

REVIEW

Nodal Lymphangiography and Embolization for Postoperative Lymphatic Leakage

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Abstract:

Intranodal lymphangiography has replaced conventional pedal lymphangiography and has advanced lymphatic intervention. In this method, a lymph node is punctured and Lipiodol is injected to visualize the subsequent lymphatic vessels. This has facilitated the widespread adoption of lymphatic interventional radiology due to the simplicity of the technique and the shortened examination time of the procedure, which allows easy mapping of lymphatic vessels and lymphatic fluid dynamics. With this technique, lymphatic embolization was achieved by injecting an embolic substance into the lymph nodes upstream of the lymphatic leak. Although complications associated with lymphangiography are rare, caution should be exercised due to potential complications associated with the use of Lipiodol. This study summarizes intranodal lymphangiography techniques, complications, and lymphatic embolization.

Keywords:

intranodal lymphangiography, lymphatic embolization, lipiodol, lymphocele, lymphorrhea

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Introduction

Historically, pedal lymphangiography has been performed for diagnosis by injection of ethiodized oil (Lipiodol; Guerbet, Villepinte, France) followed by plain radiographs [1, 2]. This can diagnose the presence of Lipiodol, but does not provide a real-time view of lymphatic fluid dynamics. However, the recent development of lymphatic embolization for lymphorrhea has made it necessary to diagnose the dynamics of the lymphatic fluid flowing in the lymphatic vessels and to identify the leaking lymphatic vessels and the pathways by which the embolization material reaches them. Until around 2011, thoracic duct embolization was performed using pedal lymphangiography with lymphatic mapping [3, 4]. Pedal lymphangiography requires skilled techniques. However, with the development of cross-sectional imaging, pedal lymphangiography is no longer performed and fewer interventional radiologists have this technique. Furthermore, lymphangiographic pumps for injecting Lipiodol are no longer manufactured. It was also difficult to ascertain the dynamics of the lymphatic fluid due to the length of time required for the procedure. However, recent lymphatic embolization procedures for lymphatic leaks require identifica-

tion of the site of the leak and the pathway to it, and more rapid mapping of the lymphatic vessels and diagnosis of lymphatic fluid dynamics were now required. These problems were solved around 2011 with the introduction of intranodal lymphangiography instead of pedal lymphangiography [5, 6]. Intranodal lymphangiography is a method of puncturing lymph nodes with a small needle and injecting Lipiodol into the node to contrast the lymphatic vessels. This was reported as early as 1967 [7]. At that time, the enlarged lymph nodes were identified by palpation and punctured, and if the node was not enlarged, it was exposed by incision and punctured. However, current intranodal lymphangiography uses ultrasound to puncture lymph nodes. The use of intranodal lymphangiography in lymphatic intervention is probably due to the improved performance of the ultrasound equipment. The time required to obtain the lymphangiographic information necessary for lymphatic interventional radiology was reduced and the lymphangiography could be more easily repeated. Lymphatic mapping became easier to obtain, resulting in a major leap forward in lymphatic interventional radiology [5, 8]. In addition, intranodal lymphangiography can be performed not only in the inguinal lymph nodes but also in the para-aortic, iliac, abdominal,

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Table 1. Intranodal Lymphangiography Techniques.

Author and year	Frequency of probe used for puncture	Puncture needle	Lipiodol injection rate (mL/min)	Lipiodol injection volume
Inoue M, 2016	>7.5 MHz	23-gauge Cathelin needle	0.2–0.4	No more than 10 mL
Kariya S, 2014	13 MHz	23-gauge Cathelin needle	0.3	10–16 mL
Lee EW, 2014	-	25-gauge spinal needle	0.2–0.4	10–20 mL
Nadolski, 2012	-	25- or 26-gauge spinal needle	0.2	-
Sun X, 2021	>7.5 MHz	25-gauge Cathelin needle	0.2–0.4	Limited to 0.25 mL/kg

axillary, and cervical regions by image-guided puncture of lymph nodes upstream of the area to be visualized [9, 10]. Thus, intranodal lymphangiography has not only streamlined the diagnostic process but has also greatly improved the diagnosis of lymphatic fluid dynamics, which is essential for lymphatic embolization.

