

# Percutaneous Aspiration and Ethanolamine Oleate Sclerotherapy for Sustained Resolution of Symptomatic Polycystic Liver Disease: An Initial Experience

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**OBJECTIVE.** Surgical therapy for symptomatic polycystic liver disease is effective but has substantial mortality and morbidity. Minimally invasive options such as percutaneous aspiration with or without ethanol sclerosis have had disappointing results. The purpose of this study was to evaluate percutaneous aspiration with ethanolamine oleate sclerosis in the management of symptomatic polycystic liver disease.

**SUBJECTS AND METHODS.** The study included 13 patients (11 with polycystic liver disease, two with simple cysts) with 17 cysts. All patients underwent percutaneous aspiration of the liver cyst under ultrasound guidance followed by insertion of a 7-French pigtail catheter, instillation of ethanolamine oleate (10% of cyst volume), and aspiration of the ethanolamine oleate. The catheter was kept in place for 24 hours of open drainage and then removed.

**RESULTS.** All but one of the cysts resolved with one instillation. The one cyst, in a patient with polycystic liver disease, required two instillations 3 months apart. The mean initial volume of cysts was 589.8 mL, and the mean reduction in volume was 88.8%. Both the simple cysts resolved completely. In the cases of polycystic disease, the volume of cysts larger than 10 cm in diameter was reduced by 92.8%. Cyst resolution was gradual, and clinically significant cyst reduction was achieved within 1 year of therapy. None of the patients needed surgery. The median follow-up period was 54 months (range, 1 week–95 months). There were no significant adverse effects, and all patients had relief of symptoms after therapy.

**CONCLUSION.** This initial experience with a single session of percutaneous aspiration and ethanolamine oleate sclerosis resulted in sustained resolution of symptomatic polycystic liver disease with minimal morbidity, avoidance of surgery, and improvement in quality of life.

**Keywords:** ethanol sclerosis, ethanolamine oleate, hepatic cysts, polycystic liver disease, sclerotherapy

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The management of polycystic liver disease (PLD) is notoriously difficult and challenging. Symptomatic cysts first require careful differential diagnosis from cystadenoma, cystadenocarcinoma, and hepatic metastasis. Symptoms can be attributed to hepatic cysts after exclusion of biliary colic, gallstones, reflux disease, peptic ulcer, nonulcer dyspepsia, chronic pancreatitis, and irritable bowel syndrome as potential causes of symptoms [1]. Most patients have no symptoms, but the minority who do have symptoms need to be considered for treatment.

Management options for PLD include needle aspiration with or without injection of a sclerosing solution, internal drainage with cystojejunostomy, deroofing of the cyst by open laparotomy or laparoscopy, varying degrees of liver resection, liver transplantation, and hepatic arterial embolization [2, 3]. Percuta-

neous ultrasound- or CT-guided needle aspiration of hepatic cysts has a high recurrence rate (78–100%) due to the presence of epithelial cell lining [4, 5]. Percutaneous aspiration and ethanol sclerosis for PLD is largely useless because of a high recurrence rate, greater than 75% [1, 6]. The procedure is generally safe and effective in the management of solitary cysts, however, and is associated with a low recurrence rate in that circumstance [6]. Alcohol destroys the cells lining the cyst cavity, disabling cystic fluid secretion [7] and resulting in cyst resolution. Ethanol injected as a sclerosing agent after aspiration of the cyst contents can cause complications if it leaks from a cyst or is systemically absorbed [8]. Therefore, percutaneous sclerosis has been attempted with other substances, such as iophendylate [9], tetracycline chloride [10], doxycycline [11], minocycline chloride [12], and hypertonic saline solution [13]. The surgical options, including

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laparoscopic deroofing with or without hepatic resection and liver transplantation, are effective but have substantial morbidity and mortality and require technical expertise. Surgery therefore is reserved for the few selected cases caused by one or a few dominant cysts superficially located in anterior segments of the right hepatic lobe [14].

Ethanolamine oleate has been used with immense success in sclerotherapy for esophageal varices [15]. Like alcohol, ethanolamine oleate destroys the cystic epithelial cells immediately, bringing about cyst resolution [16]. In a study with a small number of subjects [17], ethanolamine oleate was used successfully for sclerosis of simple hepatic and renal cysts. To our knowledge, in no previous study has ethanolamine oleate been used in sclerotherapy for PLD. Ethanolamine oleate sclerosis is minimally invasive; if it is successful, surgery can be avoided and the quality of life of patients improved. The purpose of this study was to evaluate the usefulness of percutaneous aspiration and ethanolamine oleate sclerosis of symptomatic hepatic cysts, most of which were associated with PLD.

