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DECREASING AND PREVENTING LYMPHATIC-INJURY-RELATED COMPLICATIONS IN PATIENTS UNDERGOING VENOUS SURGERY: A NEW DIAGNOSTIC AND THERAPEUTIC PROTOCOL

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ABSTRACT

Lymphatic complications following great and small saphenous vein surgery show a varying and non-negligible incidence in the literature. We undertook this study to investigate a new protocol to reduce lymphatic injuries in patients undergoing venous surgery. Eighty-six patients with lower limb venous insufficiency and varices were treated. Lymphoscintigraphy was performed preoperatively in 65 of them and postoperatively in 19. Blue dye was used in all patients and blue lymph nodes and lymphatics were identified intra-operatively and preserved or used to perform multiple lymphatic-venous anastomoses (MLVA). Patients were followed up for a period varying from 3 months to 6 years. Sixty-six patients were treated by greater saphenectomy and varicectomy, 12 patients had crossectomy and varicectomy, 4 patients underwent greater saphenectomy and varicectomy associated with MLVA, and 4 patients were treated by small saphenous vein stripping and varicectomy. No lymphatic complications occurred in any of the patients. A decrease of over 75% of excess volume was observed in 4 patients treated by MLVA. Lymphoscintigraphy showed normalization in the Transport Index in 4 patients treated with MLVA. Our results demonstrate that accurate diagnostic investigation and proper surgical technique is of paramount importance in the effort to avoid lymphatic complications during venous surgery.

Keywords: venous surgery, lymphatic injuries, prevention, phlebolymphedema, lymphoscintigraphy, microsurgery

Lymphatic complications following great and small saphenous vein surgery show a varying and non-negligible incidence in the literature (1-3). They are often long lasting and cause bothersome and costly problems for both patients and surgeons (4-6). Lymphatic complications after surgery for varicose veins mainly involve lymphocele and lymphorrhea localized at the groin due to the disruption of lymphatics surrounding the saphenous-femoral junction (lymphocele 1.3%, lymphorrhea 0.7%), lymphangitis (diffuse lymphangitis localized at the leg or at the thigh, 4-6%) and lymphedema mainly at the foot and the leg (1). Generally speaking, lymphatic morbidity occurs in 2.2% of cases in venous surgery (1), and lymphangitis is reported in 4-6% of patients after saphenous venectomy for coronary artery bypass surgery (7-10). Some risk factors include lymphatic insufficiency, obesity, and lipedema (11-13).

The anatomical relationship between lymphatic collectors and the veins may explain the appearance of lymphatic injuries

during surgical procedures. Anatomical studies of human legs identified areas at risk during surgery, and knowledge of these studies is of the utmost importance to prevent lymphatic complications (14). Lymphatic vessels of the dorsum of the foot are separated from one another and not assembled in one single bundle whereas lymphatic collectors in the groin and in the knee region cluster around the saphenous vein. The main lymphatic bundle is at the ventromedial area of the thigh, and even minimal dissection of subcutaneous tissue in this area may cause unnecessary and harmful lymphatic damage.

A new approach is needed to prevent or reduce the frequency of post-operative lymphatic morbidity. We have developed a protocol to prevent lymphatic injuries in conventional vein surgery for great saphenous varicose veins and report here on its use as a preventive protocol for patients with latent or clinically manifest lymphatic insufficiency as well as for patients at risk of developing lymphatic complications.

MATERIALS AND METHODS

Patients

Between January 2010 and December 2016, 86 consecutive patients with lower limb venous insufficiency and varices were studied and treated by the Unit of Lymphatic Surgery, IRCCS San Martino-IST in Genoa. Informed consent was obtained by all patients and the study was approved by the Hospital Ethical Board. The mean age of patients was 55.04 years (range 21 to 81 years) with 31 men and 55 women.

