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Reconstructive

Lymphatic Fistula Treatment: Indocyanine Green Lymphography-guided Microsurgery

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Background: Lymphatic fistulas are a common complication from surgery or interventional procedures resulting in persistent lymphatic leakage and delayed wound healing. The management of lymphatic fistula remains a subject of debate, ranging from conservative treatment to surgical lymphatic ligation. The implementation of a novel microsurgical approach involving lymphatic fistula ligation and/or lymphovenous anastomosis (LVA) using indocyanine green (ICG) lymphography is expected to decrease occurrence and complications. In this study, we share our experience in treating lymphatic fistula–guided microsurgical treatment.

Methods: A total of 13 patients from our hospital with persistent lymphatic fistula were enrolled in this retrospective study. Lymphatic fistulas and their leakages were identified and ligated by using ICG lymphography and a surgical microscope. In two cases, additional LVA surgery was performed.

Results: We were able to precisely identify lymphatic fistulas and treat them in all 13 patients. Lymph ligation was performed in all 13 cases, with additional distal LVA in two cases. In all patients, wound healing occurred following lymphatic ligation, except in one patient due to persistent infection. Patients with a lymphatic fistula were referred to our unit within 3 weeks to 1 year after onset, with an average consultation occurring after 5 months of persistent lymphatic fistula.

Conclusions: Targeted lymphatic vessel ligation with or without LVA with ICG-guided surgical microscope represents a promising highly efficacious therapy for persistent lymphatic fistula. This technique may accelerate wound healing and reduce hospitalization duration, thus advocating for its preferential use in managing lymphatic fistulas. *(Plast Reconstr Surg Glob Open 2024; 12:e6168; doi: 10.1097/GOX.0000000000006168; Published online 15 October 2024.)*

INTRODUCTION

Lymphatic fistula is a well-known complication resulting from lymphatic leakage after trauma, surgery, or interventional procedures that can cause injury to the nearby lymphatic channel.[1] The extent of fluid outflow from a lymphatic fistula varies depending on the severity of the underlying lymphatic vessel injury. Currently, there is no consensus definition of lymphatic fistula.[2] The incidence of postoperative lymphatic complications, regardless of their location, ranges between 10% and 45%.[3] The treatment of lymphatic fistula remains controversial, with various options ranging from conservative treatment to negative pressure wound therapy,[4] interventional radiologic embolization,[5] and immediate surgical lymphatic ligation in the suspected area.[6] Although these treatment methods are rather nonspecific, the use of indocyanine green (ICG) offers targeted localization of lymphatic vessels. The application of this dye in ICG lymphography has been documented and has demonstrated utility in both the evaluation of lymphedema and intraoperative navigation in lymphatic supermicrosurgery.[7,8] The successful

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use of ICG lymphangiography with lymphatico-lymphatic anastomosis for treating lymphatic fistulas has also been demonstrated.[9] We anticipate that implementing a novel approach involving lymphatic fistula ligation with and without lymphovenous anastomosis (LVA) will decrease lymphatic fistula occurrence and related complications in patients. This study aims to assess the effectiveness of these interventions, offering insights into enhanced surgical management strategies for lymphatic fistulas. In this study, we present our experience in treating lymphatic fistulas at a single medical institution between 2018 and 2023.

MATERIALS AND METHODS

All data from lymphatic fistula patients who were admitted to the Hospital of the Divine Savior in Vienna Austria from 2018 until March 2023 were retrospectively collected and analyzed. Thirteen patients were referred to plastic and reconstructive surgery for lymph fistula treatment due to wound healing problems with high volume lymph discharge after surgical or vascular interventional procedures. Our study was conducted according to the ethical principles of the Declaration of Helsinki. The diagnosis of lymphatic fistula was made on the basis of history and clinical examination. This can be done by visualization of lymphatic discharge through the wound, which can be exaggerated by deep palpation of distal surrounding tissue.

The study evaluated the recurrence of lymphorrhea after 6 months (yes/no) as the primary outcome measure, with statistical analysis relying solely on descriptive values. Patients were scheduled for postoperative follow-up appointments in the outpatient setting.

