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Donor limb assessment after vascularized groin lymph node transfer for the treatment of breast cancer-related lymphedema: Clinical and lymphoscintigraphy findings

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Summary *Introduction:* Vascularized lymph node transfer is an established treatment for secondary lymphedema. Different donor sites of lymph node flap have been described. In our institute, vascularized groin lymph node (VGLN) flap is the workhorse flap for treating breast cancer-related lymphedema (BCRL). Potential complications of VGLN flap harvesting include seroma formation, thigh dysaesthesia, and iatrogenic lymphedema.
Methods: Between August 2013 and June 2016, 30 consecutive patients with a mean age of 60 years underwent VGLN transfer for BCRL. Reverse mapping of lower limb lymphatics with patent blue solution was performed in all cases. The donor limb conditions were assessed clinically with limb circumference measurement and radiologically with lymphoscintigraphy. Postoperative lymphoscintigraphy findings and transport indexes were compared between the donor and nonoperated limbs.
Results: The mean follow-up period was 22.11 ± 7.83 months. Three (10%) patients developed groin seroma and 18 (60%) patients complained of transient thigh dysaesthesia. There was no clinically detectable donor limb lymphedema.
Lymphoscintigraphy was performed at a mean of 13 months after operation. The mean transport indexes of the nonoperated limbs and donor limbs were 2.04 and 3.32, respectively. For the donor limbs, all patients had normal distribution pattern of contrast uptake. No dermal backflow pattern was demonstrated.

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Conclusion: With good knowledge of groin anatomy and meticulous surgical skills, VGLN flap can be harvested without causing major consequence to the donor limb.

Introduction

Vascularized lymph node transfer (VLNT) is an established treatment of secondary limb lymphedema. Different donor sites have been described in the literature, which include neck, axilla, groin, and intra-abdominal donor sites.[1-7]

In our institute, VGLN flap is the workhorse flap for the treatment of BCRL. The advantages of groin donor site include concealed scar and the relatively straightforward flap harvesting procedure. However, iatrogenic lymphedema is a potential complication of VGLN harvest.

In this article, we focused on the donor site condition of 30 BCRL patients who underwent VGLN transfer in our previous cohort.[8] Postoperative clinical and lymphoscintigraphy findings of donor limb were described. The transport indexes were compared between the donor and nonoperated limbs.

Materials and methods

Patients

Between August 2013 and June 2016, 30 female patients with BCRL were included in this study. A total of 30 upper limbs were treated. The mean age was 60 (range, 45–79 years). The mean body mass index was 20.1 (range, 17.7–28.6). No patient had operation on pelvic, groin or lower limb regions, and pre-existing lower limb swelling prior to VGLN transfer.

The indications of VGLN transfer include recurrent bacterial cellulitis, International Society of Lymphology (ISL) stage II or later lymphedema, i.e., irreversible edema, tense, and fibrotic limb.

This was a prospective study. Institutional review board approval was obtained for this study. This study was reported using the STROBE checklist as a framework.

