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Lymphangiography and Lymphatic Embolization for the Management of Pelvic Lymphocele After Radical Prostatectomy in Prostatic Cancer

Hee Ho Chu[1] · Ji Hoon Shin[1] · Jong Woo Kim[1] · Seung Yeon Noh[1] · Woo Jin Yang[1] · Suyoung Park[1]

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Abstract
Purpose To retrospectively evaluate the short-term outcomes of lymphangiography and lymphatic embolization in the treatment of pelvic lymphocele after radical prostatectomy in patients with prostate cancer.
Materials and Methods The data of nine, consecutive patients who underwent lymphangiography and lymphatic embolization for pelvic lymphocele after radical prostatectomy with pelvic lymph node dissection (PLND) between January 2016 and May 2018, were retrospectively reviewed. Lymphangiography was performed through inguinal lymph nodes in order to identify the lymphatic leakage. When a leakage was found, lymphatic embolization was performed using a directly punctured fine needle at the closest upstream lymph node or lymphopseudoaneurysm and with *N*-butyl cyanoacrylate glue.
Results Lymphangiography demonstrated extravasation and/or lymphopseudoaneurysm in all of these patients. A total of 13 sessions of lymphangiography and lymphatic embolization were performed. The median number of lymphangiography and lymphatic embolizations required to achieve clinical success was one (range, 1–3). Three patients underwent repeated embolization with successful results. The technical and clinical success rates were 100%, respectively. The median time to resolution was 7 days (range, 2–19 days). There was no recurrence and no procedure-related complications during the follow-up period (mean, 26 weeks; range, 8–77 weeks) in all patients.
Conclusions Lymphangiography and lymphatic embolization are safe and effective for the management of pelvic lymphoceles after radical prostatectomy with PLND.

Keywords Prostatectomy · Pelvic lymphocele · Lymphangiography · Lymphatic embolization

Introduction

Pelvic lymph node dissection (PLND) represents the most accurate and reliable staging procedure at the time of radical prostatectomy for prostatic carcinoma [1]. PLND provides staging information that may help to more accurately define the extent of the disease and aid in treatment planning [2]. However, a common risk associated with the procedure is postoperative pelvic lymphocele formation. The prevalence of symptomatic lymphocele following radical prostatectomy with PLND varies between 3% and 27% depending on the extent of the lymph node dissection. Symptomatic lymphocele can be treated by parenteral nutrition, percutaneous catheter drainage, and adjunctive sclerotherapy [3–5]. Although the majority of pelvic lymphoceles are effectively managed conservatively, there is no consensus regarding a treatment strategy for patients who fail to respond to conservative management.

Recently, percutaneous management of lymphatic abnormalities, including pelvic lymphocele, chylous ascites, and chylothorax, has become well known [6–10].

✉ Ji Hoon Shin
jhshin@amc.seoul.kr

[1] Department of Radiology and Research Institute of Radiology, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea

N-butyl cyanoacrylate (NBCA) glue is injected directly into a lymph node or lymphatic vessels in order to treat the downstream lymphatic leaks. However, only a few case reports and series have described lymphangiography and lymphatic embolization that are used to treat lymphoceles and lymphorrhea following surgery [11, 12]. To our knowledge, the reports regarding lymphatic intervention of a pelvic lymphocele focused on patients with prostatectomy and are very limited [13]. In the present study, we report our clinical experience with lymphangiography and lymphatic embolization for the management of pelvic lymphoceles after radical prostatectomy in patients with prostatic cancer.

Materials and Methods

Study Design

This study was approved by the institutional review board of our hospital, and the requirement for informed consent was waived. The institutional electronic database was searched to identify eligible patients. Nine consecutive patients who underwent lymphatic embolization for management of a pelvic lymphocele after radical prostatectomy with PLND, between January 2016 and May 2018, were included. Prolonged lymphatic fluid drainage via a postoperative pelvic drain (> 500 mL/day) or a symptomatic pelvic lymphocele despite conservative management was considered the indication for lymphatic embolization. The electronic medical records and picture archiving and communication systems were retrospectively reviewed to determine the type of original surgery, a lymphocele-related symptom or sign, the daily drainage amount, and the duration of lymphatic leakage. The imaging findings on lymphangiography, lymphatic embolization procedures, computed tomography (CT), the daily drainage amount after the lymphatic embolization, and any procedure-related complications were also carefully reviewed.

