



# Treatment of Gharbi Type III Hepatic Hydatid Cysts: A Clinical Dilemma

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This article aims to compare available treatment options for type III liver hydatid cysts, including surgery and percutaneous techniques. Hydatid disease is a helminthic infection caused by *Echinococcus granulosus* and is a serious public health problem in endemic regions of the world. Hydatid cyst of the liver is the most common clinical presentation of *Echinococcus granulosus*. According to Gharbi classification, hydatid cysts of the liver are classified into 5 types. Type III hydatid cysts are those with fluid collection and septa. Treatment of Gharbi type III hydatid cysts is still controversial. Some researchers think that Gharbi type III hydatid cysts are not suitable for percutaneous drainage, and surgery is the suitable treatment option. There are not enough prospective studies comparing percutaneous and surgical techniques for the treatment of type III hydatid disease of the liver. A proper meta-analysis does not seem to be possible with the available studies in current medical literature.

*Key words:* Hydatid disease – Surgery – Percutaneous treatment – *Echinococcus granulosus* – Liver

Hydatid disease is a helminthic infection caused by *Echinococcus granulosus* (EG) and is a serious public health problem in endemic regions of the world, including the Middle East.<sup>1,2</sup> Dogs are definite hosts for EG, whereas sheep are the intermediate hosts. Humans get involved in this cycle incidentally by ingestion of food or water contaminated with dog feces containing eggs of EG.<sup>3,4</sup>

Hydatid cyst of the liver is the most common clinical presentation of EG, with a prevalence of 50% to 70% of infected cases. Infection is often acquired during childhood and becomes symptomatic in adulthood. Today, with the increasing use of imaging modalities, many hydatid cysts are diagnosed incidentally before they become symptomatic. Clinical symptoms depend on the size and location of hydatid cyst. The common symptoms are mostly

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related to mass effect and hepatomegaly, which can result in right upper quadrant discomfort, nausea, vomiting and jaundice. Rupture into the biliary system or peritoneal cavity can cause biliary colic, jaundice, cholangitis, or pancreatitis.<sup>2,5</sup> Anaphylaxis is the most undesired symptom of hydatid cyst, with a reported prevalence of 10% in intraperitoneal ruptures.<sup>6</sup>

Liver hydatid cysts are mainly diagnosed by ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI). Of these, US imaging has a special importance because of its availability, easy application, high sensitivity/specificity, and presence of robust diagnostic criteria for hydatid cysts, which enables standardized classification. Classifications of hydatid cysts are based on morphologic appearances revealed by US imaging. Today, the classification described by Gharbi *et al*<sup>7</sup> is the preferred one. According to this classification, hydatid cysts of the liver are classified into five types: type I (pure fluid collection), type II (fluid collection with a split wall), type III (fluid collection with septa), type IV (hydatid cysts with heterogeneous echo patterns), and type V (hydatid cysts with reflecting thick walls). In 2001, the World Health Organization (WHO) Informal Working Group on Echinococcosis (IWGE) standardized the classification of liver hydatid cysts based on the biologic activity of the disease and described 6 types as follows: CL (active if CE, unilocular cystic lesion with invisible wall), CE1 (active, unilocular cyst with uniform anechoic content and well-defined visible wall, may be full of hydatid sand), CE2 (active, multivesicular, multiseptated cysts with well-defined contours that look like honeycombs or wheels), CE3 [transitional, degenerating cyst with floating membrane (3a) or a unilocular cyst with a solid matrix that may contain daughter cysts (3b)], CE4 (inactive, heterogeneous hypoechoic/hyperechoic appearance without daughter cysts, may show a “ball of wool” sign), and CE5 (inactive, often calcified, which varies from partial to complete).<sup>3,8</sup>