The application of this technology has led to the use of embolization techniques in which N-butyl cyanoacrylate (NBCA) (histoacryl; B. Braun, Melsungen, Germany) is injected from upstream lymph nodes of the lymphorrhea and has been effective in the treatment of lymphatic leaks. In particular, the ability to accurately map lymphatic leakage points and the embolic material pathways has been instrumental in the successful treatment of conditions such as pelvic lymphatic leaks. The use of N-butyl cyanoacrylate (NBCA) for embolization, guided by precise lymphatic mapping, has demonstrated significant efficacy in clinical practice.

This study discusses the indication, intranodal lymphangiography techniques, complications, and upstream lymph node or lymphatic vessel embolization.

Intranodal Lymphangiography Technique

Intranodal lymphangiography is performed by puncturing the lymph node under ultrasound guidance and injecting Lipiodol into the lymph node. High-frequency (7.5–13 MHz) linear probes [8, 11, 12] are used (**Table 1**). Cathelin or spinal needles of 23–26 gauge are used for puncture (**Table 1**) [5, 8, 11–13]. The needle is connected to a Lure lock syringe via an extension tube. Fill the syringe, extension tube, and needle with Lipiodol. Ensure that no air bubbles are introduced for ultrasound-guided puncture. Extension tubes must be free of phthalates, which are eluted by Lipiodol.

The lymph nodes are lima bean-shaped and the cortex and hilum can be clearly delineated with a high-frequency probe. The long axis of the lymph node is in the direction of the body axis, and puncturing in the direction of the long axis of the lymph node allows a large stroke through the lymph node. When the needle tip reaches the lymph node, the lymph node is pushed by the needle and moves. If it does not move, the needle tip has not reached the lymph node. The needle is advanced into the lymph node, following the moving lymph node. A horizontal section is also sometimes observed to check and correct any misalignment between the lymph node and the needle. The needle tip is advanced into the lymph node and placed in the transitional

zone between the cortex and hilum of the lymph node (**Fig. 1a**) [5, 8, 11–13].

After confirming by ultrasound that the needle tip is in the lymph node, Lipiodol is injected. Lipiodol injection is started under fluoroscopy [8]. If the puncture is successful and Lipiodol has been injected into the lymph node, fluoroscopy immediately shows granular nodules and the lymphatic vessels extending from the lymph nodes (**Fig. 1b**) [8]. However, if the lymph node puncture fails, fluoroscopy shows spreading lobulated nodular pooling and the lymphatic vessels are not delineated (**Fig. 1c**). In this case, the injection should be stopped immediately. The reason for this is that if Lipiodol leaks around the lymph node, the Lipiodol is isoechoic with the cortex of the lymph node, making it difficult to delineate the lymph node when the puncture is redone. Lipiodol should be injected manually at an injection rate of 0.2–0.4 mL/min. During the injection of Lipiodol, the punctured lymph nodes and lymphatic vessels are observed intermittently with fluoroscopy [13]. Ensure that the needle tip does not detach from the lymph node, Lipiodol does not leak out of the lymph node, and large amounts of Lipiodol do not leak into the vein. Lipiodol may leak into a vein through lymphovenous communications or from a vein in the punctured lymph node [8]. There are limits to the amount of Lipiodol that can be injected. The literature suggests a maximum of no more than 14–20 mL (**Table 1**) [5, 8, 11–13]. One report stated that 3–6 mL of Lipiodol is injected into each lymph node and the injection is terminated with the delineation of the lymphatics at the level of the third lumbar vertebra [5]. In children, a 1962 report of lymphangiography in which Lipiodol was injected through a foot incision reported an injection volume of 0.25 mL/kg body weight and an injection rate of 1 mL every 8–10 min [14]. For intranodal lymphangiography in children, the infusion rate of Lipiodol has been reported to be 0.10–0.17 mL/kg body weight [6]. The dose should be reduced in patients with impaired respiratory function or in children. Lipiodol progresses slowly through the iliac and lumbar lymphatic vessels, but it rapidly advances through the thoracic duct due to the confluence of lymphatic fluid from the hepatic and intestinal lymphatic vessels in the cisterna chyli. Therefore, ensure not to miss the time to image each lymphatic vessel and the thoracic duct. If all the injected Lipiodol passes through without imaging, diagnosis may not be possible. It has been reported that if the cisterna chyli are not visualized after injection of Lipiodol, saline should be continuously injected at 1 mL every 5 min to facilitate propaga-