Technical success was defined as identification of a lymphatic leak into the pelvic lymphocele and the targeted lymph node or lymphatic vessel embolization by the NBCA glue mixture. Clinical success was defined as complete resolution of the lymphocele-related symptoms and planned removal of the drainage catheter while achieving less than 50 cc/day of drainage or more than 80% reduction of daily drainage within 3 weeks [7, 12]. The time interval between the date of the lymphatic embolization and removal of the drainage catheter was also calculated. Complications were defined and classified according to the guidelines of the CIRSE classification systems [14].

Patient Population

All of the nine patients (mean age, 69.2 years; range, 62–78 years) who underwent radical prostatectomy with PLND due to prostate cancer were included in this study. A postoperative drain in the pelvic cavity or a percutaneous drainage catheter for a pelvic lymphocele was inserted in all of the patients. All of their pelvic lymphoceles were confirmed by CT, and the median developing time of the lymphocele after the surgery was 10 days (range, 4–65 days). Prolonged lymph fluid drainage, i.e., more than 100 mL/day without a gradual decrease ($n = 4$), during the postoperative care was the most common sign of the pelvic lymphocele and was followed by lower abdominal pain with fever ($n = 4$) and abdominal distension with voiding difficulty ($n = 1$). The mean drainage amount was 626.7 mL/day (range, 100–1500 mL/day) before the lymphatic intervention.

Lymphangiography and Embolization

In all of the patients, lymphangiography with ethiodized oil (Lipiodol; Guerbet, Vellepinte, France) was performed using an intranodal approach in both inguinal areas. The largest inguinal lymph node below the leakage point and/or the lymphocele was directly accessed under ultrasound guidance using a 25-gauge spinal needle (Tae-Chang Industrial, Gongju, Korea). Lipiodol injection was observed under fluoroscopy guidance in order to identify the efferent lymphatic fluid or lymph node. On lymphangiography, extravasation or a lymphopseudoaneurysm which was defined as small, extravasated, lymphatic fluid collections contained by the surrounding tissue before draining into a large space such as the peritoneum or lymphocele, were considered to be lymphatic leak. The closest upstream lymph node was identified as the lymph node from which efferent lymphatic vessels extravasated into the lymphocele, as seen on lymphangiography. After the identification and confirmation of lymphatic leakage from the closest upstream lymph node, the direct puncture of the Lipiodol-stained lymph node was performed under fluoroscopic guidance. After this, *N*-butyl-cyanoacrylate (NBCA) glue mixed with Lipiodol oil in a ratio of 1:2 to 1:9 was directly injected into the accessed lymph node draining to the leak until the draining lymphatic vessels as well as the lymph node itself were filled with the glue mixture or extravasation of the glue was observed (Fig. 1). If the interventional radiologist concluded that there was a high risk of premature polymerization of the glue mixture before reaching the leak point, based on the lymphatic flow rate and its traveling distance, the lymph node embolization was withheld and another target lymph node was sought. When upstream lymph node access was infeasible,