All patients were planned for surgical treatment via ICG lymphography–guided microsurgery in the operation room based on clinical diagnosis. The procedure is done under general anesthesia. Before preparation and draping of the affected area, a preoperative ICG lymphography is done; 0.2 mg indocyanine green (Verdye, Diagnostic Green GmbH, Munich, Germany) is administered subdermally on the dorsum of the foot or hand, usually slightly proximal to the second interdigital webspace. It is then followed by gentle lymphatic massage with the Fill & Flush Drainage Method[10] to propel the lymphatic flow proximally. Using ICG imaging device, Hamamatsu's handheld pde-neoII (Hamamatsu Photonics K.K., Hamamatsu, Japan) or Stryker's SPY-PHI (Stryker Corporation, Kalamazoo, Mich.), the course of the lymphatic vessel is simultaneously marked with a permanent marker from distal to proximal until it reaches its fistulous opening site adjacent to the wound (Figs. 1–4).

Sterile washing and draping of the patient follow. Using the microscope with ICG visualization (Zeiss Kinevo 900, Oberkochen, Germany) with integrated high-definition augmented ICG reality, we were able to visualize the flow of dye directly under the fluorescence microscope during the procedure to accurately identify the leakage of the lymphatic vessel. This lymphatic vessel is ligated with a suitable suture (eg, Vicryl 4-0), and the wound is debrided and cleaned, followed by immediate or delayed closure depending on the suitability of the wound bed. Wound closure is done by direct closure, local flap, or split thickness skin graft, with a depth of approximately 0.5 mm. In two cases, distal of the chronic lymph fistula, the feeding lymphatic vessel was dissected and anastomosed to an adjacent vein. After careful subcutaneous preparation, the anastomosis between the lymphatic vessel and a vein of similar caliber is performed end-to-end with nylon 11/0 or 12/0. Patency of the anastomosis was confirmed with

Takeaways

Question: The study addresses persistent lymphatic leakage and delayed wound healing caused by lymphatic fistulas, common after surgery or interventional procedures. It investigates the effectiveness of a novel microsurgical approach using indocyanine green lymphography to guide lymphatic ligation and lymphovenous anastomosis.

Findings: Our retrospective analysis of 13 patients shows that indocyanine green-guided microsurgery successfully treated lymphatic fistulas with minimal complications. Lymphatic ligation, with or without lymphovenous anastomosis, was effective in all cases, with no recurrence of lymphorrhea during the follow-up period.

Meaning: ICG lymphography-guided microsurgery effectively treats persistent lymphatic fistulas, improving wound healing and reducing hospital stays.

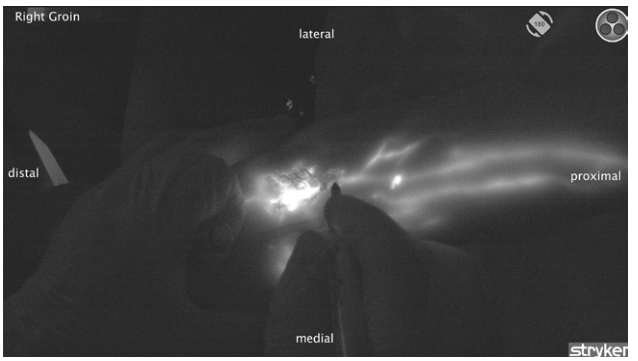

Fig. 1. Using the SPY-PHI camera, superficial lymphatic vessels are visualized and marked on the patient's skin.

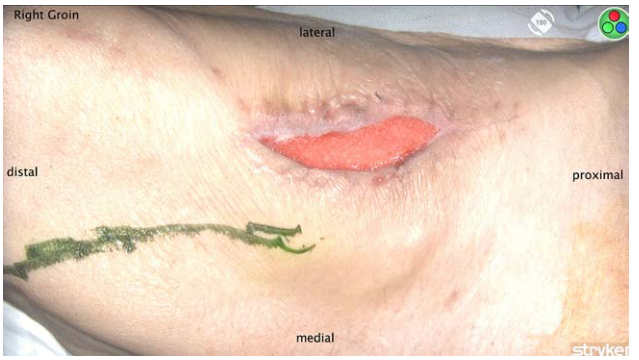

Fig. 2. A lymphatic vessel could be traced and marked just before the wound with the lymphatic fistula.

intraoperative ICG. With this LVA, the feeding lymphatic flow of the lymph fistula was diverted distally to the vein, thus reducing the discharge in the wound.

