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CLINICAL INVESTIGATION LYMPHATIC

Lymphangiography and Lymphatic Embolization for the Treatment of Refractory Chylous Ascites

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Abstract
Purpose Assess the effectiveness of conventional lymphangiography, MR lymphangiography, and lymphatic embolization for the diagnosis and treatment of refractory chylous ascites.
Materials and Methods A retrospective review of 31 patients (M/F:16/15, average age 52) who presented for the management of refractory chylous ascites was conducted to assess the diagnostic value of conventional and MR lymphangiography and outcome of lymphatic embolization.
Results Of the total 31 patients, 25 presented with chylous ascites secondary to iatrogenic trauma and six patients with a non-traumatic etiology. All patients underwent conventional lymphangiography and nine underwent MR lymphangiogram. The lymphatic leak was visualized in 17/31 (55%) of the patients (15 of which were traumatic) and in 7/9 MR lymphangiograms (six traumatic and one non-traumatic). Embolization with n-BCA glue and/or coils of the leak was performed in 11 of the 17 patients whose leak was identified (65%) with resolution of chylous ascites in 9/11 (82%) patients. Lymphangiogram alone was curative in 7/20 (35%) patients. Overall, 16/31 patients (52%) had clinical resolution of ascites. Ascites resolved in 13/17 (76%) patients in whom the site of leak could be identified compared to 3/14 (21%) of patients in whom the site of leak could not be identified ($p = 0.0038$).
Conclusions Lymphangiography and embolization can be used to treat chylous ascites. Identification of the site of leak is associated with significantly greater rate of clinical success compared to those whose site could not be identified.

Keywords Chylous ascites · Embolization · Lymphangiography

Introduction

Chylous ascites is an uncommon but difficult-to-treat condition when conservative measures have failed. It is most commonly encountered as a complication of abdominal and pelvic surgery [1, 2]. The incidence of postoperative chylous ascites ranges from 0.3 to 11% [3]. Non-traumatic causes include malignancy, cirrhosis, infection, inflammatory conditions, right heart failure, and congenital anomalies of the lymphatic system [1].

Diagnosis is generally made by the presence of milky colored fluid after paracentesis or via postsurgical drainage catheters. Many surgical series have shown that patients with chylous ascites have increased morbidity, reduced survival, and prolonged hospital stays [3–6]. In some series, survival in patients with postsurgical chylous ascites is reduced by almost 65% [1, 3, 7].

The initial approach to the treatment of chylous ascites is conservative, starting with diet modification with the goal being to reduce chyle flow thereby allowing the leak

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to heal. It includes a medium chain triglyceride (MCT) diet or nothing by mouth with concurrent use of total parenteral nutrition (TPN) [1, 2, 4]. The reported success of these measures varies but can be as low as 71% [3]. The addition of a somatostatin analogue to an MCT diet or TPN has been reported to expedite the resolution of a chyle leak [1, 2, 4] [3, 8–12]. The time to resolution of chyle leaks with conservative measures is variable, generally resolving in 1–6 weeks, but has been reported to be as long as almost 1 year [1, 8, 13, 14].

Lymphangiography, which is performed using oil-based contrast, previously has been shown to have therapeutic effect on chylous effusion probably due to its embolic or inflammatory effect on the lymphatic vessels [15]. Dynamic Contrast Enhanced MR Lymphangiogram (DCRML) is a new modality in which imaging of the lymphatic system is performed using MR after injection of the gadolinium contrast agents in the groin lymph nodes. DCMRL has been found to be of significant value for diagnosis and treatment of patients with thoracic lymphatic disorder [16]. Over the past several years, embolization techniques, which have been used routinely for thoracic duct embolization to treat chylothorax, are being adopted for treatment of chylous ascites [17–22]. The purpose of the present study is to assess the effectiveness of lymphangiography, DCRML, and lymphatic embolization for the diagnosis and treatment of refractory chylous ascites.

Materials and Methods

Patient Characteristics

Electronic databases at our institutions between January 2009 and September 2015 were reviewed to identify patients who underwent lymphangiography for chylous ascites. Institutional Review Board approval was obtained under an ongoing protocol for the retrospective study of percutaneous intervention for lymphatic disorders. Data regarding patient characteristics, treatment, and follow-up were extracted from the electronic medical record (Table 1).

