

Long-term safety and efficacy of ethanol retention therapy via percutaneous approach and/or EUS guidance for symptomatic large hepatic cysts (with video)

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ABSTRACT

Background and Objectives: Ethanol retention therapy (ERT) under EUS guidance or a percutaneous approach is a safe treatment for large symptomatic hepatic cysts. However, reports on the long-term outcomes after ERT are very rare. Therefore, we aimed to evaluate the long-term outcomes of ERT in symptomatic large hepatic cysts. **Materials and Methods:** A total of 47 consecutive patients with large symptomatic hepatic cysts treated at the Asan Medical Center from April 2009 to October 2017 were analyzed. Thirty patients with right hepatic cysts were treated with ERT through a percutaneous approach, and 14 patients with left hepatic cysts were treated with ERT under EUS guidance. Three patients were treated with ERT using both methods. **Results:** Of the 47 patients, 43 (91%) showed complete regression and four (9%) showed partial regression on abdominal computed tomography. Recurrence of the cysts was not observed during the follow-up surveillance of a median of 66 months. **Conclusions:** Percutaneous catheter drainage-guided ERT and EUS-guided ERT, based on their favorable long-term outcomes, may be considered as first-line treatments in patients with large symptomatic hepatic cysts.

Key words: Ethanol retention therapy, EUS, hepatic cyst, percutaneous catheter drainage

INTRODUCTION

Many asymptomatic hepatic cysts are found in routine imaging studies. The prevalence of simple hepatic cysts is 2.5%–18%.^[1] Simple hepatic cysts are benign lesions of the main biliary system.^[2] Most hepatic cysts are asymptomatic; however, because of their continuous growth, they can become voluminous and cause symptoms or complicated disease. Typical symptoms

include abdominal pain and distention, dyspnea, early satiety, and nausea.^[3] In the past, surgery was accepted as the treatment of choice for symptomatic simple hepatic cysts; however, high perioperative morbidity (0%–25%) was reported.^[4] Although mere aspiration of cystic fluid is safe and easy to perform, it leads to high recurrence rates (78%–100%).^[5] Various

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10.4103/eus.eus_42_19

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How to cite this article: Lee DS, Lee SK, Seo DW. Long-term safety and efficacy of ethanol retention therapy via percutaneous approach and/or EUS guidance for symptomatic large hepatic cysts (with video). *Endosc Ultrasound* 2020;9:31-6.

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Received: 2019-04-26; **Accepted:** 2019-06-19; **Published online:** 2019-09-26

protocols for aspiration with sclerotherapy have been published with good outcomes;^[6-8] however, long-term data on efficacy and safety are rare and under debate. Especially, ethanol retention therapy (ERT) with EUS guidance for hepatic cysts has not yet been fully evaluated.

EUS can provide a high-resolution image of the liver, gallbladder, and biliary tract. EUS-guided FNA is useful to diagnose relatively small hepatic lesions (<1 cm diameter) in the left hepatic lobe and proximal right lobe and in the hilum and part of the intrahepatic biliary tract.^[9] Percutaneous catheter drainage (PCD)-guided ERT or EUS-guided ERT is safe and effective to treat various symptomatic hepatic cysts. We previously evaluated the efficacy and safety of PCD-ERT and EUS-ERT during a short-term follow-up period.^[10] However, long-term data have not been obtained to date. Therefore, in this study, we aimed to evaluate the long-term outcomes of PCD-ERT and EUS-ERT.