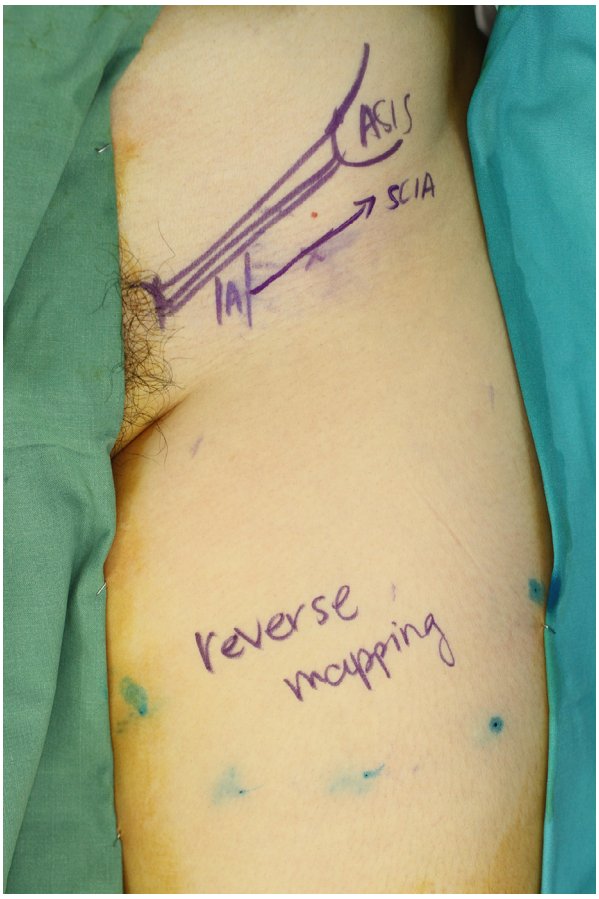

Figure 1 Markings over patient's left groin region. The course of superficial circumflex iliac artery (SCIA) was traced with handheld Doppler device. Reverse mapping of lower limb lymphatic tissues was performed with subdermal and subcutaneous injection of patent blue solution.

Surgical technique

The details of flap harvesting technique were described in author's (HL Liu) previous publication.[8] In essence; the VGLN flap was based on superficial circumflex iliac artery (SCIA) and superficial circumflex iliac vein (SCIV).

For the skin markings, the landmarks of pubic tubercle, anterior superior iliac spine, inguinal ligament and femoral artery were identified. The course of SCIA was traced with a handheld Doppler device. Reverse mapping of lower limb lymphatic tissue was performed through patent blue solution injection to the subdermal and subcutaneous planes of thigh (Figure 1).

Skin incision was made along the course of SCIA. SCIV was then identified immediately underneath the Scarpa's fascia. The flap was harvested from medial to lateral. The femoral sheath was opened for the identification of the SCIA origin.

The flap was then elevated from the muscle fascia. The medial border of flap was at the femoral artery. Lateral border was the medial border of sartorius muscle. Superior border was around 2 cm superior to inguinal ligament. Inferior border was taken at the level where SCIV joined to the saphenous bulb. Lymphatic tissues that were stained with patent blue solution from reverse mapping were preserved (supplementary video).

The flap was then transferred to the axilla. The branches of thoracodorsal or lateral thoracic vessels were used for microvascular anastomosis.

A suction drain was placed in the groin wound. The wound was closed with absorbable sutures in layers.

Table 1 Calculation of transport index.

Points	Kinetics (*K*)	Distribution (*D*)	Time to visualization of nodes	Visualization of nodes (*N*)	Visualization of vessels (*V*)
0	No delay	Normal	0.04 × min (*T*)	Clearly demonstrated	Clearly demonstrated
3	Low-grade delay	Partially diffuse		Faint visualization	Faint visualization
6	Extreme delay	Diffuse		Hardly recognizable	Hardly recognizable
9	Absence of transport	Transport stopped	No appearance	No visualization	No visualization

The formula for the calculation of transport index: $K + D + 0.04\,T + N + V$.

Postoperative care of groin donor site

All patients were kept in hospital for monitoring and discharged on day 7 after operation. Suction drain was taken off when the daily output was less than 20 ml. Pressure dressing was applied to the groin region after drain removal to prevent seroma formation

Clinical assessment of donor limb

Patients were followed up in outpatient clinic at 2 weeks and 1, 3, 6, and 12 months after operation, and once a year after that. For the lower limb assessment, history taking and physical examination were focused on symptoms and signs, e.g., subjective feeling of lower limb swelling, thigh dysaesthesia, the presence of seroma and pitting edema.

Circumferences of both lower limbs were measured before and after operation at seven levels, i.e., midsole, ankle, 10 cm above ankle, 20 cm above ankle, knee joint, 10 cm above knee joint, and 20 cm above knee joint. The circumference differences were calculated.

Iatrogenic lymphedema was defined clinically when there was a 2 cm difference in circumference between the preoperative and postoperative donor limb readings

Lower limb lymphoscintigraphy

Lymphoscintigraphy of lower limb was ordered one year after operation. For the lymphoscintigraphy protocol, 99mTc-labeled nanocolloid contrast material was injected to the subdermal plane of web spaces. Serial gamma films were taken at 0 min, 15 min, and 60 min onward.

The lymphoscintigraphy studies were interpreted by a group of radiologists specialized in nuclear medicine. The radiologists were blinded to the treatment.

