



Turkish HPB Surgery Association consensus report on hepatic cystic *Echinococcosis* (HCE)

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ABSTRACT

Objective: Cystic *Echinococcosis* (CE) is one of the important problems of the Eurasian region. We aimed to prepare a consensus report in order to update the treatment approaches of this disease. This study was conducted by Turkish HPB Surgery Association.

Material and Methods: This study was conducted with the modified Delphi model. For this purpose, we conducted a three-stage consensus-building approach.

Results: Six topics, including diagnosis, medical treatment, percutaneous treatment, surgical treatment, management of complications and posttreatment follow-up and recurrences in HCE were discussed.

Conclusion: The expert panel made recommendations for every topic.

Keywords: Liver, cystic echinococcosis, expert consensus

INTRODUCTION

Cystic *Echinococcosis* (CE) is one of the important problems of the Eurasian region that has been waiting for a solution for years. It is basically a public health issue. There has been an increase in the number of clinical cases in recent years. Despite the expansion of the health system in Turkey in recent years and the provision of health services to more people and the improvement of sanitation services, there is an increase in CE cases. This increase in the number of cases is attributed to the early detection of most asymptomatic cases. One other important reason of the increase of CE cases is that Turkey hosts too many immigrants from neighboring countries. While CE of the liver (Hepatic CE-HCE) was treated only in some centers where advanced surgical treatment was performed years ago, it can now be treated in many centers in Turkey thanks to developing facilities, medical technologies and trained personnel. Many centers have renewed their infrastructure to treat this disease with the most up-to-date approaches. Therefore, we decided to prepare a consensus report in order to update the treatment approaches of these centers and to assist in the standardization between centers. This study was conducted by Turkish HPB Surgery Association.

MATERIAL and METHODS

This study was conducted with the modified Delphi model. For this purpose, we conducted a three-stage consensus-building approach: (1) identifying the list of topics for inclusion based on literature review and the study team's experience; (2) a two-round modified Delphi exercise with a panel of experts to establish consensus

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on the importance of these features; and (3) a small in-person consensus group meeting to create options-recommendations about every topic included to the study.

Panel Selection

Turkish Association of HPB Surgery executive committee selected 34 specialists as committee members for the development of this consensus report. These specialists were selected according to their literature reports, number of ongoing cases, and clinical and surgical experience about HCE. Twelve of them were selected as authors. Authors addressed six topics, including diagnosis, medical treatment, percutaneous treatment, surgical treatment, management of complications and posttreatment follow-up and recurrences in HCE. These topics were selected according to the literature. An ongoing debate was the key point for selection of the topics. Two experts for every topic were assigned and they have performed a literature review and recommendations.

The remaining 22 specialists were assigned as expert panel members for the development of further Delphi processes. The literature review and recommendations created by the authors were evaluated and criticized by this expert panel. After the first and second Delphi rounds, a third in-person meeting was performed and the final options for every topic were created. Levels of recommendations given in this document follow the "Guide to Practice Guidelines" of the Infectious Diseases Society of America (1) (Table 1).

Exclusion/Inclusion Criteria

A literature search for every topic covering the same dates was made. For this purpose, a search was performed including the Pubmed database for English publications and the TR Index-Ulakbim database for Turkish publications. Keywords for Pubmed search were "*Echinococcal cysts, hydatid cysts, hydatid disease, cystic Echinococcosis, hydatidosis, hydatid*" and for Turkish literature search in the TR Index-Ulakbim database "*kist hidatik*" (hydatid cyst). Additional keywords were used for every single

topic according the choices of the authors. Preliminary search results were filtered for human studies, original reports, reviews and meta-analyses and studies reporting liver involvement. Animal studies, case reports and articles reporting only extra-hepatic involvement were excluded.

RESULTS

All authors created their own search for their topic. After they performed their review, they set recommendations for each topic. These reviews and recommendations were sent to the expert panel. The expert panel reviewed every recommendation and sent the results back to the authors. This was the first round of the modified Delphi procedure. The authors revised the recommendations according to the reviews and votes of the panel and sent them to the expert panel for a second round. After the second-round results were collected, an in-person meeting was performed for the establishment of final recommendations. Expert panel voted every recommendation in every round. Recommendations that were accepted below 50% of the expert panel were withdrawn. Recommendations that were accepted between 50-80% of the expert panel were revised. Recommendations that were accepted by over 80% of the panel were assigned as recommendation.

The reviews and recommendations for every topic are summarized below;

Chapter 1. Diagnosis of HCE

A literature search on the subject, covering the dates 01.01.1900-09.12.2018, was carried out using the Pubmed database for English publications and the TR Index-Ulakbim database for Turkish publications. Pubmed search with the keywords "*Echinococcal cysts, hydatid cysts, hydatid disease, cystic Echinococcosis, hydatidosis, hydatid, classification, diagnosis*" revealed a total of 6599 articles. Of these, 5466 were in English, and 3697 were on humans. After excluding 1858 case reports, 1839 articles were included in the preliminary evaluation. Of these 1839 articles, 53 were clinical

Table 1. Infectious Diseases Society of America grading system (strength of recommendation and quality of evidence)

Strength of recommendation	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
D	Moderate evidence to support a recommendation against use
E	Good evidence to support recommendation against use
Quality of evidence	
I	Evidence from ≥ 1 properly randomized, controlled trial
II	Evidence from ≥ 1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies; from multiple time series; or from dramatic results from uncontrolled experiments
III	Evidence from recommendations of respected authorities, based on clinical experience, descriptive studies, or reports of committees

trials (20 controlled, 16 randomized controlled) and 394 were Reviews. After excluding articles that did not contain liver involvement, did not relate to the diagnosis of cystic *Echinococcosis* or were not adequately included in the diagnosis, the study evaluated 15 clinical trial articles and 61 reviews.

A total of 503 articles were found in the Turkish literature search using the keyword “kist hidatik” (hydatid cyst) in the TR Index-Ulakbim database. Of these, 477 were related to medicine. After excluding the articles that did not include liver involvement, were not related to the diagnosis of cystic *Echinococcosis*, or insufficiently related to the diagnosis, a total of 26 Turkish articles were evaluated within the scope of the study.

1.1. Clinical findings

The diagnosis of CE is based on clinical findings, imaging modalities, and serological examinations. Direct evaluation of the cyst content aspirated by percutaneous puncture or obtained by surgery with microscopic, histological, and molecular methods can also confirm the diagnosis (2). Up to 60% of the patients are asymptomatic (3). Symptoms and signs that arise with the growth of the cyst over time are nonspecific. The most common symptom is abdominal pain in liver involvement and cough in lung involvement (4,5). Clinical findings depend on the complications that may occur depending on the localization and size of the cyst. Complications such as direct compression of the cyst, inflammatory reaction, distortion of neighboring organs and structures, rupture of the bile duct, pleural space, bronchial tree or peritoneal cavity, infection of the cyst, cholangitis, and pancreatitis may occur. Rupture of the cyst can cause allergic reactions. In the clinical evaluation of patients, it should also be questioned whether they are exposed to the risk of CE (living in an endemic area or having migrated from an endemic area, having a dog, or being in contact with wildlife) (6-8)

1.2. Ultrasound

Radiological imaging is one of the key components in the diagnosis of HCE. US is the primary imaging modality as it can detect pathognomonic findings for diagnosis, has a sensitivity of 88-98% and a specificity of 93-100%, is easily accessible, and is radiation-free (9,10). US has also been used in the classification of HCE, and the standardized classification proposed by the WHO Informal Working Group on *Echinococcosis* (WHO-IWGE) in 2003 is still used (11). US also plays an important role in interventional treatment methods (9,12). It can also be used in community health screenings with its portable feature, high sensitivity, and specificity (13).

