# 9 Asymptomatic Liver Hydatid Cysts: Is There a Role for Nonoperative Management?

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## Introduction

Echinococcosis, also known as hydatid disease, is a parasitic infection caused by tapeworms of the genus *Echinococcus*. It is considered by the World Health Organization (WHO) to be an important public health issue especially in endemic areas [1]. The life cycle includes a definitive host (mainly dogs) and an intermediate host (such as sheep or cattle). Humans are infected when they ingest the parasite eggs in contaminated food or water. They are considered as incidental hosts and do not play a role in the transmission of disease. Most cases occur where dogs and livestock are raised closely [2].

Human echinococcosis mainly affects the liver and lungs, although any organ can be involved. The two most common species affecting humans are *E. granulosus* and *E. multilocularis* causing cystic echinococcosis (CE) and alveolar echinococcosis (AE), respectively. CE has a global distribution including highly endemic areas such as the Middle East, North Africa, Eastern Europe, South America, China, and Central Asia. New endemic areas are being recognized as Echinococcosis is re-emerging as a health problem in certain countries [3]. The economic consequences have been estimated to reach a loss of at least one million disability-adjusted life years (DALYs) and three billion dollars in annual expenses, including treatment and loss of livestock [4]. The exact prevalence is difficult to determine with the absence of overall population surveys, especially in endemic areas. However, increased detection of new cases is currently observed with better diagnostic abilities and surveillance programs. Prevalence can reach 5–10% in endemic regions [5].

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## Clinical Manifestations

CE has a long incubation period as most infected cases are usually asymptomatic in the initial phase and clinical manifestations can appear years later. The spectrum of clinical presentations can range from completely asymptomatic to severe and even fatal disease with a reported mortality of 2–4% [6]. Signs and symptoms depend on the size and location of the cysts. They can remain asymptomatic or can present with symptoms secondary to mass effect, obstruction of nearby vessels and structures, or from complications such as cyst rupture, infections, or anaphylactic reaction. The liver is the most frequently affected organ by hydatid cyst (70% of cases). The lungs are involved in 20% of cases, and less frequently other organs such as the kidneys, spleen, muscles, and bones [7]. *E. granulosus* tends to involve a single organ (up to 90% of cases) and usually presents as a solitary cyst (up to 70% of cases). The growth rate in the liver is variable with a reported 1–5 mm growth in diameter per year. The right lobe is more frequently involved due to the nature of portal blood flow [8].

The signs and symptoms of liver CE include hepatomegaly, abdominal distention, right upper quadrant/epigastric pain, nausea, vomiting, loss of appetite, and weight loss. Growing cysts can cause portal vein and bile duct obstruction. Cyst rupture in the peritoneal cavity can lead to secondary CE. Rupture in the biliary tree can lead to secondary cholangitis, biliary obstruction by daughter cysts, portal hypertension, ascites, and abscess formation. Cyst leakage or rupture can lead to a systemic immunological response and a life-threating anaphylactic reaction induced by sensitization from a previous leakage into the systemic circulation during the life of the cyst [7].

## Diagnosis

The diagnosis of CE is based on history, clinical examination, imaging, and serologic testing. The vast majority of cases are usually found incidentally on imaging. In the case of symptomatic patients, a careful medical history should be obtained that focuses on contact with dogs or wild animals as well as living in endemic areas. Proper physical exam should be conducted, and liver imaging with or without serology testing is usually needed to confirm the diagnosis. In most cases, an ultrasound is sufficient to make the diagnosis. When in doubt, serological tests are available with variable sensitivity based on cyst location, size, and stage. Clinical laboratory tests are nonspecific in CE patients. Most will have normal serum liver enzymes tests and complete blood count tests will show eosinophilia in around 40% of patients [9]. In patients that require diagnostic aspiration, sampled fluid can be sent for microscopic examination, though this is rarely indicated. Observing protoscolices and/or free hooklets confirms the diagnosis [10].

