Intranodal Lymphangiography: Feasibility and Preliminary Experience in Children

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ABSTRACT

Purpose: To review an initial experience studying the lymphatic system using direct injection of ethiodized oil contrast medium into lymph nodes (ie, intranodal lymphangiography) in children with chylous disorders.

Materials and Methods: Children with chylous disorders who underwent intranodal lymphangiography were included in this retrospective study. Under general anesthesia, ultrasonography was used to guide the placement of a small-bore (22–25-gauge) needle into an inguinal lymph node. Ethiodized oil contrast medium was very slowly injected into the node. Opacification of the lymphatic system was documented with fluoroscopic and digital substraction imaging and videofluoroscopic clips.

Results: Five children (age range, 6 wk to 17 y) with chylous vaginorrhea (n = 1), postoperative chylothorax (n = 2), or spontaneous chylothorax (n = 2) underwent intranodal lymphangiography. The amount of ethiodized oil injected was 0.5–4.5 mL. Intranodal lymphangiography was successfully completed in four patients. One procedure was terminated because of patient motion and extravasation of contrast medium. Lymphangiographic findings included a spectrum of lymphatic channel disorders including incompetence, obstruction, collateralization, chylous reflux, and chylous leak. There were no complications.

Conclusions: The simplified technique of injecting contrast medium into a lymph node to opacify the lymphatic system in children can be an alternative to the more elaborate conventional lymphangiography.

Conventional pedal lymphangiography is a useful diagnostic tool for a wide spectrum of diseases of the lymph nodes and lymphatic channels (1). The standard technique, which involves isolation and cannulation of a lymphatic vessel in the foot and injection of oily contrast material, is time-consuming and requires an incision to expose the lymphatics. The technique is particularly challenging in small children.

Intranodal lymphangiography is a less invasive alternative. Nevertheless, the limited published literature is focused on static imaging of lymph nodes. Herein, we report our initial experience with intranodal lymphangiography in five children, with successful dynamic opacification of the central lymphatic channels.

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Videos 1 and 2 are available online at *www.jvir.org*.

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MATERIALS AND METHODS

The committee on clinical investigation at our institution approved this retrospective study. The relevant medical history, technique, and imaging findings in patients who underwent intranodal lymphangiography are described in the present report.

Technique of Intranodal Lymphangiography

After confirming the clinical indication for intranodal lymphangiography, informed written consent was obtained from the patient's guardian. Initial ultrasonography (US) of the groin was performed to confirm the presence of prominent femoral lymph nodes. General anesthesia was induced for all procedures. With sterile technique and sonographic guidance, the largest inguinal lymph node was accessed with a fine needle (22–25 gauge). Alternatively, bilateral inguinal lymph node access was preformed. Care was taken not to puncture the node more than once and to place the tip

Table. Summary of Clinical and Imaging Findings

Pt. No.	Age/Sex	Weight (kg)	Clinical Indication	Lipiodol		
				Volume (mL)	Rate (mL/h)	Dose (mL/kg Body Weight)
1	6 wk/F	2.9	Postoperative chylothorax	0.5	0.3	0.17
2	17 y/F	46.5	Chylous vaginorrhea	4.5	3	0.10
3	6 mo/F	7.3	Spontaneous chylothorax	NA*	NA*	NA*
4	10 y/F	28.8	Spontaneous chylothorax	3.5	1.2	0.12
5	4 y/M	16.7	Postoperative chylothorax	2.5	0.4	0.15

Note.—NA = not applicable.
* Procedure aborted.