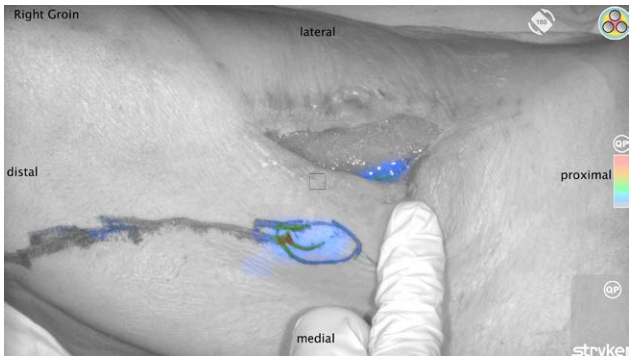

Fig. 3. The suspected leaking lymphatic vessel is shown. Here you can see how the course of the lymphatic vessel breaks off, but shortly afterward, lymph fluid can be visualized in the wound by means of ICG.

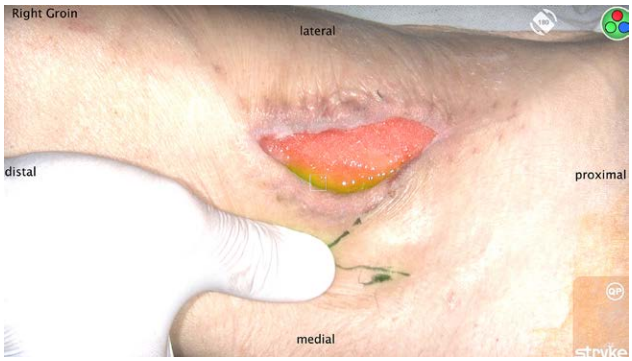

Fig. 4. Using a different ICG overlay, the suspected draining lymphatic vessel and its accumulating fluid in the wound are visualized here as well.

RESULTS

A total of thirteen cases of lymphatic fistula were clinically diagnosed in our center and treated surgically with ICG-guided lymphangiography microsurgery (Table 1). We could categorize our cases regarding the cause of the lymphatic fistula as follows (Fig. 5). Four occurred after vascular surgery, four after tumor extirpation, two after vascular intervention, one after orthopedic surgery with prosthesis, and one after lymph node extirpation.

The minimum duration of lymphatic fistula prior to referral to our unit was 3 weeks, whereas the longest was up to 1 year. The average duration of lymphatic fistula before referral was 5 months.

Before surgical intervention, conservative management of lymphatic fistula included weekly seroma aspiration and drainage, frequent wound care with conventional or modern dressing with or without negative pressure wound therapy, and several attempts of wound closure after fistulectomy.

All cases that were referred to our team proceeded with immediate ICG lymphography-guided microsurgery lymphatic ligation. These 13 cases were confirmed with lymphangiography during preoperative assessment in the operating room. Average operating time was 2 hours from the moment of lymphangiography assessment until ligation of lymphatic vessel was completed. Figures 6–9 show the successful detection and verification of a lymphatic fistula followed by ligature. The entire process is also presented in a supplemental video. [**See Video (online)**, which displays the successful detection and verification of a lymphatic fistula followed by ligature.]

