Original Research

Endoscopic Ultrasound

OPEN

EUS-guided lauromacrogol ablation with different concentrations of lauromacrogol for the treatment of pancreatic cystic neoplasm: A randomized controlled study

Fei Gao[1,2,#], Huikai Li[1,#], Xiuxue Feng[1], Qianqian Chen[1], Chen Du[1], Bingqian Cheng[1,3], Ke Han[1,3], Ningli Chai[1,*], Enqiang Linghu[1,*]

ABSTRACT

Objectives: To explore the safety and efficacy of injections of 1%, 2%, or 3% lauromacrogol during EUS–guided lauromacrogol ablation (EUS-LA) for the treatment of pancreatic cystic neoplasms (PCNs) and to determine the optimal concentration of lauromacrogol for use in EUS-LA therapeutic regimens.

Methods: From May 2021 to January 2023, patients who met the indications for EUS-LA were randomly divided into 3 groups: A, B, and C; the patients in these groups were injected with 1%, 2%, and 3% lauromacrogol during EUS-LA, respectively. Safety was evaluated based on the incidence of postoperative complications. Efficacy was comprehensively evaluated by assessing the ablation rate and ablation effect.

Results: Forty-two patients underwent EUS-LA, and 31 patients completed at least 1 postoperative re-examination. No acute pancreatitis was observed in the 1% and 2% lauromacrogol groups, and 1 case of acute pancreatitis occurred in the 3% lauromacrogol group. The total complication rate was 2.4%. The median ablation rates of the groups were 94.1%, 82.0%, and 100.0%, respectively. There were statistically significant differences in the EUS-LA ablation rate between the 1% and 3% lauromacrogol groups and between the 2% and 3% lauromacrogol groups. There was a statistically significant difference in complete disappearance between the 1% and 3% lauromacrogol groups as well as between the 2% and 3% lauromacrogol groups.

Conclusion: The short-term outcomes showed that injections of 1%, 2%, and 3% lauromacrogol were safe for use in EUS-LA, and injection of 3% lauromacrogol was the most effective for EUS-LA.

Keywords: EUS; Lauromacrogol; Ablation; Pancreatic cystic neoplasm

INTRODUCTION

The prevalence of pancreatic cystic neoplasms (PCNs) has reached 2%–45%.[1–4] The approaches that are used to treat different types of PCN vary depending on malignancy; for example, the risk of serous cystic neoplasm (SCN) is low, whereas mucinous cystic neoplasm (MCN) has the potential to develop into pancreatic cancer.[5] Radical surgical resection is the traditional treatment for PCN,[6] but resecting a tumor while removing part of the pancreas and even parts of other organs impacts the body to different degrees. Moreover, surgical resection of pancreatic tumors is technically difficult, and this treatment is associated with a high rate of perioperative complications that substantially reduce the quality of life of patients after surgery.

Since the concept of super minimally invasive surgery (SMIS) was introduced,[7] surgical approaches that preserve organs and cure disease have increasingly been accepted by patients. EUS–guided lauromacrogol ablation (EUS-LA) treats PCNs using EUS-guided fine needle aspiration (EUS-FNA) technology while preserving the anatomy of the pancreas. Our previous studies showed that EUS-LA has good efficacy and safety in the treatment of PCNs, with stable long-term efficacy.[8–10] However, the complete resolution (CR) rate for PCN was only 51.4% for patients with a follow-up time of more than 1 year. To improve the efficacy of lauromacrogol ablation, we performed animal studies and showed that injecting 1%, 2%, or 3% lauromacrogol to ablate cystic tumors in animal models had good safety and efficacy[11]; thus, we used these 3 concentrations of lauromacrogol in a single-center, randomized controlled trial of EUS-LA, and we hypothesize that the 3% lauromacrogol have the best efficacy for treating PCNs according to previous polidocanol studies. The purpose of this study was to investigate the safety and efficacy of EUS-LA with injection of 1%, 2%, or 3% lauromacrogol and to determine the optimal lauromacrogol concentration for use in EUS-LA therapeutic regimens.

[#]Fei Gao and Huikai Li contributed equally to this article.

[1]Department of Gastroenterology, the First Medical Center of Chinese PLA General Hospital, Beijing 100853, China; [2]Government Offices Administration of the Central Military Commission, Beijing 100034, China; [3]Chinese PLA Medical School, Beijing 100853, China.

* **Address for correspondence:** Fuxing Road 28, Haidian District, Beijing, China. E-mail: linghuenqiang@vip.sina.com (E. Linghu); csxlily@vip.163.com (N. Chai).

Endoscopic Ultrasound (2025) 14:1

Received: 11 October 2024; **Accepted**: 2 January 2025.

Published online: 3 March 2025.

http://dx.doi.org/10.1097/eus.0000000000000105

METHODS

Patients

Patients who received an initial diagnosis of PCN from May 2021 to January 2023 were prospectively included. The inclusion criteria for patients who met the indications for EUS-LA were as follows: (1) presence of a PCN that did not connect with the pancreatic duct on imaging, (2) age ≥18 years, (3) maximum PCN diameter ≥1.5 cm, and (4) informed consent provided. The exclusion criteria were as follows: (1) pancreatic pseudocyst (PPC)/walled-off necrosis (WON)/intraductal papillary mucinous neoplasm (IPMN)/solid pseudopapillary neoplasm (SPN) indicated by further examination after admission; (2) possibility of malignancy could not be excluded or high possibility of malignancy development; (3) intravenous anesthesia and endoscopic operation could not be tolerated; (4) high surgical risk factors, such as severe cardiovascular or respiratory disease, coagulation dysfunction, or pregnancy; and (5) refusal to cooperate with postoperative follow-up. Due to the communication between cystic tumors and the pancreatic duct, lauromacrogol that is injected into the tumor may enter normal pancreatic tissue through the pancreatic duct and cause pancreatitis, so IPMN was excluded. This study was approved by the Institutional Review Board of the Chinese PLA General Hospital (No. S2021-071-01) and registered in the Chinese Clinical Trials Registry (No. ChiCTR2100044096).

Preoperative preparation

Relevant preoperative examinations and tests, including routine blood tests, blood biochemistry tests, coagulation function analysis, tumor marker analysis, chest x-ray, electrocardiogram (ECG), pancreatic enhanced magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP), and other examinations, were completed after admission. Patients who were unable to undergo MRI underwent enhanced computed tomography (CT) of the pancreas. Patients who met the indications for EUS-LA were randomly divided into 3 groups, namely, groups A, B, and C, using a random number table that was generated by SPSS 25.0 (IBM, USA). The patients in groups A, B, and C were injected with 1%, 2%, and 3% lauromacrogol, respectively. To control bias, this study was a "triple-blind" experiment; the patients, endoscopists, and data analysts were blinded to the grouping status, and the data analysts were not involved in the clinical work.