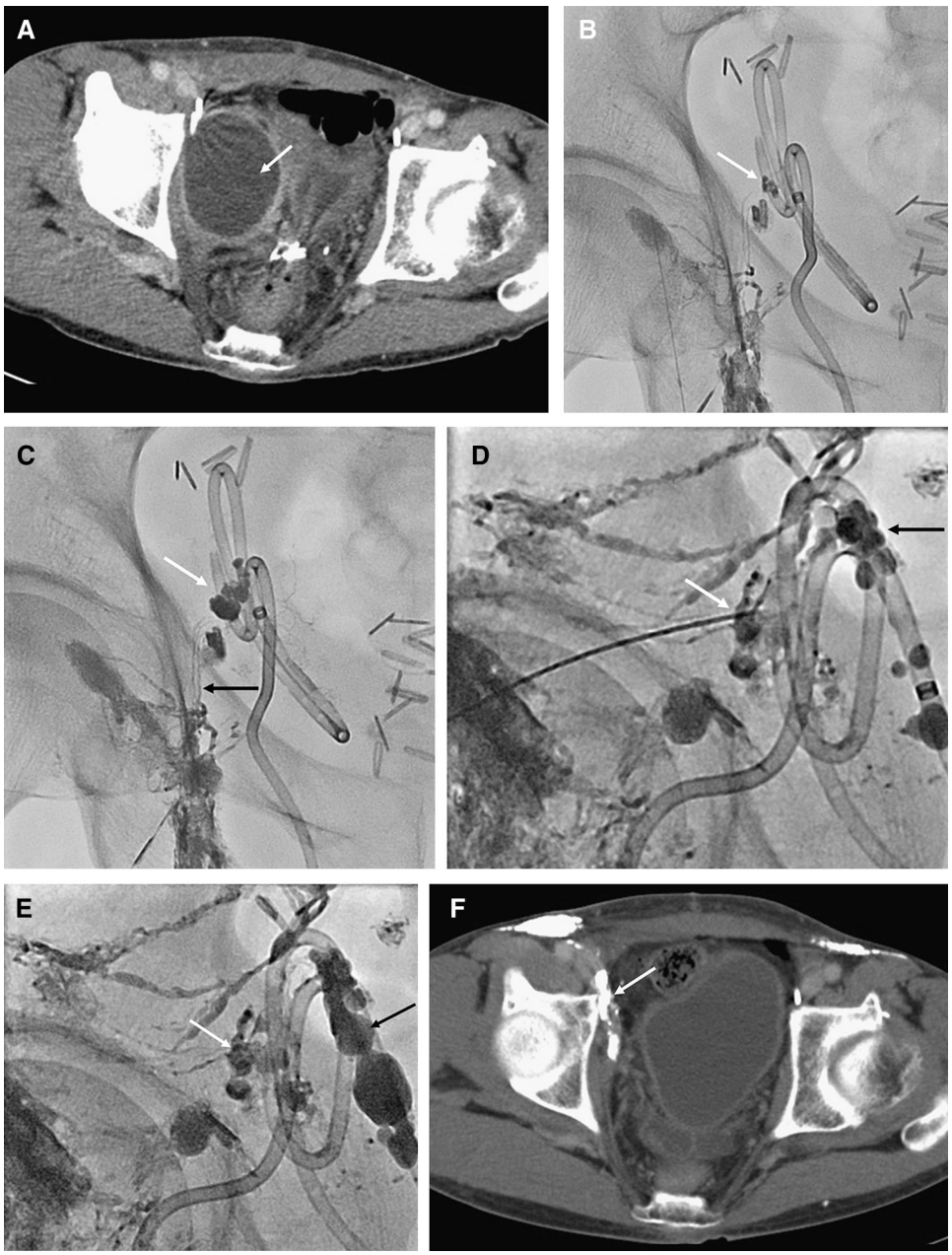

Fig. 1 Image of a 68-year-old, male patient (No. 5) with a history of radical prostatectomy and pelvic lymph node dissection. The patient complained of lower abdominal pain and tenderness 2 months after his surgery. **A** An axial contrast-enhanced CT image shows a well-defined cystic lesion (arrow) with prominent wall enhancement in the right pelvis. **B** Right intranodal lymphangiography demonstrated extravasated Lipiodol (arrow) collected around the tip of the drainage catheter. **C** Feeding lymphatic vessels (black arrow) and the lymphatic leak point (white arrow) were embolized using NBCA glue (1:7 mixture with Lipiodol). **D** However, the drainage amount did not decrease, and a second session of lymphatic embolization was performed 6 days after the first session. A 25-gauge needle was inserted at the closest upstream lymph node (white arrow) from the extravasated Lipiodol (black arrow) and lymphangiography showed residual lymphatic leakage. **E** The NBCA glue (1:3 mixture with Lipiodol) was injected, filled the lymph node (white arrow), and was extravasated along the drainage catheter (black arrow). **F** Follow-up CT performed 5 weeks after the lymphatic intervention demonstrated complete resolution of the right pelvic lymphocele without any recurrence. Only an NBCA glue cast (arrow) remained in the treated area

lymphopseudoaneurysms were directly punctured by the use of a 21-gauge Chiba needle (Cook, Bloomington, IN, USA), and followed by NBCA glue being injected through the needle in order to seal the lymphopseudoaneurysm. The ratio of NBCA to Lipiodol ranged between 1:1 and 1:3, and this glue mixture was injected in order to completely fill the lymphopseudoaneurysm (Fig. 2).