1.3. Classification of HCE

In uncomplicated HCE cases, current treatment recommendations follow a stage-specific approach. The cyst type is the most critical determinant of the treatment method to be selected (11,14).

1.4. Role of calcification in HCE classification

Hosch W et al. have followed up 78 CE patients treated with albendazole and a watch-and-wait approach (15). US and, in some cases, additional CT imaging was used in the follow-up. A total of 137 abdominal cysts (116 in the liver) were present in the patients, and calcification was detected in the cyst wall and/or cyst content in 67 *Echinococcal* cysts (48.9% of all cysts). Of the 67 calcified cysts, only 23 were compatible with CE 5 and 18 with CE 4 (46.2% of all CE 4 cysts). In the cyst content-based classification of the remaining 26 patients, one CE 1 (7.1% of all CE 1 cysts), 8 CE 2 (47.1% of all CE 2 cysts), and 17 CE 3 (40.5% of all CE 3 cysts) were detected. During follow-up, progressive involution was observed in two CE 2 cysts, 7 CE 3 cysts, and 5 CE 4 cysts, while a poor course was observed in the form of re-fluid collection in the main cyst and/or new daughter cysts in 5 CE 3 cysts.

1.5. CT and MR imaging

CT and MR imaging are indicated for the subdiaphragmatic location of the cyst, metastatic disease, complicated cyst (abscess, cystobiliary fistula), and preoperative evaluation (2). Obesity, intestinal gases, and postoperative changes are other conditions in which the US is inadequate, and CT and MR imaging are indicated. CT and MR are also used in cases with no pathognomonic findings on US, and differential diagnosis is required (9). While MR imaging (especially T2-weighted sequences) shows very good compatibility with the US in CE 1-CE 4 types, it has shortcomings in identifying the details of the cyst wall in CE 5. On the other hand, CT shows poor performance in CE 1-CE 4 types, while it performs satisfactorily in CE 5 compared to US (16). MRI is also better than CT in visualizing the liquid areas within the matrix structure of the cyst and is preferred to CT whenever possible (17).

1.6. Serological tests

Due to limitations in sensitivity and specificity, serological tests often yield up to 30% false-negative and 25% false-positive results. Therefore, the role of serology in the diagnosis of CE is limited to supporting or confirming the diagnosis rather than being a diagnostic test. Many factors that affect the performance of serological tests have been identified. The most important factors are; the measurement techniques used and the antigens used within, the patient's immune status, the organ involved, the stage, size and number of the cyst, and previous treatment and complications (3,6,9,18). Primary serological tests are:

- ELISA (enzyme-linked immunosorbent assay).
- IHA (indirect hemagglutination)
- LA (latex agglutination)
- IFA (immunofluorescence assay)
- IEP (immunoelectrophoresis) tests.

The generally accepted sensitivity of primary serological tests is 85-98% for liver cysts, 50-60% for lung cysts, and 90-100% for multi-organ involvement (2). It is recommended to use at least two of these primary tests together to improve the performance of serological tests (2,3,19,20). Another recommendation for performance is to use the WB (Western Blot) test as a secondary confirmatory test due to its high specificity of up to 100% (2,6,21-24). It is possible to find different results for each technique in the literature due to the aforementioned factors, especially the type of antigen used in the test (18,25-29).

Detection of antigens in the serum is not preferred in the serological diagnosis of CE due to its low sensitivity of 35% despite its high specificity, and most of the tests are based on the detection of antibodies against antigens in the serum (18). The most commonly used antigen source for this purpose in tests is hydatid cyst fluid (HCS). Overall, HCS provides higher sensitivity (80-99% sensitivity and 60-97% specificity), while tests in which the purified main antigenic structures of Antigen 5 (Ag5) and Antigen B (AgB) or their smaller subunits or their recombinant forms and synthetic peptides are used as antigens provide higher specificity (33-93% sensitivity and 80-100% specificity) (27-30). A double-blind, randomized study on this subject compared the diagnostic performances of HCS, natural AgB, two recombinant AgB subunits, an AgB-derived synthetic peptide, and recombinant cytosolic malate dehydrogenase (EgMDH) in the ELISA method (31). Equivalent diagnostic accuracy was found with HCS, AgB, and AgB8/1 subunit, respectively, of 81.4%, 81.3%, and 81.9%, while synthetic peptide, AgB8/2 subunit, and EgMDH yielded an accuracy of 76.8%, 69.1%, and 66.8%, respectively, and HCS was recommended as the antigen source for the primary serological test (31).

When serological tests were evaluated according to the CE stage, 30-58% false negatives were found in CE 1, 50-87% in CE 4 and CE 5, while this rate was lower in CE 2 and CE 3 with 5-20% (32). False-positive results may be associated with cross-reactions in other parasitic diseases such as alveolar *Echinococcus*, cysticercosis, fascioliasis, and filariasis, as well as malignancy and chronic immune disorders (6).

1.7. Direct diagnostic methods

In cases where diagnosis cannot be made by clinical, radiological, and serological methods, differential diagnosis can be achieved by direct examination of the aspirated cyst content. Diagnosis can be made by direct microscopic examination by detecting protoscolex and/or free hooks. Histological examination of laminar and germinative membranes is also diagnostic (2,6,9). Another direct diagnostic method is the detection of nucleic acids specific for *E. granulosus* with molecular biology methods such as Southern blot and PCR (Polymerase Chain Reaction) (2,33). Despite positive experiences with PAIR, diagnostic aspiration and biopsy remain controversial. Anaphylaxis, sec-

ondary dissemination, and the risk of tumor seeding during the differential diagnosis in malignant cases are stated as important drawbacks of the procedure (34-36).

1.8. Differential diagnosis of HCE and HAE

The differential diagnosis of HCE and HAE is usually made radiologically. In cases where this is impossible, serological tests should be used. The AgB a 8kDa subunit examined for HCE is also common to HAE, and the WB test performed is positive in 92% of HCE cases and 79% of HAE cases. On the other hand, serological tests Em2-ELISA, Em2^{plus}-ELISA, Em10-ELISA, Em18-ELISA, and Em18-Immunoblot used for HAE have high sensitivity and specificity (90-100% and 95-100%, respectively). In cases where a differential diagnosis cannot be achieved with radiological and serological methods, direct diagnostic methods (direct microscopic examination, histological examination, and PCR) can be used (2,6,9,33,37-39).

Table 2 demonstrates case definition of CE in the article "Expert consensus for the diagnosis and treatment of cystic and alveolar *Echinococcus* in humans" published by WHO-IWGE in 2010 (2).

In light of the above literature, the following recommendations were formed;

Recommendation 1.1: Most patients are asymptomatic and diagnosed incidentally in radiological examinations performed for other reasons. Since clinical findings are non-specific, HCE should be considered, especially in endemic areas, and radiological imaging should be performed in suspected cases.

Recommendation 1.2: US is the first imaging modality of choice in the diagnosis of HCE. It is diagnostic in cases with pathognomonic signs (CE 1, CE 2, CE 3a, and CE 3b). In uncertain cases, additional diagnostic methods are needed.

Recommendation 1.3: Classification should also be made during the diagnosis of HCE; our treatment approach will be determined accordingly.

Recommendation 1.4: Calcification is also possible in CE 1, CE 2, and CE 3 cysts. Calcification is not reliable for predicting the activity of the cyst. Viability assessment is more reliable with evaluating cyst content rather than wall calcification.

