Quantifying Lymph Nodes During Lymph Node Transplantation

The Role of Intraoperative Ultrasound

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Abstract: Quantifying lymph nodes in vascularized lymph node transfer (VLNT) has been performed using preoperative percutaneous ultrasound. The higher resolution and accuracy of intraoperative ultrasound (IOUS) over transcutaneous ultrasound has been demonstrated in the radiology literature for the identification and characterization of finer structures including hepatic lesions, pancreatic lesions, and biliary or pancreatic ducts. We hypothesize that IOUS during VLNT would be a superior method to quantify and map lymph nodes in our flaps. A prospectively collected database of patients undergoing VLNT over 3 years (October 2014 to October 2017) was reviewed. Patients who underwent IOUS during flap harvest, before pedicle ligation to simultaneously map and quantify the number of lymph nodes were included in the study. Twenty-one patients with an average age of 58.7 years and a mean BMI of 32.3 underwent VLNT with IOUS for chronic lymphedema during the study period. Extremity lymphedema was classified as Campisi IB (n = 7), IIA (n = 7), IIB (n = 5), and IIIA (n = 2). There were 14 superficial circumflex iliac artery flaps, including 4 performed concomitantly with a deep inferior epigastric perforator flap, 1 transverse cervical artery flap, and 6 omental flaps. The average number of lymph nodes transferred per IOUS was 4.3 for superficial circumflex iliac artery flaps, 4 for the transverse cervical artery flap, and 5.2 for the omental flaps. Intraoperative ultrasound allows the lymphatic surgeon to precisely map the location of lymph nodes which can guide intraoperative decision making. As there is no data correlating the number of lymph nodes transferred and outcomes after VLNT, developing a precise intraoperative quantification method is important.

Key Words: vascularized lymph node transfer, intraoperative ultrasound, lymph node quantification, lymphedema

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Surgical treatment of chronic lymphedema includes excisional procedures (eg, Charles and Sistrunk procedures) and physiological procedures (eg, lymphovenous anastomosis and vascularized lymph node transfer [VLNT]).[1] The first VLNT performed in a patient was in 1982 by Clodius et al.[2] Subsequently, this technique has been widely adopted by lymphatic surgeons and has shown to be highly effective in volume reduction, symptomatic relief, reduction of cellulitis episodes, and quality of life improvement in patients with intermediate stage lymphedema.[3–10] The main mechanisms of actions have been attributed to "pumping" of interstitial lymph into the transferred lymph node and, subsequently, pedicle vein and enhanced lymphangiogenesis via locally secreted growth factors.[10–12]

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Preoperative imaging studies such as percutaneous duplex ultrasonography (US), computed tomography (CT), and magnetic resonance imaging are routinely used for flap characterization and planning preoperatively.[13–16] Specifically, percutaneous duplex US is a noninvasive and inexpensive modality that also negates the harmful effect of ionizing radiation. Patel et al. used this technology to identify certain donor-site characteristics such as flap volume, thickness, and number of lymph nodes with reasonable accuracy.[14]

Several landmark studies have shown that intraoperative ultrasound (IOUS) can improve the localization and characterization of finer anatomical structures in various surgical fields.[17–19] In those studies, IOUS guidance affords the surgeon even more accuracy and precision than percutaneous ultrasound or other cross-sectional modalities such as CT and magnetic resonance imaging. In addition, omental flaps, which have more recently gained popularity, can only be effectively assessed intraoperatively. We applied this concept in our VLNT practice and used intraoperative ultrasound to quantify the number of lymph nodes to harvest for lymph node transplantation. In addition, we sought to gain further real-time information including spatial mapping of lymph nodes in the flap to facilitate improved lymph node transfer.

PATIENTS AND METHODS

Study Population and Design

A retrospective cohort study was conducted on a prospectively maintained database on all patients undergoing VLNT for lymphedema and IOUS from October 2014 to October 2017. Patient demographics, lymphedema location and staging, and donor lymph node locations were recorded. Institutional review board approval was obtained.