Color Doppler scanning was carried out in all patients. Lymphoscintigraphy was performed preoperatively in 65 patients who presented clinical signs of lymphatic impairment or were at risk for lymphatic complications (obesity, familial predisposition, clinical history, etc.). Lymphoscintigraphy was not done in all the patients because in those cases in which there were no sign of lymphatic disorders and history was negative the protocol did not include this investigation. Inclusion and exclusion criteria were generated based on our previous work (15,16). Exclusion criteria were post-thrombotic syndrome and tumors of the extremities. Demographic and pathologic characteristics of the patients undergoing vein surgery with prevention of lymphatic damage are reported in *Table 1*. Inclusion criteria were venous insufficiency, C2-C3 according to the CEAP classification (C: clinical findings; E: etiological factors; A: anatomical cause; P: pathophysiological cause). Also patients at lymphedema stage IIB, considered for lymphatic reconstruction along with venous treatment, were included in the series because prevention of lymphatic disruption together with microsurgical reconstruction allowed improvement of the lymphatic disorder where lymphatic dysfunction is usually ignored.

Patients were followed clinically and instrumentally (color Doppler duplex scan and lymphoscintigraphy) for a period varying from 3 months to 6 years. Limb volume measurements were obtained by measuring serial limb circumferences according to LEL Index (17). Lymphoscintigraphy was performed pre- and post-operatively in 4 patients who also underwent lymphatic microsurgical procedures and in 15 patients who underwent only venous surgery.

Protocol Groups

Patients were treated according to three possible clinical scenarios. In the case of no signs of lymphatic disorders but with a history of previous peripheral edema (i.e., after long flights, during summertime, etc.), positive family history, obesity, and/or lipedema, we injected the blue dye (Patent Blue V 2.5%, 2 ml; E131, Acid Blue 3, Disulfine Blue), which allowed sparing the lymphatics around the veins. Patients with varicose veins and clinical signs of lymphatic disorders (slight peripheral edema, fibrotic subcutaneous tissue, episodes of lymphangitis,

TABLE 1
Patients' Demographic and Pathologic Characteristics

Number of patients	86
Age (years)	21-81 (mean 55.04)
Gender	Female 55
	Male 31
Lymphedema stage in 4 patients with phlebolymphedema (according to Campisi's lymphedema staging (9-20)	
Ib	1
IIa	2
IIb	1
CEAP Clinical Score	
C2	82
C3	4
Duration of Disease (months)	10-18
BMI	20-32 (26)

TABLE 2
Groups of Patients Divided According to the Preventive Protocol

Surgical procedure	Number of patients	Blue Dye	Pre-op Lympho-scintigraphy	Post-op Lympho-scintigraphy	MLVA
Patients with no signs of lymphatic disorders but positive history, obesity or lipedema	21	21	-		-
Patients with signs of lymphatic disorders	61	61	61	15	-
Patients with phlebolymphedema	4	4	4	4	4
Total	**86**	**86**	**65**	**19**	**4**

etc.) underwent preoperative lymphoscintigraphy and the blue dye was used during surgery. In this group, the procedure consisted of treatment of venous pathology with prevention of lymphatic injuries by sparing lymphatics and lymph nodes. For patients with phlebolymphedema of the lower limbs with positive lymphoscintigraphy, the surgical procedure consisted of injection of blue dye and performance of a lymphatic-venous anastomosis (*Fig. 1, Table 2*).

Surgical Technique

Blue dye was injected into the thigh (or calf for small saphenous vein surgery) and below the internal (or external) malleolus in all patients 10 minutes prior to surgery. This procedure allowed visualization of both inguinal and popliteal lymphatics and nodes. Blue lymph nodes and lymphatics were identified intraoperatively and preserved (*Fig. 2*) or used to perform multiple lymphatic-venous anastomoses (MLVA) with a competent collateral branch of the great or small saphenous vein (*Fig. 3*) in patients affected by mixed venous and lymphatic insufficiency. The vein used for anastomosis was either a collateral branch of the great saphenous vein (after checking