Recommendation 1.5: CT and/or MR imaging are indicated in cases where the patient is obese or has excess intestinal gases, in cases of subdiaphragmatic localization of the cyst or metastatic disease, in cases requiring preoperative and postoperative evaluation, in cases without pathognomonic findings in the US that require differential diagnosis, and in cases of complicated HCE. When CT or MR imaging is required to diagnose HCE, MR has a superior imaging potential and is preferred to CT.

Recommendation 1.6: Negative serological tests do not exclude diagnosis. False negativity may occur due to lack of standardization of the antigens used in serological tests and labo-

Table 2. Case definition of CE in the article “Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans” published by WHO-IWGE in 2010

<p>A. Clinical criteria</p> <p>At least one of the following three:</p> <ol style="list-style-type: none"> 1.A slowly growing or static cystic mass(es) (signs and symptoms vary with cyst location, size, type and number) diagnosed by imaging techniques. 2. Anaphylactic reactions due to ruptured or leaking cysts. 3. Incidental finding of a cyst by imaging techniques in asymptomatic carriers or detected by screening strategies. 	<p>B. Diagnostic criteria</p> <ol style="list-style-type: none"> 1. Typical organ lesion(s) detected by imaging techniques (e.g. US, CT-scan, plain film radiography, MR imaging) 2. Specific serum antibodies assessed by high-sensitivity serological tests, confirmed by a separate high specificity serological test 3.Histopathology or parasitology compatible with cystic echinococcosis (e.g. direct visualization of the protoscolex or hooklets in cyst fluid) 4.Detection of pathognomonic macroscopic morphology of cyst(s) in surgical specimens. 	<p>C. Possible versus probable versus confirmed case</p> <p>Possible case. Any patient with a clinical or epidemiological history, and imaging findings or serology positive for CE</p> <p>Probable case. Any patient with the combination of clinical history, epidemiological history, imaging findings and serology positive for CE on two tests.</p> <p>Confirmed case. The above, plus</p> <p>either</p> <p>(1) demonstration of protoscolexes or their components, using direct microscopy or molecular biology, in the cyst contents aspirated by percutaneous puncture or at surgery,</p> <p>or</p> <p>(2) changes in US appearance, e. g. Detachment of the endocyst in a CE1 cyst, thus moving to a CE3a stage, or solidification of a CE2 or CE3b, thus changing to a CE4 stage, after administration of ABZ (at least 3 months) or spontaneous.</p>
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ratories, the patient’s immune status, the organ, type and size of the cyst, etc. A single primary serological test is unreliable to exclude false positives; at least two primary tests should be considered together. If the two primary tests are not positive together, results should be confirmed with WB.

Recommendation 1.7: In cases where US findings are compatible with HCE but not pathognomonic, additional radiological imaging should be performed together with serological tests.

Recommendation 1.8: In cases that cannot be diagnosed by clinical, radiological, and serological methods, a direct diagnostic approach with aspiration may rarely be required for differential diagnosis. In the differential diagnosis, the application should be limited due to the risk of anaphylaxis, secondary dissemination, and tumor seeding in cases of malignancy.

Recommendation 1.9: The “CE case definition” section in the article “Expert consensus for the diagnosis and treatment of cystic and alveolar *Echinococcosis* in humans” published by WHO-IWGE in 2010 is suitable for clinical applications in the light of current information (Table 2).

Recommendation 1.10: The differential diagnosis of HCE and HAE is usually made radiologically. In cases where this is impossible, specific serological tests should be performed for HAE. In cases where a differential diagnosis cannot be achieved with

radiological and serological methods, cyst aspiration and/or FNAB can be performed for direct diagnosis (direct microscopic examination, histological examination, and PCR).

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 2. Medical Treatment in HCE

The relevant literature was searched using the Pubmed database, covering 01.01.1900 and 18.03.2018. In Pubmed search, two columns were chosen as keywords. In the first one, the words “albendazole OR mebendazole OR praziquantel OR drug OR drugs OR medical OR benzimidazole* OR flubendazole” were searched in the title, abstract, and keywords of the articles (n= 9633333). In the second column, articles with the words “(*Echinococ** OR *hydati**) AND (liver OR hepatic)” in the title were searched (n= 3517). The combination of both columns revealed a total of 963 studies. Narrowing these down to studies that included words in the first column in their title revealed 87 studies. No distinction was made between them in terms of date or language.

A total of 503 articles were found in the Turkish literature search using the keyword “kist hidatik” (hydatid cyst) in the TR Index-Ulakbim database. Of these, 477 were related to medicine. After excluding the articles that did not include liver involve-

ment and were not related to medical treatment in cystic *Echinococcosis*, a total of 17 Turkish articles were evaluated within the scope of the study.

Points to be clarified about drug use in the treatment of cystic *Echinococcosis* (CE) in the liver:

2.1. Drugs used in the treatment of HCE, medicines that have not entered clinical use, drug doses, and drug combinations

The drugs used in the treatment of HCE are mainly benzimidazole group drugs. The drug that first came into use is mebendazole. However, Albendazole has become the primary drug used over time due to its greater effectiveness. Albendazole is determined to be effective in the germinative layer. Its sulfoxide (SO) metabolite is more effective than albendazole itself. Intra-cyst concentrations of Albendazole were also found to be more important than blood levels. It was also revealed that there was no significant difference between the intra-cystic and blood levels of the drug. However, it was noted that intra-cyst concentrations could not be predicted from blood concentrations. Besides, hepatic localization of the cyst and the calcification of its wall were found to cause higher drug concentration in the cyst. The intra-cystic drug concentration is inversely proportional to the diameter of the cyst. While the duration of drug use does not increase the intra-cystic drug concentration, long-term exposure of the germinative layer to the drug increases the effectiveness of the treatment (40). Experimental studies have been conducted with flubendazole as a drug not used in clinical practice to treat HCE. These studies have not yet been put into clinical practice (41). The dose of Albendazole is determined as 10 mg/kg/day. There is no evidence that increasing the drug's dose will increase the drug's effectiveness during medical treatment (2,41,42). The most commonly combined drug with Albendazole is Praziquantel. Praziquantel has been found to increase the blood level of Albendazole significantly. However, this combination has not been shown to increase intra-cystic concentrations. Therefore, the clinical efficacy of combining these two drugs has not been proven (40).

2.2. Role of drug use in the treatment of HCE

In the treatment of HCE, drug therapy is administered either as the sole treatment or as an adjuvant to the interventional procedure.

CE1 cysts with a diameter of less than 5 cm have an indication for drug therapy alone. The rate of transformation of these cysts to inactive cysts after 1-2 years of drug treatment has been reported as 75% in some studies. Studies have also reported that the effectiveness of drug therapy decreases as the cyst diameter increases and the stage progresses. Medical therapy alone has also been used in patients with medical conditions not suitable for surgical treatment, patients with diffuse peritone-

al hydatidosis with or without liver cysts, and CE3b patients in some studies. However, no study compared the effectiveness of medical treatment alone with surgical treatment in this patient group. Nevertheless, drug therapy alone has a high recurrence rate. In two-year follow-ups, it was determined that cysts that became inactive with medical treatment became active in 25% in some series and 50-60% in others (11,43-45). The response rate to drug therapy is even lower in CE2 and CE3 cysts (30-50%). There is no definite duration of treatment in patients who will receive drug therapy alone. Different durations have been specified in the literature, such as 1-2 years (46,47). There is no study comparing the duration of medical treatment. Studies predominantly compare drug therapy with watch-and-wait therapy. Nonetheless, WHO/IWGE states that membrane detachment should occur three months after drug initiation in CE1 cysts to evaluate the efficacy of the intra-cystic drug. In some studies, the mean duration of drug intake was reported as 12 months (46). In addition, there are studies suggesting that CE3b cysts should be treated with Albendazole alone instead of surgery or followed by ultrasound without treatment (46). However, these studies are retrospective, and some CE4 cysts have been reported to revert to the CE3b state. The most important criterion for drug therapy success is the cyst stage change. The World Health Organization classifies CE1 and CE2 as active, CE3a and CE3b as transitional, and CE4 and CE5 as inactive cysts. Success in medical treatment can be defined as changes in US appearance (e.g., conversion to CE 3a with membrane detachment in a CE 1 cyst or conversion to CE 4 with solidification of a CE2 or CE3b cyst) after albendazole administration (at least three months). Regarding the complication rate of cysts in HCEs under drug therapy, a study comparing medical treatment with albendazole and wait and watch treatment in CE3b cysts reported the complication rate in cysts treated with albendazole was the same as in other cysts (46). Albendazole has side effects that can sometimes be serious. Except for nausea and rare hair loss, this drug is hepatotoxic and may cause bone marrow depression. Liver functions and hemogram parameters should be followed in long-term treatments.

