Korean J Thorac Cardiovasc Surg 2019;52:409-415 □ CLINICAL RESEARCH □
ISSN: 2233-601X (Print) ISSN: 2093-6516 (Online) https://doi.org/10.5090/kjtcs.2019.52.6.409

Lymphangiographic Interventions to Manage Postoperative Chylothorax

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Background: Postoperative chylothorax may be caused by iatrogenic injury of the collateral lymphatic ducts after thoracic surgery. Although traditional treatment could be considered in most cases, resolution may be slow. Radiological interventions have recently been developed to manage postoperative chylothorax. This study aimed to compare radiological interventions and conservative management in patients with postoperative chylothorax. **Methods:** We retrospectively reviewed periprocedural drainage time, length of hospital stay, and nil per os (NPO) duration in 7 patients who received radiological interventions (intervention group [IG]) and in 9 patients who received conservative management (non-intervention group [NG]). **Results:** The baseline characteristics of the patients in the IG and NG were comparable; however, the median drainage time and median length of hospital stay after detection of chylothorax were significantly shorter in the IG than in the NG (6 vs. 10 days, p=0.036 and 10 vs. 20 days, p=0.025, respectively). NPO duration after chylothorax detection and total drainage duration were somewhat shorter in the IG than in the NG (5 vs. 7 days and 8 vs. 14 days, respectively). **Conclusion:** This study showed that radiological interventions reduced the duration of drainage and the length of hospital stay, allowing an earlier return to normal life. To overcome several limitations of this study, a prospective, randomized controlled trial with a larger number of patients is recommended.

Key words: 1. Chylothorax
2. Lymphography
3. Postoperative care
4. Thoracic duct
5. Thoracic surgery

Introduction

Postoperative chylothorax may be caused by iatrogenic injury of the collateral lymphatic ducts after thoracic surgery. In most cases, traditional treatment is prescribed; however, recent studies reported success rates of 16%–75% depending on the daily output [1-4]. It is especially difficult for elderly patients to endure nil per os (NPO) status during the postoperative period, as it causes lethargy and prevents active rehabilitation. To maximize the likelihood of early recovery, pleurodesis may be the treatment of

Received: January 4, 2019, Revised: June 3, 2019, Accepted: June 5, 2019, Published online: October 5, 2019
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Table 1. Prior operations in patients with chylothorax

Group	Underlying disease	Operation	No. of patients
Intervention group (n=7)	Lung cancer	Lobectomy	4
	Esophageal cancer	Ivor-Lewis operation	2
	Thyroid cancer invasion to the trachea	Tracheal end-to-end anastomosis	1
Non-intervention group (n=9)	Lung cancer	Lobectomy	4
	Lung cancer	Sleeve lobectomy	2
	Esophageal cancer	Ivor-Lewis operation	1
	Esophageal cancer	3-Hole operation	2

choice [5-7]. However, the associated chest pain may prevent lung rehabilitation; patients develop a cough and cannot take deep breaths. Chemical agents may trigger acute respiratory distress syndrome in cases where postoperative air leakage is prolonged [8-10]. Although surgery or another intervention may serve as a last resort, surgery might be problematically invasive, especially in the postoperative status.

However, an intervention may be worthwhile if it reveals the leakage site and is therapeutic [2,11-17]. Thoracic duct lymphangiography (TDL) with or without thoracic duct embolization (TDE) may solve several of the above-mentioned problems. Although only a few patients at Pusan National University Hospital have undergone radiological interventions, we herein present a retrospective evaluation of the efficacy of radiological interventions in comparison to conservative management.

Methods

1) Study groups

The intervention group (IG) included patients with postoperative chylothorax who underwent radiological interventions (n=7) from January 2017 to September 2018. The non-intervention group (NG) included 9 patients who underwent conservative management from January 2010 to December 2015. In the IG, 5 patients underwent TDE and 2 underwent TDL only.