### Subjects and Methods

All patients gave a written consent for the study, and the study protocol was approved by

the ethics committee at our institution. From June 1998 through June 2007, all patients consecutively referred to our department with symptomatic liver cysts were included in this prospective study. These 13 patients (10 women, three men) had 17 cysts. The symptomatic liver cysts were classified into two groups: simple solitary or multiple liver cysts or cysts of PLD. The latter included autosomal dominant PLD and PLD in the presence of polycystic kidney disease.

Simple liver cysts typically were visualized on ultrasound images [18] as anechoic smooth borders with strong posterior echo enhancement and an accentuation of echoes beyond the cyst wall. On CT scans, simple liver cysts appeared as well-demarcated lesions with fluid attenuation and without enhancement after contrast administration. The cysts of PLD typically appeared as multiple homogeneous lesions with fluid attenuation and without wall or content enhancement after IV contrast administration [19]. The volume of the cyst was estimated as the volume of an ellipse, as suggested previously [16].

The procedure was performed on an inpatient basis. The puncture site, needle angle, and depth were chosen in real time at sonography. In patients with multicystic disease, the cyst most probably responsible for the symptoms was chosen for treatment according to location and size. After antiseptic preparation of the skin and local anesthe-

sia with lidocaine, the cyst was punctured with an 18-gauge percutaneous transhepatic aspiration needle. A guidewire was inserted, and a 7-French single pigtail catheter was placed over the guidewire. As much as possible of the contents of the cyst were aspirated, and the cystic fluid was sent for cytologic and bacteriologic examination.

To avoid leakage of ethanolamine oleate, a puncture line traversing normal liver parenchyma was determined. The cyst was opacified by injection of contrast medium to verify the absence of communication between the cyst cavity and the biliary tree and of leak to the peritoneal cavity, urinary tract, or surrounding hepatic vessels. The amount of contrast medium injected was the same as the volume aspirated from the cyst cavity (Table 1).

During cystography in this study, no vessel, bile duct, or urinary structure was visible before ethanolamine oleate sclerosis. In such a situation, percutaneous aspiration with ethanolamine oleate would be contraindicated because of the risk of tissue toxicity. Because 5% ethanolamine oleate is effective for management of varices [15], we used that concentration for cytolysis of the cyst epithelium. There is no consensus, however, on the appropriate volumes of ethanol and ethanolamine oleate for resolution of hepatic cysts. As suggested in a study of ethanol sclerosis [17], a volume of sclerosant equivalent to 10% of the volume of aspirated cystic fluid was injected in this study.

**TABLE 1: Demographic and Cyst Characteristics of Patients with Symptomatic Hepatic Cysts**

Patient No.	Age (y)	Sex	Symptoms	Diagnosis	Size (cm)	Estimated Cyst Volume (mL)	Volume Aspirated (mL)	Amount of Ethanolamine Oleate Injected (mL)	Follow-Up Period (mo)
1	67	M	Back pain	PLD	16×15	1,885	1,700	120	17
2	72	F	Epigastralgia	PLD	10.4×8.7	412	500	70	63
				Second episode	5.2×5.2	73	150	20	
3	86	F	Epigastralgia	PLD	7.7×6.8	185.7	150	16	1
4	72	F	Epigastralgia	PLD	9.1×8.3	328.2	400	40	2
5	45	F	Right hypochondrial pain	PLD	15×15	1,767.2	1,500	100	<1
6	63	M	Epigastralgia	PLD	14×11	887	1,550	100	<1
7	79	F	Abdominal distention	Simple cyst	4.3×3.4	26	34	10	84
8	70	F	Epigastralgia	PLD	7.4×7.2	200.9	120	15	9
9	75	M	Epigastralgia	PLD	8×7.1	211.6	400	60	56
				PLD	11.5×7.8	366.3	400	60	28
10	51	F	Abdominal distention	PLD	10.1×8.8	409.5	600	80	63
				PLD	6.5×6	122.5	350	40	62
11	60	F	Epigastralgia	PLD	11.9×10.8	726.8	1,620	120	54
				PLD	8.4×6.2	169.1	150	20	54
12	59	F	Epigastralgia	Simple cyst	9×9	381.7	350	40	72
13	54	F	Epigastralgia	PLD	15×15	1,767.2	1,000	100	95
				PLD	7×7	179.6	100	20	95

Note—PLD = polycystic liver disease.