EUS-LA procedures

The equipment, instruments, and drugs that were used in the EUS-LA procedure are listed in Tables 1 and 2.

EUS-LA was performed by 3 experienced endoscopists. The procedure was as follows. (1) linear array EUS was used to scan the PCN to observe its size, cyst wall, septum, nodules, relationship with the pancreatic duct, and blood supply. The contrast agent, sulfur hexafluoride microbubbles, was intravenously injected, and contrast-enhanced EUS (CE-EUS) mode was used to further confirm whether septa, nodules, or pancreatic duct connection was present. (2) EUS-FNA was performed, and as much cystic fluid was aspirated as possible until the PCN almost completely disappeared. (3) The color, viscosity, transparency, and volume of the extracted cyst fluid were recorded, the fluid was sent for cytological and biochemical tests, and the inside of the PCN was fully lavaged with normal saline. If communication between the pancreatic duct and the PCN could not be confirmed, the relationship between the 2 tissues was evaluated by observing the enhancement of the pancreatic duct after intracapsular injection of sulfur hexafluoride microbubbles. (4) SpyGlass fiber optics was inserted via a 19A puncture needle to directly observe the inside of the PCN. EUS-guided through-the-needle biopsy (EUS-TTNB) was performed to obtain cyst wall tissue samples for histological examination to confirm the diagnosis. (5) The indicated concentration of lauromacrogol was injected into the PCN until the cyst volume recovered to approximately the original volume. (6) Injection and extraction of lauromacrogol were repeated 2–3 times, and lauromacrogol remained in the PCN for approximately 1 minute after each injection to ensure its concentration in the PCN. After the last injection, part of the lauromacrogol injection was aspirated, and a lauromacrogol volume equal to 1/2–2/3 of the maximum volume of PCN was retained. (7) Finally, the puncture needle was withdrawn. The EUS-LA procedure is shown in Figure 1.

Postoperative care and follow-up

Patients were closely monitored after EUS-LA. ECG monitoring was performed within 2 hours after the procedure, routine blood tests and blood biochemistry were repeated on the first day after the procedure, and body temperature and physical signs were recorded daily. The patients fasted for 3 days postoperatively and then gradually transitioned to a normal diet. Proton pump inhibitors (PPIs) and antibiotics were intravenously administered for 2–3 days, followed by oral PPI therapy for 3–7 days. Somatostatin was intravenously administered until the serum amylase levels returned to normal. Possible adverse events (AEs) and acute pancreatitis were recorded in detail. Patients were re-examined by imaging 3, 6, and 12 months after EUS-LA, and then annual re-examinations were recommended.

Definitions

The preliminary diagnosis of PCN was based on the characteristics of the cyst fluid, combined with medical history, clinical manifestations, MRI or CT, EUS and CE-EUS, the cyst fluid string sign, and

Table 1

Equipment and instruments used in EUS–guided lauromacrogol ablation.

Equipment and instruments	Model	Company	Country
Ultrasound endoscope	GF-UCT260	Olympus	Japan
EUS mainframe	Prosound F75	Aloka	Japan
Endoscopy mainframe	CLV-290SL	Olympus	Japan
EUS-guided puncture needle	19A	Cook	Ireland
	19G	Cook	Ireland
	22G	Cook	Ireland
Biopsy forceps for puncture needle	KG0208–230	H. + H. Maslanka Chirurgische Instrumente GmbH	Germany
SpyGlass fiber optics	Lightsource 4619	Boston Scientific	USA
SpyGlass camera	SpyGlass Camera 4610	Boston Scientific	USA

Table 2

Drugs used in EUS–guided lauromacrogol ablation.

Drug	Dosage	Manufacturer	Country
Lauromacrogol for injection	10 mL:100 mg (1%)	Shaanxi Tianyu Pharmaceutical Co., Ltd	China
	10 mL:200 mg (2%)	Shaanxi Tianyu Pharmaceutical Co., Ltd	China
	10 mL:300 mg (3%)	Shaanxi Tianyu Pharmaceutical Co., Ltd	China
Sulfur hexafluoride microbubbles for injection		Bracco Suisse SA	Switzerland

SpyGlass imaging. Considering factors such as the high cost of EUS-FNA, the risk of repeated intravenous general anesthesia for patients, and the reduction in the volume of the PCN after the first EUS-FNA, which affects the second EUS-FNA, patients who met the indications for EUS-LA underwent EUS-LA in sequence after EUS-FNA. If the diagnosis of PCN was not definitive, EUS-LA was not performed until the diagnosis was confirmed through pathological diagnosis and cyst fluid analysis.

Rapid on-site evaluation (ROSE) is not available during each EUS-LA procedure in our center, so the suggestive diagnosis of PCN was based on EUS-TTNB histopathological diagnosis as the gold standard; if there was not enough tissue for biopsy pathology, EUS-FNA cyst fluid cytopathological diagnosis was used as the gold standard; and if cytology could not confirm the diagnosis, cyst fluid biochemical tests were used for the diagnosis. If a single endoscopist could not make a clear diagnosis, the diagnosis was decided upon by 3 experienced endoscopists after discussion.

The cyst fluid string sign was considered positive when cyst fluid could be stretched by >3 mm after a drop of cyst fluid was placed between the thumb and index finger and the 2 fingers were slowly separated.[12,13] The biochemical cyst fluid tests included carcinoembryonic antigen (CEA), amylase, and glucose analyses. Cyst fluid CEA levels >192 ng/mL or cyst fluid glucose levels <50 mg/dL often suggest that the PCN is a mucinous cystic tumor.[14] Cyst fluid amylase levels <250 IU/L essentially rule out the possibility of pancreatic pseudocysts.[15]

The diagnosis of acute pancreatitis was defined as typical pain with an amylase/lipase level >3 times the upper limit normal level.[16]

The preoperative original volume (OV) and postoperative final volume (FV) of the PCN were determined by importing the patient's MR or CT images into Materialize's interactive medical image control system (MIMICS; Materialise Company, Switzerland) software. After manually marking the PCN range layer by layer, tumor models were automatically reconstructed in 3D, and the tumor volume was calculated. Part of the software interface is shown in Figure 2.