Of the patients in the IG, 4 underwent thoracoscopic lobectomies to treat lung cancer, 2 underwent Ivor-Lewis operations to treat esophageal cancer, and 1 underwent an end-to-end tracheal anastomosis to treat thyroid cancer invasion of the trachea. Of the patients in the NG, 4 underwent thoracoscopic lobectomies and 2 underwent sleeve lobectomies to treat lung cancer, while 1 patient underwent an Ivor-Lewis operation and 2 patients underwent 3-hole operations to treat esophageal cancer (Table 1).

2) Radiological interventions

TDL was performed in patients who suffered from postoperative chylothorax, followed by TDE when the lymphatic duct was accessible.

3) Thoracic duct lymphangiography

We preassembled a 26G needle and a short catheter (Cook, Bloomington, IN, USA) fitted to a Luer-lock syringe containing 3–5 mL of lipiodol. Intranodal lymphangiography was performed via the bilateral inguinal or femoral lymph nodes. Lymph node puncture was performed under ultrasonographic guidance. Subsequently, a small amount of lipiodol was injected under fluoroscopic guidance to confirm puncture of the intranodal lymphatic vessel. Lipiodol was then hand-injected at 3 mL/min under intermittent fluoroscopic guidance (to reduce the radiation dose). When the punctured lymph node became ruptured during the injection, the upper lymph nodes were directly punctured under fluoroscopic guidance and lipiodol injection continued. Lipiodol injection ceased after opacification of the lumbar duct or cisterna chyli. The total amount of lipiodol was limited to 20 mL to minimize the risk of pulmonary fat embolism.

4) Thoracic duct embolization

Thoracic duct access was obtained via direct puncture of the lumbar duct or cisterna chyli with a 21G Chiba needle using the transabdominal route. Prior to access, cone-beam computed tomography was used to assess the relationship between the duct and surrounding anatomical structures (such as the aorta). After transabdominal puncture of the cisterna chyli, we attempted to enter the thoracic duct using a 0.018-inch (0.46-mm) Transend guidewire (Boston Scientific Corp., Natick, MA, USA). If the guidewire