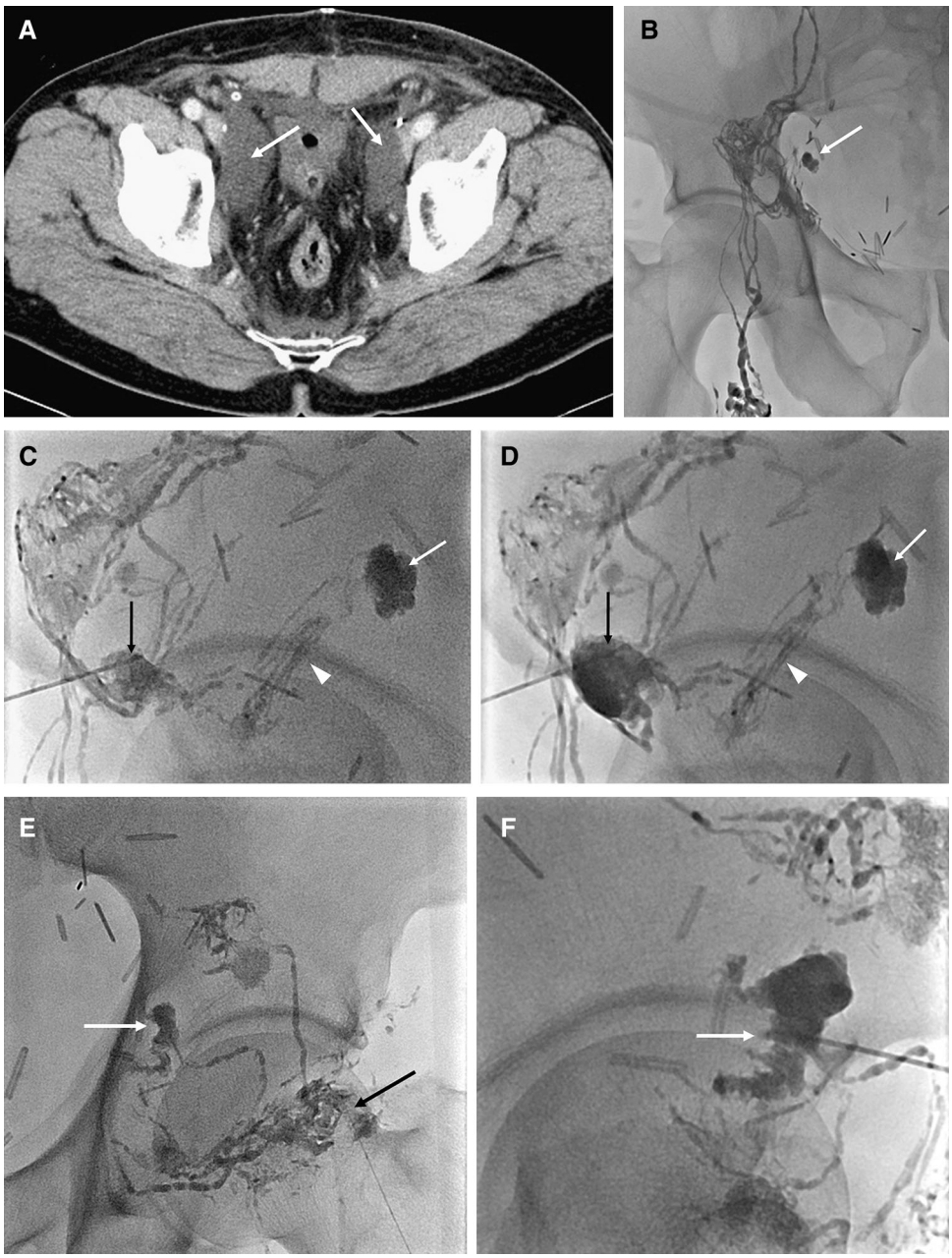

Fig. 2 Image of a 68-year-old, male patient (No. 8) with a history of radical prostatectomy and pelvic lymph node dissection. Prolonged lymphatic fluid (> 500 mL/day) was drained after the surgery. **A** Four days after the operation, an axial contrast-enhanced CT image showed lymphoceles (arrows) along the bilateral external iliac vessels. **B** Intranodal lymphangiography through a right inguinal lymph node showed extravasated Lipiodol (arrow). **C** Direct puncture of the closest upstream, external iliac lymph node (black arrow) using a 25-gauge needle and followed by lymphangiography showed extravasating Lipiodol (white arrow) with multiple, feeding lymphatic vessels (arrow head). **D** A fluoroscopy image shows complete occlusion of the lymph node (black arrow), injured lymphatic vessels (arrow head), and a lymphatic leak point (white arrow) of NBCA glue (1:5 mixture with Lipiodol). **E** Left intranodal lymphangiography through an inguinal lymph node (black arrow) shows a lymphopseudoaneurysm (white arrow). **F** Direct puncture of the lymphopseudoaneurysm with a 21-gauge needle and followed by immediate NBCA glue (1:2 mixture with Lipiodol) injection (arrow) was performed to seal the lymphatic leakage. After the lymphatic embolization, the amount of drainage gradually decreased to less than 50 mL/day and the postoperative drain was removed 6 days later