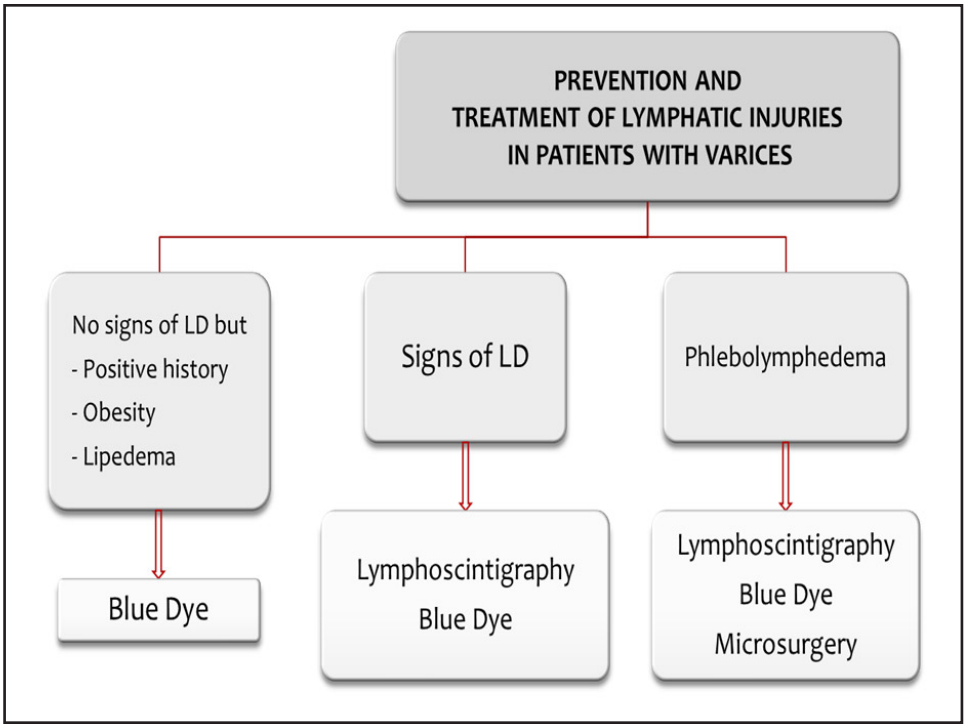

Fig. 1. Flow chart of treatment protocols to prevent lymphatic injuries for use in patients undergoing venous surgery.

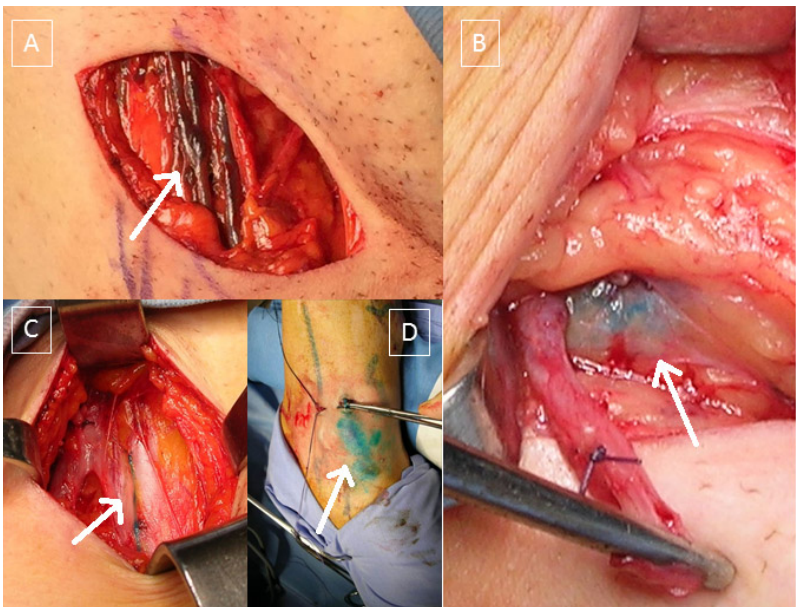

Fig. 2. Identification of perivenous lymphatic vessels highlighted by blue dye (arrows). A-C: lymphatic vessels in the groin; D: lymphatic vessels in the internal malleolus.

