

Review Article

Diagnosis, treatment and prognosis of simple hepatic cyst: Clinical practice guideline

Seoung Yoon Rho¹, Jeong-Moo Lee², Min-Su Park³, Woo-Hyoung Kang⁴, Yoonhyeong Byun⁵, Seung Jae Lee⁶, Aesun Shin⁷,
Jeong Hee Yoon⁸, Bohyun Kim⁹, Nam-Joon Yi²;

Clinical Practice Guideline Development Committee of Korea Association Hepato-Biliary-Pancreatic Surgery

¹Department of Hepato-Biliary-Pancreatic Surgery, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Korea,

²Department of Surgery, Seoul National University College of Medicine, Seoul, Korea,

³Department of Surgery, School of Medicine, Kyung Hee University, Seoul, Korea,

⁴Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea,

⁵Department of Surgery, Uijeongbu Eulji Medical Center, Uijeongbu, Korea,

⁶Department of Surgery, Konyang University Hospital, College of Medicine, Konyang University, Daejeon, Korea,

⁷Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, Korea,

⁸Department of Radiology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea,

⁹Department of Radiology, The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, Korea

Simple hepatic cysts are now diagnosed in over 8,000 individuals annually in South Korea, largely due to the widespread adoption of medical check-ups and advancements in imaging techniques. However, no appropriate clinical practice guideline has been established to address this condition. While international guidelines have recently been published, differences in clinical and epidemiological contexts have highlighted the need for a tailored guideline to assist domestic clinicians. To address this, the Clinical Practice Guideline Development Committee of Korea Association Hepato-Biliary-Pancreatic Surgery gathered input from surgeons, physicians, radiologists, pathologists, and epidemiology experts to adapt and modify pre-existing international guidelines to better suit domestic realities. This clinical practice guideline aims to provide a clear and appropriate pathway for the management of patients with simple hepatic cysts. It is anticipated that, based on this guideline, clinicians will have a practical framework for diagnosis and treatment. In the near future, it will be necessary to collect high-level evidences to further refine and strengthen recommendations for subsequent guideline updates.

Key Words: Cysts; Liver disease; Practice guideline

INTRODUCTION

Over the past few decades, advancements in radiological imaging techniques and the widespread adoption of routine

medical check-ups have significantly improved the detection of hepatic cystic lesions. Proper diagnosis and management of these lesions are essential when they are identified. However, simple hepatic cysts, the most common hepatic lesions that are frequently detected in recent screenings, are often overlooked in terms of diagnosis, treatment, and prognosis.

Hepatic cysts are lined by single epithelial cells filled with transudate fluid, arising from ductal plate malformations during fetal development. These cysts are disconnected from the biliary tree and filled with isotonic fluid that resembles bile but lacks bile acids and bilirubin. A simple hepatic cyst, the most common benign cystic lesion, is found in approximately 2.5% to 18% of adults. Most are asymptomatic at the time of detection. They measure less than 3 cm in size. Cysts larger than 10 cm are referred to as giant hepatic cysts. Among cysts

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Corresponding author: Nam-Joon Yi, MD, PhD
Department of Surgery, Seoul National University College of Medicine, 101
Daehak-ro, Jongno-gu, Seoul 03080, Korea
Tel: +82-2-2072-3550, Fax: +82-2-766-3975, E-mail: gsleenj@gmail.com
ORCID: <https://orcid.org/0000-0002-5467-425X>



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treated with aspiration or surgery, approximately 60% were over 10 cm [1,2]. They are usually asymptomatic, often incidentally discovered, and more common in females and older individuals. Their diagnosis is typically made via grayscale ultrasound, with a sensitivity and specificity of 90%, showing homogeneously anechoic structures with a thin wall. Computed tomography (CT) and magnetic resonance imaging (MRI) can also characterize simple cysts, showing typical imaging features such as hypodensity on CT, hyperintensity on T2-weighted images of MRI, and lack of enhancement on dynamic imaging [3].

With increasing number of diagnoses, large cohort studies and case reports have encouraged classification of simple hepatic cysts based on their pathophysiology and expansion of treatment indications. Despite this progress, there remains no consensus on treatment indications or methods for hepatic cystic lesions due to their diverse presentations. The need for practical clinical guidelines has been recognized, prompting the American College of Gastroenterology (ACG) and the European Association for the Study of the Liver (EASL) to provide such guidelines since 2010 [4,5].