Five parameters of lymphoscintigraphy were assessed, which included lymphatic transport kinetics, distribution pattern of contrast, time to appearance of lymph nodes, visualization of lymph nodes, and visualization of lymph vessels. Transport index was calculated from these five parameters (Table 1). The transport indexes of both lower limbs were compared.

Statistical analysis

Paired sample *t*-test was used to determine the statistical significance of the results. A *p*-value of <0.05 was considered statistically significant.

Results

Clinical findings of donor limb

The mean follow-up period was 22.11 ± 7.83 months (range, 12–34 months). There was no wound infection. Three patients (10%) developed persistent seroma (duration >14 days) who were treated with needle aspiration at outpatient clinic. Eighteen (60%) patients complained of transient thigh dysaesthesia, mainly numbness and pins and needles sensation, along the distribution of the branches of anterior femoral cutaneous nerve. Most of the patients had improvement of sensation 6 months after operation.

No patient complained of donor limb swelling after operation. No pitting edema was detected during the follow-up period. There were no significant differences between preoperative and postoperative donor limb circumference measurements. There were also no significant differences between the limb circumferences of the donor limbs and the nonoperated lower limbs after VLNT.

Lymphoscintigraphy findings and transport index

The 30 sets of lower limb lymphoscintigraphy were performed at a mean of 13 months after operation (range, 12–15 months). The lymphoscintigraphy findings were compared between the donor limbs and the nonoperated limbs.

The mean transport index of the nonoperated limbs was 2.04 (range, 0.6–2.4). In all nonoperated limbs, the time to appearance of groin lymph nodes was less than or equal to 60 min. All patients had normal distribution pattern of contrast uptake. No dermal backflow pattern was demonstrated. All groin lymph nodes and lower limb lymphatic vessels were clearly demonstrated.

The mean transport index of the donor limbs was 3.32 (range, 0.6–8.4). All patients had normal distribution pattern of contrast uptake. No dermal backflow pattern was demonstrated. In all limbs, the time to appearance of groin lymph nodes is less than or equal to 60 min. The difference between the transport indexes of the donor limbs and those of the nonoperated limbs was statistically significant ($p = 0.008$).

Eight patients had a higher transport index than their nonoperated limb, which included 3 patients with prolonged contrast transport time as well as faint visualization of lymphatic vessels and 5 patients with faint visualization of lymphatic vessels (Figure 2). For all the 3 patients with prolonged contrast transport time, the time to appearance of