According to the consensus by WHO-IWGE,<sup>9</sup> the treatment approach for liver hydatid cysts is determined based on the cyst type obtained in imaging and consists of the following alternatives: (1) percutaneous treatment, (2) surgery (3) antiparasitic drugs, and (4) a “watch and wait” approach. In addition, treatment indications are more complex and depend on many circumstances, including the patient status (age, pregnancy, accompanying diseases, patient preferences, and adherence to long-

term follow-up), the cyst characteristics (type, size, number, location, complications), the clinician’s experience, and the hospital’s resources.<sup>9,10</sup> Surgery still retains its place as the treatment of choice for complicated liver hydatid cysts, but in recent years percutaneous drainage techniques have evolved and became widely accepted, especially in uncomplicated types I and II cysts, with large series reported in the literature.<sup>9,11</sup> Treatment of Gharbi type III (WHO, CE2, and CE 3b) hydatid cysts is still controversial. Some researchers think that Gharbi type III (WHO, CE2, and CE 3b) hydatid cysts are not suitable for percutaneous drainage and surgery is the suitable treatment option. However, some authors reported different percutaneous drainage techniques for the treatment of Gharbi type III (WHO, CE2) hydatid cysts.<sup>12,13</sup> Chemotherapy can be used either alone, or adjuvant to surgery or percutaneous drainage. A “wait and observe” approach is recommended for types IV and V<sup>14,15</sup> cysts.

This review article aims to compare the available treatment options for type III liver hydatid cysts, including surgery and percutaneous techniques.

## Surgical Treatment

For many years, before the introduction of anti-helminthic drugs and percutaneous techniques, surgical treatment was the only option for liver hydatid cysts. Surgery should be considered carefully against other options, especially for uncomplicated hydatid cysts. However, it is still the first choice for (1) complicated cysts, including CE2 and CE3b cysts with multiple daughter vesicles; (2) solitary liver cysts situated superficially, which carry a risk for spontaneous or traumatic rupture when percutaneous techniques (PTs) are not available; (3) infected cysts; and (4) cysts that open into the biliary tree and compress adjacent vital organs.<sup>16,17</sup>

The most commonly used surgical techniques are classified as either conservative or radical. Conservative techniques aim to sterilize and evacuate the cyst cavity, including the endocyst, and obliterate the residual cavity, whereas radical techniques remove the cyst totally, even by hepatic resection.<sup>18,19</sup> Conservative surgical techniques include tube drainage, marsupialization, capitonnage, deroofting, partial simple cystectomy, and open/closed total cystectomy with or without omentoplasty. Radical techniques involve total pericystectomy, partial hepatectomy, and lobectomy.

In the last decade, radical procedures became the preferred techniques, rather than conservative procedures, because the former pose fewer complications, lower recurrence rates, and a shorter duration of hospital stay.<sup>19,20</sup> In a study by Yorganci and Sayek,<sup>19</sup> the authors treated 95 patients who had liver hydatid cyst not suitable for PT. The most common indication for choosing surgical treatment rather than PT was the presence of type III or IV cysts (68.4%) that had nondrainable solid material. In this study the authors compared conservative and radical techniques and showed that conservative surgical approaches and common bile duct exploration are significantly associated with increased rates of complications, risk of recurrence, and length of hospital stay. Their overall complication and recurrence rates were 40% and 25%, respectively, and the cysts that were treated by radical techniques did not recur. Biliary fistula and residual cavity infection were the most pronounced major complications, which were only seen in patients treated with conservative techniques. Because these authors evaluated their results in terms of surgical techniques there is no information about the correlation between the cyst type, surgical technique chosen, and type of recurrent cysts.

In another study by Tagliacozzo *et al*,<sup>20</sup> the authors treated 454 patients with 695 liver hydatid cysts surgically and compared the results of conservative and radical techniques. A total of 87% of the treated cysts were multivesicular. In their 87-month follow-up, the results showed higher operative morbidity (79.9% versus 16.2%), higher recurrence rate (30.4% versus 1.2%), and longer hospital stay (33.7 days versus 13.8 days) in conservative procedures when compared with radical procedures. They also stated that in patients with clear cysts no recurrences occurred after conservative surgery. In this series the most pronounced major complications were biliary fistula and residual cavity infection, which also occurred with a higher incidence in conservative techniques. There were more deaths in the radical surgery group ( $n = 22$ ; 9.2%) than in the conservative procedures group ( $n = 14$ ; 6.5%), but this was not statistically significant. The authors' conclusion was to limit alternative treatments and conservative surgical procedures to (1) clear cysts, (2) severely ill patients, and (3) when pericyst tissue adhered to main vessels.