of the needle within the central portion of the lymph node. To confirm the proper position of the needle within the lymph node and rule out extravasation, small amounts (<0.5 mL) of normal saline or water-soluble contrast medium (Optiray 320; Mallinckrodt, St. Louis, Missouri) were slowly injected into the lymph node under sonographic and magnified collimated fluoroscopic visualization, respectively. Signs of successful cannulation of the node were gradual swelling of the node with the injection, visualization of the microbubbles flowing into the medulla of the node, and lack of perinodal leak. In the absence of extravasation, ethiodized oil contrast medium (Lipiodol Ultra-Fluid; Laboratoire Andre Guerbet, Aulnay-sous-Bois, France) was slowly infused into the lymph node by manual injection using a small (1–3-mL) syringe. The ethiodized oil was followed by normal saline in one patient and with Optiray 320 (ioversol) contrast medium in four patients; these boluses were administered at the same rate as the ethiodized oil. Single fluoroscopic and digital substraction images, as well as videofluoroscopic clips, were recorded at different intervals. After the required diagnostic information was obtained, the needles were removed and gentle pressure was applied at the puncture site for a few minutes. Subsequently, the patients were extubated and transferred to the recovery unit.

Endpoint

Intranodal lymphangiography was deemed as technically successful if the lymphatic channels of interest were adequately visualized and the lymphatic anatomic derangement was documented.

RESULTS

Five children (age range, 6 wk to 17 y; four female, one male) with disorders of the chylous circulation underwent intranodal lymphangiography under general anesthesia. The indication was chylous vaginorrhea (n = 1), iatrogenic chylothorax (n = 2), or spontaneous chylothorax (n = 2).

Intranodal lymphangiography was technically successful in four children. In one infant (patient 3), the procedure was terminated because of patient motion and extravasation of contrast medium. The volume of ethiodized oil injected during each procedure was 0.5–4.5 mL. The average injection rate ranged from 0.3 to 4.5 mL/h, although initial injection rates were performed at a slower pace. The total dose of ethiodized oil ranged from 0.10 to 0.17 mL/kg body weight.

The clinical and imaging findings are summarized in the **Table**. Intranodal lymphangiography successfully demonstrated the spectrum of lymphodynamic disorders including incompetence, obstruction, collateralization, chylous reflux, and chylous leak.

Follow-up ranged from 2.5 to 9 months. No complications occurred apart from minor, clinically insignificant extravasation of contrast medium.

First Patient

Patient 1 was a 6-week-old female infant with complex congenital heart disease. The infant was small for gestational age (2.9 kg). After palliative surgical repair, she developed extensive thrombosis of the superior vena cava and innominate and jugular veins with persistent bilateral chylothoraces. Medical management and drainage with chest tubes failed to control the leak. Intranodal lymphangiography was performed with the intent to percutaneously embolize the thoracic duct if a chylous leak was identified. The study showed an intact cisterna chyli and thoracic duct without visible extravasation of contrast medium. However, instead of normally draining into the left subclavian vein, ethiodized oil was diverted into the lymphatics and nodes of the chest wall, axilla, mediastinum, and neck, very likely secondary to obstruction of the terminal portion of the thoracic duct by central venous thrombosis (**Fig 1a, 1b**). In this infant, we avoided the use of a larger volume of ethiodized oil because of the bidirectional intracardiac admixture of blood. For several weeks, on follow-up chest radiographs, these regional nodes retained most of the ethiodized oil injected (**Fig 1c**). Unfortunately, needle maceration of the cisterna chyli (performed at the same time as the lymphangiogram) and surgical ligation of thoracic duct failed to lessen the leak and the infant died 1 month later as a result of cardiopulmonary failure.