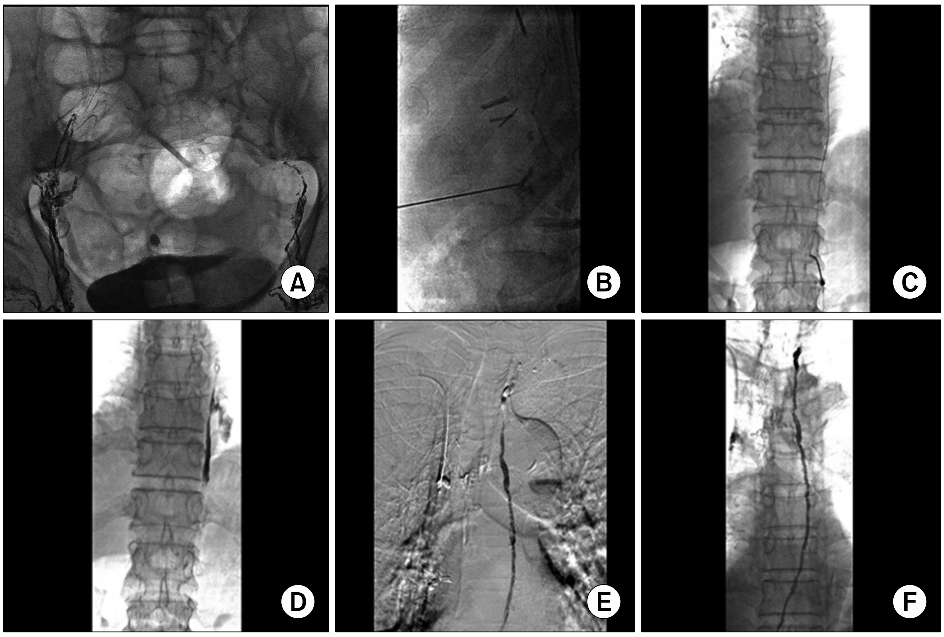

Fig. 1. Thoracic duct embolization. (A) Intranodal lymphangiography via the bilateral inguinal lymph nodes. (B) Thoracic duct access via direct puncture of the lumbar duct. (C) Introduction of a microcatheter after insertion of a guidewire. (D) Digital subtraction angiography to establish the chyle leakage site. (E) Microcoil embolization above the leakage site. (F) Embolization using a mixture of N-butyl cyanoacrylate and lipiodol.

entered the duct, we advanced it further and then introduced a 2.0- or 2.2F microcatheter (Terumo, Tokyo, Japan), employing the over-the-wire technique. Digital subtraction angiography was performed with the aid of the microcatheter to establish the chyle leakage sites; these were subjected to Concerto microcoil embolization (Medtronic, Jacksonville, FL, USA) proximal to (above) the leakage sites, which were then embolized using a mixture of N-butyl cyanoacrylate (NBCA, Histoacryl; B Brown, Melsungen, Germany) and lipiodol (weight ratio 1:1). Coil embolization prevented NBCA migration to the left subclavian vein; the NBCA polymerization time is longer in the lymphatic vessels than in blood vessels. If the needle accessed the lymph node, lipiodol was injected. Fluoroscopic images of the cisterna chyli were then obtained. Direct cisterna chyli puncture using a 21G Chiba needle was performed under fluoroscopic guidance, and an 0.018-inch (0.46-mm) guidewire and microcatheter were used to cannulate the thoracic duct, which was then embolized using Concerto 3EA microcoils and an NBCA/lipiodol mixture (weight ratio 1:1) (Fig. 1).

5) Medical records

We recorded the patients' age, total drainage duration, drainage duration after detection of chylothorax, preprocedural and postprocedural drainage duration, day of postoperative chylothorax detection, interval from detection to intervention, interval from detection to oral feeding, postprocedural oral feeding status, total length of hospital stay, length of hospital stay after detection of chylothorax, postprocedural length of hospital stay, complications, and in-hospital mortality in the IG and NG and in the TDE and TDL patients (Fig. 2). The study protocol was approved by the Institutional Review Board of Pusan National University, Busan, Republic of Korea (IRB no., 1908020082), which waived the need for informed patient consent.

6) Statistical analysis

We used the Student t-test, the Mann-Whitney U-test, and the Kolmogorov-Smirnov test as appropriate. All data are expressed as medians with ranges. A p-value <0.05 was considered to indicate statistical significance. All analyses were conducted using IBM SPSS ver. 24.0 (IBM Corp., Armonk, NY, USA).

Results

In the IG, the median age was 70 years (range, 62–76 years), and chylothorax was detected at mean postoperative day (POD) 3 (range, 1–7 days), although 5 patients (71.4%) exhibited chylothorax earlier, only 1 day after NPO ended. The 2 patients who