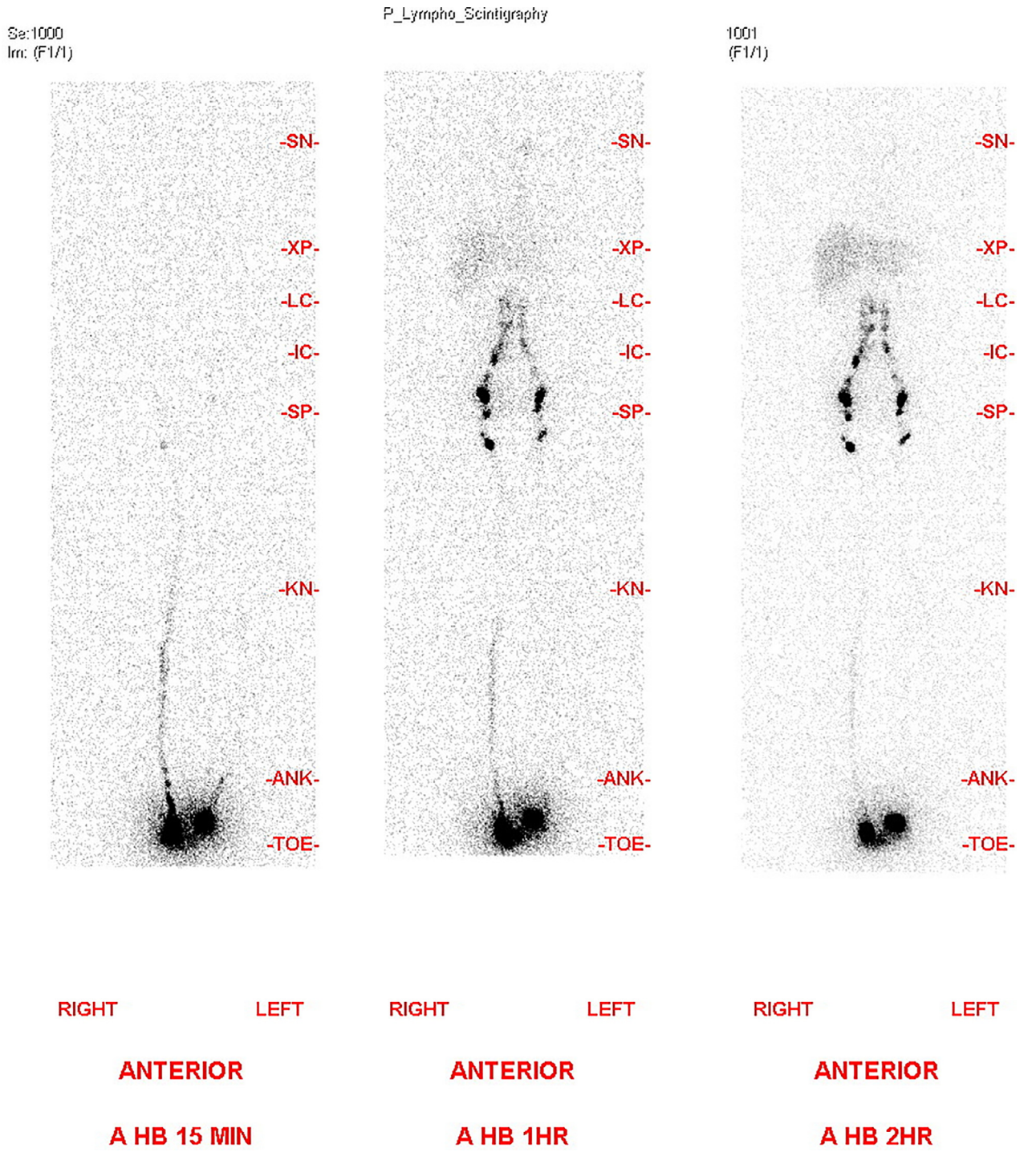

Figure 2 Vascularized groin lymph node (VGLN) flap was harvested from left groin. In the postoperative lymphoscintigraphy, the lymphatic vessel of right lower limb was clearly demonstrated. However, the left lower limb lymphatic vessel was only faintly demonstrated in postinjection 1- and 2-hour films. However, no dermal backflow pattern was found.

groin lymph nodes was 15 min for the nonoperated limb and 60 min for the donor limb (Figure 3).

Eleven patients had less groin lymph nodes visible in the donor limb when compared to the nonoperated limb. However, the remaining nodes were clearly demonstrated (Figure 4).

The details of lymphoscintigraphy findings are listed in Table 2.

Discussion

Different donor sites of lymph node flap that have been described in the literature include submental region, supraclavicular region, axilla, groin, and intra-abdominal donor sites.[1-7]

There is no single perfect donor site. Each donor site has its advantages and downsides. The chance of iatrogenic