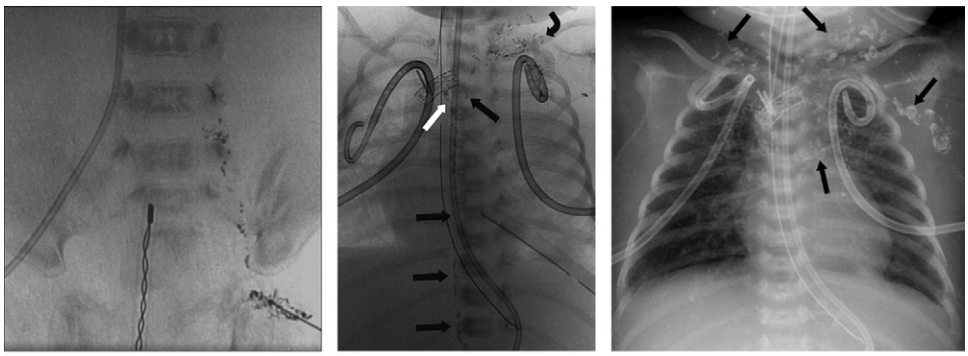

Figure 1. Patient 1. **(a)** Spot radiograph of the left groin shows the initial phase of intranodal injection with opacification of a left inguinal lymph node and pelvic lymphatic channels. **(b)** Spot radiographs (obtained 70 min after starting injection) shows diverted flow from the thoracic duct into the lymphatics of the neck and axilla (bent arrow) denoting obstruction of the terminal portion of the thoracic duct. Note opacification of normal cisterna chyli and left thoracic duct (black arrows) as well as the right thoracic duct (white arrow). There is a metallic stent in the left innominate vein (overlapping with surgical clips) and bilateral chest, endotracheal, and nasogastric tubes. **(c)** Chest radiograph 25 days after the procedure shows retained ethiodized oil in the lymph nodes of the neck, chest wall, axilla, and mediastinum (arrows).

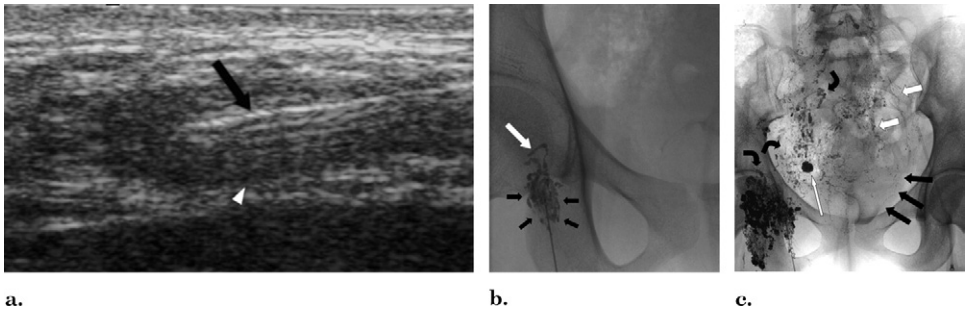

Figure 2. Patient 2. **(a)** US image shows the proper position of the needle (arrow) within the lymph node (arrowhead). **(b)** A spot radiograph of the right groin demonstrates the initial phase of intranodal injection of ethiodized oil, with opacification of the lymph node (black arrows) and adjacent efferent femoral lymphatic channels (white arrow). **(c)** There is extensive ectasia and incompetence of the femoral, iliac, and retroperitoneal lymphatics (bent arrows), with focal areas of leak (long white arrow). Note reflux from incompetent right external and common iliac lymphatics into ipsilateral and contralateral iliac chains (thick white arrows) as well as into the pelvic organs. The faintly opacified uterus is marked by black arrows overlapping with contrast in the urinary bladder.

Second Patient

A 17-year-old female patient was referred to our center for management of chronic chylous vaginorrhea and arteriovenous malformation of the left femur. Clinical examination showed slightly prominent labia and a faint capillary stain over the right thigh. In addition, the right thigh was warmer with a thrill.

Magnetic resonance (MR) imaging showed an extensive intraosseous arteriovenous malformation involving the entire length of the right femur. There were no abdominal tumors or signs of lymphedema. US showed a mildly enlarged uterus with small ascites. The patient underwent three embolization procedures at an outside institution, during which proximal closure of the main feeding arteries was performed with coils.