Follow-up

After successful lymphangiography and embolization, careful monitoring of the daily drainage amount was performed. If the drainage amount was not gradually decreased or prolonged at more than 100 mL/day, additional lymphangiography and embolization were performed due to the suspicion of a residual lymphatic leak. If the

drainage amount gradually decreased to less than 50 mL/day, the drainage catheter was removed [7, 12]. Follow-up visits were scheduled at 1 week and then every three to 6 months, depending on the patients' circumstances and the discretion of the referring physician. A contrast-enhanced CT was performed at each visit.

Results

The patient demographics and procedure details are summarized in Table 1. Three patients, each with a large, single lymphocele abutting the bilateral pelvic wall, underwent bilateral intranodal lymphangiography to determine the lymphatic leakage. Two patients underwent bilateral intranodal lymphangiography due to two, separated lymphoceles in both pelvic cavities. Four patients had a unilateral single lymphocele, and we performed unilateral lymphangiography in the involved area. In all nine patients, successful intranodal lymphangiography was obtained and lymphatic leakage was demonstrated. Lymphatic leakage manifested as Lipiodol extravasation in six patients and as both Lipiodol extravasation and lymphopseudoaneurysm in three patients (Figs. 1, 2). The technical success rate of the lymphangiography and lymphatic embolization was 100%. A total of 13 sessions of lymphangiography and lymphatic embolization were performed. In six patients, clinical success was achieved after a single embolization session, and three patients (Patients No. 1, 2, and 5) required a second embolization session in order to achieve clinical success. The time interval between the first and second attempt was 7 and 6 days, respectively. Multiple lymphatic leak points were identified in all of these three patients.

After the targeted lymph node embolization for lymphatic leakage, all of the patients showed a significant decline in the amount of daily drainage. The mean amount

Table 1 Patient demographics and procedure details

Pt. no.	Age (year)/sex	Symptoms and sign	Average drainage (mL/day)	Lymphangiography	Embolization no.	Last amount on day of drainage removal (mL)	Time to resolution (day)	Final outcomes	Follow-up period (week)
1	78/M	Prolonged lymph fluid drainage	700	Extravasation + LPSA	2	35	7	CR	77
2	63/M	Abdominal distension with voiding difficulty	1500	Extravasation	2	40	12	CR	51
3	70/M	Abdominal discomfort with fever	620	Extravasation	1	25	7	CR	19
4	69/M	Abdominal discomfort with fever	370	Extravasation	1	15	4	CR	10
5	68/M	Lower abdominal pain with fever	100	Extravasation + LPSA	2	2	18	CR	8
6	62/M	Prolonged lymph fluid drainage	500	Extravasation	1	50	2	CR	18
7	71/M	Prolonged lymph fluid drainage	820	Extravasation	1	20	19	CR	34
8	68/M	Prolonged lymph fluid drainage	500	Extravasation + LPSA	1	50	6	CR	8
9	74/M	Lower abdominal pain with fever	530	Extravasation	1	20	7	CR	12

M male, *LPSA* lymphopseudoaneurysm, *CR* complete resolution

of the last drainage on the day of the drain removal was 28.5 mL (range, 2–50). The median time to resolution was 7 days (range, 2–19 days).

The overall clinical success rate was 100%. Follow-up CT (the median time interval after the drainage catheter removal was 27 days; range, 2–74 days) showed complete resolution without residual or recurrent pelvic lymphocele in all of the patients. There was no recurrence and no procedure-related complications during the follow-up period (mean, 26 weeks; range, 8–77 weeks) in all of the patients.

Discussion

In the current study, our experience demonstrates that lymphangiography and lymphatic embolization for pelvic lymphocele after radical prostatectomy with PLND are safe and effective with a 100% technical and clinical success rate without procedure-related complications. Lymphangiography shows that lymphatic leak from the disrupted lymphatic vessel runs into the pelvic lymphocele and that following NBCA glue injection through the closest upstream lymph node blocks the lymphatic leak. Most of the patients required just one session of the procedure (66.7%, 6 of 9) and which resulted in rapid resolution (median time to resolution, 7 days; range, two-19 days). There was no recurrent pelvic lymphocele during the median follow-up time of 26 weeks.