However, directly applying Western clinical practice guidelines is challenging due to differences in disease presentation and treatment indications in the domestic context. According to data retrieved using the KCD-8 code for simple cyst of the liver (K76.81) and the procedure code for marsupialization (Q7213) from the Health Insurance Review and Assessment Service of the Republic of Korea, the number of patients diagnosed with hepatic cystic diseases had increased from 4,591 in 2013 to 7,667 in 2020 and 8,852 in 2023. Additionally, the number of marsupialization procedures, a surgical treatment for simple hepatic cysts, had increased from 139 cases in 2022 to 207 cases in 2023 [6].

Given the growing elderly population and its expected acceleration, the prevalence of simple hepatic cysts is anticipated to increase, along with associated patient numbers and medical expenses. There is a widespread consensus on the need for reliable, context-specific guidelines to assist domestic clinicians in making practical clinical decisions. Recognizing this, our treatment guideline committee aimed to establish an evidence-based guideline tailored to the domestic reality, providing a systematic approach to the diagnosis and treatment of simple hepatic cysts to support informed clinical decision-making.

GUIDELINE DEVELOPMENT METHODOLOGY

The Clinical Practice Guideline Development Committee was assembled in March 2023. By May of the same year, the committee completed its formation and finalized the practice guideline development direction, focusing on adaptation and modification of pre-existing guidelines. Through eight meetings held by December 2023, the Clinical Practice Guideline

Development Committee determined specific topics, selected principal investigators, and finalized key questions. In January 2024, advisory committee members were appointed and the invitation list for a public hearing was finalized. In June 2024, during the Liver Week conference, expert review and public hearing were conducted and the final guideline was revised accordingly.

To enhance the transparency and credibility of the development process, the committee was composed of not only surgeons affiliated with the Korean Association of Hepato-Biliary-Pancreatic Surgery, but also two radiologists and one expert in preventive medicine. The committee held a total of ten full meetings and workshops to establish the overall methodology and framework of the guideline. After selecting the adaptation and modification approach, key clinical questions were defined for each category (diagnosis, treatment, and prognosis) and draft recommendations were developed based on a thorough review of the most current and relevant literature.

Subsequently, two rounds of Delphi survey letters were sent to a panel of leading experts representing major academic societies, including another three members from the Korean Association of Hepato-Biliary-Pancreatic Surgery, three from the Korean Association of Liver Surgery, two from the Korean Society of Abdominal Radiology, one from the Korean Society of Interventional Radiology, three from the Korean Association for the Study of the Liver, one from the Korean Society of Pathologists, and two from the Korean Society for Preventive Medicine. Final recommendation statements were developed based on expert feedback and only those with a consensus agreement rate of 90% or higher were included. In June 2024, during the Liver Week conference, a public hearing was held to obtain additional external validation. Feedback from this event was also incorporated into the final version of the guideline.

This guideline was primarily developed through adaptation and modification of EASL and ACG guidelines, with key questions tailored to domestic conditions. In light of limited human and financial resources, members of the Clinical Practice Guideline Development Committee decided to focus the scope of the guideline on simple hepatic cysts—the most common and fundamental type—rather than conducting a review of all hepatic cystic lesions as seen in previous published guidelines. This approach was intended to ensure an efficient use of available resources while addressing the most clinically relevant issues in the current domestic healthcare context. The guideline was structured into three categories: diagnosis, treatment, and prognosis. Each question was formulated using the PICO format (P, patient, problem, or population; I, intervention; C, comparison, control, or comparator; O, outcome). Its contents were reviewed by a team of 10 specialists, including surgeons, radiologists, and preventive medicine experts.

Evidence grading followed the modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system (Table 1) [7,8]. Strong recommendations

Table 1. Modified GRADE system and strength of recommendation

Criteria		Subject	Grade
Quality of evidence			
High quality	Further research is very unlikely to change our confidence in the estimate of effect	Randomized trials without important limitations	A
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	Randomized trials with important limitations or observational studies with special strengths	B
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	Observational studies without special strengths or important limitations	C
Strength of recommendation			
Strong	Factors influencing the strength of the recommendation	-	1
Weak	Variability in preferences and values, or more uncertainty. Recommendation is made with less certainty, higher cost, or resource consumption	-	2

were based on high-quality evidence, while recommendations with limited or unclear evidence were decided through expert consensus and public hearing discussions. Although the overall level of evidence for simple hepatic cysts was limited, the committee acknowledged this gap and emphasized the need to establish clear, practice-oriented recommendations based on expert consensus. While numerous high-level evidence studies, including randomized controlled trials, are available for malignant or premalignant cystic lesions, simple hepatic cysts—despite being more common—are comparatively underrepresented in the literature. Recognizing this, the committee regarded it essential to develop a definitive and authoritative guideline to assist clinicians in the absence of robust data.