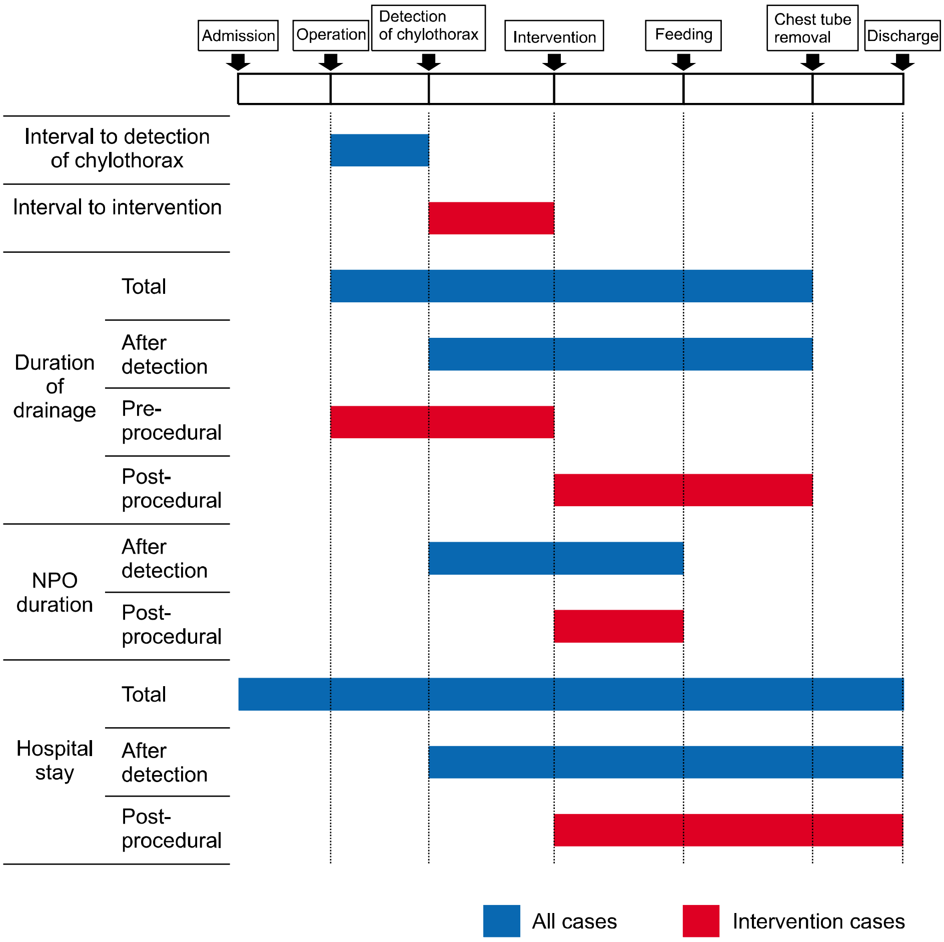

Fig. 2. Schematic of the measurement schedule. The measured parameters in all cases include interval to detection of chylothorax, total duration of drainage, duration of drainage after detection, NPO duration after detection, total length of hospital stay, and length of hospital stay after detection, whereas the measured parameters in the intervention cases include interval to intervention, preprocedural/postprocedural duration of drainage, postprocedural NPO duration, and length of hospital stay after intervention. NPO, nil per os.

underwent an Ivor-Lewis operation exhibited chylothorax on PODs 5 and 7 because NPO duration was prolonged. The median interval between chylothorax detection and the intervention was 4 days (range, 1–7 days). The median duration of chest tube drainage was 7 days (range, 5–26 days); of the total drainage days, the preprocedural and postprocedural durations were 5 days (range, 3–13 days) and 4 days (range, 1–12 days), respectively. Although the median time from the intervention to postprocedural oral feeding was 3 days (range, 1–3 days), 3 of 7 patients (42.9%) commenced oral feeding the day after their procedures. The median time from detection of chylothorax to oral feeding was 5 days (range, 2–10 days). The median length of hospital stay after detection of chylothorax was 10 days (range, 7–20 days), and the median postprocedural length of hospital stay was 7 days (range, 6–13 days) (Table 2, Fig. 1).

Compared with the IG, the median age of the NG was 61 years (range, 52–75), and the median chylothorax detection time was POD 2 (range, 1–8 days). The median total drainage duration in the NG was 14 days (range, 10–31 days), and the median total length of hospital stay was 21 days (range, 14–49 days), which did not differ significantly from the IG. In the NG, the median drainage time after detection of chylothorax was 10 days (range, 9–24 days) and the median length of hospital stay after detection of chylothorax was 20 days (range, 12–42 days), which were significantly different from the IG ($p=0.036$ and $p=0.025$, respectively). The NPO duration after detection of chylothorax in the NG was 7 days (range, 1–20 days), which was not significantly different from the IG (Table 2).