MATERIALS AND METHODS

Ethics and study population

From April 2009 to October 2017, a total of 47 consecutive patients (40 women, 7 men; median age, 62 years) with 59 symptomatic large hepatic cysts were treated with EUS-ERT or PCD-ERT at the Asan Medical Center [Table 1]. This single-center, single-arm study was approved by the Institutional Review Board of the Asan Medical Center, Seoul, Korea (2014-0528), and all patients gave a written informed consent on the use of personal information in the manuscript. The inclusion criteria were as follows: (1) the presence of an abdominal symptom such as pain, early satiety, and/or

bloating; (2) intrahepatic bile duct dilatation on imaging; and/or (3) rapidly increased size on imaging without symptoms. The exclusion criteria were the presence of cystic tumors and infected hepatic cysts and an abnormal coagulation profile. All patients underwent abdominal computed tomography (CT) before and after ethanol therapy.^[10]

Drainage route and techniques

The approach route of the EUS-ERT or PCD-ERT was determined by the size, location, and complexity of the lesion. EUS-ERT was mainly performed in patients with left-sided, multiple, and relatively small hepatic cyst. However, a large hepatic cyst is sometimes difficult to treat with EUS-ERT monotherapy. Huge hepatic cysts can contain more than 3 L of cystic fluid. The needle aspiration procedure under EUS guidance takes too much time and can cause discomfort for the patient. PCD-ERT might be a better approach to reduce the patient's discomfort and the procedure time. PCD-ERT was mainly performed in patients with right-sided and large hepatic cysts. Therefore, in our experience, both methods are necessary to treat huge or multiple hepatic cysts. In patients with multiple hepatic cysts, both EUS-ERT and PCD-ERT were performed.

For EUS-ERT, a therapeutic curved linear array EUS (GF-UCT 260; Olympus Corp., Tokyo, Japan) and a 19- or 22-G needle (EchoTip Ultra; Cook Medical LLC, Bloomington, IN USA) were used to aspirate cystic fluid and inject ethanol. In most cases, a 22-G needle was used. However, a 19-G needle was used for some large cysts to reduce aspiration time. We thought a 19-G needle may increase the risk of leakage of ethanol during patient rotation. Therefore, a 22-G needle was used more frequently. When the cyst volume was small, the amount of ethanol injected was the same as that of the aspirated cystic fluid. However, if the aspirated cystic fluid was more than 200 cc, the maximal amount of ethanol injected was approximately 200 cc considering the risk of possible complications. Antibiotics were administered to all patients before the intervention to prevent infection. The aspirated fluid was submitted for laboratory biochemical analyses.

The EUS-ERT was performed according to the following protocol: (1) the maximum possible volume of cyst fluid was aspirated, and 99% ethanol was injected. Pure (99%) ethanol was used as a sclerosing agent to fix the cells lining the cyst cavity and to disable fluid secretion. The amount of ethanol injected

Table 1. Baseline characteristics of the included patients and hepatic cysts

Characteristics	Values
Median age (years)	62
Number of patients (male/female)	47 (6/41)
Number of cysts (one/two)	59 (35/12)
Reason for intervention	
Early satiety	10
Increased size	5
Abdominal pain	20
IHD dilatation	2
Location of the cyst within the liver	
Right lobe	28 (47)
Left lobe	31 (53)

IHD: Intrahepatic duct

ranged from 10 to 200 cc, which was determined according to the endosonographer's discretion. (2) The procedure of EUS-ERT is not lavage but retention after ethanol injection. Therefore, alcohol injection was performed only once per cyst. After ethanol injection, the echoendoscope was removed from the patient, and the position of the patient was changed to enhance uniform contact with the cyst wall. Injected ethanol was retained for 40 min while rotating the patient's position in succession: supine for 5 min, left lateral decubitus for 5 min, prone for 5 min, and right lateral decubitus for 5 min. Two full rotations took about 40 min. After two rotation cycles, EUS was repeated to ensure the existence of epithelial debris within the cyst cavity [Figure 1], and a cyst puncture and drainage were then performed. Video 1 demonstrates the EUS-ERT procedure performed in a study participant.

PCD-ERT was mainly performed in patients with right-sided and relatively large hepatic cysts. At first, a 7- or 8-Fr percutaneous catheter was inserted into the hepatic cyst for the drainage of the cystic fluid. For large hepatic cysts, it took a long time to drain the cystic fluid. After the drainage of the cystic fluid for 1–2 days, ERT was performed through the PCD catheter. The basic steps of PCD-ERT are similar to those of EUS-ERT, except for the route of injection and reaspiration of ethanol. The injected ethanol was then completely drained, and the PCD catheter was kept in the cyst cavity for 1 day. After the confirmation of drainage, the PCD catheter was removed.