In total, 31 patients with chylous ascites were referred for lymphangiography and potential lymphatic intervention. In all cases, conservative measures were deemed to have failed based on joint consultation between the referring provider and interventional radiology. Lymphatic drainage volume was evaluated before and after lymphangiography if the patient had an indwelling drainage catheter or one was placed at the time of the procedure. For patients in whom a drainage catheter was not placed, lymphatic drainage volume was determined based on serial paracentesis.

Of the 31 patients who were identified, 25 had a traumatic-iatrogenic etiology and six had a non-traumatic etiology of their chylous ascites (Table 1). The average age of patients was 52 years (range 8–88). The gender distribution of the patients was 16 males and 15 females.

Lymphangiography Technique

The first nine patients underwent bilateral bipedal lymphangiography. After the description of intranodal lymphangiography by Nadolski and Itkin in 2012, a nodal approach was used for lymphangiography for the remaining 22 patients [23]. The techniques of both pedal and intranodal lymphangiography (IL) have been described extensively in literature [23, 24]. In short, pedal lymphangiogram was performed using a skin cut-down and cannulation of the lymphatics at the dorsal aspect of the foot bilaterally, following by injection of lipiodol (Guerbet LLC, Bloomington, IN). IL was performed by accessing bilateral groin lymph nodes with 26-gauge needles under ultrasound guidance with injection of lipiodol at a rate of approximately 1 mL per 5 min by hand. Transit of the oily contrast agent in both techniques was monitored using intermittent fluoroscopy.

After the introduction of Dynamic Contrast Enhanced MR Lymphangiography (DCRML), the last nine patients underwent DCRML in attempt to identify the source of the leak [25]. MR imaging was performed in an XMR suite that couples a 1.5 MR scanner with a catheterization laboratory (Siemens, Erlangen, Germany). Bilateral access to the groin lymph nodes was performed similar to IL as described above. Between 1 and 5 mL of water-soluble iodinated contrast (Isovue 300; Bracco, Princeton, New Jersey) was injected under fluoroscopic guidance to confirm the correct position of the needles inside the lymph nodes. The patients were then transferred into the MRI suite. MR was performed on a 1.5 T Siemens Magnetom Avanto scanner (Siemens, Erlangen, Germany). MR lymphangiography included T2 W sequence for identification of lymphatic masses followed by intranodal injection of 2–8 mL of undiluted Gadovist (Bayer Healthcare Pharmaceuticals Inc., Wayne, NJ) and dynamic imaging using a syngo time-resolved angiography with stochastic trajectories [TWIST] sequence. Delayed imaging using high-resolution navigator gated 3D flash IR sequence was then used to determine final details of contrast distribution in the lymphatic system [16].

Lymphatic Embolization Technique

The first embolization case in this series was performed in January of 2013. Prior to then, lymphangiography alone