Treatment options for pelvic lymphocele can vary depending on the severity of the clinical symptoms, the treating urologist, and patient factors such as the location, size of the lymphocele, whether the lymphocele is infected, the overall health condition of the patient, and recurrence of the lymphocele [15–17]. The drainage catheter placement into the lymphocele is a simple method used to decompress the lymphatic fluid collection. The drains are usually left in place until there is minimal lymphatic fluid drainage; however, if the drain continues to have a high output of more than 100 mL/day without a gradual decrease, other methods should be considered. Sclerotherapy injection of sclerosing agents such as povidone-iodine, alcohol, talc, bleomycin or tetracycline, and fibrin sealants via the percutaneous drain tube helps to seal the lymphatic channels within the lymphocele. The reported success rates of sclerotherapy for pelvic lymphoceles vary from 70 to 100% depending on the study and the type of sclerosing agents being used. Most of the drains are in place ranging from one to 60 days, with a mean range of 10–20 days. In these studies, there was a moderate recurrence rate of 20–25%, but it was mostly resolved with an additional session of sclerosis [18–23]. Although little is known regarding the reasons for failure of sclerotherapy for pelvic lymphoceles, Shih et al. [24] have described a lymphocele in which sclerotherapy failed that was cured by percutaneous ligation of the inflow lymphatic vessel. This means that occlusion of the lymphatic inflow within the pelvic lymphocele is crucial for preventing recurrence of the lymphocele.

Lymphangiography and lymphatic embolization are emerging in the spotlight for the management of lymphatic leakage, especially in postsurgical lymphatic leaks [6–10]. Baek et al. [8] described a case series of five patients with pelvic lymphocele after gynecologic surgery and who underwent lymphatic embolization by direct needle targeting of the leaking vessel and injection of NBCA glue after identification by lymphangiography. The authors reported an immediate clinical success rate of 100% with a recurrence in only one of four patients during follow-up. In an additional study by Baek et al. [7], they reported the results of lymphangiography and lymphatic embolization in 21 consecutive patients who were referred for lymphatic intervention after surgical lymph node dissection. After one treatment session, 17 of the 21 patients showed a significant decline in the amount of drainage and the drainage catheter could then be removed. In four patients who failed in initial treatment session, additional leak or multiple leakage sites were demonstrated during the second procedure. Among these patients, three had clinical success after the second attempt. The overall clinical success rate was 95.2%. Our results are comparable to those studies as we could achieve 100% technical and clinical success of lymphangiography and lymphatic embolization for pelvic lymphoceles encountered following radical prostatectomy with PLND. Six patients required just one session of the procedure and it resulted in rapid resolution with a median time to resolution of only 7 days. Three patients who did not show a good response to the initial treatment due to additional lymphatic leak points were not treated, but experienced other leaks were identified on the second procedure performed within 7 days after the initial treatment. The second attempt was successful in these patients, and the drainage catheter was removed after the drainage amount declined the target range. There was no recurrent pelvic lymphocele during the median follow-up of 26 weeks (range, 8–77 weeks).

As shown in the text above, the most common cause of initial treatment failure was multiple sites of postsurgical lymphatic leak after lymph node dissection. Because of its nature of complexity in the lymphatic system and injury to the lymphatic vessels that can be extensive depending on the invasiveness of the surgery, postoperative lymphatic leakage may be broad and need multisession procedures for complete occlusion of lymphatic leakage. For this reason, if the initial treatment shows poor results, the response should be evaluated within 1 week and further intervention should be considered in order to shorten the hospital stay

and morbidity period caused by postsurgical lymphatic leakage.

We acknowledge that this study has inherent limitations, mostly as a result of the small number of patients and its retrospective nature. Studies with larger patient cohorts and longer follow-up data are required in order to verify the safety and efficacy of the lymphatic intervention in the management of lymphoceles. However, our study suggests that lymphangiography and lymphatic embolization may have an important role in the treatment of lymphoceles that fails using conservative methods. A well-designed, prospective study to determine the proper protocols and adequate standards for lymphatic intervention in the management of postsurgical lymphocele is warranted in the future.

In conclusion, this retrospective study indicates that lymphangiography and lymphatic embolization are safe and effective for the management of pelvic lymphoceles after radical prostatectomy with PLND.

Compliance with Ethical Standards

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

Consent for Publication For this type of study, consent for publication is not required.

Ethical Approval This is retrospective study, for this type of study formal consent is not required.

Informed Consent This study has obtained IRB approval from our institution, and the need for informed consent was waived.

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