In this study, the primary outcome is the efficacy of EUS-LA, which was assessed via 2 methods. (1) The ablation rate ($1-\frac{FV}{OV}\times 100\%$) was quantitatively assessed by determining changes in tumor volume before and after EUS-LA. (2) To determine the ablation effect, we previously used the "3 grades" criterion: (1) complete resolution (CR): FV was <5% of the OV; (2) partial resolution (PR): FV was 5%–25% of the OV; and (3) stable: FV was >25% of the OV. According to the previous consensus, the "3 grades method" for evaluating EUS-guided ablation included 2 grades that were considered to indicate efficacy, namely, CR and PR[17]; however, this approach is not accurate enough for cystic tumors. Therefore, in our study, we used the "six grades" criterion[10] that was recently proposed by our team: (1) complete disappearance: no PCN in imaging (FV = 0); (2) nearly complete disappearance: FV was <10% of the OV; (3) significantly effective: FV was 10%

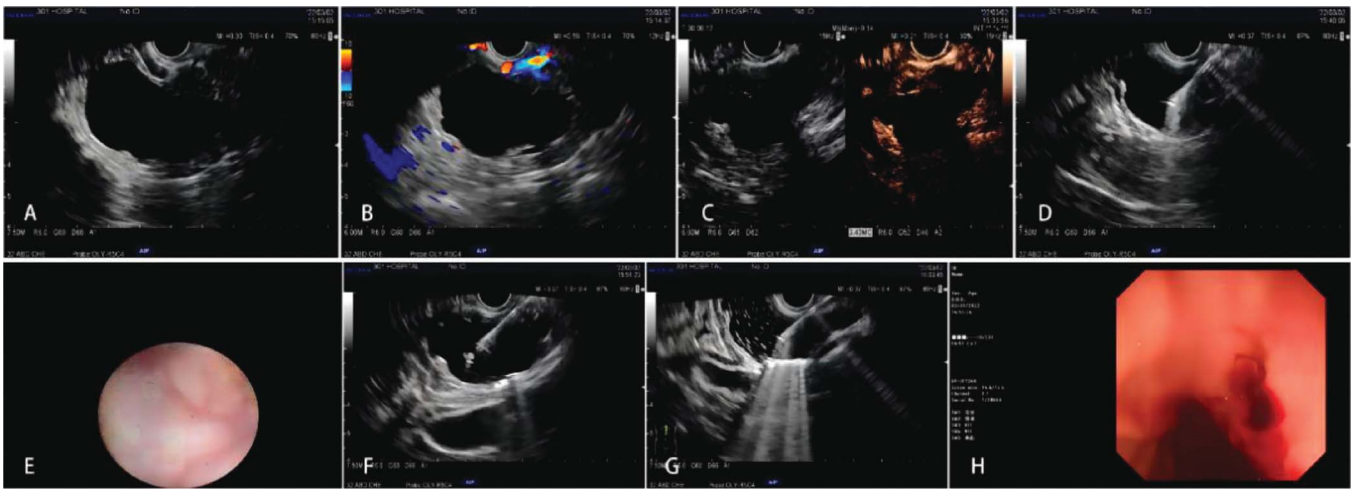

Figure 1. EUS-LA procedure. A, PCN was scanned by EUS. B, Color Doppler flow imaging showed no obvious blood flow signal inside the PCN. C, PCN was scanned by CE-EUS to further evaluate the internal structure. D, The fluid inside the PCN was aspirated using EUS-FNA and was sent for examination. E, SpyGlass revealed a "branch-like" vascular network on the cyst wall. F, EUS-TTNB, biopsy specimen was sent for pathology examination. G, EUS-LA, microbubbles can be seen inside the PCN after the injection of lauromacrogol. H, The needle was retracted to observe whether there was active bleeding at the puncture site.

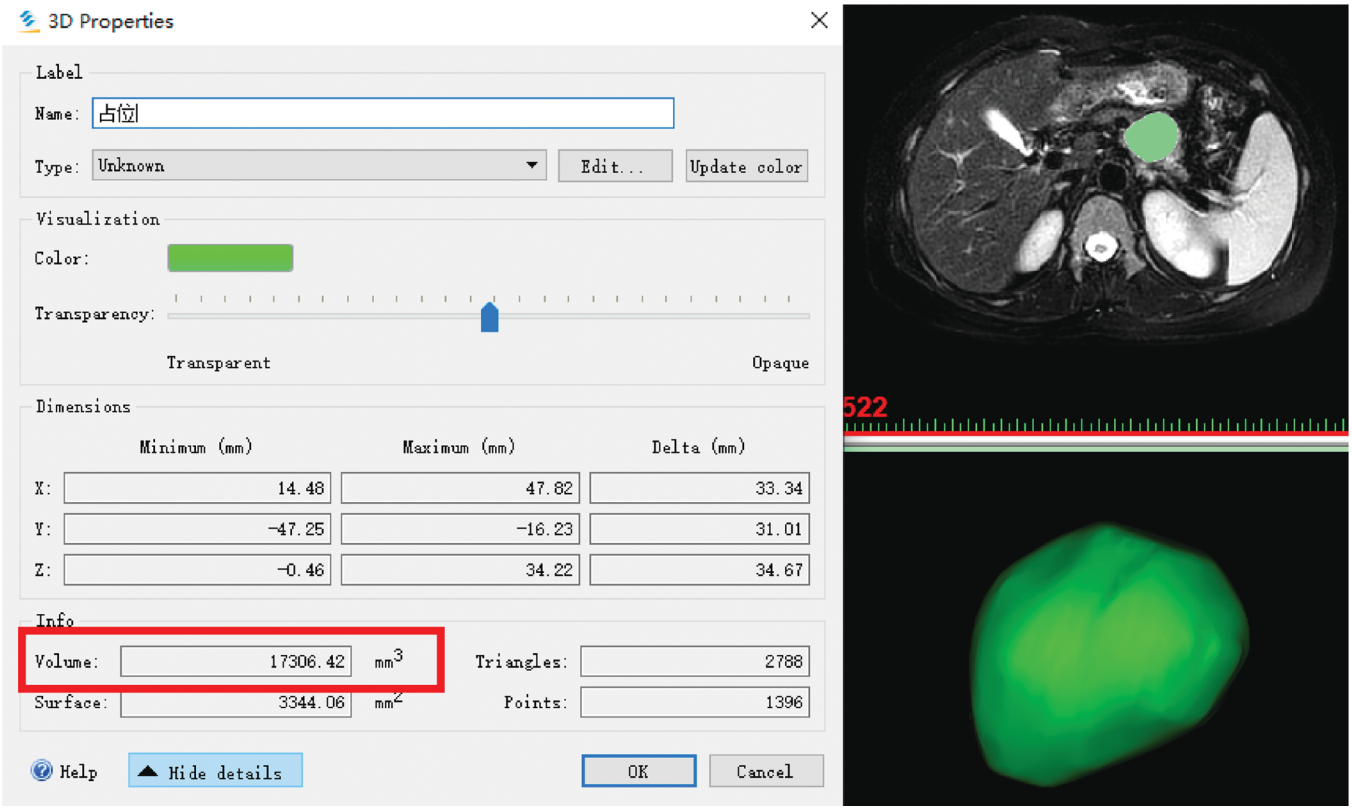

Figure 2. MIMICS automatically calculate and display the volume of the tumor after 3D reconstruction (the volume shows in the red box).