2.3. Drug therapy and duration before or after intervention (percutaneous or surgical) in HCE

Medical indication for hepatic hydatid cyst is mainly adjuvant therapy used in the preoperative and postoperative period. It is known that Albendazole used before surgery reduces intracystic pressure and scolex vitality. In addition, the intracystic viable scolex ratio decreases as the duration of preoperative use is prolonged. Studies have shown that the concentration of Albendazole in the cyst is close to the values in the blood. Different sources have specified different durations for the use of the drug. Still, various sources recommend using drugs for 15 days-1 month preoperatively and 1-3 months postoperatively (2,41,42).

In light of the above literature, the following recommendations were formed;

Recommendation 2.1: The most effective drug currently in use in the medical treatment of HCE is albendazole. Treatments with other medications have not yet entered clinical use.

Recommendation 2.2: There is no evidence that the concomitant use of praziquantel or any other drug in medical treatment increases the effectiveness of the treatment.

Recommendation 2.3: The dose of albendazole is determined as 10 mg/kg/day. There is no evidence that increasing the drug's dose will increase the drug's effectiveness during medical treatment.

Recommendation 2.4: Indications for medical treatment of HCE; If CE1 cysts have a diameter less than 5 cm medical treatment can be attempted.

Recommendation 2.5: Although some studies consider medical treatment sufficient in patients with CE3b cysts, the primary treatment is interventional or surgical. An appropriate dose of albendazole is first given preoperatively in these patients, and then surgical/interventional treatment is applied.

Recommendation 2.6: There are no definitive studies in patients with peritoneal hydatidosis along with HCE. If surgical treatment is applied in these patients, drug therapy may be preferred as an adjuvant, but it can also be administered alone without surgical treatment.

Recommendation 2.7: The duration of medical treatment without any other treatment approaches should be six months at least and twelve months on average. However, the change in the cyst stage should also be evaluated in the follow-ups.

Recommendation 2.8: Liver function tests and hemogram should be monitored monthly to follow up on drug side effects seen during drug treatment of HCE.

Recommendation 2.9: There is no defined period for the use of Albendazole before and after the intervention (surgery or percutaneous treatment). However, based on limited information in the literature, a minimum of ten days of drug use can be recommended. Similarly, at least two months of postoperative use can be recommended.

Recommendation 2.10: Studies have shown no relationship between Albendazole blood levels and intra-cystic concentration, but these two levels are close to each other, and the intra-cystic concentration is more effective in treatment. Therefore, blood level monitoring has not been included in clinical practice.

Recommendation 2.11: Drug use during pregnancy has been reported as teratogenic and embryotoxic in experimental studies; however, high doses used in experimental studies are not used in humans in clinical practice. Nevertheless, its embry-

toxic effects have not been clearly demonstrated. Yet, there is also no evidence that it is safe for use in pregnant women.

Recommendation 2.12: There are two recommendations for drug administration in patients who will use albendazole for a long time (six months or more). Recommended treatments for long-term use are continuous and intermittent therapy. In continuous therapy, the treatment continues with two divided daily doses without interruption, while in intermittent therapy, the drug is given for 20 days, and a break is given for ten days. The more preferred treatment is intermittent therapy.

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 3. Percutaneous Treatment in HCE

The relevant literature was searched using the Pubmed database, covering 01.01.1900 and 18.03.2018. In Pubmed search, two columns were chosen as keywords. In the first one, the words "PAIR OR puncture OR percutaneous" were searched in the articles' title, abstract, and keywords (n= 418508). In the second column, articles with the words "(*Echinococ* OR hydatid) AND (liver OR hepatic)" in the title were searched (n= 3699). The combination of both columns revealed a total of 346 studies. Narrowing these down to studies that included words in the first column in their title revealed 73 studies. Of these, four were comparative clinical studies, five were reviews, 16 were case reports, and one was a meta-analysis, and the remaining majority were retrospective clinical studies. No distinction was made between them in terms of date or language.

A total of 503 articles were found in the Turkish literature search using the keyword "kist hidatik" (hydatid cyst) in the TR Index-Ulakbim database. Of these, 477 were related to medicine. After excluding the articles that did not include liver involvement, were not related to the treatment of cystic *Echinococcus*, or insufficiently related to the diagnosis, a total of nine Turkish articles were evaluated within the scope of the study.

3.1. Common evaluation

Especially in the last three decades, percutaneous treatments in HCE have increased and improved. It can be performed with low complication rates, especially for CE1 and CE3a cysts (48). Today, the success of percutaneous treatments in HCE is quite high. From this point of view, joint planning of the treatment for HCE by an interventional radiologist, general surgeon, and endoscopist who can perform ERCP will increase the chance of success.

3.2. Cyst localization

Especially cysts located deep in the liver parenchyma are more suitable for percutaneous treatment (PT). There may not be enough parenchyma in exophytic cysts to enter the cyst, and sclerosis of the cyst pouch is often more difficult in these cysts.

Therefore, surgical treatment is more appropriate in these cysts that grow towards the abdomen (49).

3.3. Cyst diameter and type

While PAIR therapy is successful in CE1 and CE3a cysts, it is more likely to fail in CE2 and CE3b cysts. Failure rates of up to 60% have been reported in some series (50,51). Therefore, percutaneous catheter applications are used in this patient group. Generally, PAIR treatment with a needle is appropriate for CE1, CE3a, and CE4 cysts with fluid content up to 10 cm. If possible, catheter treatment should be performed in larger cysts, CE2 medium-large CE3b cysts, cysts with biliary content, and postoperative collections. Different methods have been tried for catheter treatment. However, there are no controlled studies comparing these methods. PT can be performed on all cysts with live or liquid contents. However, since the risk of recurrence is high in CE3b cysts with a high solid component and especially with exophytic extension, primarily surgical treatment should be considered (11,12,48,50-54).

3.4. Treatment in HCE in case of bile leakage into the cyst

If PT is to be performed in these patients, they should be treated with catheter drainage, if possible. Since most cystobiliary fistulas become evident after cyst drainage, the inserted catheter should not be removed immediately but should be removed after waiting for about one week, making sure there is no obvious fistula, and performing cystography and sclerotherapy (12).

3.5. Treatment in HCE in case of bile leakage into collections or cyst pouch after surgery or PT

Cystobiliary fistula is more likely in centrally located cysts close to the porta hepatis. These cysts should be treated with catheter drainage if possible. The catheter should not be removed until the daily bile leakage is below approximately 10 cc. Sclerotherapy should be performed after the presence of cystobiliary fistula is evaluated cystography. If bile leakage is not reduced or is increased, ERCP and ES, Stent, or NBD can be applied. In this process, care should be taken for the cyst not to become infected (12).