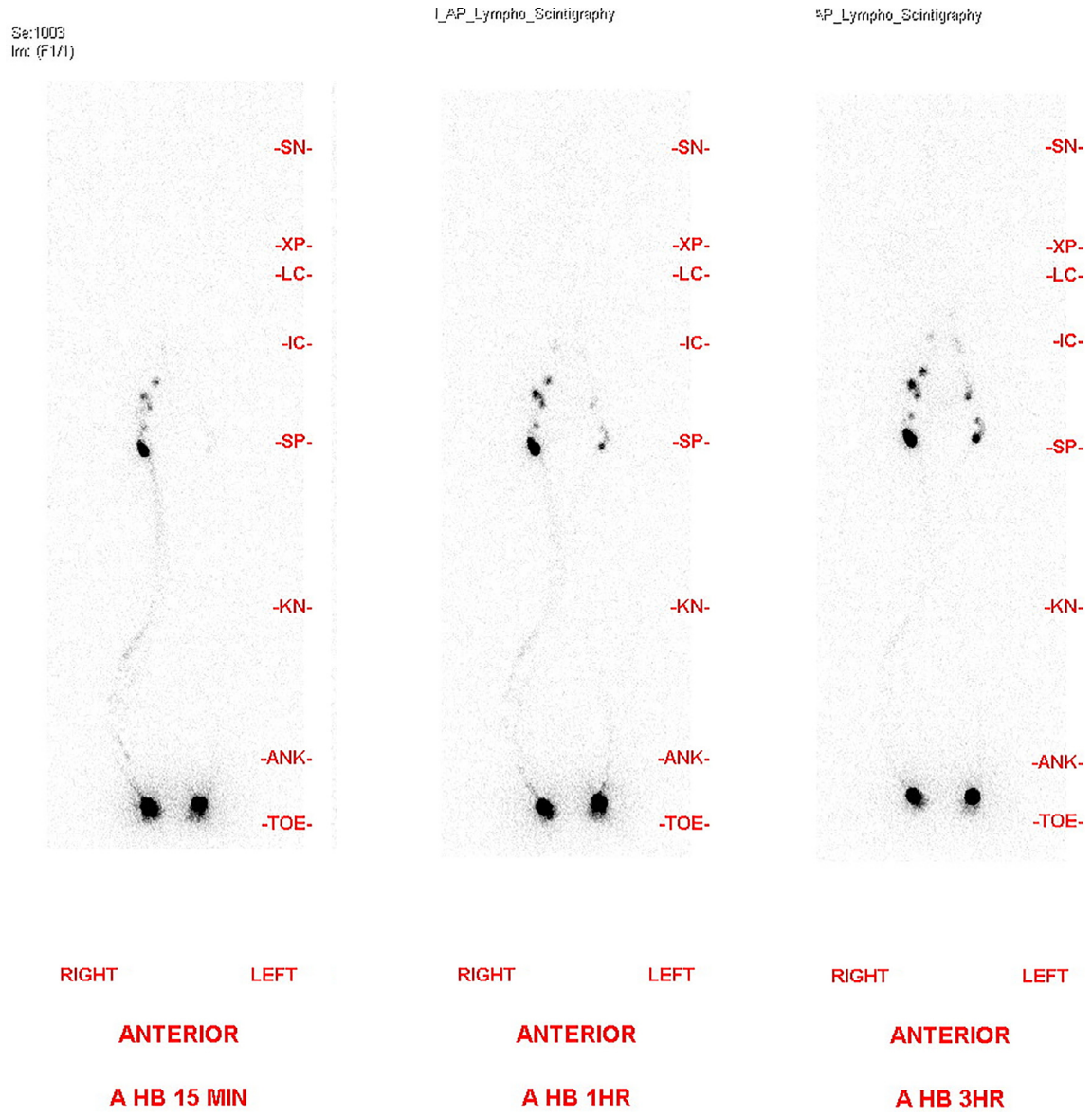

Figure 3 Vascularized groin lymph node (VGLN) flap was harvested from left groin. The groin lymph nodes of nonoperated limb were visualized in postinjection 15 min film. However, the groin lymph nodes of donor limb were only visualized in postinjection 1 h film. This demonstrated a low grade delay of contrast transport.

lymphedema is low for neck donor sites, i.e., submental and supraclavicular regions. However, in submental lymph node flap harvesting, tedious dissection is required for the protection of the marginal branch of facial nerve.[4] Other disadvantages include visible depression and scar at the upper neck region.

On the other hand, we consider supraclavicular node harvesting not appropriate for BCRL. The reason for avoiding ipsilateral supraclavicular node harvesting is obvious. Animal study by Suami et al. showed that new lymphatic connections were formed between the treated axilla and the contralateral normal lower neck.[9] This kind of new lymphatic connections was also observed in unpublished human indocyanine green studies. Because of the theoretical risks of worsening the pre-existing BCRL, we reserve supraclavicular lymph node flap for lower limb lymphedema exclusively.

The harvesting of lateral thoracic lymphatic is not straightforward due to the lack of landmarks. Donor limb lymphedema is a possible complication. In addition, we prefer not to operate on the contralateral normal axilla in patients who already had breast cancer.

Intra-abdominal donor sites mainly include mesenteric and gastroepiploic lymph nodes.[1,6,7] If the microsurgeon is not familiar with abdominal procedure, the flap harvesting part may need to be performed by general surgeons.