Ultrasound has played a major historical role in the diagnosis of CE. The disease was previously only detected late as complications occur or incidentally on autopsies. It is now being detected in its earliest stages in asymptomatic affected

individuals. Ultrasound has allowed for population-based surveys of CE and has uncovered the true prevalence rates across the world. It has been the preferred imaging modality in CE due to its global availability, lack of radiation, and excellent ability to diagnose stage and follow up most abdominal cysts. In addition, field surveys are easily performed with portable ultrasound as a screening tool [11]. This led to the development of classification systems based on ultrasound findings. Gharbi et al. developed the first widely implemented CE ultrasound classification system in 1981 [12]. The WHO Informal Working Group on Echinococcosis (WHO-IWGE) improved the previous system and developed in 1995 a standardized classification that can be universally applied and replaced the plethora of previous classifications [13]. The WHO system divides the cysts into three categories: active, transitional, and inactive (Table 9.1). This classification has important implications in terms of prognosis and treatment decision-making [14]. CE1 and CE2 are active, usually fertile cysts with viable protoscoleces. CE3 is classified as transitional and is divided into CE3a (with detached endocyst) and CE3b (predominantly solid with daughter vesicles). Some studies based on magnetic resonance spectroscopy (MRS) have suggested that CE3b are usually viable and should be considered more active as compared to CE3a that tend to be more transitional and equally likely to be viable or nonviable [14]. CE4 and CE5 are considered inactive.

Cysts can also be assessed using other modalities including computed tomography (CT) and magnetic resonance imaging (MRI). MRI is superior to CT in detecting the structural components and stage-defining features of cysts that are usually seen on ultrasound. However, it has a limited role in detecting cyst wall calcification. MR cholangiopancreatography (MRCP) plays a role in the preoperative evaluation of cysto-biliary fistulas. It has been reported that it can be as sensitive as endoscopic retrograde cholangiopancreatography (ERCP) in detecting biliary obstruction as a noninvasive technique [10].

**Table 9.1** World Health Organization Informal Working Group (WHO-IWG) ultrasound classification of cystic echinococcosis

| Cyst | Status | Ultrasound features |
|---|---|---|
| CE1 | Active | Unilocular simple cyst with uniform anechoic content |
| CE2 | Active | Multivesicular multiseptated cysts<br>Daughter cysts may partly or completely fill the mother cyst |
| CE3a | Transitional | Anechoic content with detached laminated membrane<br>Floating membrane "water-lily" sign |
| CE3b | Transitional | Unilocular cyst with anechoic daughter cysts and echoic areas<br>"Complex mass" appearance |
| CE4 | Inactive | Heterogeneous hypoechoic cyst without daughter cysts<br>"Ball of wool" indicating degenerative membrane |
| CE5 | Inactive | Thick calcified wall with cone-shaped shadow |

Adapted from 2003 World Health Organization Informal Working Group (WHO-IWG) International classification of ultrasound images in cystic echinococcosis [15]

## Treatment

The available treatment options for CE include surgery, percutaneous drainage, chemotherapy, and the "watch and wait" approach. The decision to choose the best therapeutic approach should be based on the cyst stage, size and location, the available medical and surgical expertise, and adherence of patients to long-term monitoring. The WHO has issued recommendations on the best treatment approach based on the cyst stage (Table 9.2). However, despite the WHO attempts, a consensus is still lacking on a standardized disease management for CE. The best individual treatment option for patients is still controversial as the evidence supporting any of the four available modalities from solid clinical studies is limited. The reasons are mainly due to the chronicity of the disease requiring years of follow-up on the effectiveness of treatment, the relatively small number of patients presenting with homogenous conditions to allow adequate comparison, and finally the heterogeneity of studies in the literature that hinders appropriate comparison [16]. The current evidence is based on small randomized trials, cohort studies, and case series with few controlled studies to compare the four treatment options [17].

Historically, surgery has been considered the only definitive curative option for CE. However curative surgery is not always feasible and has considerable risks of morbidity and relapse. The overall recurrence rate is around 6%, and mortality can range between 0.5% and 4% depending on the type of surgery and the available surgical experience and medical facility [18]. In addition, surgery cannot be applied in cases where general contraindications for surgery apply such as pregnancy and very small or unreachable cysts. PAIR (puncture-aspiration-injection-reaspiration) procedure and laparoscopic surgical approach have been introduced as minimally invasive techniques, but morbidity, recurrence, and mortality rates, albeit low, should be considered. This has paved the way for implementing less invasive

**Table 9.2** Treatment of uncomplicated CE stratified by cyst stage

| Cyst | Surgery | Percutaneous | Medical therapy | Watch and wait | Expert consensus recommendation |
|---|---|---|---|---|---|
| CE1 | | ✓ | ✓ | | < 5 cm ABZ<br>> 5 cm PAIR + ABZ |
| CE2 | ✓ | ✓ | ✓ | | Other PT + ABZ<br>Or surgery + ABZ |
| CE3a | | ✓ | ✓ | | < 5 cm ABZ<br>> 5 cm PAIR + ABZ |
| CE3b | ✓ | ✓ | ✓ | | Other PT + ABZ<br>Or surgery + ABZ |
| CE4 | | | | ✓ | |
| CE5 | | | | ✓ | |

Adapted and reprinted from 2010 WHO Informal Working Group on Echinococcosis (WHO-IWGE) stage-specific treatment approach [13] with permission from Elsevier
Abbreviations: *ABZ* albendazole, *PAIR* puncture, aspiration, injection, reaspiration, *Other PT* other percutaneous procedure

treatment strategies such as the "wait and observe" approach and the option of medical therapy.