Under general anesthesia, vaginoscopy showed chylous leak from the cervical os, with small lymphatic vesicles. After successful embolization of the thigh arteriovenous malformation, lymphangiography demonstrated extensive ectasia and incompetence of the right femoral, iliac, and retroperitoneal lymphatics, with focal areas of contrast medium leakage (**Fig 2a–2c**). Marked reflux of contrast medium from incompetent right external and common iliac lymphatics into ipsilateral and contralateral iliac chains, as well as the pelvic organs, primarily opacifying the uterus, was noted (**Fig 2d**; **Video 1** [available online at *www.jvir.org*]).

Third Patient

A 6-month-old female child was admitted with respiratory distress. Examination showed increased head circumference and hepatosplenomegaly. A large chylous left pleural effusion noted on initial chest radiograph was drained with a chest tube. Follow-up chest radiographs demonstrated thickened interstitial lung markings.

MR imaging and computed tomography (CT) of the chest demonstrated thickening of the pulmonary interstitium with retroperitoneal and posterior mediastinal soft tissue density, very suggestive of abnormal mediastinal and retroperitoneal lymphatic channels. These imaging findings

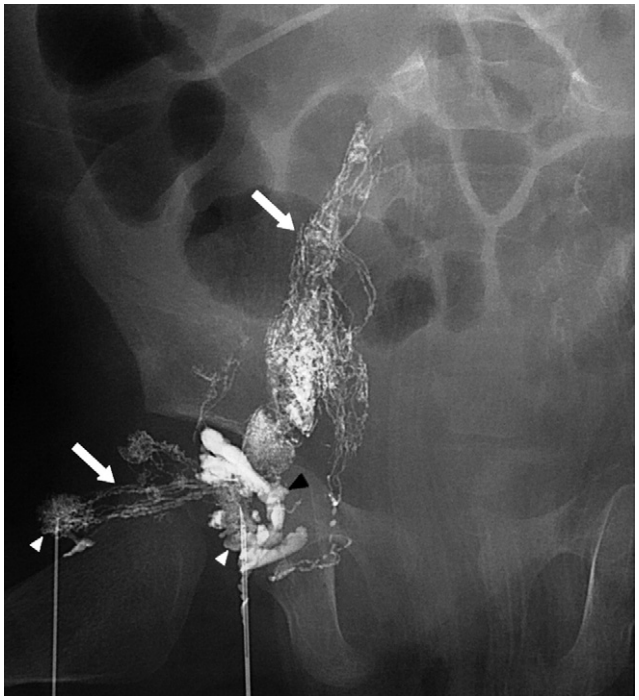

Figure 3. Spot radiograph of right groin in patient 3 shows opacification of two lymph nodes (white arrowheads) with extravasation (black arrowhead). There is also opacification of normal femoral and iliac efferent lymphatic channels (arrows).

were suggestive of extensive pulmonary and systemic lymphatic abnormalities.

Intranodal lymphangiography was attempted under general anesthesia to identify the source of chylous leak. Initial injection of ethiodized oil into the largest lymph node in the left groin was terminated as a result of extravasation. Access to a second lymph node successfully opacified the efferent lymphatic channels up to the common iliac group (**Fig 3**). Unfortunately, the needle was dislodged as a result of patient motion. Further attempts to securely access lymph nodes in the left inguinal region were unsuccessful as a result of the small size of the nodes. Therefore, the procedure was aborted. After further workup, the infant was found to have Niemann–Pick disease.

Fourth Patient

A 10-year-old girl with diffuse thoracic lymphatic disease and multiple respiratory tract infections was refereed to our center with a 9-month history of dyspnea and fatigue. Chylous right pleural effusion was drained with a chest tube. A chest CT scan demonstrated a diffuse, low-attenuating infiltrative abnormality involving the mediastinum with extension into the pulmonary perihilar regions and bronchovascular bundles, with thickening of the pulmonary interstitium. In addition, there was contiguous extension into the retroperitoneum, right axilla, and chest wall.

Lung and thymus biopsy specimens demonstrated diffuse lymphatic disease with extensive pulmonary involvement, fibrosis, abundant macrophages, and spindle cell proliferation.