After ethanolamine oleate injection, the pigtail catheter was clamped for 30 minutes. The patient was positioned supine for 10 minutes, on one side for 10 minutes, and on the other side for 10 minutes so that all of the cystic epithelium was exposed to the ethanolamine oleate. The ethanolamine oleate was aspirated from the cyst at the end of the procedure. The pigtail catheter was left in place for 24 hours of open drainage and was removed at the end of that period.

The effectiveness of ethanolamine oleate sclerosis of hepatic cysts was evaluated with follow-up ultrasound imaging or CT within 1 week of the procedure. Results of routine clinical blood tests (cell count, aspartate aminotransferase level, alanine aminotransferase level, bilirubin level) were followed for another week. In this series, follow-up ultrasound imaging or CT was performed 3, 6, 12, and 24 months after the procedure. The patients were monitored for adverse effects.

We calculated the data as mean, median, and SD and analyzed them with a spreadsheet program (Excel 2003, Microsoft). The Student's *t* test was used to test significance, which was set at *p* < 0.05.

**Results**

The patient and cyst characteristics are shown in Table 1. The symptoms included abdominal distention and abdominal pain. Nine patients had one cyst, and four patients had two cysts. The mean age of the patients was 65.6 ± 11.7 (SD) years (range, 45–72 years). Fifteen of the 17 cysts managed with percutaneous aspiration and ethanolamine oleate sclerosis were related to PLD; the other two were simple cysts. Both simple cysts were smaller than 10 cm in diameter. Eight PLD cysts had a maximum diameter greater than 10 cm, and seven measured less than 10 cm in diameter. The mean volume of the hepatic cysts was 589.8 ± 618.9 mL (range, 26–1,885 mL), and the mean amount of ethanolamine oleate needed for sclerosis was 57.3 ± 38.2 mL (range, 10–120 mL; median, 50 mL). The mean follow-up period was 44.4 ± 34.1 months (range, 1 week–95 months; median, 54 months).

The results of percutaneous aspiration and ethanolamine oleate sclerosis of symp-

tomatic hepatic cysts and the complications are shown in Table 2. In all patients, pain and symptoms were relieved. The mean volumetric reduction of hepatic cysts with percutaneous aspiration and instillation of ethanolamine oleate was 88.8% ± 14.8% (range, 47.1–100%; median, 93.1%). The reduction was greatest for simple cysts (100% reduction) followed by PLD cysts larger than 10 cm (92.8% reduction) and PLD cysts smaller than 10 cm (80.7% reduction). The mean reduction 1 week, 3 months, and 1 year after treatment was 62.6%, 84.4%, and 96.4% respectively. All but one cyst resolved with a single session of ethanolamine oleate sclerosis; the one cyst required two sessions of instillations 3 months apart. There was no recurrence in any patient.

Table 3 compares the mean, median, and range of characteristics of the hepatic cysts. There are no significant differences in reduction between PLD cysts smaller than 10 cm and those larger than 10 cm. Nor were there

**TABLE 2: Results and Complications of Percutaneous Hepatic Aspiration and Ethanolamine Oleate Sclerosis of Symptomatic Hepatic Cysts**