to 25% of the OV; (4) effective: FV was 25% to 75% of the OV; (5) stable: FV was 75%–100% of the OV; and (6) progression: PCN volume increased (FV was >OV). The "six grades" criterion for evaluating EUS-LA included four grades that were considered effective: complete disappearance, nearly complete disappearance, significant effect, and effective. The flowchart for this study is shown in Figure 3. The secondary outcome is the incidence of AE, postoperative acute pancreatitis, which indicates the safety of EUS-LA.

Statistical methods

SPSS 25.0 (IBM Corp, Armonk, NY) was used for data entry and analysis. Quantitative data with a normal distribution are presented as the mean ± standard deviation (SD), and data with a nonnormal distribution are presented as the median (range). Quantitative data were analyzed using the nonparametric Kruskal-Wallis *H* test. Categorical variables are presented as counts (constituent ratios). Categorical variables were analyzed using the chi-square test and Fisher's exact test. $P < 0.05$ was considered to indicate statistical significance. Bonferroni correction was used to make pairwise comparisons between the 3 groups, and $P < 0.02$ was considered to indicate statistical significance.

RESULTS

From May 2021 to January 2023, a total of 54 patients with suspected PCN were included in this study, and 12 patients were excluded after the preoperative examination was completed. Three patients were excluded because the lesion was found to be connected to the pancreatic duct during the EUS examination, and IPMN was diagnosed based on pathological diagnosis and cyst fluid analysis after EUS-FNA. Two patients were excluded because CE-EUS showed high enhancement, and NEN was diagnosed based on the pathological results after EUS-FNA. One patient was excluded because a cystic lesion with suspected communication with the pancreatic duct was observed during EUS examination, coffee-like fluid was extracted by EUS-FNA, and PPC was considered based on the cyst fluid analysis results combined with medical history. One patient was excluded due to insufficient diagnostic evidence and the inability to determine the type, even after discussion. One patient was diagnosed with PCN by imaging examination, but EUS suggested that the lesion was an abdominal cyst adjacent to the pancreas. Two patients were diagnosed with PCN by imaging examination, but EUS showed no obvious pancreatic space-occupying lesions; these patients were excluded. One patient was determined to have self-absorbed PPC based on medical history, and 1 patient was considered to have an MCN that achieved CR from the last imaging re-examination to readmission after EUS-LA. Imaging examination of one patient indicated that the maximum diameter of the PCN was ≥1.5 cm, but the diameter measured by EUS was less than 1.5 cm, which does not meet the indications for EUS-LA. One patient refused EUS-LA or regular follow-up after signing the informed consent form and was excluded.

A total of 42 patients received EUS-LA. The baseline characteristics for each group are summarized in Table 3.

Safety outcomes

No postoperative acute pancreatitis was observed in the 1% or 2% lauromacrogol group after EUS-LA. A young female patient in the