Of the 7 patients who underwent TDL, 5 successfully underwent TDE, but 2 did not. Although the TDL-only subgroup contained only 2 patients, the median postoperative chylothorax detection time in

Table 2. Comparison of clinical findings between the intervention and non-intervention groups of patients with postoperative chylothorax

Variable	Intervention group (N=7)	Non-intervention group (N=9)	p-value
Sex (male:female)	4:3	8:1	0.29
Age (yr)	70 (62–76)	61 (52–75)	0.06
Postoperative detection day (POD)	3 (1–7)	2 (1–8)	0.72
Drainage duration (day)			
Total	8 (5–26)	14 (10–31)	0.15
After detection	6 (3–19)	10 (9–24)	0.036
NPO duration after detection (day)	5 (2–10)	7 (1–20)	0.72
Hospital stay (day)			
Total	24 (14–29)	21 (14–49)	0.37
After detection	10 (7–20)	20 (12–42)	0.025

Values are presented as median (range), unless otherwise stated.
POD, postoperative day; NPO, nil per os.

Table 3. Comparison of post-procedural findings between patients who underwent TDE and TDL only in the intervention group

Variable	TDE (N=5)	TDL only (N=2)	p-value
Sex (male:female)	3:2	1:1	0.82
Age (yr)	70 (62–74)	72 (68–76)	0.57
Postoperative detection day (POD)	3 (1–7)	3 (2–3)	0.72
Interval from detection to intervention	4 (3–7)	1 (1)	0.09
Drainage duration (day)			
Total	8 (5–26)	14 (10–31)	0.38
Pre-procedural	6 (3–19)	10 (9–24)	0.09
Post-procedural	4 (1–12)	3 (2–4)	0.86
NPO duration after detection (day)	3 (1–3)	2 (1–3)	0.09
Hospital stay (day)			
After detection of chylothorax	11 (11–20)	8 (7–9)	0.09
Post-procedural	7 (6–13)	7 (6–8)	0.86

Values are presented as median (range), unless otherwise stated.
TDE, thoracic duct embolization; TDL, thoracic duct lymphangiography; POD, postoperative day; NPO, nil per os.

the TDE and TDL subgroups was 3 days (range, 1–7 days) and 3 days (range, 2–7 days), respectively. The median interval between chylothorax detection and the intervention in the TDE and TDL subgroups was 4 days (range, 3–7 days) and 1 day (range, 1 day), respectively. The median total duration of chest tube drainage was 11 days (range, 7–26 days) and 7 days (range, 5–8 days), respectively; the preprocedural drainage duration was 7 days (range, 5–14 days) and 4 days (range, 3–4 days), respectively; and the post-procedural drainage duration was 4 days (range, 1–12 days) and 3 days (range, 2–4 days), respectively. The median time to postprocedural oral feeding in the TDE and TDL subgroups was 3 days (range, 1–3 days) and 2 days (range, 1–3 days), respectively. The median length of hospital stay after detection of chylothorax in the TDE and TDL subgroups was 11 days (range, 11–20 days) and 8 days (range, 7–9 days), respectively, and the median postprocedural length of hospital stay was 7 days (range, 6–13 days) and 7 days (range, 6–8 days), respectively (Table 3). No postprocedural complications, such as bleeding, infection, or empyema, were noted. The mean follow-up duration was 5±3.02 months (range, 1–8 months).

Discussion

The results of our study showed that the baseline characteristics of the patients in the IG and NG were generally comparable; however, the median drainage time and median length of hospital stay after detection of chylothorax were significantly shorter in the IG than in the NG. NPO duration after detection and total drainage duration were somewhat shorter in the IG than in the NG.