Intranodal lymphangiography was performed via a tiny lymph node in the left groin by instilling 3.5 mL of ethiodized oil, followed by 5 mL of Optiray 320, very slowly over a period of 3 hours. The study revealed a normal appearance of the pelviabdominal lymphatic system. The flow of contrast medium into the cisterna chyli and thoracic duct was delayed, with reflux of contrast medium from the thoracic duct into mediastinal and cervical lymphatic channels. The thoracic duct was dilated and tortuous with continuous to-and-fro peristaltic motion (**Video 2** [available online at *www.jvir.org*]). The findings were suggestive of occlusion or incompetence of the terminal portion of the thoracic duct.

Fifth Patient

A 4-year-old boy with double-inlet left ventricle and transposed great vessels underwent a lateral tunnel fenestrated Fontan operation at our institution. He later presented with a chronic right-sided chylous pleural effusion that was managed with diuresis, intermittent drainage, and a low-fat diet. Intranodal lymphangiography was preformed using a small amount of ethiodized oil because of the concerns for a right-to-left shunt and risk of systemic embolization. Lymphangiography was preformed via simultaneous injection of the lymph nodes in both groins. The study demonstrated patency of the iliac lymphatics, lumbar trunks, and cisterna chyli. The thoracic duct was intermittently opacified by a small amount of contrast medium, which quickly flowed into the chest. Percutaneous cannulation of the thoracic duct was attempted. Despite successful opacification of the duct during several direct retroperitoneal injections, a guide wire could not be passed into the duct. No contrast extravasation was directly visualized, possibly because of the limited use of ethiodized oil. Follow-up CT scan showed extensive reflux of ethiodized oil into the bronchovascular and mediastinal lymphatic channels and nodes. No contrast medium was seen within the pulmonary arteries, signifying poor flow through the terminal portion of the thoracic duct, presumably as a result of obstruction.

DISCUSSION

With the advent of cross-sectional imaging, pedal lymphangiography has been replaced largely by CT and MR imaging. Nevertheless, the procedure may be indicated in patients with chylous reflux or iatrogenic chylothorax for preoperative localization or transabdominal catheterization and embolization (2–7).

Intranodal injection of iodized oil contrast material was described initially as a promising technique to avoid the difficulties of conventional lymphangiography. Funaoka (8) described direct injection of contrast material into lymph nodes in 1930. Shanbrom and Zheutlin (9,10) described the procedure of "lymphadenography" with radiologic visual-

ization of lymph nodes and lymph channels by injecting contrast medium directly into a palpable lymph node. The procedure was developed during an attempt to evaluate the tumoral involvement of inguinal, pelvic, and lumbar lymph nodes. Thirty-five procedures were initially performed in 20 patients. The lymph node was held firmly between the fingertips, accessed with a needle, and injected with 2–8 mL of oily contrast medium, depending on the size of the lymph node, ease of injection, and spread of contrast medium (9,10). In a more recent study, Xu et al (11) described their experience with intranodal lymphangiography in 40 patients, mostly adults (14 female; age range, 16–64 y). Forty-five intranodal lymphangiography procedures were performed to study patients with chyluria, perineal chylous leak, or pelvic or genitourinary masses. The technique simply involved palpating a superficial inguinal lymph node (>0.5 cm), percutaneously placing a fine needle into the node, and injecting 3 mL of 0.5% procaine followed by the oily contrast medium. They reported a success rate of 87%; failed procedures were attributed to difficult access of indurated or metastatic lymph nodes, multiple punctures, and excessive pressure leading to extravasation of contrast medium (11). There were minor complications such as local pain, cough, and low-grade fever, all of which resolved without intervention. Other reported complications from intranodal lymph node injections include extravasation of the contrast material and direct injury to the lymph nodes, leading to lymphovenous shunts (12). Unfortunately, studies of intranodal lymphangiography on humans have included little or no documentation of the lymphodynamics, diagnostic and clinical relevance of the procedure, incidence of extravasation, and whether the contrast material opacified the central conducting lymphatics of interest or the thoracic duct.