Table 1 Patients' clinical data

Patient	Gender	Age	Indication for the procedure	Lymphangiography	Visualization of the leak	Output	Types of intervention	Outcome
1	Male	57	S/p AAA repair	Bipedal	No	Weekly 4–6 L	Lymphangiography	Denver shunt
2	Female	63	Ovarian cancer, TAH/SBO, pelvic radiation	Nodal	Yes	Monthly 2–3 L	Proximal lymph node embolization	Resolved
3	Female	54	Primary sclerosing cholangitis, s/p OLT × 2 and partial colectomy	Nodal	Yes	High volume	Lymphangiography	Denver shunt
4	Male	85	Pancreatic CA, s/p Whipple	Bipedal	No	150 mL/day	Lymphangiography	Resolved
5	Male	54	Left RCC, s/p nephrectomy and retroperitoneal lymph nodes dissection	Nodal	No	Weekly 1 L	Lymphangiography	Chylous ascites persisted
6	Female	51	AAA, s/p open repair	Nodal	No	300 cc daily	Lymphangiography	Resolved
7	Male	79	RCC, s/p right nephrectomy	Bipedal	No	500 cc daily	Lymphangiography	Chylous ascites persisted
8	Male	36	Testicular cancer, s/p retroperitoneal lymph nodes dissection	Nodal	yes	Daily 1 L	Proximal lymph node embolization	Denver shunt
9	Male	61	RCC, s/p left nephrectomy	Nodal	yes	Monthly 6.5 L	Embolization of the site of the leak with coils and glue	Resolved
10	Female	57	Pancreatic neuroendocrine cancer, s/p pancreatectomy	Nodal	No	Daily 400 cc	Lymphangiography	Chylous ascites persisted
11	Female	23	Idiopathic chylous ascites, intestinal lymphangiomatosis	Bipedal	yes	Daily 1–3 L	Lymphangiography	Chylous ascites persisted
12	Male	50	AML, s/p right nephrectomy	Bipedal	No	Weekly 4–7 L	Lymphangiography	Denver shunt
13	Male	56	Colon CA, s/p colectomy	Bipedal	Yes	Daily 1 L	Embolization of the site of the leak with coils and glue	Resolved
14	Male	53	B cell lymphoma	Nodal	No	Weekly 10 L	Lymphangiography	Chylous ascites persisted
15	Male	46	Metastatic neuroendocrine tumor, s/p pancreatectomy, splenectomy, partial liver lobectomy	Nodal	No	Daily 3.5 L	Lymphangiography	Denver shunt
16	Female	37	Ovarian CA, s/p TAH/BSO, right hepatectomy retroperitoneal lymph nodes resection	Nodal	Yes	Daily 500 ml	Lymphangiography	Resolved
17	Male	67	RCC, s/p right nephrectomy	Nodal	Yes	Daily 3.5 L	Proximal lymph node embolization	Resolved
18	Female	57	B-cell lymphoma	Nodal	No	Every 10 days 1–3 L	Lymphangiography	Denver shunt

Table 1 continued

Patient	Gender	Age	Indication for the procedure	Lymphangiography	Visualization of the leak	Output	Types of intervention	Outcome
19	Female	45	Retroperitoneal lymphangioma, s/p surgical biopsy	Bipedal	Yes	Daily, 1 L	Lymphangiography	Resolved
20	Female	88	Idiopathic chylous ascites	Nodal	No	Weekly 4 L	Lymphangiography	Denver shunt
21	Male	67	Idiopathic portal vein thrombosis	Nodal	No	Weekly 4–6 L	Lymphangiography	Denver shunt
22	Male	66	S/p Whipple for pancreatic cancer	Bipedal	No	Daily 200–500 ml	Lymphangiography	Chylous ascites persisted
23	Female	74	S/p Whipple for pancreatic cancer	Bipedal	No	Daily 220–500 ml	Lymphangiography	Resolved
24	Female	75	Angiomyolipoma, s/p left nephrectomy	Nodal	Yes	12 L/week	Proximal lymph node embolization	Resolved
25	Male	57	RCC, s/p left nephrectomy and lymph node dissection	Nodal	Yes	Daily 1.2 L	Lymphangiography	Resolved
26	Female	40	Retroperitoneal LAM with chylous ascites after biopsy.	Nodal	Yes	Weekly 7–10 L	Embolization of the site of the leak with coils and glue	Resolved
27	Female	57	Cervical cancer s/p TAH, BSO, b/l pelvic lymph node dissection	Nodal	Yes	Monthly 3–4 L	Proximal lymph node embolization	Resolved
28	Male	18	Retroperitoneal dissection for testicular cancer	Nodal	Yes	1 L a day	Lymphangiography	Resolved
29	female	8	Idiopathic chylous ascites, since early childhood	Nodal	Yes	800 CC a day	Proximal lymph node embolization	Resolved
30	Male	28	Testicular cancer s/p retroperitoneal node dissection p/w	Nodal	Yes	Weekly 1 L	Lymphangiography	Resolved
31	Female	12	S/P portosystemic anastomosis for idiopathic splenic vein thrombosis	Nodal	Yes	800 CC a day	Proximal lymph node embolization	Resolved

was used for both diagnostic and therapeutic purposes based on the available literature at that time.

For the most part, two different techniques for lymphatic embolization were utilized: (1) embolization of the lymph node proximal to the leak with glue; (2) embolization of the site of the leak with endovascular coils and n-BCA glue.