Intraoperative Duplex Ultrasonography

An attending radiologist performed IOUS after the anticipated flap was exposed superficially and before committing to the boundaries of the flap or pedicle ligation to quantify the number of lymph nodes present. This was always done with the guidance of the same lymphatic surgeon (D.S.) to minimize interoperator variability. The intraoperative information obtained from IOUS allowed adjustments to be made in the creation of the flap to maximize lymph node presence before harvest. Lymph nodes seen intraoperatively were marked with a superficial Prolene suture to facilitate mapping (Fig. 1). All detected lymph nodes that were deemed safe for harvest were transferred.

RESULTS

Twenty-one patients with an average age of 58.7 years and a mean BMI of 32.3 underwent VLNT for chronic lymphedema during the study period. Nineteen patients were with upper extremity edema, one with lower extremity edema, and one with breast edema. The average follow-up was 3.4 years. Extremity lymphedema was classified as Campisi IB (n = 7), IIA (n = 7), IIB (n = 5), and IIIA (n = 2). There were 14 superficial circumflex iliac artery (SCIA) flaps, including 4 performed concomitantly with deep inferior epigastric perforator flaps, 1 transverse cervical artery (TCA) flap, and 6 omental flaps (Figs. 2 and 3).

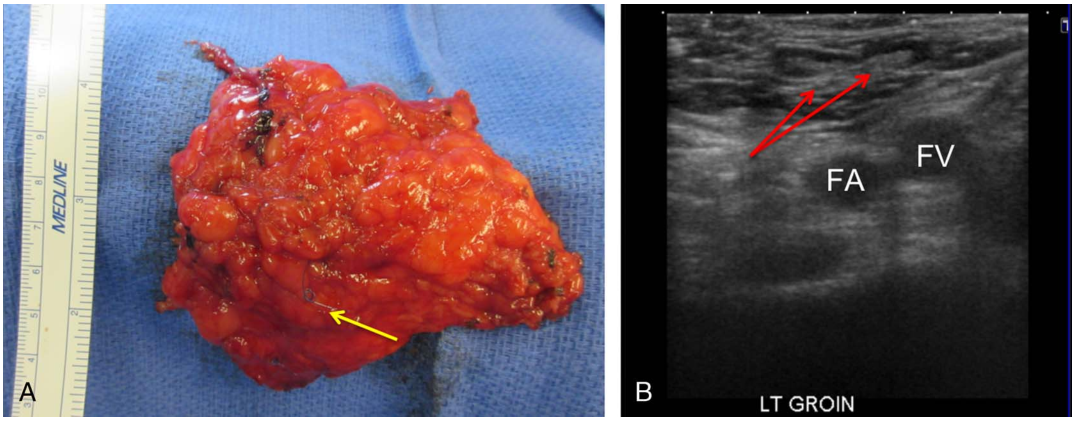

FIGURE 1. A, Harvested lymph node transplant based on the left superficial circumflex iliac artery. The white arrow points to a Prolene suture which marks the location of 2 lymph nodes mapped by IOUS. B, IOUS screenshot demonstrating the 2 lymph nodes (grey arrows), each with the characteristic "kidney bean" shape and a fatty hilum. The femoral artery (FA) and vein (FV) are also visualized. A total of 5 lymph nodes were mapped using IOUS in the flap.

The average number of lymph nodes transferred per IOUS was 4.3 for SCIA flaps, 4 for the TCA flap, and 5.2 for the omental flap (Table 1).

DISCUSSION

Our results indicate that IOUS allowed for precise quantification and mapping of lymph nodes in VLNT. Knowing exactly where lymph nodes were located within each basin often affected the boundaries of the flap, facilitating real-time decisions to capture more tissue to include more lymph nodes in the flap to be harvested. In addition, IOUS allowed for avoidance of nodes in certain locations such as near the femoral triangle, which if removed are more likely to cause iatrogenic injuries and/or lower extremity lymphedema.