3.6. Treatment of recurrent cysts after surgery or PT in HCE

It would be correct to approach the cases with recurrence or residual postoperatively as if they had not been operated on. Since the mortality and morbidity of the second open surgery are higher in these patients, and surgical treatment is more difficult due to surgical adhesions, they should be treated with PT if possible. Similarly, percutaneous treatment should be planned primarily in recurrences or residues after percutaneous procedures (12,55-58).

3.7. Postprocedure follow-up

After the procedure, routine controls with US and blood tests should be performed at the 1st, 3rd, 6th, 9th, and 12th months. Bile

leakage into the cyst pouch is usually seen in the first months, while cyst recurrence develops in a longer term. If there is deterioration in blood values, the dose of the drug should be adjusted accordingly, and if there are GI side effects, it should be given with stomach protectors. In the follow-up, recovery criteria such as the absence of fluid in the cyst, collapse of the membranes, reduction in size, and development of calcification should be considered.

In light of the above literature, the following recommendations were formed;

Recommendation 3.1: When planning treatment for HCE, the patients should be discussed in a MDT board including an interventional radiologist or, at least should be consulted with an interventional radiologist prior to surgery.

Recommendation 3.2: In terms of cyst localization, surgical or percutaneous treatment can be planned for superficial cysts or cysts growing towards the abdomen. Surgical treatment is preferred in cases where safe percutaneous access is not available.

Recommendation 3.3: Percutaneous treatment is applied with the PAIR technique in CE1 and CE3a cysts. If the aspirated content has bile, catheterization should be started. PAIR and catheterization can be applied in CE1 and CE3a cysts larger than 10 cm in diameter, but catheterization is preferred for a safer and shorter procedure. If there is no bile content, the catheterization process can be completed in a single session by removing the catheter at the end of the procedure. Surgical treatment is the standard treatment for CE2 and CE3b cysts, but percutaneous treatment is also possible in experienced centers with the modified catheterization technique (MoCaT), in which the cyst content (daughter vesicles and solid degenerative content) is completely evacuated.

Recommendation 3.4: PT should be planned first in recurrent cysts or collections after surgery and PT.

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 4. Surgical Treatment of HCE

The relevant literature was searched using the Pubmed database, covering 01.01.1900 and 30.09.2018. In Pubmed, the keywords (surg* OR lap*) AND [(cystic AND *Echinococ**) OR (hydatid)] AND (liver OR hepatic) were searched in the title, abstract, and keywords of the articles. As a result, 1557 studies were obtained. Of these, 548 were case reports, 25 were comparative clinical studies, 65 were reviews, four were meta-analyses, and the remaining majority were retrospective clinical studies. No distinction was made between them in terms of date or language.

A total of 92 articles were found in the Turkish literature, using the keywords “kist hidatik VE karaciğer VE cerrahi” (“hydatid cyst

AND liver AND surgery") in the TR Index-Ulakbim database. After excluding the articles that did not include liver involvement and were not related to cystic *Echinococcosis* surgery, a total of 47 Turkish articles were evaluated within the scope of the study.

4.1. Surgical treatment

With the increase in percutaneous interventions, surgical treatment indications have narrowed, and their number has decreased. The current indications for surgical treatment are as follows. Surgical treatment indications (2);

1. In large uncomplicated CE2 and CE3b cysts with many daughter vesicles.
2. In uncomplicated large cysts that compress neighbouring vital organs.
3. In cases where percutaneous treatment is not possible.
 - a. Against the possibility of spontaneous or traumatic rupture in superficial and large single cysts.
 - b. In infected cysts.
4. As an alternative to percutaneous treatment in cysts with cysto-biliary communication.

4.1. Surgical treatment options

The main purpose of surgical treatment in hepatic hydatid cyst is to eliminate the parasite and minimize recurrence, morbidity, and mortality (59). Surgical treatment can be done as radical or conservative. Surgical treatment is chosen according to the patient, the cyst, the surgeon's experience in different surgical treatments, and the institution's facilities.

4.2. Conservative surgery

The principle of conservative surgical treatment is to empty and sterilize the cyst cavity and manage the remaining cavity (60-62). Although conservative surgical procedures are easier to perform than radical procedures, the rate of postoperative morbidity is higher (2).

In conservative surgery, various scolical agents are used to evacuate the cyst content and sterilize the inside of the cavity. Mostly, 3-30% NaCl (hypertonic NaCl), chlorhexidine, cetrimide (0.5%), povidone-iodine (10%), hydrogen peroxide (3%), silver nitrate (0.5%) and ethyl alcohol (75-90%) are used as scolical agents. The application time of these agents is 5-15 minutes. However, some of these agents are no longer in use. Today, the most commonly used agents are hypertonic NaCl and cetrimide. A concentration below 10% hypertonic NaCl is considered insufficient scolical activity. The ideal concentration is 20% (63,64). Contact of all scolical agents with the biliary tract should be avoided. Because all of them are likely to cause caustic sclerosing cholangitis.

The part of the emptied cavity outside the liver parenchyma should be removed as much as possible. This procedure is de-

finied as a partial cystectomy. After reducing the cystic cavity, management methods for the remaining space include unroofing, marsupialization, tube drainage, capitonage, Roux-en-Y cystojejunostomy, and omentoplasty (65). There are studies comparing tube drainage, capitonage, and omentoplasty in the literature. Comparisons were made in terms of biliary fistula and cavity infection. In general, the risk of biliary fistula and cavity infection was lower in capitonage than tube drainage and omentoplasty compared to capitonage (66-70).

Radical surgery

Radical surgical procedures are pericystectomy and hepatectomy. The rate of radical surgery reported in the literature is only 10% of all surgical procedures in the series. Radical surgical treatment is performed without opening the cyst with its contents, either by removing only the pericyst (Pericystectomy-total cystectomy) or removing the pericyst and some parenchyma around it (hepatectomy). The rate of pericystectomy in radical surgical procedures is reported to be 80-90% in the literature (71). Unlike conservative procedures, radical procedures are more complex and challenging and are only applied in units performing advanced HPB surgeries.

Pericystectomy is more preferred among radical procedures. This is because healthy parenchyma is tried to be preserved as much as possible. There is a good dissection plane between the liver tissue and the cyst. Identifying and advancing this plane will provide a comfortable dissection (72). Pericystectomy or cystoprostatectomy method is the removal of the pericyst together with the cyst. This method can be performed closed or open. In the closed method, the cyst content is not opened, while in the open method, the cyst is opened, the pericyst is removed, and its contents are emptied. The open method is especially preferred for deeply located cysts close to the hepatic and portal vein (59).

Considering the series, the rate of hepatectomy in radical surgical treatment remains at 10-20% (59,72-76). Indications for hepatectomy are a large cyst filling a lobe, multiple cysts, complicated cysts, as well as lesions close to hilar vascular structures, according to some authors (77). Erosion of the large bile ducts has been suggested as an indication for hepatectomy. Studies have stated that especially lesions close to the inferior vena cava constitute a partial contraindication. Particular attention should be paid to segment VIII, IV, and I lesions, lesions close to hepatic veins and right atrium (78).