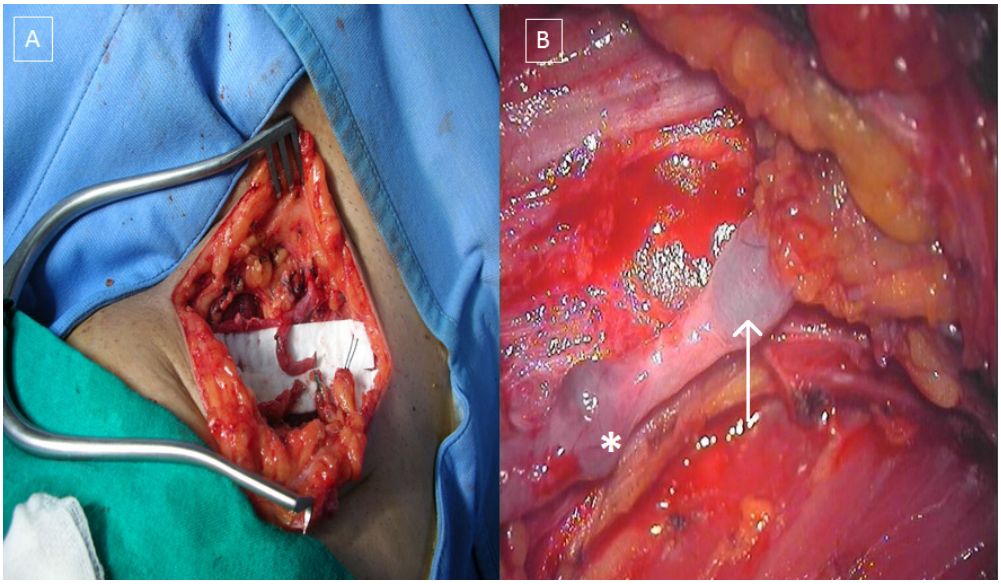

Fig 3. Multiple lymphatic-venous anastomoses. A: vein and lymphatics prepared for anastomosis; B: Completed MLVA at the end (arrow). Note the vein filled with lymph and a competent valve (*).

for perfect competence of the vein valve), or the cut end of the great saphenous vein at the saphenofemoral junction (SFJ) after proper external valvuloplasty. Lymphatic-venous anastomoses consisted of an end-to-end shirt sleeve-shaped anastomosis (18,19). During groin dissection, lymphatic collectors were highlighted in blue and were spared when ligating the great saphenous vein near the SFJ and its collateral branches. The blue dye allowed us to find lymphatics and lymph nodes to avoid causing any damage. Likewise, the dye that was injected distally to the malleolus allowed us to spare the lymphatics around the vein in this area. The incisions at the groin and at the popliteal region are the same size as for standard venous surgery. Lymphatics can be found very near the veins, and this is the reason they can be damaged during standard venous surgery. Regarding lymph nodes, they can more easily be seen at the groin than in the popliteal area but sometimes they can also be seen at the junction of the saphenous vein with the popliteal vein.

RESULTS

Sixty-six patients were treated by greater saphenectomy and varicectomy, 12 patients had crossectomy and varicectomy, 4 patients underwent greater saphenectomy and varicectomy associated with MLVA, and 4 patients were treated by small saphenous vein stripping and varicectomy (*Table 3*). The surgical procedure was chosen based on the preoperative assessment of the patients by physical examination and diagnostic investigation (echo-Doppler). No lymphatic complications occurred. A decrease of over 75% of excess volume between pre- and post-op measurements was observed in 4 patients with lower limb phlebolymphedema treated by MLVA (*Fig. 4*). Lymphoscintigraphy showed no post-operative lymphatic impairment and normalization (T.I. <10) in the Transport Index in 4 patients with phlebolymphedema treated with MLVA (20). These 4 patients were followed clinically and instrumentally for at least 5 years (4 times a year for the first year, then twice a year