In two cases of prolonged lymphatic fistula in the right groin, both after aortobifemoral bypass, we were able to successfully treat the lymphatic fistula with LVA. This allowed us to redirect the lymphatic fluid from the

Table 1. Thirteen Patients with Secondary Lymphedema

No	Age	Sex	Cause	Location of Lymph Fistula	Treatment	Postoperative Results*	
					ICG and ligation/LVA	Recurrence of lymphorrhea (Yes/No)	Postoperative complications
1	78	M	Extirpation of tumor	Right groin	Ligation	No	—
2	70	F	Vascular intervention	Right lower leg	Ligation	No	—
3	59	F	Extirpation of tumor	Left groin	Ligation	No	—
4	36	F	Extirpation of tumor	Right groin	Ligation	No	—
5	51	M	Vascular intervention	Right groin	Ligation	No	—
6	79	F	Vascular surgery	Left groin	Ligation	No	—
7	67	M	Vascular surgery	Left groin	Ligation	No	Wound infection with delayed wound closure
8	76	M	Orthopedic intervention with prosthesis	Left elbow	Ligation	No	—
9	50	F	Lymph node extirpation	Right thigh	Ligation	No	—
10	77	F	Lymph node extirpation	Right and left groin	LVA + ligation	No	—
11	58	F	Vascular surgery	Right groin	LVA + ligation	No	—
12	79	F	Vascular surgery	Left groin	Ligation	No	—
13	69	M	Vascular surgery	Left groin	Ligation	No	—

*During the minimum 6-month follow-up period.

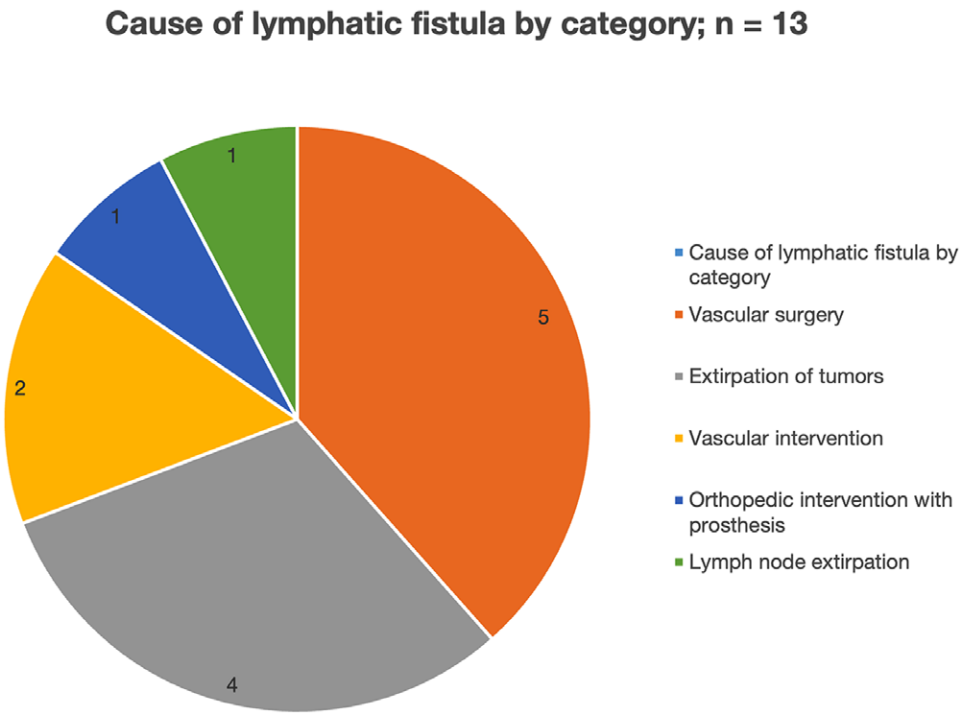

Fig. 5. Cause of lymphatic fistula by category.

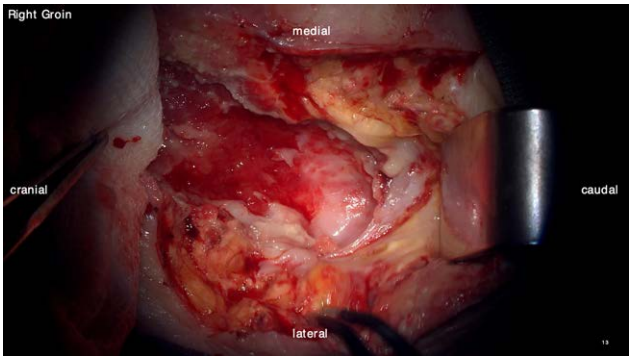

Fig. 6. Visualization of a surgical site with a lymphatic fistula in the right groin resulting from lymph node extirpation following vulvar carcinoma.

lymphatic vessel that had previously emptied into the wound into a healthy vein. Additionally, the lymphatic fistula was precisely identified under the operating microscope and the leaking lymphatic vessel was securely ligated.