Patient No.	Cyst Volume (mL)					Percentage Reduction			Complications
	Initial (n = 17)	1-wk Follow-Up (n = 16)	3-mo Follow-Up (n = 8)	1-y Follow-Up (n = 6)	Final (n = 17)	3-mo Follow-Up (n = 8)	1-y Follow-Up (n = 6)	Total (n = 17)	
1	1,885	294.5		157.3	157.4		91.7	91.7	Mild pain, no treatment required
2 <sup>a</sup>	412	59.1	73.6	0.1	0	82.2	99.9	100	None
3	185.7	68.7			69.4			62.6	Mild pain, no treatment required
4 <sup>b</sup>	328.2	N/A			173.9			47.0	Moderate abdominal and back pain, relieved with oral analgesic
5	1,767.2	238.9			238.9			86.5	Mild abdominal pain, right shoulder pain, no treatment required
6	887	139.1			139.1			84.4	None
7	26	26			0			100	Vasovagal reflex, improved with atropine; mild abdominal pain, no treatment required
8	200.9	70.8	31.5	0.7	0.7	84.3	99.7	99.7	Mild abdominal pain, no treatment required
9	211.6	171.9	43.6		29.4	79.4		86.1	None
	366.3	112.5		45.3	13.7		87.6	96.3	None
10	409.5	298.2	12.7		29.1	96.9		92.9	Mild right abdominal pain, no treatment required
	122.5	107.4	40.6		7.5	66.9		93.9	Right abdominal pain, distention; no treatment required
11	726.8	243.7	73.5		49.8	89.9		93.2	None
	169.1	60	32.3		41.6	80.9		75.4	None
12	381.7	50.3	19.6		0	94.9		100	Severe abdominal pain, relieved with oral analgesics
13	1,767.2	84.1		3.7	2.8		99.8	99.8	Mild abdominal pain, no treatment required
	179.6	14		0.3	0		99.8	100	Mild fever, no treatment required
Mean	589.8	122.6	44.4	34.6	56.2	84.4	96.4	88.4	

Note—N/A = not available.

<sup>a</sup>Patient 2 underwent two treatment sessions.

<sup>b</sup>Patient 4 underwent only a 1-month follow-up examination.

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**TABLE 3: Mean Reduction of Cyst Volume With Respect to Sex, Diagnosis, and Size of Cysts**

Characteristic	No. of Cysts	Initial Cyst Volume (mL)			Mean Volume Reduction (%)	p
		Mean	Median	Range		
Patient sex						
Male	3	1,287.99 ± 933.9	1,767.2	1,885 – 211.6	87.3 ± 3.8	0.62
Female	14	440.2 ± 447.7	328.2	1,767.2 – 26	90.6 ± 16.1	
Nature of cystic disease						
Simple cyst	2	203.9 ± 251.5	203.9	381.7 – 26	100	0.99
Polycystic liver disease	15	641.3 ± 633.7	366.3	1,885 – 73.5	88.8 ± 15.2	
Size of cysts in polycystic liver disease						
> 10 cm	8	1,027.6 ± 669.5	806.9	1,885 – 366.3	94.5 ± 5.4	0.87
< 10 cm	7	199.7 ± 63.4	185.7	328.2 – 122.5	80.7 ± 20.1	

Note—NS = not significant.

differences between simple cysts and PLD in regard to efficacy of resolution with ethanolamine oleate therapy. Men and women also had similar results regarding resolution of cysts. Figure 1 shows the CT images of a liver cyst before and after sclerosis with ethanolamine oleate. That none of the patients needed surgical therapy for symptomatic PLD in the follow-up period resulted in excellent quality of life.

No major complications occurred that could have been considered life-threatening or precluding treatment. There was, however, one episode of vasovagal attack, which was managed with conservative treatment without stopping the ethanolamine oleate sclerosis treatment session. In six of the 17 cases of cyst treatment (35.3%), the patient had no pain or complications. In nine cases (52.9%), the patient had mild pain, which did not require analgesics and two patients had moderate to severe abdominal pain necessitating oral analgesics, and one patient (11.1%) had a self-resolving mild fever.

### Discussion

Minimally invasive techniques such as ethanol sclerosis have been disappointing in the management of PLD in spite of relative success in resolution of simple hepatic cysts. Previous reports [1, 7] have suggested high recurrence rates among patients with PLD, some reports showing a greater than 75% recurrence rate. Furthermore, resolution with ethanol as a sclerosing agent occurs in fewer than 25% of patients with PLD. The results are better for simple cysts, in the range of 80–90% [3–7]. The poorer long-term treatment response among PLD patients may be due to the more rigid hepatic architecture in polycystic than in normal livers, which

results in inadequate cyst collapse [19–23] during the aspiration phase of treatment. In our study, percutaneous aspiration and ethanolamine oleate sclerosis led to resolution of 15 of 15 PLD cysts in only one treatment session in 93.3% (14/15) of cases and two sessions in 6.7% (1/15) of cases.