Asymptomatic hydatid cyst can be defined as the incidental finding of a cyst in patients who do not have any symptoms or have symptoms not attributed to CE. The diagnosis can be made during ultrasound or other imaging techniques for other abdominal conditions or during mass surveys for CE in endemic areas [18]. Mass ultrasound surveys allowed a better understanding of the natural course of the disease and demonstrated that the vast majority of cases are asymptomatic at diagnosis. The current practice is that all asymptomatic hydatid cysts must be subjected to a type of treatment. The rationale behind such belief is the fear for any future complications that can happen if the cyst is left untreated. This practice, however, is not supported by strong evidence [19]. The major risk for any hepatic hydatid cyst is the possibility of rupture and leakage which can lead to serious complications such as anaphylactic shock and seeding to nearby structures. The host's defenses, however, are capable of containing the disease leading to cyst calcification which can remain dormant and inactive for years. The questions remain if asymptomatic hydatid cysts should be treated, what the best treatment approach would be, and if there is a role for nonoperative management.

## The "Watch and Wait" Approach

The "watch and wait" approach corresponds to regular ultrasound follow-up on an asymptomatic uncomplicated hydatid cyst without any further interventions. According to the WHO-IWG guidelines, it is the current recommended approach for CE4 and CE5 inactive cysts. This recommendation was based on long-term follow-up of asymptomatic hydatid cysts, and it was shown that the majority of patients remain symptom-free for years with a low risk for complications. The widespread use of ultrasound and the incidental detection of asymptomatic hydatid cysts lead to a controversy on the best way to manage them. The current evidence to support a "watch and wait" approach is still based on a limited number of studies with a small number of patients [18]. In recent years, experience at some referral centers showed promising results to support a watchful approach to asymptomatic cysts. A study at a referral center in Italy using an ultrasound-based follow-up of at least 2 years on 53 patients with 66 inactive cysts (CE4 and CE5) showed that 52 (98.1%) patients remained stable with no complications and only one patient (1.9%) had a documented reactivation [20]. Such an approach would have promising socioeconomic implications in managing large numbers of asymptomatic carriers, especially in endemic areas. Adapting this strategy requires close follow-up with ultrasound monitoring to avoid unnecessary treatment and/or the risk of any therapeutic intervention. A prospective survey was carried in an endemic area on 127 patients with 137 liver cysts with a median follow-up of 6 years. It showed that while 81% of the cysts have favorable outcomes, 5.8% of the cysts developed complications, and the size increased in 13% [19]. This highlights the importance of close monitoring as experts recommend a minimum

follow-up of 5 years to confirm the stability of inactive cysts [21]. Another study on the "watch and wait" showed that this approach is also feasible on CE3b cysts [16]. To note, cysts that reached inactivity by means of medical treatment have a higher relapse rate (up to 50% within 2 years) as compared to naturally inactivated cysts and should be followed up more closely [21]. The exact biological mechanism to explain the process of inactivation or reactivation remains unknown. Clinical experiences in recent years have suggested that a conservative approach for selected asymptomatic hydatid cysts is reasonable. This was based on the observation that a good proportion of cysts becomes calcified and inactivated without treatment, and asymptomatic cysts that do not affect nearby structures seem to stabilize and remain quiescent. However, it is important to stress on the necessity of an adequate and regular follow-up using ultrasound in addition to a good doctor-patient relationship when the "watch and wait" approach is selected. Currently, this option should be offered to selected patients with CE4 and CE5 cysts. The evidence for this appealing approach is still far from ideal and deserves better evaluation to specify the indications and limitations.