In a series by Yagci *et al*,<sup>21</sup> the authors compared an open surgical approach with laparoscopic surgery and percutaneous treatment in 355 patients with 510 liver hydatid cysts. The cysts treated by an

open surgical approach consisted mainly of types III and IV cysts. On the other hand, uncomplicated cysts, types I and II, were mainly treated by percutaneous techniques. Their results showed significantly higher total morbidity (28.1%, 13.3%, and 9.2%, respectively), recurrence rates (16.2%, 3.3%, and 3.6%, respectively), and length of hospitalization (12 days, 8 days, and 1 day, respectively) in the conservative open surgery group compared with the laparoscopic surgery and percutaneous treatment groups. They also compared open surgical techniques and showed that morbidity in conservative procedures, including wound infection, cavity infection, and bile leakage, was higher than in radical procedures. When complication rates were compared based on treated cyst types, cavity infection/abscess and bile leakage rates were higher in types III and IV cysts (20.1% and 25%, respectively), which were treated mainly by an open surgical approach. In this study, the cyst type heterogeneity in the groups affects the comparison of the results. Complicated cysts, including types III and IV cysts, accumulated in the open surgery group, so morbidity, recurrence rate, and hospitalization period were higher in this group. With these results the authors stated that radical surgery could be performed safely for suitable cases; hence, the conventional procedures were associated with greater morbidity. In this study, laparoscopic surgery and percutaneous techniques seemed to be effective and safe in accessible localizations for types I to III cysts, with lower morbidity and recurrence rates.

In a landmark study by Khuroo *et al*,<sup>22</sup> the authors randomized 50 patients and divided them into 2 arms to receive either percutaneous drainage or surgery (each arm having 25 patients). There were 9 patients with multivesicular cysts in each group. Authors did not subanalyze multivesicular cysts separately. Mean hospital stay was shorter and number of complications was lower in the percutaneous treatment group; these values were statistically significant. Of note, there were more patients with disappearance of cysts in the surgery group, although this was not statistically significant. When analyzed further, 7 multivesicular cysts in the surgery group and 8 multivesicular cysts in the percutaneous drainage group disappeared in follow-up. The authors' final word was that percutaneous drainage of uncomplicated hepatic hydatid cysts could be performed safely and resulted in the disappearance of the cyst during a period of up to 2 years. The advantages of percutaneous drainage

included shorter hospital stay and a lower complication rate, but close monitoring was necessary during percutaneous drainage for anaphylaxis and laryngeal edema.

Prousalidis *et al*<sup>23</sup> reported on their experience regarding 220 patients, 187 of whom had multivesicular cysts. They divided patients into conservative and radical surgery groups. The mortalities were in the radical surgery group, with an overall rate of 1.36% and a recurrence rate of 8.2%. The authors' conclusion was that there is a small place for percutaneous treatment for hydatid disease.

In a retrospective study by Gupta *et al*<sup>24</sup> involving 128 patients, puncture, aspiration, injection, and reaspiration (PAIR) was applied to types I and II cysts, and surgery was performed for types III and IV cysts. In this series, type III cysts were the most common type and were seen in 71 patients (55.4%). Bile leak occurred in 13 patients (13.8%), and the recurrence rate was 5.3% in the surgery group. Because the authors did not use percutaneous treatment for type III cysts, there is not any comparison reported in this study.

### Percutaneous Treatment

Since Mueller *et al*<sup>25</sup> first described the percutaneous drainage technique of a recurrent liver hydatid cyst in 1985, the treatment of liver hydatid cysts by percutaneous techniques has evolved and has proven to be safe and efficient, with data from more than 4000 PAIRs.<sup>9,10</sup> Percutaneous techniques aim to destroy the germinal layer with scolicedal agents in the classical PAIR technique, and to evacuate the entire endocyst in modified catheterization techniques.

Classical PAIR technique was stated to be safe and efficient in active unilocular cysts [types I (WHO CE 1) and II (WHO CE II)].<sup>10</sup> However, treatment of multivesicular cysts with PT is controversial because of the high recurrence and complication rates reported in different series.<sup>26–28</sup> In the study by Kabaalioglu *et al*,<sup>26</sup> the authors reported a success rate of less than half (39%) of the total type III cysts that were treated using a modified PAIR technique (short-term follow-up). In the studies by Giorgio *et al*,<sup>27,29</sup> the authors reported short- and long-term follow-up recurrence rates of 30% and 50%, respectively, for type III hydatid cysts treated with double percutaneous aspiration and injection of alcohol technique. They also stated that after retreatment of the recurrent type III hydatid cysts with multiple double percutaneous aspiration and