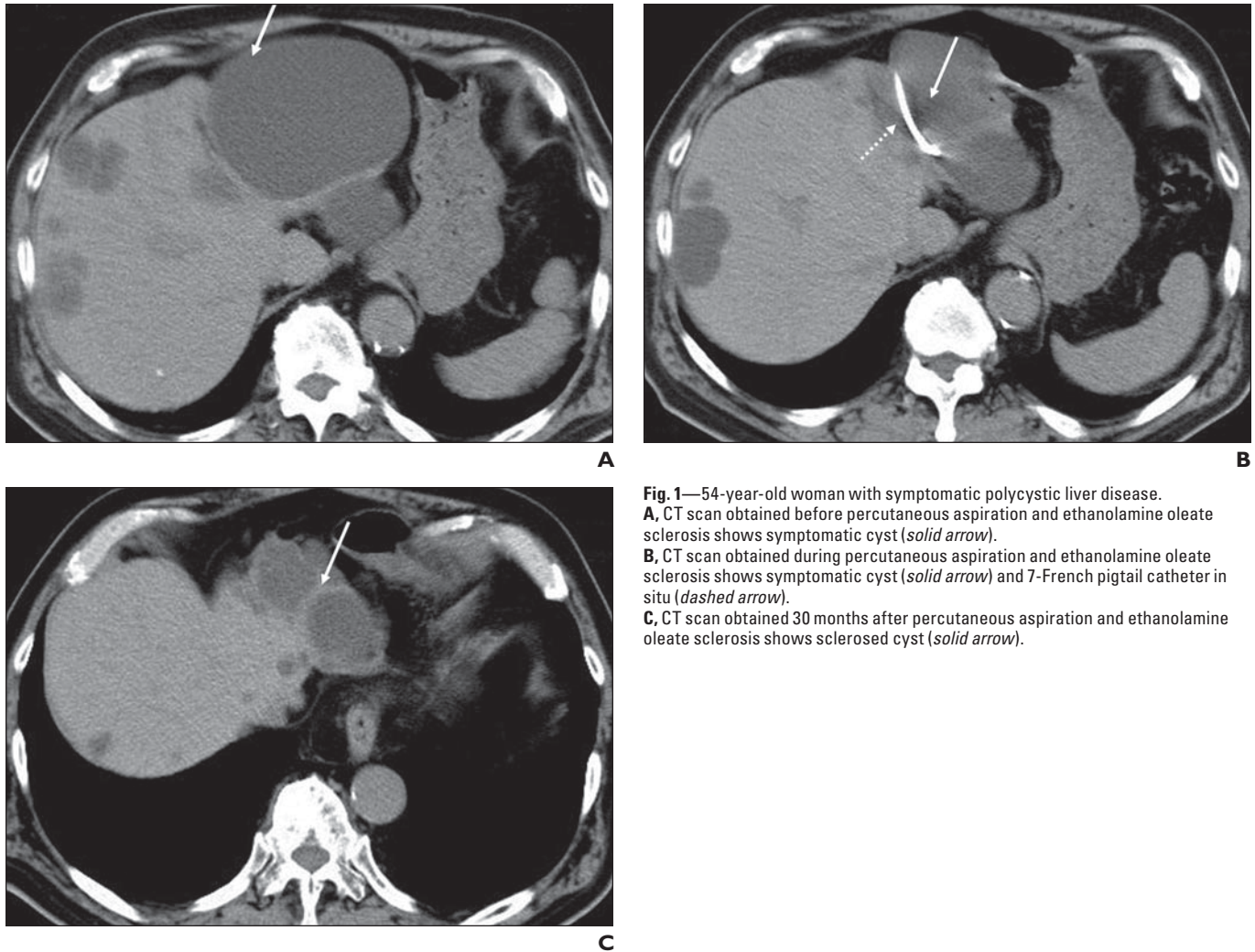
Our results are groundbreaking compared with the previous techniques of simple percutaneous aspiration with or without ethanol sclerosis and surgical therapy. Percutaneous aspiration alone has an almost 100% recurrence rate [4], and its role is limited only to a diagnostic tool for establishing the link between the hepatic cyst and the symptoms [1]. Percutaneous aspiration of a cyst followed by instillation of ethanol has not resulted in sustained reduction in cyst volume. Erdogan et al. [1] found a recurrence rate of 78.7% within a few months of ethanol sclerosis of PLD, and a second attempt at sclerosis did not improve the efficacy of cyst resolution. Other studies [7, 20] have shown similarly high recurrence rates and poor cyst and symptom resolution. We believe the success of percutaneous aspiration with ethanolamine oleate sclerosis for cyst resolution in our study may have been primarily due to the use of ethanolamine oleate and the technique used. Improved resolution with ethanolamine oleate probably occurred because ethanolamine oleate is more effective than alcohol in destroying the epithelium of the cyst. Exposure to ethanolamine oleate leads to cytolysis followed by thrombogenesis. The ethanolamine oleate functions as a cytolytic agent owing to its anionic surfactant properties that brings about a change in cellular permeability [17].