KEY QUESTIONS (KQ) AND RECOMMENDATIONS

Diagnosis

KQ1. Which imaging technique is recommended to diagnose simple hepatic cysts?

Ultrasound is the first choice of imaging modality to diagnose a simple hepatic cyst [3,9-14]. Additional imaging studies such as CT, MRI, and contrast-enhanced ultrasound that can be used to further characterize simple hepatic cysts are not indicated for asymptomatic or uncomplicated hepatic cyst on ultrasound.

Recommendation:

- Ultrasound is the first choice of imaging modality to diagnose a simple hepatic cyst.
- Additional imaging studies such as CT and MRI that can be used to further characterize simple hepatic cysts are not indicated for asymptomatic or uncomplicated hepatic cyst on ultrasound.

- Cyst fluid analysis is not recommended to diagnose simple hepatic cysts.

Level of Evidence & Recommendation: C1

KQ2. Which imaging technique is recommended for symptomatic simple hepatic cysts?

Simple hepatic cysts may present with a variety of symptoms associated with complications such as cyst infection, intracystic hemorrhage, cyst rupture, and compression of surrounding organs [3,9,15]. If symptoms occur in patients with simple hepatic cysts, ultrasound may be the first diagnostic modality. Additional imaging studies, such as CT or MRI, may be indicated depending on symptoms and complications.

Recommendation:

- Simple hepatic cysts may present with a variety of symptoms associated with complications such as cyst infection, intracystic hemorrhage, cyst rupture, and compression of surrounding organs.
- If symptoms occur in patients with simple hepatic cysts, ultrasound may be the first diagnostic modality.
- Additional imaging studies such as CT and MRI may be indicated depending on symptoms and anticipated complications.

Level of Evidence & Recommendation: C1

KQ3. What are the diagnostic criteria for hepatic cyst infection?

Cyst infection should be considered as definite in the presence of a cyst aspiration showing evidence of infection (neutrophils debris and/or microorganism). However, cyst aspiration is relatively rarely performed as it does not contribute to the diagnosis in the majority of cyst infections. Other sources of infection should be excluded for diagnosing cyst infection. Cyst

infections are more frequently diagnosed using other clinical, laboratory, and imaging findings, such as fever without other sources of fever, tenderness in the liver area, leukocytosis, increased C-reactive protein, positive blood culture, and imaging studies detecting gas in cyst or cyst wall thickening (Table 2) [16-21]. ¹⁸FDG PET-CT can only be considered for evaluating cyst infection in patients with autosomal dominant polycystic kidney and liver disease and when cyst infection is clinically suspected but not detected on CT or MRI [18,19,22].

Recommendation:

- Cyst infection should be considered as definite in the presence of a cyst aspiration showing evidence of infection (neutrophils debris and/or microorganism).
- The diagnosis of hepatic cyst infection should be considered in patients who present with clinical signs of infection alongside supportive laboratory and imaging findings (Table 2).
- ¹⁸FDG PET-CT can only be considered for evaluating cyst infection in patients with autosomal dominant polycystic kidney and liver disease and when cyst infection is clinically suspected but not detected on CT or MRI.

Level of Evidence & Recommendation: C2

KQ4. Which imaging modality is recommended to diagnose hepatic cystic hemorrhage?

If a patient with a simple hepatic cyst develops sudden and severe abdominal pain, imaging studies may be performed to suspect cystic hemorrhage [23]. Ultrasound, CT, and/or MRI may be used to diagnose cystic hemorrhage [24-28].

Recommendation:

- If a patient with a simple hepatic cyst develops sudden and severe abdominal pain, imaging studies may be performed to diagnose cystic hemorrhage.
- Ultrasound, CT, and/or MRI may be used to diagnose hepatic cystic hemorrhage.

Level of Evidence & Recommendation: C2

Treatment

KQ1. Which antibiotic therapy is recommended for cyst infection?

Escherichia coli is known to be the most common cause of infection in simple hepatic cysts. It has been reported that the same strain is found in cyst aspiration culture and blood culture tests in more than 80% of cases. Antibiotic treatment has been attempted in more than half of cases where hepatic cyst infection is clinically suspected. However, the treatment success rate is as low as 30% [29]. Antibiotic penetrance into the cyst appears to be related to the therapeutic effect. Antibiotics such as carbapenem and cefazolin are known to have low concentrations within the cyst [30,31]. There has been no report on the result after direct administration of antibiotics into the cyst. Quinolone is known to have an ability to achieve sufficient intracystic concentrations in hepatic cysts [32] with sufficient bactericidal activities against Gram-negative bacteria [33]. Therefore, it is recommended to first use ciprofloxacin and third-generation cephalosporin alone or in combination empirically.