injection of alcohol technique, a healing rate of 93.3% was achieved. In the study by Bosanac and Lisanin,<sup>28</sup> the authors reported long-term follow-up results of their experience in percutaneous drainage technique (*i.e.*, PAIR with catheterization and povidone iodine as a scolicedal agent) in liver hydatid cysts. They found no recurrence in any type of the treated hydatid cysts, but development of secondary infection was noted in 3 patients with type III hydatid cysts. To prevent this complication, the authors used larger catheters (18–20 Fr) in the treatment of type III cysts, which enabled evacuation of all cyst contents initially. In the study by Akhan *et al*,<sup>1</sup> the authors treated type III liver hydatid cysts with a catheterization technique and destroyed all of the daughter cysts with saline except one, which required absolute alcohol for destruction. In their short-term follow-up they reported no recurrence in any type III cysts, but they also emphasized that type III hydatid cysts should be selected carefully for percutaneous treatment, and they stated that if the choice of technique is PAIR, every daughter cyst has to be punctured separately.

Complexity of the treatment of type III hydatid cysts mainly depends on how effective the destruction and evacuation of nondrainable contents of a cyst are. To cope with this difficulty, different centers reported new percutaneous drainage techniques.<sup>13,18</sup> One of these techniques was reported by Saremi and McNamara<sup>13</sup> in 32 patients, 9 of whom had multivesicular cysts. To avoid catheter occlusion by the nondrainable contents, the authors used a coaxial system and a large-bore cutting aspiration device to evacuate all cyst contents, including the laminating membranes and daughter cysts. Catheter drainage was also performed. Their major complication rate was low (3%), and short-term follow-up (mean, 25.5 months) showed no recurrence.

In a study by Schipper *et al*,<sup>14</sup> the authors reported a different PAIR method for multivesicular hydatid cysts with or without cystobiliary fistula that contained nondrainable material. The method was named as percutaneous evacuation of cyst content and consisted of the following steps: puncture of cyst and aspiration of cyst fluid, insertion of a large-bore catheter, aspiration and evacuation of cyst content using isotonic saline, cystography, injection of scolicedal agent if no cystobiliary fistula was present, external drainage of cystobiliary fistulas combined with endoprosthesis or sphincterotomy, catheter removal after com-

plete cyst collapse, and closure of the cystobiliary fistula. They reported their short-term follow-up (17.9 months) results. They reported zero recurrence, but cyst infection and cystobiliary fistulas were their main complications, and these complications prolonged hospital stay and increased morbidity, especially in patients with cystobiliary fistula. In patients with cystobiliary fistula the authors reported longer mean catheter time and hospital stay than patients without cystobiliary fistula (72.3 and 38.1 days catheter time and hospital stay versus 8.8 and 11.5 days catheter time and hospital stay, respectively). With their early follow-up results they stated that percutaneous evacuation of cyst content would not replace surgery but would offer a less invasive approach.

In another study by Mohan *et al*,<sup>15</sup> the authors reported their short-term follow-up results of the treatment experience with type III hydatid cysts by using a large-bore drainage catheter and active mechanical suction in 11 patients. After puncturing of the cyst under US guidance and obtaining an aspirate for microbiologic analysis, the authors inserted a 0.035-inch, super-stiff guide wire to dilate the tract up to 18 to 24 Fr, and inserted a large-bore sheath and stabilized it manually. First they used a suction catheter of 14-Fr size through this sheath, and cyst contents were sucked mechanically using a suction apparatus. After evacuation of all solid portions, the suction catheter was withdrawn, retaining the large-bore catheter, and a cystogram was obtained to look for any residual solid component and/or biliary fistula. When the cyst unilocularity was achieved, the large-bore sheath was exchanged with a 16- to 20-Fr large-bore catheter, which was connected to a bag for drainage. The 48-hour drain output was evaluated for any biliary ductal communication, and then absolute alcohol was instilled as a scolicial agent. Patients were discharged 48 hours later after downsizing of the catheter to 12 to 14 Fr. The authors reported zero recurrence in their short-term follow-up results, but their most common problem was biliary fistula (3 of 11 patients), which was effectively managed with prolonged catheter drainage and/or endoscopic intervention. Their mean hospital stay was 3 days in patients without complications and 4 days in patients with bilio-cystic communication.