Formal follow-up protocol

During the initial period of this study, residual sizes of the cysts were evaluated using abdominal CT at 1, 3, 6, and 12 months after ERT because of concerns of possible complications. Later, we changed the follow-up CT to 3 and 12 months after ERT for the 1st year. After 1 year, abdominal CT scan was conducted yearly or every 2 years.

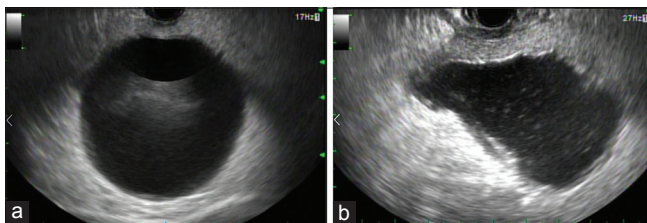


Figure 1. (a) EUS image showing the hepatic cyst before ethanol retention therapy. (b) EUS image showing the existence of epithelial debris within the cystic cavity after ethanol retention therapy

Definition of events

Clinical response means a volume reduction of the hepatic cyst on repeat CT imaging after ERT. Clinical response was divided into complete regression (CR) and partial regression (PR) regression according to the decrease in the size of the hepatic cyst. CR was defined as volume reduction of >90% of the hepatic cyst on repeat CT imaging, and PR was defined as volume reduction of 50%–90% of the hepatic cyst on repeat CT imaging. Symptom resolution was defined as the disappearance of the previous complaints of the patient.

Statistical analysis

Statistical analysis was performed using SPSS software, version 21 (IBM, Armonk, NY USA). Results are reported as mean (standard deviation) for quantitative variables, median (range) for nonparametric variables, and percentages for categorical variables. Descriptive statistics was used to describe patients' characteristics and procedures.

RESULTS

Baseline characteristics of patients are described in Table 1. PCD-ERT was conducted in thirty patients with right hepatic cysts, EUS-ERT was conducted in 14 patients with left hepatic cysts, and both PCD-ERT and EUS-ERT were conducted in three patients with multiple hepatic cysts. The median cyst volume drained before treatment was 347 mL (interquartile range [IQR], 139–801 mL). Two patients with large cysts complained of moderate abdominal pain and nausea that resolved after 2 days. One patient showed ethanol intoxication; however, severe intoxication did not occur, and the symptoms were mild and disappeared after 1 day. The remaining patients showed no changes in the results of the laboratory tests. There were no procedure-related major adverse events, such as infection or mortality. Outcomes of the PCD-ERT and/or the EUS-ERT are shown in Table 2. After treatment, pain or discomfort related to the hepatic cyst completely disappeared in all patients (100% clinical success rate). The median follow-up period after therapy was 66 months (IQR, 41–84 months). After treatment, 43 patients (91%) showed CR and four (9%) showed PR. Further, two patients showed PR to EUS-ERT and two showed PR to PCD-ERT; these patients had relatively large hepatic cysts and multiple cysts compared with other patients. Partial response was defined as volume reduction of 50%–90% on CT imaging. These four patients

Table 2. Clinical and radiological outcomes of patients treated with ethanol retention therapy

Characteristics	Values
Drainage type, n (%)	
PCD	30 (63)
EUS	14 (30)
Combination-ERT	3 (6)
Median amount of injected ethanol, mL (range)	100 (20-200)
Cystic volume	
Median volume of cyst before therapy, mL (IQR)	347 (139-801)
Median volume of cyst after therapy, mL (IQR)	0 (0-6)
Median volume reduction, % (IQR)	100 (99-100)
Cases of clinical response, n (%)	
CR	43 (91)
PR	
EUS-ERT (n = 2)	4 (9)
PCD-ERT (n = 2)	
Median period of clinical response after treatment, months (IQR)	
EUS-ERT	17 (10-36)
PCD-ERT	12 (7-27)
Combination-ERT	22 (12-31)
Recurrence	0
Adverse event, n (%)	
Bleeding	0
Wound infection	0
Alcohol intoxication	1 (2)