There was no immediate recurrence of lymphatic fistula postoperatively. Twelve cases had immediate wound closure by either direct suture or flap coverage, whereas one had delayed closure with skin mesh graft due to chronic wound infection. The average hospital stay after ICG-guided lymphatic fistula microsurgery was 3 days. During the minimum 6-month follow-up period, 12 cases demonstrated complete wound healing without any complications.

DISCUSSION

The lymphatic system is a complex network composed of lymph nodes, lymphatic vessels, lymph tissue, and lymphatic duct. Our study found that using ICG lymphography combined with lymphatic ligation and, when appropriate, LVA is effective in treating lymphatic fistulas, reducing prolonged wound healing times, and lowering associated healthcare costs. The flow of lymphatic circulation, beginning with the collecting lymphatic capillaries and ending with reentry in the blood stream via lymphatic tissues and organs has been well described in literature.[1] Any injury to a lymphatic vessel may cause lymphatic leakage, which includes lymphatic fistula. A fistula leakage can be directed into the skin, producing lymphorrhea or accumulate in the body to form a lymphocele. We will relate in this work on lymphatic fistulas causing lymphorrhea into cutaneous wound.

The etiology of lymphatic fistulas is often iatrogenic due to interventional or surgical vascular bypass procedures, as well as lymph node dissections and lymph node transfers.[11,12] Studies indicate that lymphatic fistulas occur in approximately 2% of patients following vascular surgical incisions in the groin, highlighting their relative importance.[13,14] A visceral lymphatic fistula is less reported, such as lymphatic fistula at lumbar region due to posterior lumbar transpedicular screw fixation.[15] This condition can be debilitating due to the prolonged wound healing, not to mention the cost of frequent dressing changes over a long period of time, which is exacerbated by higher risk of wound infection.

Many treatments[16,17] that have been described to treat this debilitating condition fall into the spectrum of conservative methods. That includes applying negative pressure[18] wound therapy and conventional regular dressings. Although some of these methods have proven successful, optimal outcomes remain elusive, with the attainment