TABLE 3
Surgical Procedures That Were Performed

Surgical procedure	Number of patients	Lymphatic complica-tions	Volume reduction	Pre-op Lympho-scintigraphy Transport Index (T.I.)*	Post-op Lympho-scintigraphy Transport Index (T.I.)
Greater saphenectomy and varicectomy	66	0	-	-	-
Crossectomy and varicectomy	12	0	-	-	-
MLVA + Greater saphenectomy and varicectomy	4	0	75-100%	Pt 1: TI= 23 Pt 2: TI= 18 Pt 3: TI= 27 Pt 4: TI= 16	Pt 1: TI= 8 Pt 2: TI= 6 Pt 3: TI= 9 Pt 4: TI= 4
Stripping of the small saphenous vein and varicectomy	4	0	-	-	-
Total	86				

*Normal T.I.≤10; Pathological T.I. over 10

Fig. 4. Example of patient with phlebolymphedema of LEFT lower limb before (a) and after (b) treatment with varicectomy and lymphatic-venous anastomoses demonstrating the effectiveness of the therapeutic protocol to prevent further development of lymphedema even in the setting of phlebolymphedema.

thereafter), and they showed no signs of impairment or relapse. Lymphoscintigraphy did not depict any subclinical lesions to the lymphatics in 15 patients who underwent only venous surgery reflecting the efficacy of the preventive protocol, and the Transport Index remained within normal limits (*Fig. 5*).

DISCUSSION

The reported frequency of lymphatic injury (lymphocele, lymphatic fistula, lymphorrea, and lymphangitis) after surgery for varicose veins varies in the literature (2.2-8.7% and 26% in redo surgery in the groin),

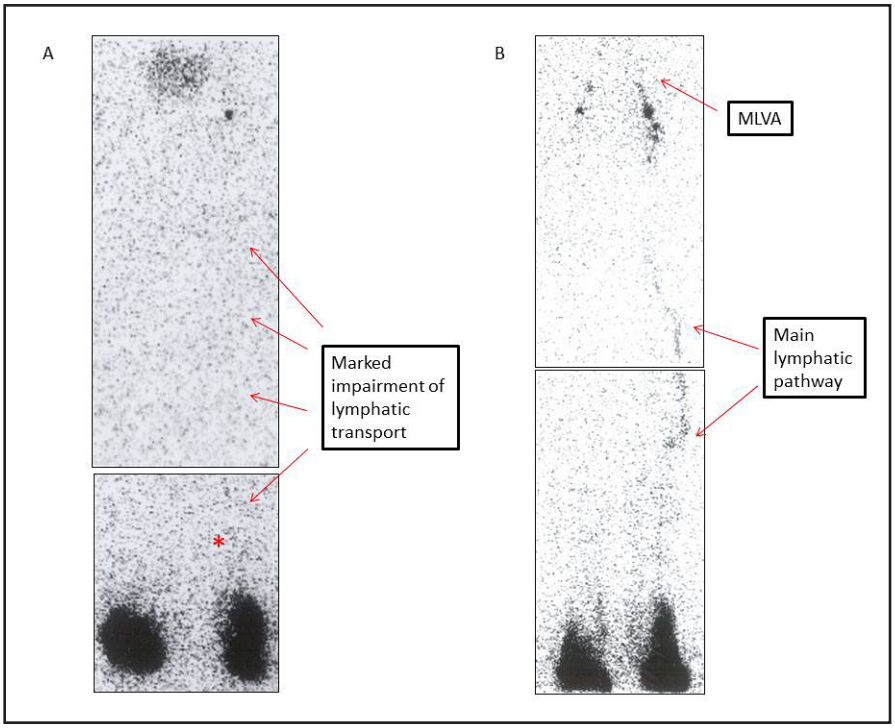

Fig. 5. Pre (A) and post (B) lymphoscintigraphy in patient who underwent venous treatment with the prevention of lymphatic injuries. Preoperatively Transport Index was 15 with dermal back flow at the left leg (*) and postoperatively T.I was 6 with improvement of lymphatic transport, shown also by a clearly evident main lymphatic pathway flowing up to the inguinal-iliac region (arrows).