CR: Complete regression, PR: Partial regression, ERT: Ethanol retention therapy, PCD: Percutaneous drainage, Combination-ERT: Ethanol retention therapy using both EUS and PCD guidance, IQR: Interquartile range

with PR by volume definition showed good response clinically. The symptoms resolved, and no recurrence was observed during follow-up.

Cases of ERT are shown in Figure 2. The median period of clinical response after EUS-ERT was 17 months (IQR, 10–36 months), and the median period of clinical response after PCD-ERT was 12 months (IQR, 7–27 months). There was no recurrence during the long-term follow-up in any patient with a simple hepatic cyst [Figure 3].

DISCUSSION

Several studies have reported on the high technical and clinical success rates of aspiration sclerotherapy for hepatic cysts; however, there are no standardized protocols concerning the frequency, interval, ethanol amount, or timing of indwelling catheter removal.^[11,12] In addition, there are few studies on the long-term treatment outcomes of ethanol sclerotherapy.^[12,13]

In our previous study, we evaluated 19 hepatic cysts in 17 patients treated with EUS-ERT or PCD-ERT between 2009 and 2012 (short-term follow-up of

a median 11.5 months).^[10] PCD-ERT is a favorable option for right-sided huge hepatic cysts because large amounts of ethanol can be injected and drained without repetitive puncture. EUS-ERT is a favorable option for left-sided hepatic cysts and multiple hepatic cysts because of the possibility of repeated procedures. EUS-ERT permits easy access to the posterior and left segments of the hepatic lobe. In particular, EUS-ERT is the best option for caudate lobe lesions. EUS-ERT can be performed in a single-step approach without catheterization. However, in EUS-ERT, it takes a long time to aspirate large volumes of fluid, thus increasing the risk of alcohol leakage during the procedure.^[14] Therefore, EUS-ERT is favorable for left-sided, relatively small, and multiple cystic lesions.^[10]

The characteristics of the patient group in this study are the same as those of the patient group in our previous study.^[10] Further, patients who were enrolled in the previous study were also included in this study. However, the number of patients increased from 17 to 47 patients. The median follow-up period after therapy increased from 11.5 to 66 months. Although the previous study focused on the technical feasibility and initial safety, this study was focused on the long-term follow-up results. In this study with a long-term follow-up of a median of 66 months, the overall results were satisfactory, as those obtained in our previous study with a short-term follow-up. Both PCD-ERT and EUS-ERT showed favorable clinical outcomes, including volume reduction and symptomatic relief as well as procedural safety. There was no recurrence of hepatic cysts during the follow-up period.

This study has some limitations. First, the single-center design might have an inherent selection bias. Second, there was no control group for a comparison of the effectiveness and safety.

CONCLUSIONS

PCD-ERT and EUS-ERT are useful methods for the treatment of various large hepatic cysts and are associated with a high success rate, excellent procedural safety, and low recurrence rate. On the basis of their favorable long-term outcomes, PCD-ERT and EUS-ERT may be considered as first-line treatments in patients with large simple hepatic cysts.

Consent for publication

Patients provided written informed consent on the use of personal information in manuscripts.