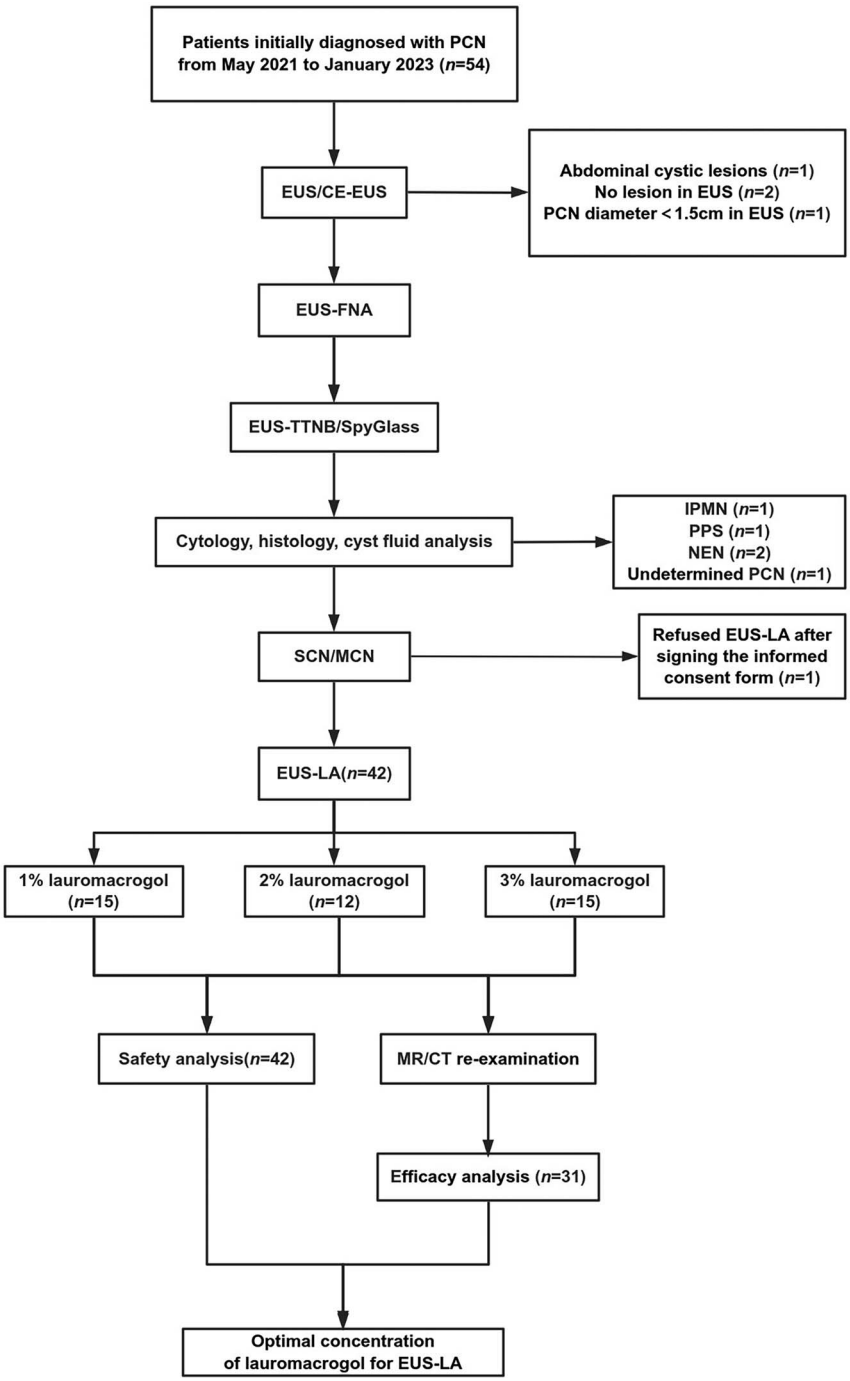

Figure 3. Study flowchart.

3% lauromacrogol group developed abdominal pain after resuming a liquid diet after EUS-LA. The patient indicated that the pain could be tolerated without the need for medication. Abdominal CT revealed pancreatic edema and peripheral exudation, so the patient was diagnosed with acute pancreatitis after EUS-LA. After acid suppression, enzyme suppression, anti-infection, and other symptomatic treatments, the patient's symptoms significantly improved after 2 days, and her blood amylase levels decreased to within the normal range. The patient was discharged without obvious discomfort.

The total complication rate was 2.4%, and the complication rate in group C was 6.7%. There was no significant difference in the complication rates among the 3 groups ($P = 1.000$). No patients had serious complications that were unresponsive to conservative drug treatment or required surgical intervention. The specific complications in each group are listed in Table 4.

Efficacy outcomes

As of January 2023, 1 patient had been excluded because she refused follow-up, and 10 patients had not been re-examined with

Table 3

Baseline characteristics of the patients and PCNs.

Characteristics	Group A (*n* = 15)	Group B (*n* = 12)	Group C (*n* = 15)	Total (*n* = 42)	*P*
Age, mean ± SD, y	39.7 ± 9.1	45.3 ± 16.0	43.2 ± 17.2	42.5 ± 14.2	0.873
Sex, *n* (%)					0.662
Male	5 (33.3)	5 (41.7)	4 (26.7)	14 (33.3)	
Female	10 (66.7)	7 (58.3)	11 (73.3)	28 (66.7)	
PCN diameter, mm	26.2 (16.1–60.1)	32.9 (20.1–64.0)	28.5 (19.3–40.4)	28.7 (16.1–64.0)	0.207
PCN location, *n* (%)					0.294
Head	8 (53.3)	6 (50.0)	3 (20.0)	17 (40.5)	
Body	6 (40.0)	4 (33.3)	8 (53.3)	18 (42.9)	
Tail	1 (6.7)	2 (16.7)	4 (26.7)	7 (16.7)	
PCN septum, *n* (%)					0.414
Yes	10 (66.7)	10 (83.3)	9 (60.0)	29 (69.0)	
No	5 (33.3)	2 (16.7)	6 (40.0)	13 (31.0)	
PCN nodules, *n* (%)					0.739
Yes	0 (0.0)	1 (8.3)	1 (6.7)	2 (4.8)	
No	15 (100.0)	11 (91.7)	14 (93.3)	40 (95.2)	
PCN diagnosis, *n* (%)					0.200
SCN	10 (66.7)	7 (58.3)	5 (33.3)	22 (52.4)	
MCN	5 (33.3)	5 (41.7)	10 (66.7)	20 (47.6)	

MCN: mucinous cystic neoplasm; PCN: pancreatic cystic neoplasm; SCN: serous cystic neoplasm.

enhanced MRI or CT at our center or at another hospital because the required re-examination time was not reached. Thus, 31 patients were included in the evaluation of EUS-LA efficacy. The specific data for each group are shown in Table 5.

The Kruskal-Wallis *H* test was used to compare the differences in the EUS-LA ablation rate among the groups that received different concentrations of lauromacrogol. The EUS-LA ablation rate differed among the groups, and the difference was statistically significant ($H = 10.849$, $P < 0.05$). The average EUS-LA ablation rates for the 1%, 2%, and 3% lauromacrogol groups were 12.86, 11.29, and 23.70%, respectively. Post hoc pairwise comparison after correcting for significance levels using the Bonferroni method indicated that there were statistically significant differences in the EUS-LA ablation rates between the 1% and 3% lauromacrogol groups (adjusted $P = 0.011$) and between the 2% and 3% lauromacrogol groups (adjusted $P = 0.016$); the difference between the 1% and 2% lauromacrogol groups was not statistically significant.

The ablation effects for 31 patients who were re-examined after EUS-LA were as follows: complete disappearance was observed in 8 patients (25.8%), almost complete disappearance was observed in 11 patients (35.5%), significantly effective outcomes were observed in 5 patients (16.1%), effective outcomes were observed in 6 patients (19.4%), stable outcomes were observed in 1 patient (3.2%), and no patients exhibited progression. The effective rates of the 1%, 2%, and 3% lauromacrogol groups were 92.9% (13/14), 100% (7/7), and 100% (10/10), respectively. The ablation effects for each group are summarized in Table 6.

Table 4

Acute pancreatitis of 42 patients in each group after EUS-LA.

Acute pancreatitis, *n*	Group A	Group B	Group C	*P*
No	15	12	14	
Yes	0	0	1	
Total	15	12	15	1.000

The results of Fisher's exact test ($2 \times C$) indicated that the ablation effect of complete disappearance was statistically significantly different among the 3 groups ($P = 0.001$). Pairwise comparisons were made using the Bonferroni method to adjust the α level. The results showed that the ablation effect complete disappearance significantly differed between group A and group C ($P = 0.01$) and between group B and group C ($P = 0.002$).

Postoperative re-examination of the patients revealed ideal curative effects at all concentrations of lauromacrogol. Figure 4 shows enhanced MR images of the pancreas during reexamination after EUS-LA.