However, most patients included in reviewed studies on infected hepatic cysts have autosomal dominant polycystic kidney disease. Clinical courses of these patients might be somewhat different from those of patients with simple hepatic cysts that are managed in this guideline. Moreover, due to a significant failure rate of antibiotic treatment [34], selecting appropriate antibiotics based on sensitivity testing of culture results and considering conversion to percutaneous procedures or surgery should be prioritized [17,35].

Recommendations:

- Since *E. coli* is the most common strain in infected hepatic cysts, ciprofloxacin and/or 3rd generation cephalosporin alone or combination therapy are recommended empirically as the first antibiotic to be tried.
- Empirical antibiotic use for about 4–6 weeks is recommended. Percutaneous procedures or surgery should be actively considered based on culture results and clinical progress.

Level of Evidence & Recommendation: C1

Table 2. Criteria for hepatic cyst infection

Criteria for definite hepatic cyst infection	Criteria for probable hepatic cyst infection (after exclusion of other infection source)
• Cyst aspiration showing evidence of infection (neutrophils debris and/or microorganism)	• Fever with no other source • Tenderness in liver area • Increased C-reactive protein • Leukocytosis • Positive blood culture • Gas in a cyst on CT or MRI • Cyst wall thickening on CT or MRI

CT, computed tomography; MRI, magnetic resonance imaging.

KQ2. When should drainage be considered for treating an infected hepatic cyst?

Because initially used empiric antibiotics often fail to treat infected hepatic cysts, drainage should be considered for more effective treatment [29,32]. If the temperature persists above 38.5 degrees even after 48 hours of empiric antibiotic use, resistance to antibiotics is confirmed in culture, or there is a problem with the patient's immune system, drainage procedures should be actively considered. Additionally, it should be considered if intracystic gas shadows are detected on CT or MRI, or the size of the infected hepatic cyst is larger than 5 cm [17].

Recommendations:

Drainage may be considered for infected hepatic cysts that meet the following conditions:

- Temperature persists above 38.5 degrees even after 48 hours of empiric antibiotic use
- Resistance to antibiotics is confirmed by culture
- Severely compromised immune system
- Intracystic gas shadows are detected on CT or MRI
- Larger than 5 cm sized infected hepatic cysts

Level of Evidence & Recommendation: C1

KQ3. What is the most effective volume reduction therapy option for patients with symptomatic simple hepatic cyst?

Non-surgical treatments such as simple percutaneous drainage with or without sclerosis, minimally invasive deroofing, and complete resection as surgical treatments have been reported.

Aspiration sclerotherapy and laparoscopic unroofing (deroofing) have been reported to be effective for partial or complete obliteration of cysts and relief of symptoms [36]. In non-surgical procedures, due to limited outcomes of simple aspiration [37], sclerosing therapy is frequently being combined. There are various materials for sclerotherapy, such as ethanol [38,39], minocycline [40-42], and polidocanol [43]. In addition, endoscopic transgastric procedures have been reported [41,44].

In comparison between open and laparoscopic methods, the laparoscopic method has been reported to be effective in showing lower morbidities and improving symptoms [23,45]. It has been reported that there is no difference in recurrence [46]. Various methods are being attempted for liver resection. According to one meta-analysis, laparoscopic liver resection is more effective in reducing pain than open surgery [47]. Cases of robotic unroofing [48,49] and liver resection [50] have also been reported.

However, high-quality studies that show the superiority of a particular method have not been reported yet. Even in guidelines for hepatic cysts published to date, no specific method has been proven superior. Thus, it is recommended to select an appropriate method according to the experience and facilities

of each center [4,5,11,51].

Recommendations:

- There are various methods for volume-reducing treatment method, such as percutaneous drainage with or without sclerosing, minimally invasive deroofing, and complete resection. The most accessible and experienced method should be selected according to specific circumstances of each center.

Level of Evidence & Recommendation: C1

KQ4. Is prophylactic coverage of antibiotics necessary for preventing recurrence?

There is no evidence for prophylactic antibiotic treatment for infected hepatic cysts that have completed treatment. Further research is needed on eradication treatment to prevent translocation from the digestive tract, which is one of the hypotheses for causing hepatic cyst infection [52].