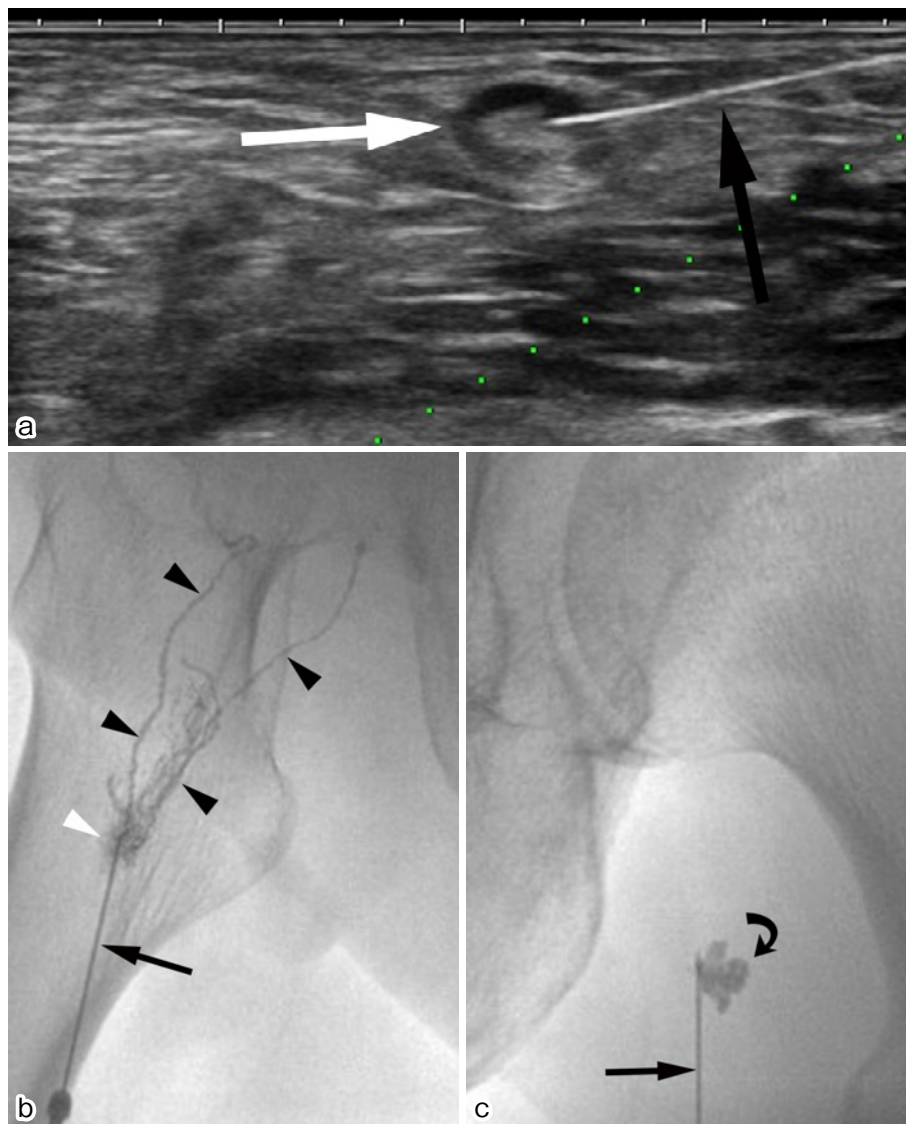


Figure 1. Intranodal lymphangiography.