DISCUSSION

The concentration of lauromacrogol that was previously used in clinical application was 1% (10 mL:100 mg). From 2015 to 2021, we carried out many studies on clinical treatment and short-term and long-term efficacy and safety. Through our continuous exploration and improvement of EUS-LA technology, the long-term effective rate of EUS-LA has gradually increased to 77.1%, and the CR rate was 51.4% in patients who were followed up for more than 12 months.[8,9] However, there are still a small number of patients who do not achieve an ideal CR after EUS-LA. If postoperative re-examination shows that the PCN has not completely disappeared, a second EUS-LA increases the psychological burden on patients, especially for patients with preoperative anxiety and financial difficulties.

Lauromacrogol injection is often used in sclerotherapy to treat varicose veins. Polidocanol, which is another sclerosing agent, has been studied by different teams with different follow-up times. Studies on the treatment of great saphenous varicose veins have reported similar complication rates after injection of 1% lauromacrogol compared to 3% polidocanol, which showed that injection of 3% polidocanol has similar efficacy to injection of 1% lauromacrogol.[18–20] Injections of 2% and 3% polidocanol also have good effects on the clinical treatment of varicose veins and hemorrhoidal disease.[21–26] Our animal

Table 5

Changes in PCN volume in 31 patients who underwent re-examination.

Features	Group A (n = 14)	Group B (n = 7)	Group C (n = 10)	Total	P
Follow-up time, mo	10.1 (3.1–12.9)	11.6 (4.5–14.4)	5.0 (3.0–12.5)	8.3 (3.0–14.4)	0.097
PCN volume, mm^3					
Before EUS-LA	7499.5 (693.8–107,719.1)	20,218.9 (6946.2–86,081.1)	11,510.4 (2668.3–30,450.2)	12,599.0 (693.8–107,719.1)	0.212
Last follow-up after EUS-LA	611.2 (38.2–8683.8)	3646.2 (210.2–14,729.7)	0.0 (0.0–9489.1)	520.0 (0.0–14,729.7)	0.004
Ablation rate, %	94.1 (2–100)	82.0 (42–99)	100 (69–100)	95.5 (2–100)	0.004

EUS-LA: EUS–guided lauromacrogol ablation; PCN: pancreatic cystic neoplasm.

experiments preliminarily indicated that injections of 1%, 2%, or 3% lauromacrogol are safe and effective and that these concentrations can be used in clinical trials.[11] Therefore, these 3 concentrations of lauromacrogol were used in a triple-blind prospective randomized controlled clinical study.

The overall complication rate in this study was 2.4%, and the complication rate in the 3% lauromacrogol group was slightly higher (6.7%). However, the complications could be controlled in a short period without serious complications, such as intracapsular hemorrhage, splenic vein thrombosis, portal vein thrombosis, peritonitis, pancreatic duct stenosis, duodenal stenosis, or death,[10] which indicated that injection of 1%, 2%, and 3% lauromacrogol has ideal safety.

The overall ablation rate for EUS-LA in the 3 groups was 95.5%, and the median ablation rate was as high as 100% in the 3% lauromacrogol group, followed by the 1% lauromacrogol group (94.1%) and the 2% lauromacrogol group (82.0%). The ablation of PCNs with reticular septa is more difficult to perform because multiple punctures cannot ensure that all the cystic cavities are connected, which greatly affects the contact between the lauromacrogol injection and the cyst wall. Ninety percent of patients in the 2% lauromacrogol group who were involved in the efficacy evaluation had reticular septa in the PCN, and some patients in this group were not reexamined because they did not reach the follow-up time, which may potentially explain the low ablation rate in this group. Pairwise comparisons of the data for the 3 groups indicated that there was no significant difference in the ablation rate between the 1% and 2% lauromacrogol groups, but the ablation rates were significantly different between the 1% and 3% lauromacrogol groups and between the 2% and 3% lauromacrogol groups. We hypothesize that the difference between the 1% and 2% lauromacrogol concentrations is not sufficient to affect the ablation rate, whereas increasing the concentration above 2%, despite the same 1% increase, results in a difference in the ablation rate.

Combining the 2 methods that were used to evaluate efficacy showed that injection of 3% lauromacrogol had the best efficacy. However, the overall median follow-up time of these patients was only 8.3 months, and the re-examination rates of the patients in each group differed. In addition, in a 1-year follow-up study, 3% polidocanol foam seemed to be more effective than 1% polidocanol foam[18]; however, 2 other studies demonstrated equivalent efficacy of 1% and 3% polidocanol foam at the 2-year follow-up and 3-year follow-up.[19,20] Therefore, the results of this study can only reflect the short-term efficacy of EUS-LA with different concentrations of lauromacrogol. As the number of patients who undergo EUS-LA and the number of patients who complete re-examination after EUS-LA continue to increase, we will further study whether the long-term efficacy of EUS-LA is the same as the short-term efficacy.

We perform EUS-LA in some patients with SCN due to some reasons: First of all, our aim is to preserve pancreas, but the best method to diagnose serous cystic neoplasm (SCN) is pathological examination of the tumor, which means the pancreas will be removed surgically, besides most EUS-TTNB results still remain uncertain. Secondly, although SCNs do have a very low probability of developing into a malignant tumor, but we cannot exclude the possibility. Thirdly, some SCNs grow rapidly in size and may produce symptoms, so some patients are eager to accept EUS-LA. Finally, having unknown PCN can also increase pressure of patients, both psychologically and financially: anxiety about the possible development of carcinogenesis of the SCN will affect the quality of life and have adversely effect on health status; incessant imaging will increase financial burden. Our aim is to stop the SCN from becoming cancerous and to treat it before it progresses.

This study has certain limitations. First, PCN is still a rare disease relative to other pancreatic tumors, and the overall sample size is relatively small. Our randomized controlled study included 3 groups, which resulted in smaller sample sizes in each group, potentially influencing the results. Second, our team developed EUS-LA, and the 3 endoscopists who participated in this study are experienced and skilled EUS experts; these skillsets are not

Table 6

Ablation effect in each EUS-LA group.