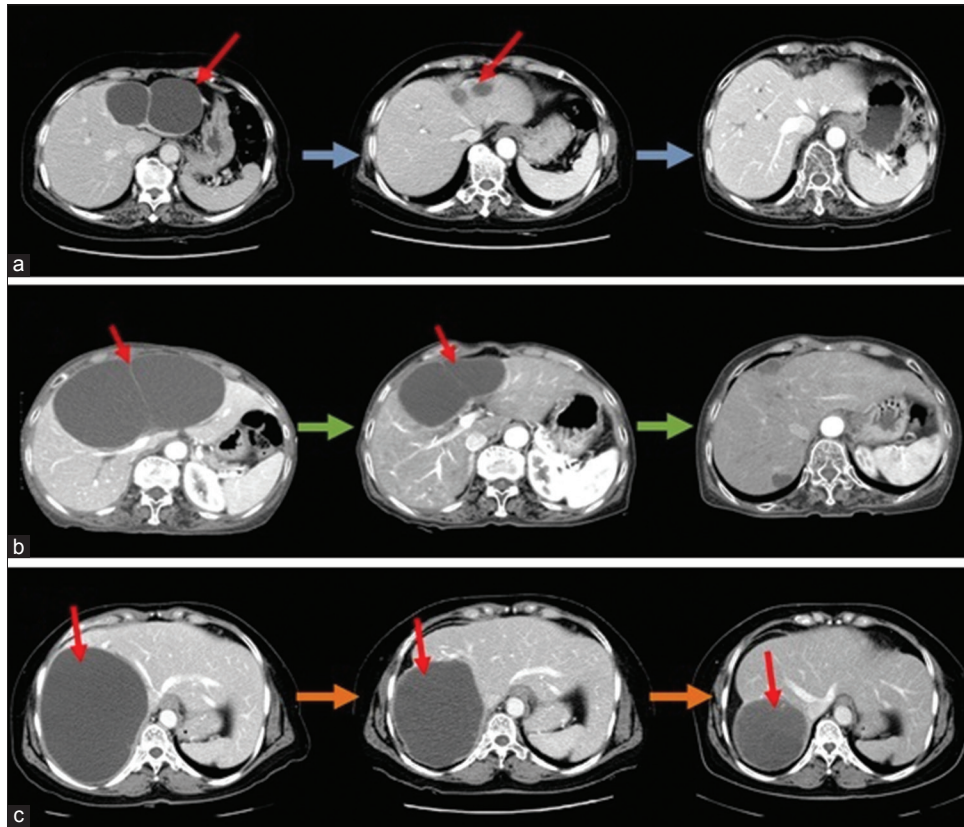


Figure 2. Cases of EUS-ethanol retention therapy and percutaneous catheter drainage-ethanol retention therapy. (a) Complete regression after EUS-ethanol retention therapy for multiple hepatic cysts (left to right: computed tomography scan before therapy, at the 5-month follow-up, and at the 4.8-year follow-up). (b) Complete regression after percutaneous catheter drainage-ethanol retention therapy of multiple hepatic cysts (left to right: computed tomography scan before therapy, at the 1-month follow-up, and at the 2.8-year follow-up). (c) Partial regression in percutaneous catheter drainage-ethanol retention therapy (left to right: computed tomography scan before therapy, at the 1-year follow-up, and at the 3-year follow-up). Abdominal computed tomography scan shows the reduced cyst and re-expansion of the liver parenchyma in the right lobe

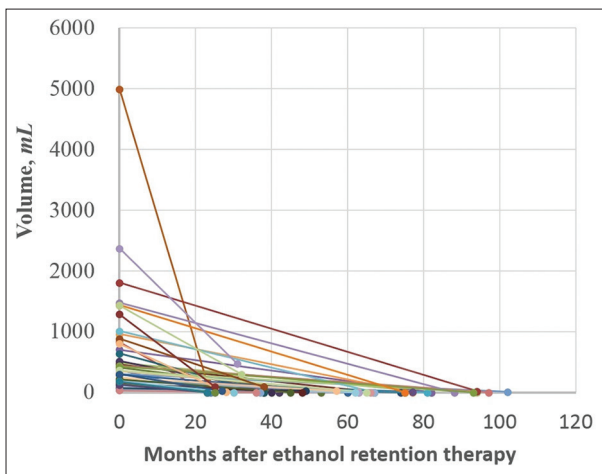


Figure 3. Trend of cyst volume changes before and after ethanol retention therapy

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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