and the risk of late complications (lymphedema) is not negligible. These complications arise because of unnecessary lymphatic disruption occurring during the incision and dissection of varicose veins due to the close relationship between lymphatic collectors and veins (21). In the literature, some studies can be found on the use of minimally invasive venous surgery techniques but none deal with the assessment of preventive methods to avoid lymphatic damage during venous surgery. Our study shows that it is possible to prevent lymphatic complications following vein surgery by identifying which patients are at risk, by performing proper preoperative diagnostic assessment and using blue dye during surgery, and by performing lymphatic-venous anastomoses when necessary. There are three possible clinical scenarios regarding patients affected by chronic venous insufficiency and varices. The first situation involves patients with no signs of lymphatic disorders but with a history of previous peripheral edema (i.e., after long flights, during summertime, etc.), positive family history, obesity, and/or lipedema. In these cases, our protocol calls for the use of blue dye, which allows sparing of the lymphatics around the veins. The same can be performed using indocyanine green (ICG) even though it allows study of only the subdermal lymphatic circulation up to 1.5 cm. A second scenario involves patients with varicose veins and clinical signs of lymphatic disorders (slight peripheral edema, fibrotic subcutaneous tissue, episodes of lymphangitis, etc.) for whom performing preoperative lymphoscintigraphy and using blue dye during surgery is recommended. Lymphoscintigraphy is an inexpensive non-invasive investigation that

should be performed only in patients who present clinical signs of lymphatic impairment or are at risk for lymphatic complications. This group of patients does not undergo microsurgery because the treatment of venous pathology with the prevention of lymphatic injuries is sufficient to obtain a successful outcome. The third group includes patients with phlebolymphedema of the lower limbs for whom the protocol recommends preoperative lymphoscintigraphy, blue dye injection, and lymphatic-venous anastomosis (*Fig. 1*).

Patients with lower limb lympho-phlebedema and varices generally undergo only venous surgery but the lymphatic disorder is neglected. The novelty of our research is to perform the treatment of both pathologic conditions at the same time. This report may also provide a tool to avoid lymphatic complications that are also frequent after saphenous vein harvest for aortocoronary bypass and lymphatic fistula and cysts after femoropopliteal bypasses.

The limitations of this study include its retrospective nature and the limited number of patients. Nonetheless, these positive results encourage consideration of preventive procedures in every venous operation we undertake with particular focus on patients at risk of developing lymphatic complications. This protocol can help improve the patients' quality of life and reduce social and health-care costs. The disadvantages of the protocol are negligible and consist of the use of blue dye and lymphoscintigraphy. However, these are very inexpensive and low risk, and there is no significant increase in the duration of the surgical procedure.

The anatomical relationship between the lymphatic collectors and the veins is of paramount importance to prevent lymphatic injuries during venous surgical procedures. Accurate diagnostic investigation and proper surgical technique (associated with micro-surgical procedures when necessary) proved to be of great importance in the effort to avoid lymphatic complications during venous surgery and to treat combined lymphatic and venous insufficiency. Accordingly, our study confirms that a proper preventive protocol during the surgical approach to chronic venous disease with varicose veins can reduce the frequency of postoperative lymphatic morbidity. Further investigation is warranted in a larger series of patients at multiple centers.

CONFLICT OF INTEREST

All authors declare that no competing financial interests exist.