Postoperative chylothorax has previously been difficult to manage. Generally, most patients are initially conservatively treated employing NPO, total parenteral nutrition, and pleural drainage [1-4]; however, an operation may be required if leakage persists for longer than 2 weeks or is greater than 1,000 mL/day for more than 5 days despite conservative therapy [1-3]. In such cases, bedside pleurodesis may obviate the need for surgery [5-7,18,19]. However, pleuritic chest pain that prevents lung rehabilitation may develop; patients may also develop a cough and be unable to take deep breaths. Chemical agents could trigger acute respiratory distress syndrome [8-10].

Developments in radiological interventions have led to new therapeutic options (such as TDL and TDE) for treatment of chylous leakage [1,2,17]. In recent studies, lymphangiography identified 64%–86% of leakage sites, and the TDE success rate was >90% when the thoracic duct could be accessed [1,12,14]. Traditional management in postoperative chylothorax was performed at our hospital before the development of the intervention technique; however, most patients with postoperative chylothorax opted for the intervention treatment as soon as possible after detection of chylothorax. Generally, in patients with lung cancer, chylothorax could be detected on POD 1 or 2, since oral feeding might be started on POD 1. However, in patients with esophageal cancer, chylothorax tended to be detected later, such as on POD 5–7, when oral feeding was usually initiated. Although variation in timing is possible due to different timelines for the initiation of oral feeding depending on the disease, we try to let patients undergo the intervention as soon as possible after the detection of chylothorax.

We performed radiological interventions to treat 7 patients with postoperative chylothorax from January 2017 to September 2018. To evaluate the efficacy of the interventions, we compared these patients to 9 who underwent conservative management and were enrolled from January 2010 to December 2015. We found that the median drainage and the median length of hospital stay after detection of chylothorax were significantly shorter in the IG than in the NG ($p=0.036$ and $p=0.025$, respectively) and that oral feeding after detection of chylothorax was possible sooner in the IG than in the NG (Table 2). Patients who require thoracic surgery are usually older, and a reduced NPO duration improves quality of life in the elderly.

Of 7 IG patients, 5 underwent TDE, but 2 underwent TDL only because of access failure that was attributable to anatomical variations of the thoracic duct, which occur in up to 30% of all subjects. We found no significant difference in postprocedural chest tube drainage duration, the postprocedural oral feeding day, or the postprocedural length of hospital stay between the TDE and TDL subgroups ($p=0.857$, $p=0.095$, and $p=0.857$, respectively). All cases resolved soon after their procedures regardless of TDE status. This might be explained by the use of "scratching" to reduce lymphatic flow via multiple needle punctures of the prevertebral lymph vessels; this releases lymphatic wall tension, allowing lymphatic leaks to heal [1,17,20]. Although the details of healing after TDL remain unclear, the TDL subgroup had better postprocedural outcomes than the TDE subgroup (Table 3). However, for these findings to reach statistical significance, the number of patients in both subgroups must be increased.

Our study had several limitations. First, the number of patients in both the IG and NG was low. Second, the IG and NG were formed at different periods, because of developments in interventional techniques. Third, our work was retrospective in nature. A prospective, randomized controlled trial with more patients is required. Finally, we could not compare the efficacy of the radiological interventions; however, those interventions reduced the duration of drainage and length of hospital stay, allowing an earlier return to normal life. The TDE and TDL subgroups did not differ significantly; evaluation of chyle production via contrast-enhanced imaging is required for TDL-only cases. Animal experiments might confirm the need for embolization.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

This study was supported by a Grant of the Samsung Vein Clinic Network (Daejeon, Anyang, Cheongju, Cheonan; Fund no. KTCS04-129).