Ablation effect, n (%)	Group A (n = 14)	Group B (n = 7)	Group C (n = 10)	Total	P
Complete disappearance	1 (7.1%)	0 (0.0%)	7 (70.0%)	8 (25.8%)	
Nearly complete disappearance	7 (50.0%)	2 (28.6%)	2 (20.0%)	11 (35.5%)	
Significantly effective	2 (14.3%)	3 (42.9%)	0 (0.0%)	5 (16.1%)	
Effective	3 (21.4%)	2 (28.6%)	1 (10.0%)	6 (19.4%)	
Stable	1 (7.1%)	0 (0.0%)	0 (0.0%)	1 (3.2%)	
Progression	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
					0.008

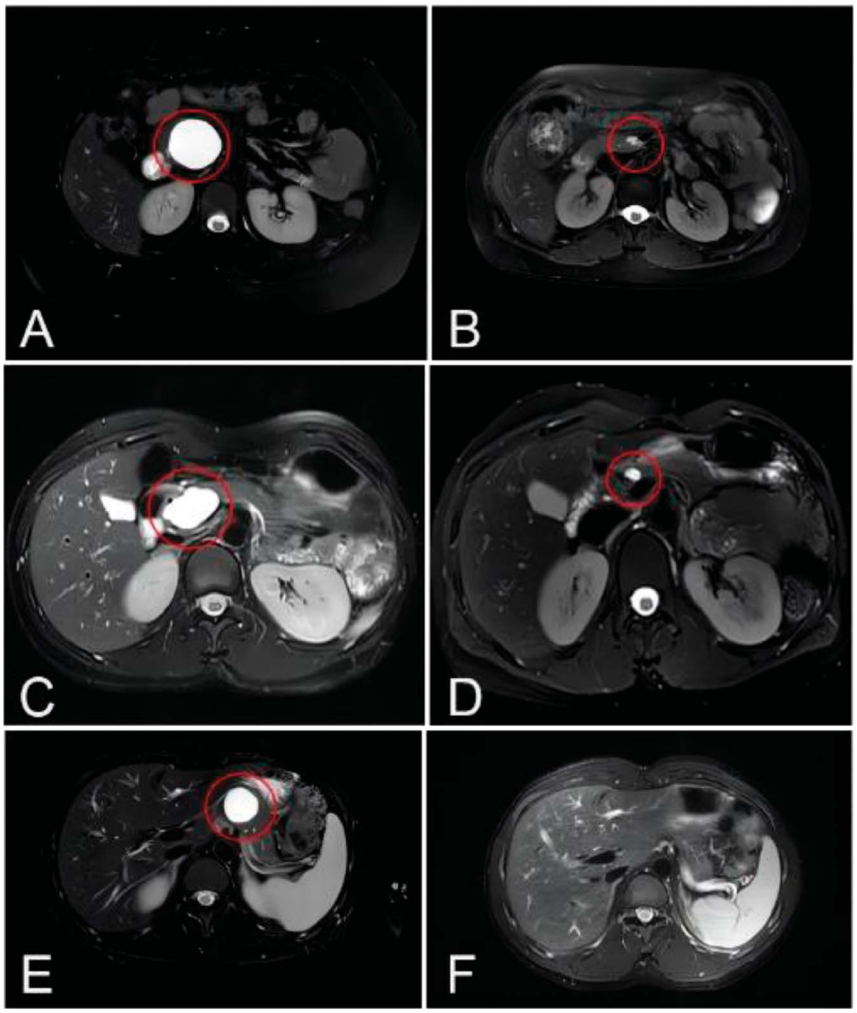

Figure 4. PCNs almost completely disappeared after EUS-LA with different doses lauromacrogol injection. A, Preoperative MRI showed a cystic lesion (SCN) with a maximum cross-sectional area of approximately 50 mm × 42 mm in the head of the pancreas. B, Follow-up MRI at 11 months after EUS-LA (with 1% lauromacrogol injection) showed that the lesion had almost completely disappeared (red circle). C, Preoperative MRI showed a cystic lesion (SCN) with a maximum cross-sectional area of approximately 36 mm × 25 mm in the head of the pancreas. D, Follow-up MRI at 12 months after EUS-LA (with 2% lauromacrogol injection) showed that the lesion had almost completely disappeared (red circle). E, Preoperative MRI showed a cystic lesion (MCN) with a maximum cross-sectional area of approximately 24 mm × 20 mm in the pancreatic body. F, Follow-up MRI 3 months after EUS-LA (with 3% lauromacrogol injection) showed that the lesion had disappeared completely (red circle).

universal. Third, the follow-up time was short, and some patients had not yet reached the time for re-examination; thus, the evaluation of EUS-LA efficacy may not have been sufficiently comprehensive. Fourth, for PCNs with a septum, it is technically difficult to pierce each septum so that lauromacrogol can fully act on the epithelial cells of the PCN; this could lead to a failure to achieve the ideal ablation rate and ablation effect despite the use of relatively high concentrations of lauromacrogol. To address the limitations of this study, we have the following plans for future studies: first, we will continue to recruit patients to conduct long-term follow-up studies to further evaluate the safety and efficacy of EUS-LA; second, we will train more endoscopists on EUS-LA technology and carry out multicenter research to increase the generalizability of the evaluation of EUS-LA safety and efficacy; third, we will research and develop new EUS instruments that can be applied to destroy the PCN septum as much as possible so that lauromacrogol can act on the entire inner wall of the PCN.

CONCLUSION

This triple-blind randomized controlled study showed that EUS-LA with 3% lauromacrogol had the best efficacy for treating PCNs, and the complications were easily controlled. The long-term efficacy of this approach still needs to be further validated by long-term follow-up studies.

Acknowledgments

We thank all doctors and nurses in department of gastroenterology of the first medical center of Chinese PLA General Hospital for their efforts to cure every patient, and all patients' cooperation in this study.

Source of Funding

This study is supported by Beijing Natural Science Foundation (7244302), the National Key Research and Development Program

of China (2022YFC2503603), the National Key Research and Development Program of China (2022YFC2503604), and the National Key Research and Development Program of China (2022YFC2503605).

Ethical Approval

This study has been approved by the Ethics Committee of Chinese PLA General Hospital (No. S2021-071-01), all patients have signed informed consent, and all methods were performed in accordance with the relevant guidelines and regulations.

Clinical Trial Registration

This study (No. ChiCTR2100044096) was registered in the Chinese Clinical Trials Registry (http://www.chictr.org.cn/; http://www.ctri.in/).

Conflicts of Interest

Enqiang Linghu is an Associate Editor of the journal. The article was subjected to the standard procedures of the journal, with a review process independent of the editor and his research group.

Author Contributions

The authors' contributions were as follows—FG, HKL, XXF, QQC, DC, BQC, HK, NLC, EQLH: designed research; FG, HKL, NLC, LHEQ: conducted research; XXF, QQC, DC, BQC: provided essential materials; KH: performed statistical analysis; FG, HKL: wrote paper; NLC, EQLH: had primary responsibility for final content. All authors have read and approved the final manuscript.