(a) A femoral lymph node (white arrow) was punctured with a 23-gauge Cathelin needle (black arrow) under ultrasound guidance. The needle was advanced until the tip reached a position between the cortex and hilum.

(b) Lipiodol was injected under fluoroscopy. If the puncture is successful, fluoroscopy immediately shows granular nodules and the lymphatic vessels (black arrowheads) extending from the lymph nodes (white arrowhead). Cathelin needle (black arrow).

(c) If the lymph node puncture fails, fluoroscopy shows spreading lobulated nodular pooling (curved arrow) and the lymphatic vessels are not delineated. Failure to puncture the lymph node results in a lobulated dark shadow (curved arrowheads) of leaking Lipiodol outside the node. In this case, the injection should be stopped. Cathelin needle (black arrow).

tion [5].

Pitfalls of Lipiodol Lymphangiography

Lipiodol has a specific gravity of 1.270-1.292 g/cm³, which is higher than that of lymph fluid (1.012-1.025), and it sinks in lymph fluid. It is not uniformly present in the thoracic ducts and the sinking oil droplets move through the ducts. Therefore, if there is lymphorrhea but the leakage is small, or if the leakage is from the ventral branch of the thoracic duct, Lipiodol may not reach the area of leakage. In

these cases, lymphoscintigraphy, magnetic resonance lymphangiography, or transcatheter thoracic ductography with water-soluble iodinated contrast is required for diagnosis [15-22].

Lymphatic leakage is inferred by a combination of whether the leaking lymphatic fluid is chylous or not and whether the cavity of the reservoir is thoracic, abdominal, or other [15]. For example, chylous and nonchylous ascites is thought to be a disorder of the intestinal and postoperative iliac lymphatics, respectively. However, if the thoracic duct or lymphatic vessels are ligated, lymphatic drainage via col-

lateral channels may result in leakage of intestinal lymph fluid from the lumbar lymphatic vessels. Caution should also be exercised if the compartment is ruptured during surgery. Postoperative chylothorax due to damage to the thoracic duct is a known complication after surgery for esophageal cancer. The surgical technique for esophageal cancer involves ligation of the thoracic duct and opening of the abdominal cavity to the thoracic cavity. When the thoracic duct is ligated and the lymph nodes around the celiac artery are dissected, the internal pressure in the lymphatic vessels is increased, and a large amount of chylous leakage may occur from the lymphatic vessels in the abdominal cavity [23, 24]. The lymph fluid leaking into the abdominal cavity, which would normally be chylous ascites, may flow into the thoracic cavity, where the pressure is lower, and drain out of the thoracic cavity as a chylothorax. Percutaneous transhepatic lymphangiography may confirm leakage around the celiac artery, which can be cured by subsequent embolization [12, 25].