VGLN flap is our preferred flap for the treatment of BCRL. The major advantages include the relatively straightforward harvesting technique and concealed scar. Iatrogenic donor limb lymphedema is the most dreadful complication. Other downsides and possible complications include small caliber of SCIA, dysaesthesia of thigh region and seroma formation.

From our experience, the caliber of SCIA at its origin can be less than 1 mm. This renders difficulties in pedicle

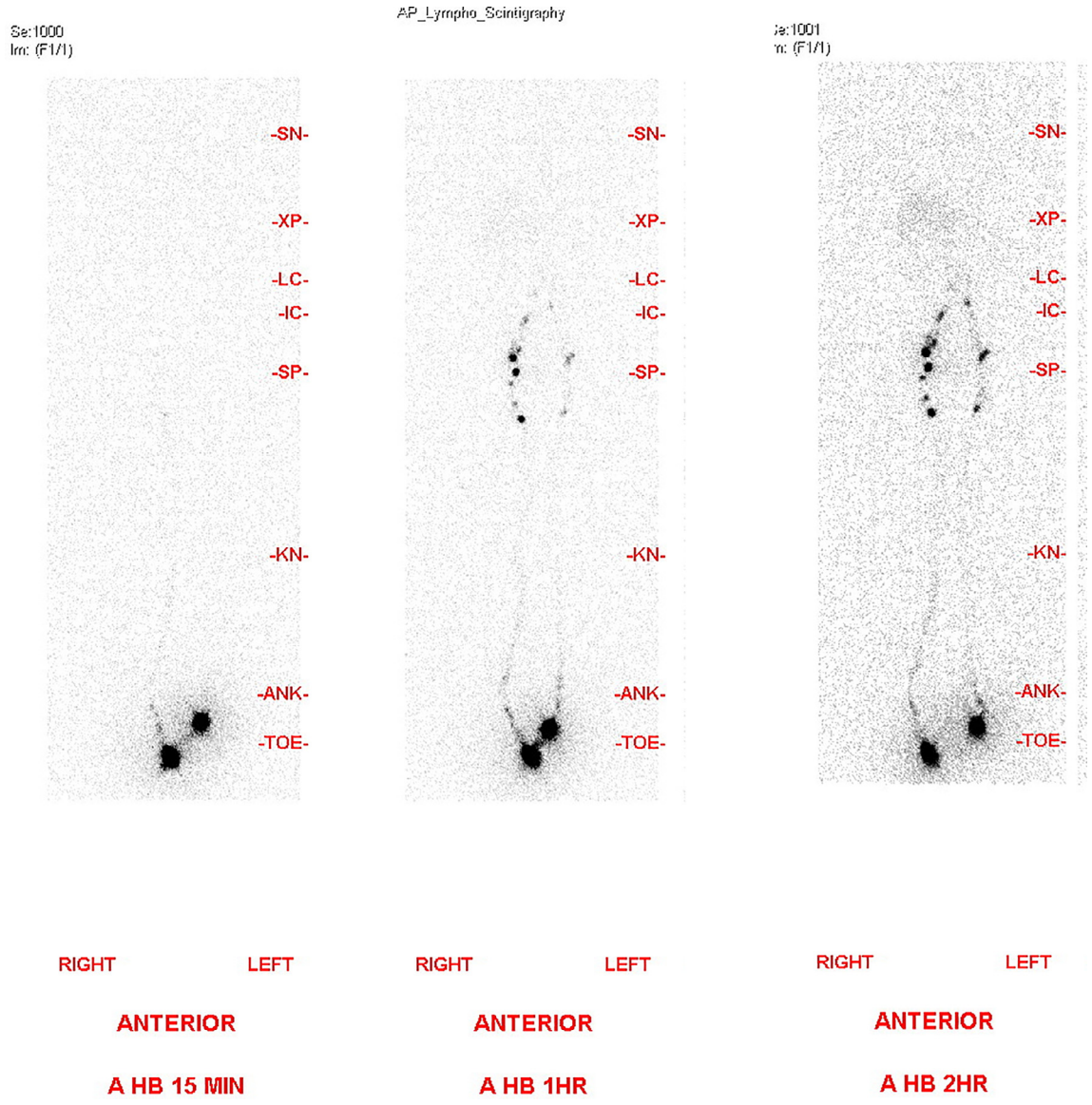

Figure 4 Vascularized groin lymph node (VGLN) flap was harvested from left groin. Postoperative lymphoscintigraphy showed a decreased number of visualized groin lymph nodes in the donor limb.

dissection and microvascular anastomosis. Ciudad et al. suggested harvesting a cuff of femoral artery to make microvascular anastomosis easier.[10] This maneuver, however, has never been adopted in our center.