Complications vary depending on the surgical method used in radical surgery. Complications of liver surgery are observed in general, and postoperative morbidity ranges between 3-30% (71). This rate is lower than conservative surgery. The advantage of radical surgery is that there is no cavity infection and less probability of biliary fistula (0-7.7%) (79,80). In patients who undergo radical surgery, the incidence of infection in the operation area after resection is less than 3%. Low postoperative

morbidity naturally reduces hospital stay in patients undergoing radical surgery. Besides, the probability of local recurrence is also lower in radical surgery. The local recurrence rate reported in the literature is 20-25% after conservative methods (59,81,82) and 0-6.4% after radical surgery (71).

Examination of the studies comparing the radical and conservative surgery reveals that the radical surgery group is preferred according to anatomical localization in many studies, indicating a bias. Besides, a significant portion of the comparison studies was conducted in specialized centers (83).

Minimally invasive surgery

The role of laparoscopy in the surgical treatment of liver hydatid cysts has always been discussed. The first studies were reported in the 1990s. The general advantages of laparoscopy, such as less hospital stay, fewer wound problems, and less pain, are also valid here (84). However, the difficulty in reaching the cysts in some localizations and aspiration of the cyst contents have led to concerns about disseminating the contents and question marks about laparoscopy.

Reaching the cysts in the posterior and superior liver segments poses some technical difficulties. However, access to cysts in the II, III, IVB, V, and VI segments can be achieved more easily (85). This also enables patient selection in liver hydatid cysts. In other words, laparoscopic or minimally invasive surgical treatment seems more reasonable in patients with anterior segment cysts (86). It can even be deduced that laparoscopy is a relative contraindication for segment VII and I cysts.

In addition, the complete evacuation of the cyst contents and the possibility of spreading around during evacuation are among the problems experienced. In the current literature, there are various studies on the use of special aspirators, liposuction catheters, or trocar systems (85,87-89). After the cavity is emptied and sterilized, cavity management can be performed with the same methods as in open cases. After the evacuation of the cyst, bile leaks can be detected thanks to the magnification by laparoscopy. Leaks can be sutured (87,90-92).

Conversion to open surgery in laparoscopic surgical treatment is usually due to inaccessibility of the cyst, calcifications, and other complications (bleeding, etc.) (85). The transition to open surgery rate has been reported as 1.7% (86,90). Currently, there is no obstacle to the treatment of liver hydatid cysts with minimally invasive surgical methods (93). In the published series, the recurrence rate in patients who underwent minimally invasive surgery was not higher than in open surgery patients (85). However, it is essential that minimally invasive surgical treatment is well planned and the indications are not forced because it is easy to apply. Minimally invasive radical surgery for hepatic hydatid cysts will increase as minimally invasive hepatectomy becomes more common.

In light of the above literature, the following recommendations were formed;

Recommendation 4.1: Indications for surgical treatment in HCE mainly apply to CE2 and CE3b cysts where percutaneous evacuation of the cavity is difficult, centrally located cysts with cysto-biliary communication, and superficially located or ruptured cysts where percutaneous treatment is not possible.

Recommendation 4.2: Conservative and radical surgery can be safely performed in HCE. Conservative surgical methods are sufficient in all cases with an indication for surgical treatment.

Recommendation 4.3: During conservative surgery for HCE, one of the currently used agents can be preferred for sterilization of the cyst cavity, but attention should be paid to its harmful effects on the biliary tract. Attention should be paid to hypernatremia when using hypertonic NaCl.

Recommendation 4.4: Although there is no difference in postoperative morbidity and mortality between conservative methods in HCE, biliary fistula is seen at a lower rate in omentoplasty than other methods. Therefore, despite the low level of evidence, omentoplasty should be preferred in cases where fistula may develop in conservative surgery. The main drawbacks in the application of omentoplasty are:

- The possibility of not seeing the fistula opening.
- Its ineffectiveness in preventing bile leakage in some studies.
- The fact that sphincter pressure is more important in preventing fistula. In addition, the fact that experienced centers predetermine the cases with fistula and take precautions reduces the interest in this method.

Recommendation 4.5: Radical surgical treatment should be performed in specialized HPB centers. The radical surgical method to be preferred should be parenchyma sparing, if possible. The relevant center should decide on what kind of procedure will be performed in which cases according to the patient's condition.

Recommendation 4.6: Minimally invasive surgical treatment should be preferred according to the patient, the physician's experience, and the institution's facilities. As the experience of minimally invasive surgery and open HPB surgery increases, it should be practiced by HPB surgeons. In other words, laparoscopic interventions should be performed by HPB surgeons.

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 5. Complication Management in HCE

A literature search on the subject, covering the dates 01.01.1990-09.12.2018, was carried out using the Pubmed database for English publications and the TR Index-Ulakbim database for Turkish publications.

Pubmed search with the keywords “Complications of *Echinococcal* cysts, complications of hydatid cysts, complications of cystic *Echinococcosis*” revealed a total of 3124 articles. Of these, 3102 were related to humans. These 3102 articles were subjected to preliminary evaluation. Of these articles, 299 were clinical studies, 351 were reviews, 14 were meta-analyses, and 2438 were case reports. After excluding the articles that did not include liver involvement, were not related to the diagnosis of cystic *Echinococcosis*, or insufficiently related to the diagnosis, 65 clinical study articles, 10 reviews, and 25 case reports were evaluated within the scope of the study.

A total of 24 articles were found in the Turkish literature, using the keywords “kist hidatik VE karaciğer VE komplikasyon” (“hydatid cyst AND liver AND complication”) in the TR Index-Ulakbim database. After excluding the articles that did not include liver involvement and were not related to cystic *Echinococcosis* surgery, a total of 11 Turkish articles were evaluated within the scope of the study.

Cysts can remain as they are, enlarge, collapse, or calcify in their natural course. It is also possible for the cysts to become complicated in their clinical course, and the complication rate reaches 30-60%. Complications in HCE can be classified as local complications in the cyst and systemic complications. Systemic complications include allergic reactions. Allergic reactions or anaphylaxis may develop preoperatively or intraoperatively in HCE. Although these allergic findings are not very common, they can be fatal in some cases. Allergic complications can be seen in the preoperative period as well as intraoperatively. Bile duct involvement (cystobiliary fistula), related complications, and free rupture in the peritoneum, pleural, and pericardium are the most common local complications. Infection of the cyst is also one of the most important complications. The suppuration rate of the cyst is over 20%.

5.1. Allergic reactions in the preoperative or intraoperative period due to hydatid cyst

Literature on the management of allergic and anaphylactic reactions due to hydatid cysts are limited to case reports, and recommendations in case-based patient management for the handling of allergic reactions detected in the preoperative period is to administer antihistamines orally for mild skin lesions at first and to start oral prednol (methylprednisolone) treatment if the reaction does not regress. Intravenous steroid administration is recommended as prophylaxis at the beginning of surgery to prevent anaphylaxis and allergic reaction in the perioperative period. In addition, it is recommended to start albendazole treatment to prevent recurrence of allergy and anaphylaxis after an allergic reaction that developed in the preoperative period. In more severe allergic reactions, if hemodynamics are affected, intravenous (IV) use of antihistamines and steroids is recommended. When anaphylaxis develops, it is recommended to

provide airway patency, give IV fluid replacement therapy, provide nasal oxygen support, and discontinue other drugs that may cause allergy (anesthesia drugs given when it occurs in the preoperative period) and administer IV antihistamines and steroids (94-97).

5.2. Detection of cysto-biliary fistula in the preoperative period

Retrospective clinical studies are predominant in the literature on predictive parameters in detecting hydatid cysts with biliary fistula in the preoperative period. Many articles have reported elevations in the enzymes (ALP, GGT, Total and Total Direct Bilirubin) that indicate biliary duct obstruction (98-101). Literature indicates an increase in the biliary tract relationship with the increasing cyst size, and studies have reported a cut-off value between 7.5-14 cm (98,99,102-104). There are studies showing that the risk is increased in hydatid cysts located centrally in the liver and located in the liver dome. Literature has revealed that the high white blood cell value and eosinophilia are significant for biliary fistula, although not alone, together with the elevation in the other parameters mentioned above (98,104-112). Several studies have also indicated that male gender and age of the cyst are risk factors for the development of biliary fistula (100,101,108,109).