Complications of Lymphangiography

Complications associated with lymphangiography are not frequent. However, Lipiodol should be avoided in patients with severe respiratory failure or right-to-left cardiac or pulmonary shunt. Particular attention should be paid to the presence of right-to-left cardiac shunt, especially in children, and if right-to-left cardiac or pulmonary shunt is present, Lipiodol should be avoided and water-soluble iodinated contrast agent or magnetic resonance lymphangiography should be considered [26, 27]. Cerebral oil embolism is caused not only by right-to-left cardiac or pulmonary shunt but also by disruption of the filtering ability of the pulmonary capillaries due to overloading with Lipiodol or by lymphovenous shunt to the pulmonary veins [28-34]. A large survey of complications was reported at a time when pedal lymphangiography was widely used for diagnosis. The incidence of pulmonary complications (not including pulmonary oil embolism) was 0.3%-0.4%, hypersensitivity reactions to oily contrast medium were 0.1%, hypotensive crises were 0.02%, death were 0.05%-0.06%, and cerebral disorders were 0.03%. [35, 36]. Lipiodol lymphangiography results in pulmonary oil embolism. Reported complications associated with this were as follows: pulmonary infarction (0.25%), lipid pneumonia (0.04%), pulmonary edema (0.03%), and hemoptysis (0.03%) [35]. The frequency of Lipiodol complications correlates with the volume of Lipiodol injected. A report of 522 lymphangiographic patients stratified by the amount of Lipiodol injected showed that the risk of complications was 13% for those injecting less than 18 mL, 24% for those injecting between 18 and 20 mL, and 48% for those injecting 20 mL or more [37]. The severity of reactions is also highly dependent on the amount of contrast injected. The more severe reactions were seen in patients who received injections of 18 mL or more. Cardiopulmonary disorder should be noted in the presence of Lipiodol infusion greater than 20 mL or lymphovenous communications [38].

Therapeutic Lymphangiography

It is known that diagnostic lymphangiography is effective in the treatment of lymphorrhea with subsequent reduction of leakage [39-45]. Although not proven, two mechanisms have been postulated: (1) an inflammatory response to Lipiodol leaks from the site of lymphatic disruption, resulting in obstruction of the lymphatic vessels, and (2) Lipiodol acts as an embolic agent. Matsumoto et al. reported that conservative treatment after lymphangiography stopped lymphorrhea in 89% of patients with a mean duration of 17 days (range, 4-31) [39]. Alejandro-Lafont et al. reported that 51% of lymphorrhea stopped within 2 weeks and 44% within 1 week after lymphangiography and 63% of lymphorrhea decreased by more than 50% [46]. Therapeutic lymphangiography is effective, but it does not always completely stop lymphatic leakage; instead, it only reduces leakage, potentially necessitating subsequent conservative management. Intranodal lymphangiography is simpler than pedal lymphangiography and, even when repeated, is less invasive for the patient and less procedurally complex for the surgeon. Therefore, repeated intranodal lymphangiography may shorten the duration of conservative treatment [9].

Upstream Lymph Node or Lymphatic Vessel Embolization

Injecting an embolic material into the lymphatic vessel can stop lymphatic leakage [47-56]. NBCA mixed with Lipiodol is used as the embolic material. The embolic material is injected into the lymphatic vessels by puncturing the lymph node directly with a fine needle, as in intranodal lymphangiography. Intranodal lymphangiography injects Lipiodol through the lymph node, whereas lymphatic embolization injects NBCA mixed with Lipiodol. Direct puncture of the lymphatic vessels has also been reported [47, 50]. However, lymph node puncture has been reported more frequently, probably due to the limited conditions under which lymphatic vessels can be punctured. Lymphatic embolization involves puncturing the upstream lymph nodes or vessels near the site of the leak. For example, in the thoracic cavity, the para-aortic lymph nodes should be punctured at the level of the lower thoracic or upper lumbar spine. If the puncture is only CT-guided, lymphangiography is not necessary to identify the lymph node to be punctured. However, there are many reports of lymph node puncture under fluoroscopic guidance [47-56]. For fluoroscopic puncture, intranodal lymphangiography should be performed first in the groin or thigh lymph node so that the lymph node upstream of the leak to be punctured can be identified under fluoroscopic guidance. Once the lymph node upstream of the leak is punctured, lymphangiography using nonionic water-soluble iodinated contrast agent, carbon dioxide, or Lipiodol is performed to confirm the site of the leak and the path of the lymphatic vessels leading to it. If the contrast medium reaches the punctured lymph node to the site of leakage relatively quickly, the mixture should be adjusted to

Table 2. Upstream Lymph Node or Lymphatic Vessel Embolization.