Embolization of the Lymph Node Proximal to the Leak with n-BCA Glue

If a leak of lipiodol was identified, a lymph node just proximal to the site of the leak was accessed under fluoroscopic guidance with a 22-25 G Chiba needle (Cook Inc., Bloomington, IN). Water-soluble iodinated contrast (Isovue 300; Bracco, Princeton, New Jersey) was then injected via the needle to confirm needle positioning in the lymph node and presence of the leak (Fig. 1). Once confirmed, a 1:3–6 mixture of *n*-butyl cyanoacrylate (n-BCA) glue (TruFill, Codman Neuro, Raynham, MA) and lipiodol was injected through the needle until stasis was achieved (Fig. 2). The dilution ratio of the glue with lipiodol depended on the volume and rate of extravasation as well as distance of the accessed lymph node to the site of the actual leak. Embolization was not performed if the leak was not identified.

Embolization of the Site of the Leak with the Endovascular Coils and n-BCA Glue

In patients with leak confined to the retroperitoneal cavity, transabdominal access to the site of the leak with a

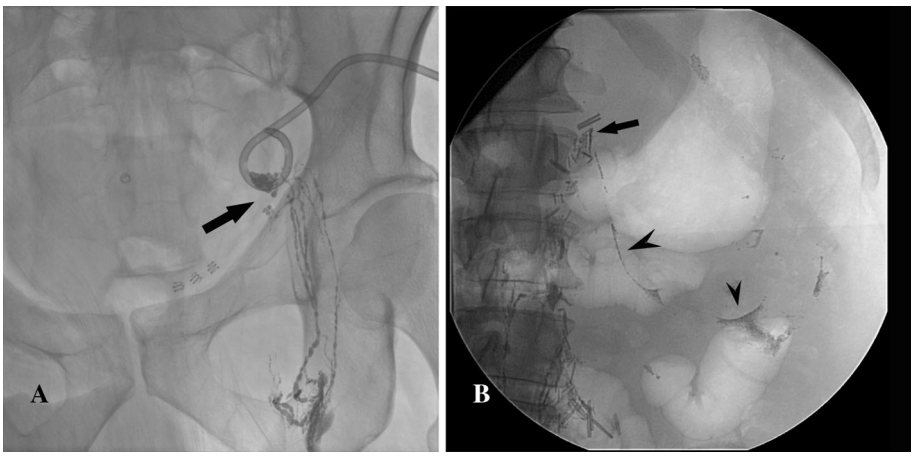

Fig. 1 **A** Fluoroscopic image of the extravasation of the contrast injected in the groin lymph nodes into the pelvis (arrow); **B** fluoroscopic images demonstrated leakage of the contrast material from the retroperitoneal lymph chain (arrow) in the abdominal cavity (arrowheads)

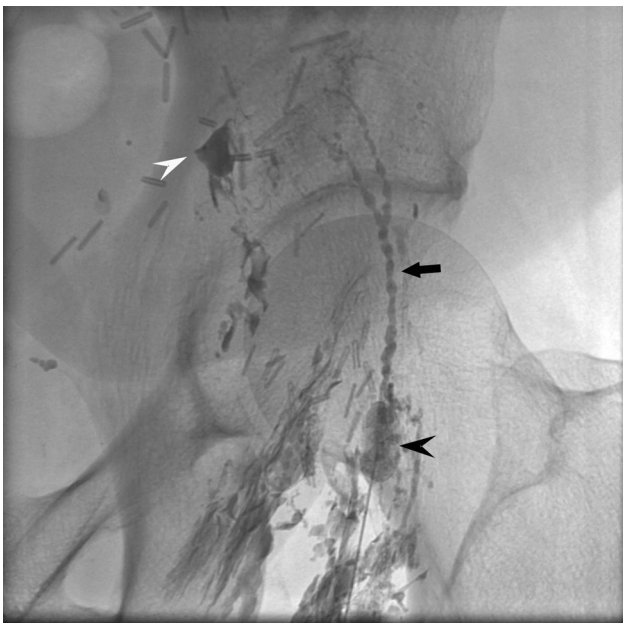

Fig. 2 Fluoroscopic image of the glue cast in the lymphatic duct (black arrow) leading to the leak (white arrowhead) following of the upstream embolization with n-BCA glue from the lymph node (black arrowhead)