Recommendations:

- Prolongation of antibiotic treatment to prevent recurrence in infected cysts is not recommended.

Level of Evidence & Recommendation: C2

KQ5. In case of cyst hemorrhage, when can anticoagulants and antiplatelet therapy be resumed?

There is no high-quality randomized study regarding discontinuation of antithrombotic agents in cases of cyst hemorrhage. However, according to related clinical treatment guidelines, it is recommended to take a rest period of about 1 to 2 weeks, considering the balance between risks due to bleeding and thromboembolism [53,54]. Because benefits and risks of discontinuing treatment vary depending on the patient, it is recommended to determine the duration of treatment discontinuation according to individual patients.

Recommendations:

- In case of cyst hemorrhage, the period of discontinuation of antithrombotic agents is about 1 to 2 weeks. However, it should be decided through an individualized approach considering the risk of bleeding and thrombosis for each patient.

Level of Evidence & Recommendation: C2

Prognosis

KQ1. Do simple hepatic cysts require follow-up?

Simple hepatic cysts are benign lesions that usually do not change significantly in size over time. They follow a slow course. Ultrasound is the first diagnostic tool used when symptoms develop in patients with simple hepatic cysts. If a patient shows symptoms, an ultrasound is used to evaluate the size and determine whether there are complications. Symptomatic hepatic cysts can be treated surgically or with percutaneous

aspiration sclerotherapy. Although some hepatic cysts can grow in size, most simple hepatic cysts are generally benign lesions that do not cause significant changes in size over time or symptoms. Therefore, routine follow-up with imaging is not recommended for most simple hepatic cysts [3,55,56].

Recommendations:

- It is not recommended to follow-up asymptomatic patients with simple hepatic cysts.

Level of Evidence & Recommendation: C1

KQ2. Is follow-up of hepatic cysts necessary after non-surgical treatment?

Imaging may be used to better assess the volume of the residual cyst after non-surgical treatment, such as aspiration sclerotherapy. However, follow-up through regular imaging tests after non-surgical treatment is not recommended, as measuring the size of the cyst regularly through imaging does not affect the degree of treatment success. The success of treatment depends on alleviating symptoms, not reducing the volume of hepatic cysts [57]. Therefore, imaging should be performed if symptoms related to hepatic cysts recur after non-surgical treatment.

Recommendations:

- Follow-up through regular imaging tests after non-surgical treatment is not recommended. Imaging should be performed if symptoms related to hepatic cysts recur after a non-surgical treatment.

Level of Evidence & Recommendation: C1

KQ3. What imaging techniques are recommended for follow-up of hepatic cysts after surgical treatment?

Routine follow-up with imaging after surgical treatment for hepatic cysts is not recommended. It is not advisable to routinely assess the size of the cyst or monitor for recurrence solely through regular imaging after surgical treatment. However, imaging tests should be performed if symptoms related to hepatic cysts recur after surgical treatment [57,58]. If cyst recurrence is suspected after surgical treatment, ultrasound, CT, MRI, and contrast-enhanced ultrasound may be used [3]. The choice of imaging depends on factors such as characteristics of the cyst, patient history, and clinical suspicion of complications.

Recommendations:

- Routine follow-up with imaging after surgical treatment for hepatic cysts is not recommended. If cyst recurrence is suspected after surgical treatment, ultrasound, CT, MRI, and contrast-enhanced ultrasound may be used.

Level of Evidence & Recommendation: C1

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Seoung Yoon Rho, <https://orcid.org/0000-0002-1265-826X>
 Jeong-Moo Lee, <https://orcid.org/0000-0001-7806-8759>
 Min-Su Park, <https://orcid.org/0000-0002-0707-2969>
 Woo-Hyoung Kang, <https://orcid.org/0000-0002-3734-3352>
 Yoonhyeong Byun, <https://orcid.org/0000-0002-4258-891X>
 Seung Jae Lee, <https://orcid.org/0000-0002-3302-6624>
 Aesun Shin, <https://orcid.org/0000-0002-6426-1969>
 Jeong Hee Yoon, <https://orcid.org/0000-0002-9925-9973>
 Bohyun Kim, <https://orcid.org/0000-0003-1157-415X>
 Nam-Joon Yi, <https://orcid.org/0000-0002-5467-425X>

AUTHOR CONTRIBUTIONS

Conceptualization: NJY. Data curation: JML. Methodology: MSP, WHK. YB, SJL. Visualization: JML. Writing - original draft: SYR. Writing - review & editing: AS, JHY, BK.

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