Intranodal lymphangiography has also been successfully performed in animal studies with better documentation of the technique and imaging findings. Johnson et al (13) used US to guide percutaneous injection of intestinal lymph nodes with nonionic iodinated contrast medium for preoperative CT lymphography of the thoracic ducts of six dogs with chylothorax. Percutaneous CT lymphangiography was successful in delineating the cisterna chyli, thoracic duct, and other associated lymphatic vessels in all six dogs. Naganobu et al (14) injected nonionic contrast medium percutaneously into the popliteal lymph node in five dogs, successfully opacifying the thoracic ducts. Contrast medium extravasation was noted in one procedure.

Based on our initial experience in children, the ultimate success of the procedure is dependent on several factors, including US guidance, use of general anesthesia, optimization of the rate of ethiodized oil injection, and dynamic use of fluoroscopy.

Initial US screening with a high-resolution linear probe to confirm the presence of a sizable inguinal lymph node is a crucial step and should be done before induction of general anesthesia. US guidance allows for the access of smaller and deeper inguinal lymph nodes that may not be palpable, reducing the number of needle punctures. US can also detect early signs of extravasation. Recording still fluoroscopic images and videofluoroscopic clips allows for dynamic, real-time evaluation of the lymphatic flow. In children, we believe the use of general anesthesia is essential to ensure complete immobility.

The rate of ethiodized oil administration should be extremely slow, as extravasation of contrast medium seems to be the main limiting factor for this technique (15). We speculate that perinodal extravasation in several of our patients was related to high injection rates. Contrast medium leak may also be precipitated by improper needle placement within the node and repetitive punctures of the same node. We believe the intranodal ethiodized oil injection should be terminated with the first sign of extravasation, and an alternative node should be used.

In the present study, the injection rate for the small infant was approximately 0.3 mL/h, whereas it reached 4.5 mL/h for the teenager. Slow manual injection of the viscous ethiodized oil through a fine needle can be exhausting to the operator's hands and requires patience. Alternating the injection between two operators may help. Unfortunately, the newer generations of automated infusion pumps do not allow for the injection of ethiodized oil as a result of its viscosity.

The ideal dose and rate of infusion of ethiodized oil for intranodal lymphangiography in children is still to be determined. In adults, it is recommended that bipedal lymphangiography to be done with 5–7 mL of ethiodized oil per extremity (16,17). Kusik (17) used infusion rates of 0.10 mL/min for children and 0.12–0.30 mL/min for adults. Gough (18) recommended 0.25 mL/kg body weight as a maximum dose of ethiodized oil for children and adults. In the present small series, the total dose of ethiodized oil ranged from 0.10 to 0.17 mL/kg body weight. We generally estimate the volume of ethiodized oil based on the weight of the patient and the progression of contrast medium flow under fluoroscopy. Symptomatic pulmonary embolism may occur with large volumes of ethiodized oil (16,19). In patients with right-to-left cardiac shunts, ethiodized oil may egress into the systemic circulation, with subsequent arterial embolization (12). A bolus of saline solution or water-soluble contrast medium after the injection of ethiodized oil may decrease the dose and expedites the flow of ethiodized oil. Intermittent fluoroscopic observation of the contrast medium flow also helps prevent excessive administration of ethiodized oil.

Intranodal lymphangiography has several advantages versus the conventional pedal method. Accessing the groin lymph nodes requires no incisions and bypasses the lower extremity. This may decrease the procedure time, radiation dose, and volume of contrast medium. The technique is particularly appealing in children in view of the small size of the lymphatic channels and commonly enlarged inguinal lymph nodes. Intranodal lymphangiography via a groin node cannot be used for evaluation of the lymphatic disorders of the lower extremities. Lymphangiography and CT

are complementary examinations (5), and in selected patients (eg, patients 4 and 5 in the present series), CT scanning after lymphangiography provides invaluable information about delayed and subtle abnormalities of chyle flow.