## Medical Therapy

The current available options for medical therapy are the benzimidazoles (albendazole and mebendazole) and praziquantel. The introduction of benzimidazole as a main treatment option has been a landmark in the management of CE. Heath et al. were the first to establish a larvicidal effect of mebendazole (MBZ) in animal models in 1975 [22]. After that, mebendazole was introduced in small clinical trials, and Bekhti et al. reported the first successful results of treating CE with MBZ in 1977 [23]. High doses were required to achieve a pharmacological effect. Albendazole (ABZ) was later introduced, and it was shown that its metabolite albendazole sulfoxide has its own active larvicidal effect enabling more practical dosing regimens [24]. They both inhibit microtubules formation, with impairment of glucose absorption through the wall of the germinative cell layer of the larva. This leads to glycogen depletion and degeneration of the endoplasmic reticulum and mitochondria of the germinal cells leading to an increase in lysosomes and eventually cellular death [24]. The WHO guidelines of 1996 have played a key role in promoting the role of benzimidazole as an important therapeutic option in the management of CE. This expanded the design and conduction of clinical trials to assess the activity of MBZ and ABZ against the parasitic disease.

Praziquantel (PZQ) is an isoquinoline discovered in the 1980s to have antiparasitic activity against CE. It was introduced as a more tolerated and less toxic therapeutic agent than the benzimidazoles. It increases the permeability of the parasite's cell membrane to calcium leading to strong contraction and paralysis of its musculature resulting in detachment from the host tissue [24]. PZQ was demonstrated to have an active scolicidal activity in vitro and in animal models. Few clinical studies, however, have analyzed its use in hydatid disease as a monotherapy or in combination with benzimidazoles.

## The Role of Medical Therapy

Currently, the role of medical therapy in CE is highlighted in the WHO recommendations. The indications and the suggested medical therapy are summarized in Tables 9.3 and 9.4.

The value of medical agents in CE can be appreciated as a nonoperative, noninvasive treatment option. As previously discussed, complete curative surgery is not always feasible. There is a risk of relapse when choosing the options of surgery or PAIR, as well as a small but significant mortality risk. Antiparasitic drugs can be used on patients of any age and are not limited by the status of the patient as compared to surgery or PAIR. The role of medical treatment was mainly recommended for inoperable patients and patients with multiple organ involvement. Over the past decade, several studies have emphasized the role of chemotherapy as an alternative to operative management in uncomplicated cysts, increasing the use of medical drug therapy over the years. As with CE in general, the evidence to support chemotherapy is limited and based on a few randomized trials and case series with abundant heterogeneity among studies. Randomized studies have shown the superiority of albendazole when compared to mebendazole or placebo [25]. Although poorly absorbed from the gastrointestinal tract, ABZ reaches higher plasma concentration as compared to MBZ (15–49 times higher); thus lower daily doses are required. ABZ is metabolized in the liver, and the primary metabolite has also anthelminthic activity [26].

Benzimidazole use is expected to cure around 30% of patients. Another 30 to 50% will show signs of cyst degeneration and/or cyst reduction. However, 20 to 30% will show no changes with chemotherapy after 12 months of follow-up [18]. Franchi et al. [25] studied the effect of benzimidazoles on 929 hydatid cysts (from 448 patients) that were followed up for at least 1 year. They showed that 74% of the cysts treated with MBZ and ABZ had detectable degenerative changes, whereas 26% remained unchanged. Those changes were more frequent in the ABZ-treated than in MBZ-treated cysts (82.2% vs. 56.1%). Stojkovic et al. [27] reviewed data collected from 711 patients with 1308 cysts from 6 centers. They showed that after 1–2 years of benzimidazole therapy, 50–75% of active CE1 cysts can be classified as inactive or disappeared. CE2 and CE3 cysts were found to be less responsive (30% to 55%). They also observed multiple

**Table 9.3** Indications for antiparasitic drug treatment in CE according to WHO-IWGE

| |
|---|
| Inoperable patients with liver CE |
| Patients with multiple cysts in two or more organs or peritoneal cysts |
| Small (<5 cm) CE1 and CE3a cysts |
| Prevention of recurrence following surgery or PAIR |

Adapted from 2010 WHO Informal Working Group on Echinococcosis (WHO-IWGE) stage-specific treatment approach [13]
Abbreviations: *CE* cystic echinococcosis, *PAIR* puncture, aspiration, injection, reaspiration