22-gauge needle under fluoroscopic guidance was performed. A stiff 0.018″ wire (V18 Control, Boston Scientific, Natick, MA) was advanced into the cavity and the needle exchanged for a 2.3 Fr microcatheter (Rapid Transit, Cordis). Embolization of the cavity was performed with MicroNester coils (Cook Medical, Bloomington, IA) and N-BCA glue ($n = 4$) (Fig. 3). If a lymphatic leak did not resolve after the first treatment, repeat lymphangiography and/or embolization was performed ($n = 5$).

The choice of the embolization technique was at the discretion of the operator at the time of the procedure. Clinical success was defined as a decrease in drain output within 14 days allowing removal of drain or no further need for paracentesis in patients without catheters.

Statistics

Descriptive and comparative statistics were performed using Stata v10.1 (Stata Corp, College Station, Tx). Comparison of therapeutic success rate between groups based on etiology (traumatic versus non-traumatic), identification of leak, embolization versus lymphangiogram only, and type of lymphangiogram (nodal versus pedal) was performed using the Fisher exact test. P values of < 0.05 were considered to represent statistically significant differences.

Results

In 17 of the 31 patients (55%), the site of the chyle leak was visualized. Fifteen of those patients had a traumatic etiology and two a non-traumatic. DCMRL demonstrated leaks in seven out of nine patients (Fig. 4), all of which had a traumatic etiology. In one of these patients with positive DCRML, IL was negative (Table 1).

Embolization with n-BCA glue and/or coils was performed in 11/17 (64%) of patients. Of the 11 who underwent embolization, 9 had resolution of their chylous ascites (82%). Six patients in whom a leak was identified did not undergo embolization because they presented prior to the evolution of embolization in our practice. In 20 patients who did not undergo embolization, lymphangiography, was clinically successful in seven (35%) patients. Overall 16 of the 31 patients (52%) had resolution of their chylous ascites (Fig. 5). In seven patients who failed lymphangiography and embolization, Denver shunt implantation was performed.

There was no statistically significant difference as to whether clinical success was achieved based on whether the initial lymphangiogram was performed via a nodal approach (13/22) or a pedal approach (3/9, $p = 0.25$). Similarly, there was no statistically significant difference in

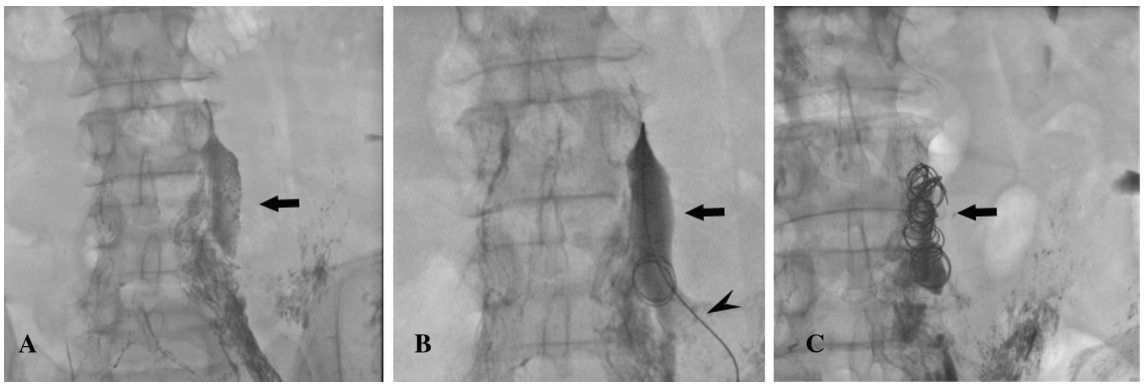

Fig. 3 **A** Fluoroscopic image of the retroperitoneal extravasation of the contrast in patient post left kidney resection (arrow). **B** Access of the extravasation cavity with 3 Fr microcatheter (arrowhead). **C** Embolization coils in the extravasation cavity (arrow)