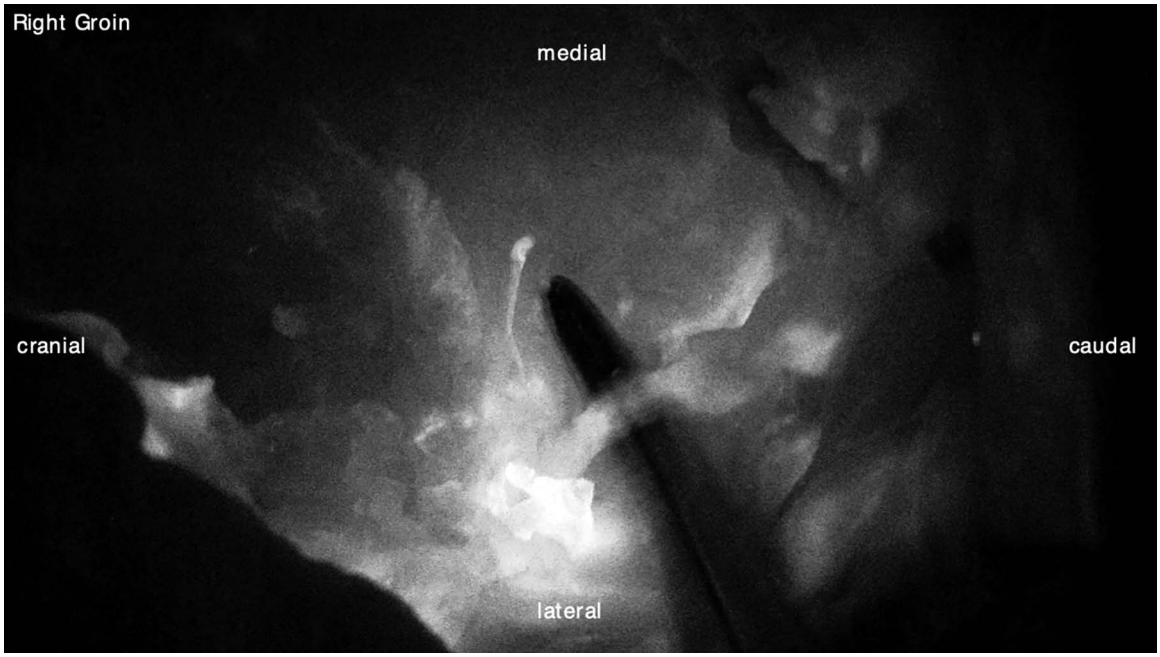

Fig. 7. Intraoperative fluorescence ICG visualization of a lymphatic vessel in the surgical site of the right groin. The image demonstrates the effective use of ICG under the surgical microscope to aid in identifying and managing lymphatic vessels.

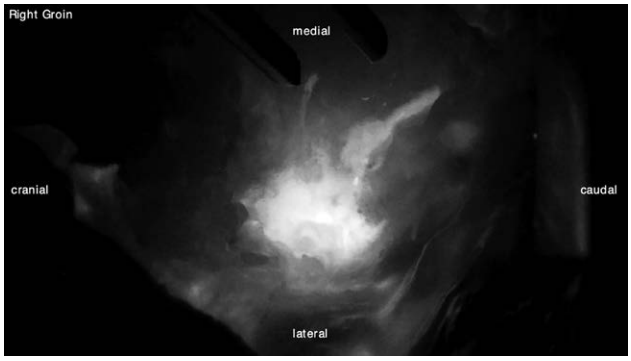

Fig. 8. Successful visualization of a lymphatic fistula draining into the wound area following manual distal propulsion of ICG toward the suspected fistula. The image demonstrates the significance of ICG in the identification and management.

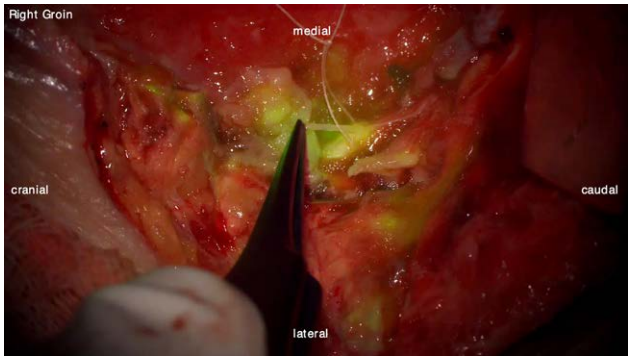

Fig. 9. Under the surgical microscope with ICG overlay, successful identification of the lymphatic vessel responsible for the lymphatic fistula is demonstrated. ICG aids in visualizing lymphatic vessels, facilitating accurate identification and proper management of lymphatic fistulas. In this case, the responsible lymphatic vessel is ligated. The green overlay in the image highlights the presence of ICG.

of adequate wound healing often necessitating weeks, months, or even years, and recurrences being a prevalent concern.[5,6] The technology of microsurgery has allowed the evolution of an efficient approach in addressing this matter. The therapeutic approach to lymphatic fistulas has evolved considerably over time, from the use of lymphatic venous anastomosis[19,20] as the first method of treatment to the current practice of using a combined approach that includes ICG[21] for both diagnostic and therapeutic purposes.[22–25]