**Table 9.4** Suggested medical therapy protocol for cystic echinococcosis

| Drug therapy | Drug | Dose | Duration |
|---|---|---|---|
| Definitive medical therapy | Albendazole | 10 to 15 mg/kg/day (up to 400 mg twice daily) | Continuous for 3 to 6 months |
| | Mebendazole | 40 to 50 mg/kg/day (three times daily) | Continuous for 3 to 6 months |
| | Praziquantel | 40 mg/kg once weekly | In combination with albendazole for 3 to 6 months |
| Uncomplicated perioperative prophylaxis | Albendazole | 10 to 15 mg/kg/day (up to 400 mg twice daily) | 4 to 30 days preoperatively and for at least 1 month postoperatively |
| | Mebendazole | 40 to 50 mg/kg/day (three times daily) | 4 to 30 days preoperatively and for at least 3 months postoperatively |
| Complicated perioperative prophylaxis | Albendazole | 10 to 15 mg/kg/day (up to 400 mg twice daily) | Recommend extending the postoperative course for 3 to 6 months |
| | Mebendazole | 40 to 50 mg/kg/day (three times daily) | Recommend extending the postoperative course for 3 to 6 months |

relapses with 25% of the cysts that initially responded reverting to active status within the first 2 years.

Some data showed that clinical and ultrasound improvement (> 25% reduction in cyst size, membrane separation, or cyst calcification) will increase with longer duration of therapy [7]. Previously, it was debatable whether cysts were inactivated by benzimidazoles or they spontaneously progressed to calcification, questioning the need for treatment. To study the effect of treatment, 80% of cysts in patients who were treated with albendazole in one study showed evidence of changes as compared to 13% of cysts in patients who received no treatment [28]. A surgical-based study demonstrated that pretreating with albendazole affects the cysts' viability and infectivity during surgical evaluation in mice models [29].

As suggested by the WHO recommendations, medical therapy is more effective for small CE1 and CE3a cysts. Benzimidazoles are less effective against CE2 and CE3b. Chemotherapy is also more effective among young patients. The outcome of treatment is also related to the size and age of the parasite. "Recent" small cysts with thin walls, as well as secondary cysts, are mostly susceptible to medical therapy as compared to "old" cysts with thick or calcified walls. Patients who experience relapse are sensitive to retreatment in the majority of cases [13].

Praziquantel is mentioned in a few studies in the literature to play a role for perioperative prophylaxis and in combination with albendazole for medical treatment.

It was introduced as a more tolerated, less toxic, and better-absorbed agent. A study suggested that a combination of PZQ plus ABZ for 1 month prior to surgery had a higher efficacy as compared to ABZ monotherapy [30]. While ABZ is potentially teratogenic, PZQ is safe in pregnancy. The currently available evidence is insufficient to guide the use of PZQ. Although it is ineffective as monotherapy, some evidence exists for a role of PZQ and ABZ combination [14].

Benzimidazoles have also an essential role to play when it comes to operative therapeutic options. Treatment outcomes were shown to be better when surgery or PAIR is combined with pre- and/or postprocedure benzimidazole therapy [17]. Blidik et al. [31], Gil-Grande et al. [29], Khuroo et al. [32], and Shams-UI-Bari et al. [33] studied this aspect of medical therapy and showed the significance of perioperative ABZ. They assessed the outcome of ABZ plus operative management as compared to operative management alone by analyzing the viability of scolex as an endpoint. The number of nonviable scolices was higher in the combination of ABZ and procedure as compared to operative procedure alone.

## Risks and Contraindications

Benzimidazoles are contraindicated in early pregnancy and in cysts at risk of rupture (such as large or superficially located cysts). ABZ was found to be teratogenic in animal models. Although the risk of exposure in early human pregnancy is low and no abnormal birth outcomes have been recorded in humans following ABZ exposure, ABZ should be avoided in pregnancy unless the benefits significantly outweigh the potential risks [13]. Benzimidazoles should be used with caution in patients with chronic liver diseases and should be avoided in patients with bone marrow depression. Benzimidazoles monotherapy is ineffective in large cysts (>10 cm) as their effect is slow in large volumes of fluid. Calcified inactive cysts should not be treated unless they become complicated [13].

## Dosage and Duration

Albendazole and mebendazole are water-soluble compounds and poorly absorbed in the gastrointestinal tract. Gastric pH and intraluminal degradation contribute to a further decrease in bioavailability. Administering PZQ with ABZ can result in a four to fivefold increase in the bioavailability of ABZ [34]. To improve absorption, benzimidazoles should be taken with fatty meals. This can lead to a four to eightfold improvement in the bioavailability of ABZ and MBZ.