Author and year	Subjected lymphorrhea	Ratio of NBCA to LPD used for embolization (NBCA:LPD)	Number of successful embolizations
Baek, 2016	Lymphorrhea occurring after surgical lymph node	1:1–1:8	20/21 (95.2)
Chu, 2019	Pelvic lymphocele after radical prostatectomy	1:1–1:9	9/9 (100)
Kim, 2020	Postoperative lymphatic leak of the abdomen and pelvis	1:3–1:4	10/10 (100)
Kim, 2019	Symptomatic lymphorrhea after pelvic surgery	1:3–1:6	20/24 (83.3)
Lee, 2023	Postoperative lymphorrhea after pelvic surgery	1:4	59/69 (83.1)
Moussa, 2021	Pelvic and retroperitoneal iatrogenic lymphoceles	1:2–1:10	20/20 (100)
Nadolski, 2018	Chylous ascites	1:3–1:6	6/7 (85.7)
Seyferth, 2023	Postoperative lymphocele in the pelvis or groin	1:1–1:4	15/18 (83.3)
Seyferth, 2023	Postoperative lymphorrhea in the pelvis or groin		8/9 (89.0)

Note: The data in parenthesis are percentages

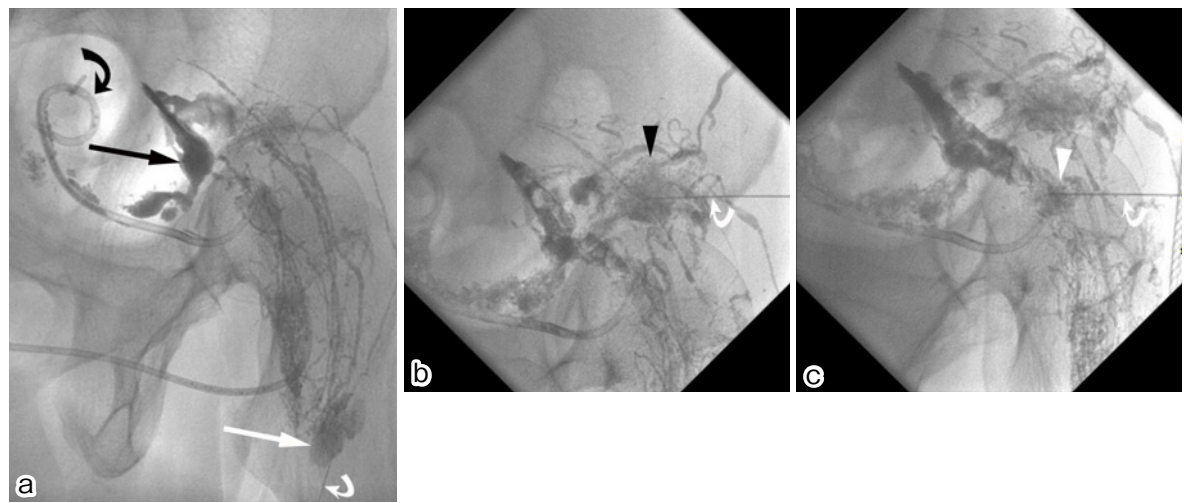


Figure 2. A 72-year-old male. A left pelvic lymphocele developed after rectal cancer surgery. A drainage catheter was placed in the lymphocele due to pressure pain. There was a daily drainage of 100 mL. After lymphatic embolization, the drainage stopped and the drainage catheter was removed 5 days after embolization.

(a) Intranodal lymphangiography. The right femoral lymph node (white arrow) was punctured with a 23-gauge Cathelin needle (curved white arrow) under ultrasound guidance and Lipiodol was injected. There is leakage of Lipiodol (black arrow) into the lymphocele. Drainage catheter placed in the lymphocele (curved black arrow).