In conclusion, intranodal lymphangiography can provide a simpler, safer alternative to the conventional procedure. Meticulous needle access with high-resolution US, slow administration of an oily contrast medium, and the use of general anesthesia are paramount for this procedure.

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REFERENCES

1. Kinmonth JB, Taylor GW. Chylous reflux. Br Med J 1964; 29:529–232.
2. Ngan H, Fok M, Wong J. The role of lymphangiography in chylothorax following thoracic surgery. Br J Radiol 1988; 61:1032–1036.
3. Sachs PB, Zelch MG, Rice TW, Geisinger MA, Risius B, Lammert GK. Diagnosis and localization of laceration of the thoracic duct: usefulness of lymphangiography and CT. AJR Am J Roentgenol 1991; 157:703–705.
4. Howarth D, Gloviczki P. Lymphoscintigraphy and lymphangiography of lymphangiectasia. J Nucl Med 1998; 39:1635–1638.
5. Guermazi A, Brice P, Hennequin C, Sarfati E. Lymphangiography: an old technique retains its usefulness. Radiographics 2003; 23:1541–1558.
6. Sheehan R, Hreshchyshyn M, Lin RK, Lessmann FP. The use of lymphography as a diagnostic method. Radiology 1961; 76:47–53.
7. Itkin M, Kucharczuk JC, Kwak A, Trerotola SO, Kaiser LR. Nonoperative thoracic duct embolization for traumatic thoracic duct leak: experience in 109 patients. J Thorac Cardiovasc Surg 2010; 139:584–589.
8. Davidson JW, Fletch AL, McIlmoyle G, Roeck W. The technique and applications of lymphography. Can J Comp Med 1973; 37:130–138.
9. Shanbrom E, Zheutlin N. Radiographic studies of the lymphatic system. Arch Intern Med 1959; 104:589–593.
10. Zheutlin N, Shanbrom E. Contrast visualization of lymph nodes. Radiology 1958; 71:702–708.
11. Xu H, Zheng W, Li H, Yang W. Groin percutaneous intranodal lymphography. Chinese J Urol 1994; 1:60–61.
12. Winterer JT, Blum U, Boos S, Konstantinides S, Langer M. Cerebral and renal embolization after lymphography in a patient with non-Hodgkin lymphoma: case report. Radiology 1999; 210:381–383.
13. Johnson EG, Wisner ER, Kyles A, Koehler C, Marks SL. Computed tomographic lymphography of the thoracic duct by mesenteric lymph node injection. Vet Surg 2009; 38:361–367.
14. Naganobu K, Ohigashi Y, Akiyoshi T, Hagio M, Miyamoto T, Yamaguchi R. Lymphography of the thoracic duct by percutaneous injection of iohexol into the popliteal lymph node of dogs: experimental study and clinical application. Vet Surg 2006; 35:377–381.
15. Brunn S, Engeset S. Lymphadenography. A new method for visualization of enlarged lymph nodes and lymphatic vessels. Acta Radiol 1956: 45:389–395.
16. Kinmonth JB. Methods of lymphography. In: Kinmonth JB, ed. The lymphatics: surgery, lymphography and diseases of the chyle and lymph systems, 2nd edition. London: Edward Arnold, 1982; 1–17.
17. Kuisk H. Technique of lymphography. In: Kuisk H.Technique of lymphography and principles of interpretation, 1st ed. St. Louis: Warren H. Green, 1971; 15–39.
18. Gough MH. Lymphangiography in children. Arch Dis Child 1964; 39: 177–181.
19. Takahashi M, Abrams HL. Arborizing pulmonary embolization following lymphangiography. Report of three cases and an experimental study. Radiology 1967; 89:633–638.