Thigh dysaesthesia is caused by the injury to the branches of anterior femoral cutaneous nerve which run on the femoral sheath. As femoral sheath has to be opened during the dissection of the SCIA origin, this can lead to injury or transection of the nerve branches. Pedicle dissection under magnification may be beneficial in preventing nerve injury.

In this series, we adopted radioisotope lymphoscintigraphy for the assessment of lymphatic function. Transport index is a scoring system derived from lymphoscintigraphy findings, which was first described in 1980s by Kleinhans et al.[11] Five parameters are assessed, which include lymphatic transport kinetics, distribution pattern of contrast, time to appearance of lymph nodes, visualization of lymph nodes and visualization of lymph vessels. Each parameter is scored on a scale from 0 to 9 i.e., the maximum score of transport index is 45. Transport index less than 10 is considered normal lymphatic function (Table 1).

Iatrogenic lymphedema from VGLN harvest has been reported in one case report and one case series.[12,13]

Pons et al. reported one case of lower limb swelling after VGLN flap harvesting.[12] The donor lower limb was found to have an increase in thigh circumference of 2 cm at 24-months follow-up. Lymphoscintigraphy of affected lower limb showed delayed drainage. Dermal backflow pattern was not found. In our opinion, the diagnosis of iatrogenic lymphedema could be more concrete if additional lymphoscintigraphy findings, such as amount of residual groin lymph node and contrast travel time to the groin region, could be provided in the article.

Table 2 Lower limb lymphoscintigraphy findings of 30 patients.

Patient number	Nonoperated limb		Donor limb			
	Transport time to groin LN (min)	Transport index	Transport time to groin LN (min)	No. of visualized inguinal lymph nodes	Visualization of lymphatic vessels	Transport index
1	15	0.6	15			0.6
2	15	0.6	15			0.6
3	15	0.6	15	Less		0.6
4[a]	15	0.6	60	Less	Faint	8.4
5[a]	15	0.6	60	Less	Faint	8.4
6[a]	15	0.6	60		Faint	8.4
7[a]	60	2.4	60	Less	Faint	5.4
8	60	2.4	60			2.4
9[a]	60	2.4	60		Faint	5.4
10	60	2.4	60	Less		2.4
11	60	2.4	60	Less		2.4
12	60	2.4	60			2.4
13	60	2.4	60			2.4
14	60	2.4	60			2.4
15[a]	60	2.4	60		Faint	5.4
16	60	2.4	60	Less		2.4
17	60	2.4	60			2.4
18	60	2.4	60	Less		2.4
19	60	2.4	60			2.4
20	60	2.4	60			2.4
21	60	2.4	60			2.4
22[a]	60	2.4	60	Less	Faint	5.4
23	60	2.4	60			2.4
24	60	2.4	60			2.4
25[a]	60	2.4	60		Faint	5.4
26	60	2.4	60	Less		2.4
27	60	2.4	60			2.4
28	60	2.4	60	Less		2.4
29	60	2.4	60			2.4
30	60	2.4	60			2.4

[a] Refers to patients who had a higher donor limb transport index than that of the nonoperated limb.

Bioimpedance analysis can be useful in detecting early stage lymphedema.

Vignes et al. reported 2 cases of iatrogenic lower limb lymphedema in 14 cases after VGLN harvest for BCRL.[13] Iatrogenic lymphedema was clinically diagnosed when there is an increase of more than 2 cm in limb circumference of the donor lower limb compared to the nonoperated lower limb. However, because Vignes et al. was not the operating team, the total numbers of operated cases were not known. Therefore, it is difficult to know the actual incidence rate of iatrogenic lymphedema. Moreover, it would be more informative if lymphoscintigraphy findings could be included in the article.