(b) Lymphatic embolization. The lymph node upstream of the leak (black arrowhead) was punctured under fluoroscopy with a 23-gauge Cathelin needle (white curved arrow). Then, 2 mL of a 1:3 mixture of N-butyl cyanoacrylate and Lipiodol liquid embolic material was injected.

(c) The other lymph node upstream of the leak (white arrowhead) was punctured under fluoroscopy with a 23-gauge Cathelin needle (curved white arrow). Then, 3.7 mL of a 1:3 mixture of N-butyl cyanoacrylate and Lipiodol liquid embolization material was injected.

a higher ratio of NBCA, and if it is slow, the ratio should be lowered. In the rabbit model, mean polymerization times of 1:2 (NBCA density of 33%), 1:4 (20%), 1:6 (14%), and 1:8 (11%) for NBCA in lymph fluid were 14 ± 3 , 88 ± 93 , 331 ± 292 , and 932 ± 540 s, respectively [57]. Polymerization of NBCA is slower in lymphatic fluid than in blood [58]. Therefore, mixed solutions with higher ratios of NBCA than those used in blood are used. In upstream lymphatic embolization, NBCA to Lipiodol ratios of 1:1-1:10 have been reported (Table 2) [48-56]. The success rates for lymphatic embolization are 83%-100% (Table 2) [48-56].

Pelvic Lymphorrhea

A complication of pelvic surgery is lymph leakage from the pelvis and groin. Lymphoceles are often monitored and treated conservatively. In cases of infection or pain, percutaneous drainage and sclerotherapy are used. Success rates vary from 42 to 100%, with recurrence and treatment lasting several weeks [53, 59]. Recently, lymphatic embolization has also been performed for lymphocele (Fig. 2 and Table 2) [48, 51, 53, 59]. The clinical success rate for lymphatic embolization for lymphocele and sclerotherapy was 15/18

(83.3%) and 15/23 (65.2%), respectively [53]. The number of treatments was also lower for lymphatic embolization than for sclerotherapy (1.3 ± 0.1 vs. 2.5 ± 0.4 [mean \pm SE]; $P = 0.003$). Treatment duration was also shorter with lymphatic embolization than with sclerotherapy (6.9 days ± 1.7 vs. 27.9 days ± 5.7 ; $P = 0.002$). In a report by Kim et al. for symptomatic postoperative pelvic lymphoceles, the clinical success rate was 20/24 (83.3%) for lymphatic embolization, which was significantly higher than 7/16 (43.8%) for sclerotherapy ($P = 0.26$) [51]. However, although the efficacy of sclerotherapy has been established by prospective studies, the efficacy of lymphatic embolization is still limited as this treatment has only recently become available [60-62].

If the fluid collection is located within a free space, such as the peritoneum, sclerotherapy is not feasible. Therefore, lymphatic embolization is the treatment of choice in this case. Lee et al. reported lymphatic embolization for postoperative lymphorrhea, excluding cases suitable for sclerotherapy because the fluid collection is confined by a discrete wall [54]. Clinical success was achieved in 59 patients (83.1%) after NBCA with Lipiodol in a ratio of 1:4 from the external iliac lymph nodes. In patients with clinical success, 41 patients were embolized once, 16 were embolized twice, and 2 were embolized three times. In a subanalysis, a daily drainage volume greater than 1,500 mL/day was also reported as a predictor of failure.

Summary

With the advent of intranodal lymphangiography, embolization for lymphorrhea is becoming more common. Although complications of Lipiodol lymphangiography are rare, it is important to know that complications of pulmonary oil embolization can occur, the use of Lipiodol should be avoided in right-to-left cardiac or pulmonary shunts, and excessive use of Lipiodol should be avoided. When therapeutic lymphangiography for lymphorrhea is ineffective, embolization by upstream injection is effective. Embolization is a treatment to consider, especially in the pelvic region where it is easier to access the upstream lymph nodes and vessels.

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