We found in almost all our cases that using ICG lymphography and lymphatic ligation was successful in treating lymphatic fistula. These cases of prolonged wound healing, some lasting up to years, have been dramatically reduced after this technique of combining low invasive ICG lymphography and ICG guided microsurgery, to an average three days hospital discharge and complete wound healing after an average of one month follow-up. Not only does it shorten the duration of this pathologic condition, but also reduces the financial burden associated with frequent dressing changes, transports, and multiple hospital admissions due to recurrent infections. It is difficult to determine the exact cost of a sick day to society, as this depends on many factors, such as the country, the industry, and the specific circumstances of the individual case. Sick leave can have both direct and indirect costs. Direct costs include, for example, continued payment of wages by the employer and

sick pay by social security. Indirect costs may include lost productivity, overtime for other employees, and possible replacement costs. Currently, there are no concrete figures that quantify these costs. In our hospital we had a rough analysis and calculation done by the medical controlling department. The total costs for the stay and the operation by means of ligation and LVA amount to approximately €5300. This assumes an operation of about 2 hours and an average stay of 4.5 days. Comparing this with the costs of vacuum-assisted closure (VAC) therapy, assuming a VAC change in the operating room twice a week and a therapy duration of 4 weeks on average, the costs here are about €22,000. Consequently, the therapy strategy using ligation and LVA costs only about a quarter compared with conservative VAC therapy in the operating room. Our cost analysis assumes that VAC changes are performed in the operating room, which is required for cases needing higher hygiene standards, such as those involving bypasses. However, it is important to note that regional differences in hygiene regulations and local hospital standards can significantly impact these costs. In some settings, VAC changes can be performed at the bedside or as outpatient procedures, which would substantially reduce costs. Therefore, the actual costs of VAC therapy could be much lower if circumstances allow for VAC changes outside the operating room. This variability should be considered when comparing the cost-effectiveness of different treatment options. Furthermore, the potential quality of life improvements from promptly identifying and addressing lymphatic leaks with ICG mapping, ideally during the initial surgery, are noteworthy. This approach could help prevent clinically significant lymphatic leaks and improve overall patient outcomes. If only ICG lymphangiography and ligation of the lymphatic vessel are planned, the requirements for the surgeon are lower, making it accessible to a larger number of people compared with the approach involving ICG lymphangiography and lymphatico-lymphatic anastomosis.

This study has several limitations, including a small sample size of thirteen patients, limiting the broader applicability of the findings. The retrospective design may introduce biases related to data collection and patient selection. The 6-month follow-up period might be insufficient to capture long-term outcomes and potential late recurrences. Additionally, the absence of a control group makes comparative analysis difficult.

However, it is also important to note certain limitations associated with the proposed technique. The availability of highly skilled microsurgeons who are proficient in supermicrosurgical techniques and experienced in ICG lymphography and ICG-guided microsurgery are a requirement of a successful therapy if additional LVA is planned. The training required for this expertise can be time-consuming and is ideally provided by plastic and reconstructive surgeons who have the necessary skills in dealing with concurrent soft tissue defects that often require reconstructive procedures for wound closure. In addition, the purchase of specialized equipment (surgical microscope and device to visualize ICG fluorescence) to perform this surgical procedure can result in significant costs. Therefore, to establish a comprehensive lymphatic fistula treatment service, a health center must have the necessary resources; that is, both expert staff and the financial means to afford the required technology. The integration of state-of-the-art equipment and expertise provides a holistic solution for patients with lymphatic fistulas.

It is important to consider potential risks associated with prophylactic LVA in oncologic patients. A study by Chungsiriwattana et al[26] focusing on melanoma skin cancer patients found adverse outcomes, such as reduced survival rates and increased recurrence after LVA. These risks were specific to melanoma patients. Current evidence suggests that prophylactic LVA, for example, in breast cancer treatment, does not seem to increase oncologic risk.[27] Further studies are necessary to confirm these findings, so cautious consideration is recommended.

CONCLUSIONS

Treating wounds with high lymphatic leakage is a major challenge, but advances in surgery have produced effective solutions. This study highlights the potential of using surgical microscopes in conjunction with ICG lymphography for the precise and rapid identification and treatment of lymphatic fistulas with ligation and LVA. Our observations indicate a reduction in wound healing time and hospital stay duration, although further research is necessary to statistically validate these findings. Although microsurgical treatment shows promise as an effective method for managing lymphatic fistulas, additional studies are required to thoroughly assess its efficacy, cost-effectiveness, and overall impact on patient outcomes.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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