs, the germinal and the laminated layer. A much less well-evaluated percutaneous technique to destroy the germinal layer by means of high temperature is radiofrequency (RF) thermal ablation. Preliminary reports are rather disappointing because nearly all the cysts treated relapsed after a few months[21].

### **Risk, benefit, and safety profile**

The major risks of percutaneous techniques are anaphylactic shock, secondary echinococcosis caused by spillage of cystic fluid, and chemical cholangitis caused by contact of the scolical agent with the biliary tree. Such major complications are reported to be only 0.38% and secondary echinococcosis as a result of spillage of fluid is reported to tune of 1.27% in the literature available. It is unclear whether this is because of spillage-free puncture, albendazole prophylaxis, or underreporting because of incomplete follow-up regarding length and imaging techniques used. Safety and efficacy of percutaneous treatments is also related to the anatomical site of the cyst[22].

- **Medical treatment**

The interest in investigating medical therapy of CE was not only facilitated by the increasing availability of ultrasonography and a better understanding of imaging features reflecting involution, but also made evaluation more objective. Mebendazole was the initial agent but due its poor efficacy has largely been replaced by the better absorbed albendazole (10–15 mg/kg/day) in LHCs[23]. Although the standard regimen is using three cycles of 1 month with a break of 14 days between courses, duration of treatment of <3 months produces less than optimal response, whereas results of extension beyond 6 months have yet to be gauged. Gil-Grande and others conducted a surgically based study of two albendazole dose regimens compared with no treatment. Evaluation in this case was made at surgery, and the cyst contents were evaluated for viability by microscopy and supravital staining after inoculation of the cyst content into mice and compared it with the ultrasound characteristics of the cysts. They showed that treatment produced a clear effect on viability and infectivity for mice, which was greater with the longer course of treatment.

Absorption of albendazole in humans is very variable and limited to between 5% and 20%. Absorption is mostly from the small intestine, and is metabolized first to albendazole sulphoxide, an active antihelminthic in its own right, and then to the relatively inactive sulphone. Improvement of systemic availability of available benzimidazoles has been explored with co-administration with a fatty meal, liposomal encapsulation, and soya bean oil emulsions, the latter two without attracting commercial interest.

### **Risk, benefit, and safety profile**

The common side effects in the short term are alopecia and gastrointestinal symptoms occurring in 1–5% of all those treated. The best-known effect of long-term benzimidazole treatment of

LHCs is elevation of liver enzymes occurring in up to 20% of treated cases and has often led to cessation of treatment. Also benzimidazoles have the potential to suppress bone marrow function, and cases of aplastic anemia have been described with both compounds[24]. Finally, benzimidazole compounds carry a risk to the fetus in the first trimester of pregnancy.

- **“Watch and wait”**

The idea of leaving certain cyst types untreated and just monitoring them over time is a logical consequence of two main findings:

1) a good proportion of cysts are consolidating and calcifying (i.e., become completely inactive) without any treatment.

2) cysts that have arrived at this stage and behave quietly (i.e., do not compromise organ functions or cause discomfort) seem to remain like this or stabilize even further. This decision must, however, be accompanied and verified by long-term ultrasonographic follow-up for a period up to ten years[25].

- **Imaging-oriented, stage-specific treatment approach**

Today management of LHCs is facilitated by consensus on cyst stages and reliable correlation of the USG-defined cyst stages. Based on current evidence a pragmatic approach to the various treatment options based on the stage of LHCs is suggested (Table 2).

**Table 2.** Treatment modalities stratified by cyst stage (uncomplicated) [23].

| <b>WHO Classification</b> | <b>Suggested practice</b>                                  |
|---------------------------|--|
| CE1                       | Albendazole alone if < 5 cm<br>PAIR + Albendazole if > 5cm |

| WHO Classification | Suggested practice  |
|--------------------|---|
| CE2                | Surgery + Albendazole<br>Or<br>Non-PAIR PT + Albendazole    |
| CE3a               | Albendazole alone if < 5 cm<br>PAIR + Albendazole if > 5 cm |
| CE3b               | Surgery + Albendazole<br>Non-PAIR PT + Albendazole          |
| CE4 and 5          | Wait and watch  |

### Conclusion:

LHC is a complex and dynamic illness with a progressing phase when the cysts expand, followed by an involution procedure throughout which the parasite is gradually dying off leaving a solidified, frequently calcified cyst or a scar. Each successive active cyst stage carries its own risks for severe and even lethal complications. For complex diseases, no "one size fits all" method is to be adopted and a stage-specific and resource-specific approach would be deemed essential. The majority of released researches conclude that radical surgical treatment is a far better option than conservative treatment. Omentoplasty related to conservative surgical treatment is effective in preventing postoperative problems. Further studies are needed to evaluate reoccurrence rates following laparoscopic surgery for liver HC. The essential issue in hydatidosis is prevention. Anthelmintic treatment of farm dogs stays presently the most effective method to reduce the occurrence of the disease.

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