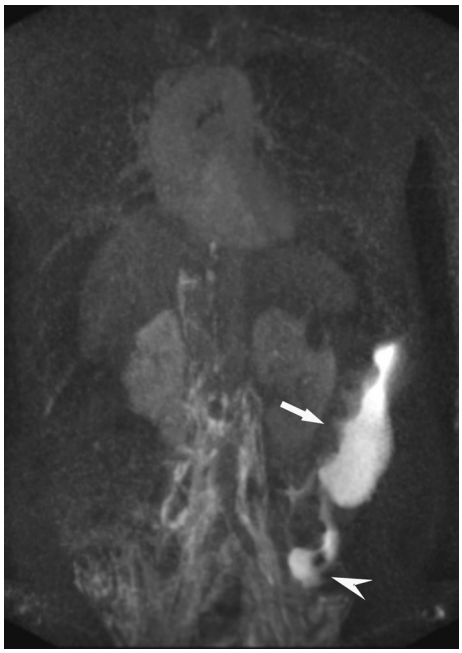

Fig. 4 DCMRL demonstrating extravasation of the contrast in the abdominal cavity (arrow) from the pelvic masses (arrowhead)

cure rate based on whether the etiology was traumatic (15/25—60%) or non-traumatic (1/6—17%, $p = 0.083$). In 17 patients in whom the leak was identified, 13 (76%) had resolution as opposed to only 3/14 patients (21%) in whom the leak was not identified ($p = 0.0038$).

One minor complication and one major complication were observed in our series. The minor complication was an asymptomatic glue/lipiodol pulmonary embolus, for which no additional therapy was administered. The major complication was a patient who suffered sustained hypoglycemia after lymphangiography requiring hospitalization in the intensive care unit to administer intravenous glucose with hourly blood glucose testing until hypoglycemia resolved. The patient suffered no permanent adverse sequelae.

Discussion

In this series, evaluating the outcomes of lymphangiography and embolization for the treatment of refractory chylous ascites, we found lymphatic embolization to be safe and clinically successful. Identification of the leak was associated with a significantly greater rate of clinical success compared to those in whom the site could not be identified. Of the 11 patients in whom the leak was identified and who were embolized, chylous ascites resolved in 9 of them for a clinical success rate of 82%.

Over the last decade thoracic duct embolization has become the primary approach for the treatment of chylothorax. Ability to visualize lymphatic anatomy and pathology of the thoracic duct using pedal or intranodal lymphangiography has significantly improved outcomes when comparing percutaneous and surgical approaches [26]. However, lymphangiography is often not able to demonstrate the source of the leak in chylous ascites. Anatomically, intestinal lymphatic ducts that carry chyle to join lumbar lymphatic ducts or cisterna chyli are often outside the pathway of the contrast that is injected in the lower extremities (Fig. 6). This may explain why the source of the leak could not be identified in 55% of the patients in this series. This may be particularly true of patients with non-traumatic chylous ascites whose leak may arise from the more proximal intestinal lymphatics which are not imaged with pedal or intranodal lymphangiography. In an attempt to identify leaks in distal intestinal lymphatic ducts, Mittleider et al. accessed the thoracic duct retrograde through a venous approach and catheterized the distal intestinal lymphatics [17]. Even though this approach has worked, advancing the catheter and contrast in a retrograde fashion is exceedingly difficult due to the presence of multiple valves in the lymphatic system.

DCRML is a new imaging modality that has proven to be essential for diagnosis and planning of the percutaneous treatment of pulmonary lymphatic disorders [16]. Using