References

1. Chang YR, Park JK, Jang JY, Kwon W, Yoon JH, Kim SW. Incidental pancreatic cystic neoplasms in an asymptomatic healthy population of 21,745 individuals: large-scale, single-center cohort study. *Medicine (Baltimore)* 2016;95:e5535.
2. de Jong K, Nio CY, Hermans JJ, et al. High prevalence of pancreatic cysts detected by screening magnetic resonance imaging examinations. *Clin Gastroenterol Hepatol* 2010;8:806–811.
3. Girometti R, Intini S, Brondani G, et al. Incidental pancreatic cysts on 3D turbo spin echo magnetic resonance cholangiopancreatography: prevalence and relation with clinical and imaging features. *Abdom Imaging* 2011;36:196–205.
4. Ip IK, Mortele KJ, Prevedello LM, Khorasani R. Focal cystic pancreatic lesions: assessing variation in radiologists' management recommendations. *Radiology* 2011;259:136–141.
5. European Study Group on Cystic Tumours of the Pancreas. European evidence-based guidelines on pancreatic cystic neoplasms. *Gut* 2018;67:789–804.
6. Linghu E. A new stage of surgical treatment: super minimally invasive surgery. *Chin Med J (Engl)* 2022;135:1–3.
7. Linghu E, Du C, Chai N, et al. A prospective study on the safety and effectiveness of using lauromacrogol for ablation of pancreatic cystic neoplasms with the aid of EUS. *Gastrointest Endosc* 2017;86:872–880.
8. Du C, Chai N, Linghu E, et al. Long-term outcomes of EUS-guided lauromacrogol ablation for the treatment of pancreatic cystic neoplasms: 5 years of experience. *Endosc Ultrasound* 2022;11:44–52.
9. Du C, Chai NL, Linghu EQ, Li HK, Feng XX. Endoscopic ultrasound–guided injective ablative treatment of pancreatic cystic neoplasms. *World J Gastroenterol* 2020;26:3213–3224.
10. Gao F, Li H, Feng X, et al. Cystic tumor ablation with different concentrations of lauromacrogol solution in an animal model. *Minerva Gastroenterol (Torino)* 2024;70:422–429.
11. Bick BL, Enders FT, Levy MJ, et al. The string sign for diagnosis of mucinous pancreatic cysts. *Endoscopy* 2015;47:626–631.
12. Oh SH, Lee JK, Lee KT, Lee KH, Woo YS, Noh DH. The combination of cyst fluid carcinoembryonic antigen, cytology and viscosity increases the diagnostic accuracy of mucinous pancreatic cysts. *Gut Liver* 2017;11:283–289.
13. Ribaldone DG, Bruno M, Gaia S, et al. Differential diagnosis of pancreatic cysts: a prospective study on the role of intra-cystic glucose concentration. *Dig Liver Dis* 2020;52:1026–1032.
14. van der Waaij LA, van Dullemen HM, Porte RJ. Cyst fluid analysis in the differential diagnosis of pancreatic cystic lesions: a pooled analysis. *Gastrointest Endosc* 2005;62:383–389.
15. Ceulen RP, Bullens-Goessens YI, Pi-VAN DE Venne SJ, Nelemans PJ, Veraart JC, Sommer A. Outcomes and side effects of duplex-guided sclerotherapy in the treatment of great saphenous veins with 1% versus 3% polidocanol foam: results of a randomized controlled trial with 1-year follow-up. *Dermatol Surg* 2007;33:276–281.
16. Hamel-Desnos C, Ouvry P, Benigni JP, et al. Comparison of 1% and 3% polidocanol foam in ultrasound guided sclerotherapy of the great saphenous vein: a randomised, double-blind trial with 2 year-follow-up. "The 3/1 study". *Eur J Vasc Endovasc Surg* 2007;34:723–729.
17. Blaise S, Bosson JL, Diamand JM. Ultrasound-guided sclerotherapy of the great saphenous vein with 1% vs. 3% Polidocanol foam: a multicentre double-blind randomised trial with 3-year follow-up. *Eur J Vasc Endovasc Surg* 2010;39:779–786.
18. Kurnicki J, Osęka M, Tworus R, Gałązka Z. Ultrasound-guided foam sclerotherapy of great saphenous vein with 2% polidocanol—one-year follow-up results. *Wideochir Inne Tech Maloinwazyjne* 2016;11:67–75.
19. Baccellieri D, Apruzzi L, Ardita V, et al. Early results of mechanochemical ablation for small saphenous vein incompetency using 2% polidocanol. *J Vasc Surg Venous Lymphat Disord* 2021;9:683–690.
20. Gallo G, Ronconi M, Trompetto M. Sclerotherapy with 3% polidocanol foam: revolutionizing outpatient treatment in patients with haemorrhoidal disease. *Updates Surg* 2021;73:2029–2030.
21. Lisi G, Campanelli M, Grande S, Milito G, Grande M. Sclerotherapy with 3% polidocanol foam for third- and fourth-degree hemorrhoids as "bridge treatment" during the COVID-19 pandemic in Italy. *Int J Colorectal Dis* 2021;36:1321–1322.
22. Lobascio P, Laforgia R, Novelli E, et al. Short-term results of sclerotherapy with 3% polidocanol foam for symptomatic second- and third-degree hemorrhoidal disease. *J Invest Surg* 2020;34:1059–1065.
23. Feng R, Jiang J, Cheng D, Lu K. Clinical efficacy comparison of sclerosing embolization with 3% polidocanol and the microsurgical subinguinal varicocelectomy in primary varicocele patients. *Andrologia* 2022;54:e14530.
24. Gallo G, Picciariello A, Pietroletti R, et al. Sclerotherapy with 3% polidocanol foam to treat second-degree haemorrhoidal disease: three-year follow-up of a multicentre, single arm, IDEAL phase 2b trial. *Colorectal Dis* 2023;25:386–395.
25. Gallo G, Pietroletti R, Novelli E, et al. A multicentre, open-label, single-arm phase II trial of the efficacy and safety of sclerotherapy using 3% polidocanol foam to treat second-degree haemorrhoids (SCLEROFOAM). *Tech Coloproctol* 2022;26:627–636.
26. Neves S, Falcão D, Povo A, Castro-Poças F, Oliveira J, Salgueiro P. 3% polidocanol foam sclerotherapy versus hemorrhoidal artery ligation with recto anal repair in hemorrhoidal disease grades II–III: a randomized, pilot trial. *Rev Esp Enferm Dig* 2023;115:115–120.