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References

1. Schild HH, Strassburg CP, Welz A, Kalff J. *Treatment options in patients with chylothorax*. Dtsch Arztebl Int 2013;110:819-26.
2. Reisenauer JS, Puig CA, Reisenauer CJ, et al. *Treatment of postsurgical chylothorax*. Ann Thorac Surg 2018;105:254-62.
3. Stange S, Sziklavari Z. *Modern treatment options for postoperative chylothorax: a systematic review*. Zentralbl Chir 2019;144:290-7.
4. Takuwa T, Yoshida J, Ono S, et al. *Low-fat diet management strategy for chylothorax after pulmonary resection and lymph node dissection for primary lung cancer*. J Thorac Cardiovasc Surg 2013;146:571-4.
5. Cho HJ, Kim DK, Lee GD, et al. *Chylothorax complicating pulmonary resection for lung cancer: effective management and pleurodesis*. Ann Thorac Surg 2014;97:408-13.
6. Borcyk K, Kamil A, Hagerty K, Deer M, Tomich P, Anderson Berry AL. *Successful management of extremely high-output refractory congenital chylothorax with chemical pleurodesis using 4% povidone-iodine and propranolol: a case report*. Clin Case Rep 2018;6:702-8.
7. Cho HJ, Na KJ, Kim DW, Choi YE, Ma JS, Jeong IS. *Chemical pleurodesis using a Viscum album extract in infants with congenital chylothorax*. Eur J Pediatr 2014;173:823-6.
8. Leuzzi G, Vita ML, Porziella V, Congedo MT, Cesario A. *Single center experience on talc poudrage morbidity: focus on high talc dosage*. J Cardiothorac Surg 2011;6:87.
9. Shinno Y, Kage H, Chino H, et al. *Old age and underlying interstitial abnormalities are risk factors for development of ARDS after pleurodesis using limited amount of large particle size talc*. Respirology 2018;23:55-9.
10. Evans TJ, Sivakumar P, Ahmed L. *Progressive respiratory failure: a rare complication after graded talc pleurodesis*. Br J Hosp Med (Lond) 2017;78:294-5.
11. Hara H, Mihara M, Yamamoto M. *Therapeutic lymphangiography for traumatic chylothorax*. J Vasc Surg Venous Lymphat Disord 2018;6:237-40.
12. Jayasinghe SA, Srinivasa RN, Hage AN, Gemmete JJ, Majdalany BS, Chick JFB. *Thoracic duct embolization: analysis of practice patterns*. Ann Vasc Surg 2018;52:168-75.
13. Jimenez Gomez J, Gomez Cervantes M, Nunez Cerezo V, et al. *Intranodal lymphangiography in pediatric chylothorax, a diagnostic and therapeutic tool*. Cir Pediatr 2019;32:41-5.
14. Kim PH, Tsauo J, Shin JH. *Lymphatic interventions for chylothorax: a systematic review and meta-analysis*. J Vasc Interv Radiol 2018;29:194-202.
15. Nadolski GJ, Itkin M. *Lymphangiography and thoracic duct embolization following unsuccessful thoracic duct ligation: imaging findings and outcomes*. J Thorac Cardiovasc Surg 2018;156:838-43.
16. Majdalany BS, Khayat M, Downing T, et al. *Lymphatic interventions for isolated, iatrogenic chylous ascites: a multi-institution experience*. Eur J Radiol 2018;109:41-7.
17. Schild HH, Naehle CP, Wilhelm KE, et al. *Lymphatic interventions for treatment of chylothorax*. Rofo 2015;187:584-8.
18. Huang PM, Lee YC. *A new technique of continuous pleural irrigation with minocycline administration for refractory chylothorax*. Thorac Cardiovasc Surg 2011;59:436-8.
19. Mares DC, Mathur PN. *Medical thoracoscopic talc pleurodesis for chylothorax due to lymphoma: a case series*. Chest 1998;114:731-5.
20. Binkert CA, Yucel EK, Davison BD, Sugarbaker DJ, Baum RA. *Percutaneous treatment of high-output chylothorax with embolization or needle disruption technique*. J Vasc Interv Radiol 2005;16:1257-62.