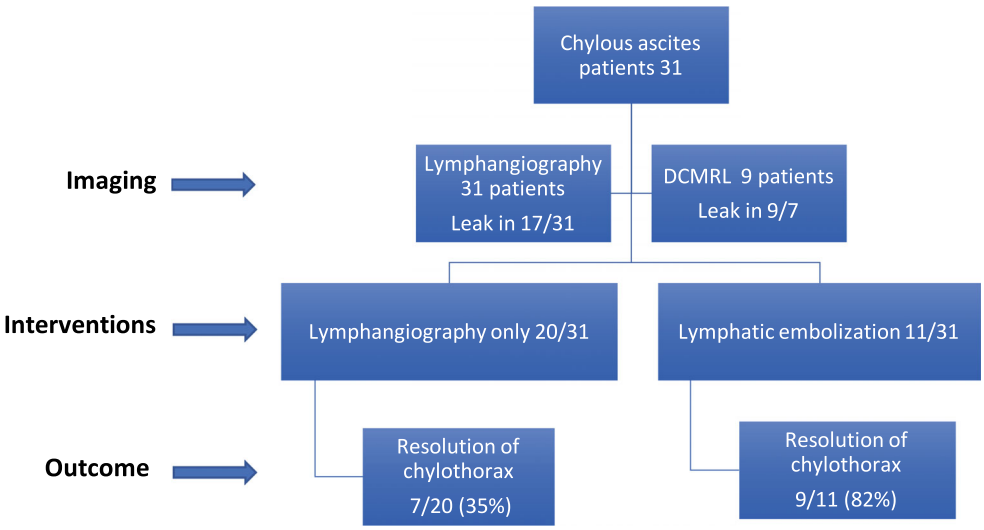

Fig. 5 Study diagram representing the outcome of the lymphatic imaging and interventions