In a study by Vuitton *et al*,<sup>16</sup> the authors treated 699 multivesicular intra-abdominal cysts with an instrument called DMFT (dilatable multifunction trocar), which was an aspiration device used to evacuate all types of cystic contents. After evacua-

tion of cyst contents, 10% to 20% saline was instilled into the cavity, and curettage was performed if necessary. Catheter was removed from the cavity after 2 to 3 days. In their short-term follow-up results they reported a recurrence rate of 2.3% *in situ* and 1% in other locations.

In a study by Akhan *et al*,<sup>17</sup> the authors treated 6 intramuscular hydatid cysts with either a catheterization with hypertonic saline and alcohol, or "modified catheterization technique," according to the type of the cyst. Of these 6 cysts, 3 were type III and were treated using the modified catheterization technique. In the modified catheterization technique, after puncturing the cyst cavity the authors aspirated up to 35% to 50% of the estimated volume and filled the cavity with hypertonic saline (20%–30% NaCl) by 5% to 10% less than the aspirated volume. Cyst puncturing, aspiration, and refilling with hypertonic saline was repeated until the complete separation of the endocyst from the pericyst was achieved (at least for 10 minutes). Then, a 14-Fr pigtail catheter was installed to thoroughly evacuate daughter cysts. The authors irrigated the cavities with hypertonic and normal saline for half an hour twice a day to evacuate all of the contents. When total emptying of the cyst cavity was shown by cystography, 95% of absolute alcohol (approximately 50% of the estimated volume) was instilled in the cavity for sclerosis. After reaspirating all of the fluid, the catheter was withdrawn. Their short-term follow-up results did not report any recurrences. Cavity infection and cellulitis were their complications; these were treated with medical therapy. Their mean hospital stay was 17.8 days (range, 1–54 days).

### Radiofrequency Ablation

Currently, radiofrequency ablation (RFA) has become an alternative treatment option for liver hydatid cysts. Although there are not any reports involving type III patients, RFA is worth mentioning in this review.

With the advance of internally cooled tip electrodes in RFA, larger volumes can be ablated safely. RFA can be performed during open/laparoscopic surgery or percutaneously for liver hydatid cysts. Successful hemostasis with fewer complications, complete elimination of the cyst, and no need for dilators, hypertonic saline, contrast injection, fluoroscopy, or catheters for external drainage are the advantages of RFA for the treatment of liver hydatid cysts.<sup>30</sup> In the study by Brunetti and Filice,<sup>31</sup> the authors reported their experience with 2 complex

liver hydatid cysts (*i.e.*, type IV) treated with RFA. They concluded that the US-guided RFA of complex cysts is feasible, safe, and simpler compared with more complex percutaneous techniques with large-bore catheters. In another study by Papaconstantinou *et al.*,<sup>32</sup> the authors treated 3 patients with liver hydatid cysts using RFA and reported no recurrence in their 2-year follow-up. They concluded that RFA-assisted pericystectomy for liver hydatid cysts provides sterile resection, eradicating both single and multiple cysts and preventing local recurrence with minimal morbidity.

Complications seen in the treatment of liver hydatid disease can also be treated with RFA. Thanos *et al.*<sup>32</sup> reported their RFA experience for the treatment of a biliocystic communication and cystocutaneous fistula after surgical treatment of liver hydatid cyst. They concluded that RFA is an effective, safe, and relatively simple and minimally invasive treatment option for bile communications.

Although promising results have been reported with limited cases in the literature, long-term results of the RFA technique are needed, with larger series enrolling patients with type III cysts.

## Conclusion

There are not enough prospective studies comparing percutaneous and surgical techniques for the treatment of type III hydatid disease of the liver. Thus, a proper meta-analysis does not seem to be possible with the studies available in the current medical literature. Nevertheless, depending on the expertise of the medical center, both techniques can be used for type III hydatid disease of the liver, with certain success and failure rates (*i.e.*, complications and recurrence). As would be expected, surgeons are in favor of radical surgery rather than conservative surgery or percutaneous techniques, but radiologists are in favor of percutaneous techniques. For a definitive judgment, a randomized study that enrolls solely patients with Gharbi type III liver hydatid disease with a similar size, number, and location of cysts should be conducted.

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