We used an innovative method of leaving the ethanolamine oleate catheter in place with open drainage for 24 hours. Aspiration of the

cystic contents led to collapse of the cyst, resulting in better exposure of the endothelium of the cyst wall to the ethanolamine oleate. We believe the walls of PLD cysts are stiffer and less likely to collapse than those of other cysts and are therefore responsible for the high recurrence rate. It is probable that this technique of open drainage for 24 hours may have caused the cyst to remain collapsed, ensuring greater contact between the cyst epithelium and the ethanolamine oleate and enabling more efficient and sustained sclerosis. None of the patients needed surgical therapy for symptomatic PLD in the follow-up period. All patients in this study experienced relief of the pretreatment symptoms and had excellent quality of life after treatment.

Except for mild to moderate pain in approximately 60% of patients, there were no major adverse effects. The other 40% of patients had no adverse effects. No late-onset adverse reactions were apparent in the long-term follow-up period of up to 95 months. In contrast, several cases of complications have been associated with ethanol sclerosis [7, 11], the incidence being approximately 6.7% [1]. Complications of the use of percutaneous ethanol for ablation therapy can occur during placement of the needle into the target organ or tissue or as a result of injection of ethanol into the body. Complications related to injection of ethanol may be secondary to absorption of ethanol into the bloodstream or to unintentional intravascular injection. Absorbed ethanol can cause various degrees of intoxication and hypotension. In addition, one of the metabolites of ethanol, acetaldehyde acetate, can cause hypotension by inducing peripheral vasodilatation. Normally, the enzyme acetaldehyde dehydrogenase neutralizes acetaldehyde ac-





**Fig. 1**—54-year-old woman with symptomatic polycystic liver disease. **A**, CT scan obtained before percutaneous aspiration and ethanolamine oleate sclerotherapy shows symptomatic cyst (solid arrow). **B**, CT scan obtained during percutaneous aspiration and ethanolamine oleate sclerotherapy shows symptomatic cyst (solid arrow) and 7-French pigtail catheter in situ (dashed arrow). **C**, CT scan obtained 30 months after percutaneous aspiration and ethanolamine oleate sclerotherapy shows sclerosed cyst (solid arrow).

etate in the blood stream. Thus persons with congenital acetaldehyde dehydrogenase deficiency are at greater risk of prolonged hypotension than those with normal levels of this enzyme. One of the late complications of ethanol sclerotherapy has been intracystic hemorrhage [21]. Therefore, in comparison with ethanol sclerotherapy, ethanolamine oleate sclerotherapy not only achieves much better reduction without recurrence or need for surgery but also has a more favorable short-term and long-term adverse effect profile.

Surgical therapy has been the mainstay of management of PLD. Open and laparoscopic fenestration procedures, which are the least invasive surgical procedures, have recurrence rates of 11–100% and 0–100%, respectively, and morbidity rates of 0–66% and 0–67% [5, 20, 24–26]. The rate of symptom recurrence for laparotomy with fenestration ranged from 11% to 26% in the largest

case series [20]. The combination of fenestration and hepatic resection has a low mortality (3–11%) but relatively high morbidity rate (20–100%) and can be considered only for patients with extreme symptoms [20, 27, 28]. Liver transplantation, the most invasive of techniques, is indicated in the care of patients with symptoms refractory to other techniques or who have liver disease combined with renal failure [29]. Experience with hepatic arterial embolization for PLD is limited to a single published report [30] and hepatic arterial embolization is a more invasive technique than percutaneous aspiration and sclerotherapy and cannot be directed at a specific cyst.

Limitations of this study were the small number of patients, that it was conducted at a single center, that patient inclusion was not randomized, and lack of a control arm. In addition, follow-up data collection varied wide-

ly; data on only 47.1% (8/17) and 35% of the cysts were available 3 months and 1 year after treatment. We conclude that a single session of percutaneous aspiration and ethanolamine oleate sclerotherapy is safe and effective, resulting in sustained resolution for a long follow-up period with minimal morbidity and preventing surgery. Further randomized control trials and comparison with existing surgical and nonsurgical options are needed.

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