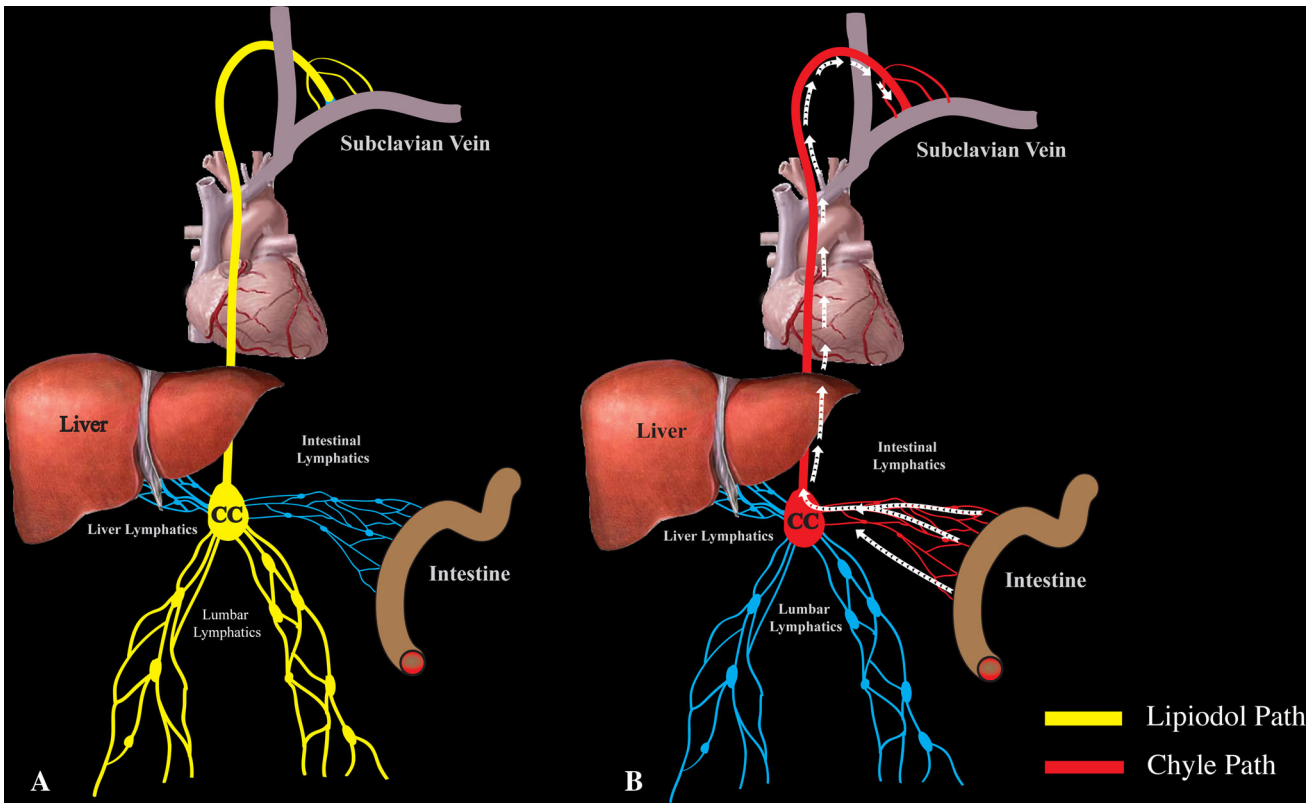

Fig. 6 **A** Schematic representation of the pathway of the contrast material injected in the lymph nodes in the inguinal lymph nodes, and ascending through the retroperitoneal lymphatic ducts, cisterna chyli and thoracic duct; **B** Schematic representation of chyle pathway, originating in the intestine and continue through intestinal lymphatic ducts into cisterna chyli and thoracic duct

this technique, we were able to identify the leak in all seven patients with traumatic chylous ascites. In addition, in one patient, DCRML was able to identify the leak, while IL was negative. Even though the pathway of contrast in DCRML and IL is the same, the lesser viscosity of the gadolinium-based contrast agents compared to lipiodol allows DCRML to be potentially more sensitive than IL for detection of abdominal lymphatic leaks. Development of dedicated intestinal and liver imaging agents and methods would provide better understanding of anatomy and pathology of abdominopelvic lymphatics and improve our ability to identify patients in whom intervention would be more likely to succeed.

Recently, several authors described a variety of percutaneous approaches to treat refractory chylous ascites in a number of case reports. Itou et al. and subsequently Ching et al. reported successful application of glue in the extravasating area in the retroperitoneum, using translumbar CT guidance [18, 19]. In our series, we used a similar approach of direct embolization of the point of leakage from the lymphatic system into the retroperitoneal space. However, we accessed the area of extravasation using an anterior transabdominal approach under real-time fluoroscopy that provided real-time observation of embolization, and thus better control of glue injection. This technique is similar to the approach for thoracic duct embolization and is expected to have a similarly low risk of complications despite potentially traversing bowel or mesentery. Kortes et al. used a similar CT-guided approach, however, used sclerotherapy and reported 72% overall success rate for therapeutic lymphangiography and sclerotherapy for traumatic chylous effusions, similar to the results reported in this series. [20].

Hur et al. have reported a success rate of 85% using the technique of embolization of the lymphatic channels supplying the leak in a group of patients with chylous ascites, lymphocele, and chylothorax [27]. We hypothesize that this approach works because intestinal lymphatic ducts are connected to the retroperitoneal lymphatics, below the chyle leakage point. In our study, the visualization of the leak was significantly lower, probably because our study included five patients with non-traumatic chylous ascites. In the majority of the patients with traumatic chylous ascites in our study the location of the iatrogenic injury was in the upper abdomen (nephrectomy, pancreatectomy, colectomy), and in Hur et al.'s study it was result of pelvic surgery (hysterosalpingo-oophorectomy). This may be because the closer the leak is to the point of lipiodol injection, the higher the odds of its visualization and subsequent successful treatment.

The present study has several limitations. First, it is a single-institution retrospective study with patients who largely have iatrogenic chylous ascites. Thus, the observations may not be generalizable to all practice settings or patient populations. Since the decision to perform lymphangiography was based on the discretion of the interventional radiologist and the referring provider, it is possible that had conservative measures been employed in some patients for longer periods of time, the chylous ascites may have resolved without intervention. Lastly, all procedures were performed by a single interventional radiologist with over 15-year experience performing lymphatic interventions. Therefore, the results may not be generalizable to operators or centers with limited experience in lymphatic interventions.

In conclusion, the study demonstrates that a percutaneous approach is an important tool in the treatment of abdominal lymphatic leaks. Visualization of the lymphatic leak on lymphangiography is associated with higher rate of clinical success, and embolization is superior to lymphangiography alone. A better understanding of the abdominopelvic lymphatic anatomy, tuning of some of the technical aspects of the treatment such as the optimal ratio of glue dilution and the rate of injection, and development of dedicated equipment would make the procedure safer and potentially improve the outcomes.

Compliance with Ethical Standards

Conflict of interest The authors declared that they have no conflict of interest.

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