5.3. Biochemical tests used for the detection of biliary fistula in the preoperative period

For the detection of biliary fistula in the preoperative period, in addition to the biochemical parameters that indicate biliary tract obstruction, which we mentioned in the previous section, studies have also identified elevated AST and ALT enzymes as a risk factor (100,101,113).

5.4. MRCP in the preoperative period

The cysto-biliary communication is divided into two; frank (major, ≥ 5 mm) and occult (minor, < 5 mm) biliary tract communication. Despite a few articles on the use of MRCP in the preoperative period, which either suggest its routine use or argue that it is unnecessary due to its low sensitivity and specificity (approximately 30%) in demonstrating the communication between the occult bile duct in the patient scheduled for surgery, majority of the articles in the literature recommend MRCP in patients with the parameters mentioned in the above sections that may raise suspicion of preoperative cysto-biliary communication, in patients with signs of cholangitis (fever, jaundice, and right upper quadrant pain) or the presence of findings showing biliary involvement in radiological imaging (113-119).

5.5. Preoperative biliary fistula detection

Literature on preoperative biliary fistula detection mentions the symptoms and signs of cholangitis, laboratory markers for biliary fistula mentioned above, demonstration of biliary tract re-

relationship in radiological imaging (germinative membrane dehiscence, daughter vesicle or debris in the biliary tract), and the presence of bile in the cyst content in the aspiration during the PAIR procedure as parameters used in diagnosis (110,113-120).

5.6. Preoperative ERCP

In the preoperative period, MRCP is preferred because it is non-invasive (120-123). Endoscopic sphincterotomy and a nasobiliary drainage catheter placement are recommended to reduce sphincter pressure with ERCP in patients with biliary fistulization in MRCP (123-125).

5.7. Management of hydatid cyst with cysto-biliary communication

Literature in the 90s reported that the treatment of hydatid cyst was surgical, and if the cyst was associated with the biliary tract during surgery, T-tube drainage might be required, and preoperative preparation should be made (126). However, today, with the advancement of radiological imaging, cysto-biliary communication can be better demonstrated preoperatively, and sphincterotomy and preoperative ERCP reduce the risk of postoperative bile leakage (124,126). There are also recommendations in the literature for the use of ERCP to reduce bile duct pressure and clear debris in hydatid cysts with an obvious cysto-biliary communication, since the incidence of detecting bile duct association greater than 5 mm is 65%, while the incidence of detecting biliary fistula below 5 mm is between 10-37% (112,126,127). In patients with signs of sepsis, such as hydatid cyst rupture, which require an emergency operation, it would be appropriate to try surgical methods for the cysto-biliary communication by taking them directly to the operating room without ERCP (107,108,111). Since ERCP is an invasive procedure, it should be performed by an experienced team (123,124).

5.8. Determining whether the intraoperative hydatid cyst is associated with the biliary tract or not.

Various methods have been described to reveal the association of the intraoperative hydatid cyst with the biliary tract, such as putting a clean sponge into the cyst pouch and waiting for 5-10 minutes, then checking whether there is bile contamination, control of the cyst pouch by performing cholecystectomy through the cystic stump or by injecting methylene blue or lipid solution by entering the common bile duct with a thin needle, checking whether there is a yellow color in the white foamy liquid formed after washing the cyst pouch with oxygenated water or filling the cyst pouch with liquid and checking whether the air exhaled from the cystic stump after cholecystectomy creates air bubbles in the cyst pouch, and checking the cyst pouch with videoscopy especially in patients in where the cyst pouch located in the liver dome cannot be fully observed with a direct examination (73,108,111,112,128,129).

5.9. Management of hydatid cyst with intraoperative biliary fistula

In the management of a hydatid cyst with an intraoperative biliary fistula, the literature recommends applying an ERCP procedure by placing an external drainage catheter into the cyst in cases where there is a biliary tract association in the cyst pouch, and no bile leakage area can be detected. If the bile ducts seen in the cyst pouch are not the main bile duct, direct suturing and placing an external drainage catheter into the cyst is recommended. In the case of a major bile duct association, it is recommended to repair the bile duct with a suture and demonstrate that the main bile ducts are not closed by placing a T-tube drainage catheter and taking a cholangiogram after common bile duct exploration. To reduce postoperative bile duct pressure, it is recommended to perform procedures such as sphincterotomy ± stent with ERCP if necessary (108,120,130-133). In addition, few studies suggest using fibrin glue as a useful method for biliary fistula (134,135).

5.10. Management of biliary fistula detected in the postoperative period

The management of biliary fistula detected in the postoperative period should be arranged according to the bile flow. Any signs of sepsis or peritonitis should be investigated immediately. If the amount of drainage is high (over 300 ccs) in the postoperative period, ERCP should be applied immediately. If the bile flow is low and no signs of sepsis or peritonitis develop (less than 300 ccs), it can be followed for three weeks with a drain (112,130). If bile flow continues despite a three-week follow-up, ERCP is performed. If the amount of drainage is high (over 300 ccs) in the postoperative period, ERCP should be applied (108-112,120,130).

5.11. Treatment of hydatid cyst abscess

Interventional or surgical drainage methods are available in the treatment of hydatid cyst abscesses, and both methods are used according to the patient's clinic and the clinician's preference. Both methods have advantages over each other. If there are no systemic and septic findings, percutaneous drainage should be performed first. Surgical perforation drainage is in the foreground if there are systemic and septic findings. Antibiotic and albendazole treatment should be given at least three weeks before percutaneous drainage (113,136-142).

5.12. Peritoneal rupture of the cyst

There are generally case series in the literature on the peritoneal rupture of the cyst. Based on the case, in which acute rupture of the cyst has the possibility of anaphylaxis and peritoneal spread of the cyst, that was urgently treated with laparotomy or laparoscopy and then albendazole administration for 3-6 months, open or laparoscopic surgery may be considered after albenda-

zole treatment for a certain period before surgery in a patient with a late-detected acute abdomen with self-limited closed perforation in the abdomen or without anaphylaxis or allergy symptoms (94,106,143-146).

5.13. Superinfection of the cyst

Since it usually occurs due to cysto-biliary communication, it is necessary to interrupt the biliary tract association with surgical or ERCP/PTK procedures and add albendazole + antibiotic therapy to the treatment. Invasive or surgical drainage of the cyst should also be provided. After the procedure, antibiotics and at least three months of albendazole treatment should be administered (147-150).

5.14. Opening of liver hydatid cysts into the thoracic cavity or pleura

The daughter vesicles and debris in the thoracic cavity can be cleaned with thoracotomy. It can be treated depending on the surgeon's experience; after laparotomy and treatment of the cyst, the diaphragm is opened, and the cyst pouch in the liver is drained, the daughter vesicle and debris are cleaned, the biliary tract communication is sutured, the diaphragm is repaired after washing with scolical agents, the abdominal drainage catheter is placed in the thorax, and the postoperative treatment is with albendazole (151-155).

5.15. Cutaneous fistulization of liver hydatid cysts

It is one of the rare complications. In the literature, there are case-level treatments such as elective surgery after 2-4 weeks of albendazole treatment, emergency surgery performed by removing the skin area and fistula tract if it is suppurative or hemorrhagic, thereby cutting the relationship between the cutaneous region and the cyst, and application of one of the surgical procedures suitable for the lesion in the liver (156).