REFERENCES

1. Pittaluga, P, S Chastanet: Lymphatic complications after varicose veins surgery: Risk factors and how to avoid them. Phlebology 27 Suppl 1 (2012), 139-142.
2. Suzuki, M, Y Unno, N Yamamoto, et al: Impaired lymphatic function recovered after great saphenous vein stripping in patients with varicose vein: Venodynamic and lymphodynamic results. J. Vasc. Surg. 50 (2009), 1085-1091.
3. Piller, N: Phlebolymphoedema/chronic venous lymphatic insufficiency: An introduction to strategies for detection, differentiation and treatment. Phlebology 24 (2009), 51-55.
4. Disselhoff, BC, DJ der Kinderen, FL Moll: Is there a risk for lymphatic complications after endovenous laser treatment versus cryostripping of the great saphenous vein? A prospective study. Phlebology 23 (2008), 10-14.
5. Mouton, WG, S Keller, M Naef, et al: Primary surgery for sapheno-femoral incompetence: A randomized controlled trial to compare two techniques to reduce lymphatic complications. Vasa 38 (2009), 234-237.
6. Diener, H, A Larena Avellaneda, ES Debus: Postoperative complications in vascular surgery. Chirurg 80 (2009), 814-826.
7. Vogt, K, J Gillner, C Bader, et al: [Postoperative complications after recrossectomy of the saphenofemoral junction.] Zentralbi Chir 137(2012), 478-484.
8. Carradice, D, AI Mekako, FA Mazari, et al: Randomized clinical trial of endovenous laser ablation compared with conventional surgery for great saphenous varicose veins. Br. J. Surg. 98 (2011), 501-510.

9. Nordon, IM, RJ Hinchliffe, R Brar, et al: A prospective double-blind randomized trial of radiofrequency versus laser treatment of the great saphenous vein in patients with varicose veins. Ann. Surg. 254 (2011), 876-881.
10. Liu, X, X Jia, W Guo, et al: Ultrasound-guided foam sclerotherapy of the great saphenous vein with sapheno-femoral ligation compared to standard stripping: a prospective clinical study. Int. Ang. 30 (2011), 231-236.
11. Olszewski, WL, PJ Ambujam, M Zaleska, et al: Where do lymph and tissue fluid accumulate in lymphedema of the lower limbs caused by obliteration of lymphatic collectors? Lymphology 42 (2009), 105-111.
12. Ouvry, PA, H Guenneguez, PA Ouvry: Lymphatic complications from variceal surgery. Phlebologie 46 (1993), 563-568.
13. Hayden, A, J Holdsworth: Complications following re-exploration of the groin for recurrent varicose veins. Ann. R. Coll. Surg. Engl. 83 (2011), 272-273.
14. Schacht, V, W Luedemann, C Abels, et al: Anatomy of the subcutaneous lymph vascular network of the human leg in relation to the great saphenous vein. Anat. Rec. (Hoboken) 292 (2009), 87-93.
15. Campisi, C, F Boccardo: Lymphedema and microsurgery. Microsurgery 22 (2002), 74-80.
16. Campisi, C, C Bellini, C Campisi, et al: Microsurgery for lymphedema: Clinical research and long-term results. Microsurgery 30 (2010), 256-260.
17. Yamamoto, T, N Matsuda, T Todokoro, et al: Lower extremity lymphedema index: A simple method for severity evaluation of lower extremity lymphedema. Ann. Plast. Surg. 67 (2011), 637-640.
18. Boccardo, F, E Fulcheri, G Villa, et al: Lymphatic microsurgery to treat lymphedema: Techniques and indications for better results. Ann. Plast. Surg. 71 (2013), 191-195.
19. Campisi, C, B Boccardo: Vein graft interposition in treating peripheral lymphoedemas. Handchir. Mikrochir. Plast. Chir. 35 (2003), 221-224.
20. Kleinhans, E, RG Baumeister, D Hahn, et al: Evaluation of transport kinetics in lymphoscintigraphy: Follow-up study in patients with transplanted lymphatic vessels. Eur. J. Nucl. Med. 10 (1985), 349-352.
21. Scaglioni, MF, H Suami: Lymphatic anatomy of the inguinal region in aid of vascularized lymph node flap harvesting. J. Plast. Reconstr. Aesthet. Surg. 68 (2015), 419-427.

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