There are only two case series in the literature that focus on the changes of donor limb lymphoscintigraphy findings after VGLN flap harvesting. Both the studies were conducted by the same group from Finland.[14,15]

In the early study published in 2012, the group performed VGLN transfer for 13 BCRL patients.[14] Lower limb lymphoscintigraphy was performed at 3–52 months after VGLN transfer. A total of 10 sets of postoperative lymphoscintigraphy were analyzed. Normal lymphoscintigraphy findings were found in 4 patients. Slower lymphatic flow was found in 6 patients. Two patients had a transport index of the donor limb greater than 10. However, none of the patients complained of lower limb lymphedema symptoms. There was no significant difference in circumferences of the limbs.

In the later study published in 2014, their VGLN flap harvesting technique was modified.[15] Lymphoscintigraphy was performed on average 7 months after operation. A total of 12 sets of postoperative lymphoscintigraphy were analyzed. However, detailed descriptions on lymphoscintigraphy were not provided. All patients had transport index of the donor limb less than 10. The mean transport index of the donor limb was 2.6 which was slightly higher than the mean value of 1.1 of the nonoperated limb. There was no clinically detectable donor limb lymphedema.

This study is the largest series in current literature describing the clinical and radiological findings of VGLN donor limb. The lymphoscintigraphy findings are described in detail.

All 30 patients had normal contrast transport time and transport index of the donor limbs after VGLN transfer, i.e., visualization of groin lymph node no more than 60 min

and transport index less than 10. However, it is observed that the number of visualized groin lymph nodes in lymphoscintigraphy decreased after VGLN flap harvesting. We consider the change in visualization pattern of lymphatic vessels, i.e., from solid to faint, reflects a certain degree of injury to the vessels.

In this study, the radiological findings and transport indexes were compared between the donor limbs and the nonoperated limbs. To make this comparison sensible, we made an assumption that the lymphatic status/function of the donor limbs prior to operation was similar to that of the nonoperated limbs. By making this assumption, the patients were spared from an extra preoperative lymphoscintigraphy study.

To prevent iatrogenic lower limb lymphedema after VGLN flap harvest, it is of utmost importance that over-harvesting of lymph nodes and injury to lower limb-draining lymphatic vessels should be avoided.

Good understanding of lymphatic anatomy of the groin region is essential for flap harvesting. Cheng et al. suggested not to harvest the deep groin nodes which are located underneath the common femoral vessels.[16] Radiological study conducted by Zhang et al. suggested not to harvest the lymphatic tissue medial and inferior to the point where SCIV joins the long saphenous vein.[17] Indocyanine green injection study conducted by Suami et al. depicted that the lower limb draining nodes and their efferent vessels are located along both sides of the long saphenous vein and medial to the femoral artery, respectively.[18] Radiological study conducted by Zeltzer et al. described the safety circle of lymph node harvesting, which is lateral to the superficial inferior epigastric vessels and superior and medial to SCIV.[19] The suggestions in common are to avoid dissection (1) medial to the femoral artery and (2) inferior to the point where SCIV join the long saphenous vein. The femoral vein and long saphenous vein should not be exposed at all times.

In theory, reverse lymphatic mapping can help to reduce iatrogenic lymphedema by identifying the donor limb lymphatic tissues that have to be preserved. The reverse mapping technique in vascularized lymph node flap harvesting has been described by Dayan et al.[5] In his study, double contrast agents, i.e., indocyanine green and radioactive isotope, were used in lymphatic mapping technique. One agent was used for the visualization of the desired lymphatic tissues. Another agent was used to reversely map the limb draining lymphatic tissues which must be preserved. To date, there is no comparative study to support its effectiveness in preventing iatrogenic donor limb lymphedema.

Besides, VGLN flap should not be harvested in patients, who are at high risk for iatrogenic lower limb lymphedema, e.g., obese patient, patients with pre-existing lower limb edema and previous pelvic surgery.

Conclusion

In this series of 30 patients, no iatrogenic lymphedema was detected both clinically and radiologically after VGLN flap harvesting. With good knowledge of the lymphatic anatomy of groin and meticulous surgical skills, VGLN flap can be harvested without causing major consequence to the donor limb.

Conflicts of interest

None to declare.

Financial disclosures

None to declare.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjps.2018.10.013.

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