5.16. Rupture of large vessels (portal vein, inferior vena cava, and aorta)

It is one of the rarest complications. Rupture of *Echinococcal* cysts of the liver into the hepatic veins or inferior vena cava may cause hydatid disease to spread to the lungs or pulmonary arteries. Its symptoms are cough, hemoptysis, and shortness of breath (157). Clinical suspicion should be increased in endemic areas. This complication should be kept in mind in patients presenting with these symptoms, especially those who have undergone liver surgery for a hydatid cyst. Thrombosis has also been reported due to opening into the inferior vena cava. One of the rare vascular complications of liver hydatid cysts is their rupture into the portal vein. A total of four cases have been reported. In this case, symptoms include abdominal pain, fever, and signs of portal hypertension (158-161). Anaphylactic shock may also develop after rupturing into large vessels (157-161). There are case-series-level treatments, but they are not mentioned because of their low success.

In light of the above literature, the following recommendations were formed;

Recommendation 5.1: In HCE, preoperative cyst diameter greater than 8 cm, central localization of the cyst, and/or presence of high ALP, GGT, and bilirubin may be indicators of possible communication between the cyst and the biliary tract.

Recommendation 5.2: In cases with clinical and laboratory suspicion of cystobiliary fistula in the preoperative period, MRCP using hepatocyte-specific agents may increase the diagnosis of cystobiliary fistula, but a standard MRCP does not completely rule out the possibility of fistula.

Recommendation 5.3: Preoperative ERCP should be performed in cases with obstructive jaundice or cholangitis, patients with dilatation of the biliary tract, daughter vesicles or debris in the biliary tract on the US examination, or a biliary tract relationship with MRCP and an obvious cystobiliary fistula (over 5 mm, major biliary tract relationship, common bile duct relationship). It is not absolutely necessary in cases where occult cysto-biliary communication (minor bile duct relationship less than 5 mm) is considered. Routine use is not recommended in uncomplicated cases.

Recommendation 5.4: In cases where intraoperative cystobiliary fistula is detected, if the bile ducts can be seen in the cyst pouch are not the main bile duct, suturing of the bile duct opening and placement of an external drainage catheter should be the choice. If a major bile duct association is observed in the cyst pouch, the repair should be performed so that it does not obstruct/narrow the large biliary tract. Intraoperative cholangiography will be useful for this. In cases where there is a bile in the cyst pouch, and no bile leakage area is detected, an external drainage catheter is placed into the cyst, and postoperative ERCP is performed if necessary.

Recommendation 5.5: If the bile flow rate is low (<300 cc) in biliary fistulas detected in the postoperative period, spontaneous closure of the biliary fistula can be expected for ten days without any action, and if the fistula closes spontaneously within ten days, no additional treatment is required. If the bile flow is high (>300 cc) and continues for more than ten days, ERCP can be planned. If the amount of fistula tends to decrease over time, ERCP can wait. ES, stent, or NBD can also be applied in ERCP. In patients with fistula, it is necessary to ensure that there is no peritonitis and sepsis. Radiological imaging of the cyst cavity is required in patients whose fistula drainage is interrupted.

Recommendation 5.6: When peritoneal rupture is detected in HCE, laparotomy or laparoscopy should be performed urgently if there are signs of acute rupture, as there is a possibility of anaphylaxis and peritoneal spread of the cyst. Afterward, albendazole treatment should be given for at least three months.

Recommendation 5.7: If superinfection of the cyst is detected, it should first be considered that it may be associated with the biliary tract and should be treated appropriately.

Recommendation 5.8: Whether or not there are septic findings or acute abdominal findings in hydatid cyst abscess, surgical or interventional drainage procedures to be preferred should be determined in accordance with the patient's clinical condition, clinician's preference, and institutional facilities. Appropriate antibiotic therapy should be initiated after the procedure.

Recommendation 5.9: If liver hydatid cysts are ruptured into the thoracic cavity or pleura, after the treatment of the cyst with laparotomy, the diaphragm is opened, the daughter vesicles and debris are cleaned, the biliary tract is sutured if a relationship is detected, then it is washed with scolical agents, the diaphragm is repaired, drainage catheters are placed in the abdomen and thorax, and the operation is terminated.

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 6- Posttreatment Follow-up and Recurrences in HCE

The relevant literature was searched using the Pubmed database, covering 01.01.1900 and 01.0.2018. In Pubmed search, [(cystic AND echinococ*) OR (hydatid)] AND (liver OR hepatic) AND (recur*) were selected as keywords. A total of 28 studies were found. One of these was a randomized controlled trial. Other studies were case reports and retrospective serial analyses. No distinction was made between them in terms of date or language.

6.1. Medium-long-term follow-up-serology-imaging

Serological tests have become negative over the years. Therefore, its sensitivity is low in recurrence cases. In the follow-up, if the serological tests have become negative and positive results are detected again, then it is significant in terms of recurrence. After the routine baseline US imaging performed in the 1st month after the treatment of hydatid cyst, control should be provided with the US, especially in the 3rd and 6th months of the first year. Then, US control should be done for at least three years in six months intervals. Suspicious cases should be evaluated with CT (162-166).

6.2. Indications for an interventional procedure in recurrences

In recurrences, treatments similar to the primary treatment indications are applied. If it is a univesicular cyst and its localization is unsuitable for surgery, percutaneous treatment and albendazole should be given together. If the cyst is risky for univesicular and radical surgery, percutaneous treatment can be tried in the recurrences of patients who have previously received conservative treatment (167,168).

6.3. Indications for surgical treatment in recurrences

In recurrences after percutaneous treatment, first of all, percutaneous treatment should be tried again. If percutaneous treatment fails, conservative surgery may be tried. Radical surgery is recommended for those who underwent conservative surgery if the patient is suitable for surgery (162,163,169,170).

In light of the above literature, the following recommendations were formed;

Recommendation 6.1: Short and medium-term follow-ups after treatment in HCE should primarily be done with US exams. CT and serological tests can be used in suspected lesions.

Recommendation 6.2: Recurrent cases of HCE are repaired like the primary disease. In cases where percutaneous treatment was applied, first of all, percutaneous treatment can be tried again. Recurrences after conservative surgery should be treated percutaneously, if appropriate. If surgical treatment is to be performed, radical surgery should be applied if possible; otherwise, a conservative approach should be applied.

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ORIJİNAL ÇALIŞMA-ÖZET

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Türk Hepato-Pankreato-Biliyer Cerrahi Derneği'nin karaciğerin ekinokok kistleri hakkındaki konsensüs bildirisi

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ÖZET

Giriş ve Amaç: Kistik ekinokokkoz (CE), Avrasya bölgesinin önemli sorunlarından biridir. Bu hastalığın tedavi yaklaşımlarını güncellemek için bir uzlaşma raporu hazırlamayı amaçladık. Bu çalışma Türk HPB Cerrahi Derneği tarafından yapılmıştır.

Gereç ve Yöntem: Bu çalışma, modifiye Delphi modeli ile yapılmıştır. Bu amaçla, üç aşamalı bir fikir birliği oluşturma yaklaşımı yürüttük.

Bulgular: KKE'de tanı, medikal tedavi, perkütan tedavi, cerrahi tedavi, komplikasyonların yönetimi ve tedavi sonrası takip ve nüksler olmak üzere altı konu tartışıldı.

Sonuç: Uzman paneli her konu için önerilerde bulundu.

Anahtar Kelimeler: Karaciğer, kistik ekinokokkoz, uzlaşma raporu

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