Albendazole is given orally at a dose of 10 to 15 mg/kg/day in two divided doses with a fatty meal to a maximum of 400 mg twice daily. It should be administered continuously without the previously recommended cyclic treatment and weekly interruption. Long-term toxicity data was not available when ABZ was first introduced and cyclic treatment was recommended. The continuous

treatment approach was followed in several centers for years now, with no evidence of any increased adverse events [35]. In cases where ABZ is not tolerated or not available, mebendazole can be used as an alternative. It is given orally at a dose of 40 to 50 mg/kg/day in three divided doses with a fatty meal. Higher doses of MBZ are required to reach a similar drug concentration level as ABZ. Praziquantel is given in a dose of 40 mg/kg once weekly in combination with ABZ [13]. The optimal duration of medical therapy with benzimidazoles has not been formally assessed. Currently, it is recommended to give ABZ for at least 3–6 months when given as a primary treatment option. Studies on large number of patients suggested an increased evidence for clinical and/or radiological improvement when longer treatment duration is applied. However, the proportion of patients with cure, defined as calcified or disappeared cysts, did not change [36].

When ABZ is given as a perioperative prophylaxis, it is recommended to start it 1 month before surgery or percutaneous procedure and to be continued for up to 1–3 months. In case of complicated cases, some recommend continuing ABZ for 3–6 months postprocedure [37]. As discussed previously, ABZ treatment before surgery leads to a higher rate of nonviable cysts at the time of surgery. A randomized controlled trial showed that patients who received ABZ for 12 weeks prior and 12 weeks after surgery had no recurrences as compared to 17% recurrence in patients who received no medical therapy [33].

## Adverse Events and Monitoring

The safety profile of benzimidazole is generally reassuring. Although the evidence is limited, adverse events are seen. Clinically, they can cause alopecia in 1–5% of cases. Gastrointestinal symptoms have been reported but are rarely severe to consider stopping treatment. Benzimidazoles have the potential to cause bone marrow suppression with reported cases of aplastic anemia and thrombocytopenia. Regular monitoring with complete blood count is required. As previously mentioned, treatment with benzimidazoles should be avoided during pregnancy as embryotoxicity and teratogenicity have been reported in animal models [38]. One of the best-known long-term effects of benzimidazoles is the rise in liver enzymes. It was reported in up to 20% of cases undergoing treatment [39]. The effect is usually limited, and liver enzymes normalize after treatment cessation. Although there is a possibility for drug-induced hepatocellular damage, it is believed that the rise in enzymes is due to the damage to the parasite and the local release of antigens by the antiparasitic drugs. Elevated liver transaminases are not seen, for example, when benzimidazoles are used to treat extra-hepatic echinococcal cysts or neurocysticercosis [39]. A retrospective study on the effect of benzimidazoles on liver function showed that the majority (85%) of elevated liver enzymes cases had liver cysts with associated structural changes [40]. Currently, it is recommended to monitor liver enzymes while on treatment, and unless changes are progressive, treatment can be continued. As previously discussed, monitoring

should be individualized as no clear evidence-based approach is currently available. It depends on the available resources and patient characteristics. Ultrasound follow-up (alternatively CT or MRI can also be used) at intervals of 3–6 months should be applied until stability is reached. After that, yearly ultrasound monitoring is advised to screen for recurrence. If stable, screening can be discontinued after 3–5 years.

## Conclusion

In conclusion, the management of liver hydatid cysts remains controversial. The approach to treatment should follow the stage-specific WHO recommendations. It is not clear if asymptomatic uncomplicated cysts should be subjected to a specific treatment protocol. The majority of hydatid cysts have a favorable outcome and do not always require invasive surgical or percutaneous intervention. Considering the operative morbidity and mortality risk as well as the risk of relapse, two nonoperative strategies should be recognized. The "watch and wait" approach is a safe noninvasive option that should be considered in inactive uncomplicated cysts. The current evidence supports its use on WHO stages CE4 and CE5 cysts. This approach should be coupled with a good doctor-patient relationship and regular ultrasound monitoring. Antiparasitic drug therapy has emerged as another important noninvasive treatment option. Enough experience in treating centers has allowed the regular implementation of benzimidazole-based therapy into current practice. Small cysts less than 5 cm (WHO stages CE1 and CE3a) can be treated with albendazole only with an expected favorable outcome in the majority of cases. An important limitation of the current treatment recommendations should be mentioned. While it is safe to assume that the majority of affected individuals are usually asymptomatic, most of the studies on medical therapy do not specify whether the treated patients are asymptomatic or not. Patients should be informed about the different therapeutic options and the risks and benefits of each approach. Treatment of CE should be individualized by taking into account the patient characteristics as well as the available resources and expertise. Finally, randomized clinical studies are needed to compare the different treatment options to provide evidence-based guidance for treatment decision-making.

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