As compared with the study by Patel et al, which used percutaneous preoperative US, our intraoperative method allowed for identification of a greater number of lymph nodes in both groin basins (4.3 vs 3.3) and transverse cervical basins (4.0 vs 0.9). Compared with 2 studies using CT to preplan for VLNT, this study identified higher number of SCIA lymph nodes on average (4.3 vs. 3.3 and 3.1).[15,22] The only study that quantified higher number of SCIA lymph node was a cadaveric dissection by Cheng et al in 2013.[4] We believe that higher resolution with IOUS accounts for the increased accuracy of this technique. Bypassing subcutaneous fat is advantageous as it has a naturally high ultrasound attenuation coefficient, and direct imaging harvest site also allows the examination depth to be decreased, allowing improvements in both imaging resolution and contrast, even for superficial basins. As with percutaneous US, IOUS is portable, cost-effective, and avoids use of ionizing radiation; OR-compatible US probes are also widely available.

Our study, to our knowledge, was the first series to describe and quantify the number of lymph nodes from a gastroepiploic omental flap in vivo (Table 2). This application differs from other harvest locations in that percutaneous US assessment of omental harvest sites is precluded by the deeper location of these nodes, which results in a prohibitive degree of ultrasonic attenuation, obscuration by bowel, and poor anatomical localization when compared with superficial groin and neck nodes. Effective US-based evaluation of this harvest site can therefore only be performed intraoperatively.

Nguyen et al has previously demonstrated a positive correlation between the number of vascularized lymph node transferred and the degree of volume reduction as well as reduction of dermal backflow on lymphoscintigraphy in a hind limb rat model.[23] Interestingly, such effects plateaued at 3 months postoperatively. The hypothesis was that the initial additive effect of multiple "lymphatic pumps" or vascularized lymph nodes subsides overtime as old lymphatic channels reopen and new ones being formed.[23] Similarly, Kwiecien et al demonstrated increasingly rapid lymph transit time in vascularized lymph node flaps in Sprague-Dawley rats with increasing numbers of lymph nodes transferred.[24] Preliminary data confirm improvement in lymphatic drainage

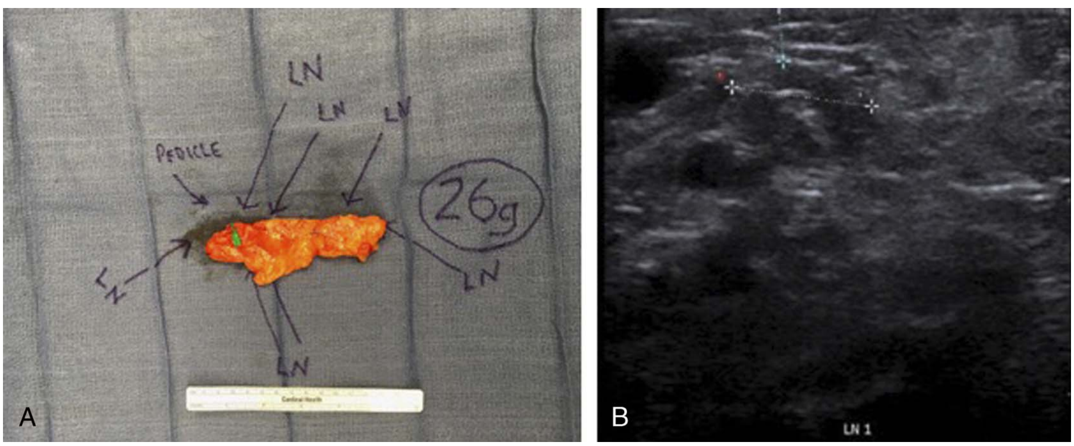

FIGURE 2. A, Harvested gastroepiploic flap. B, IOUS demonstrating 1 of 6 total lymph nodes visualized in the flap.

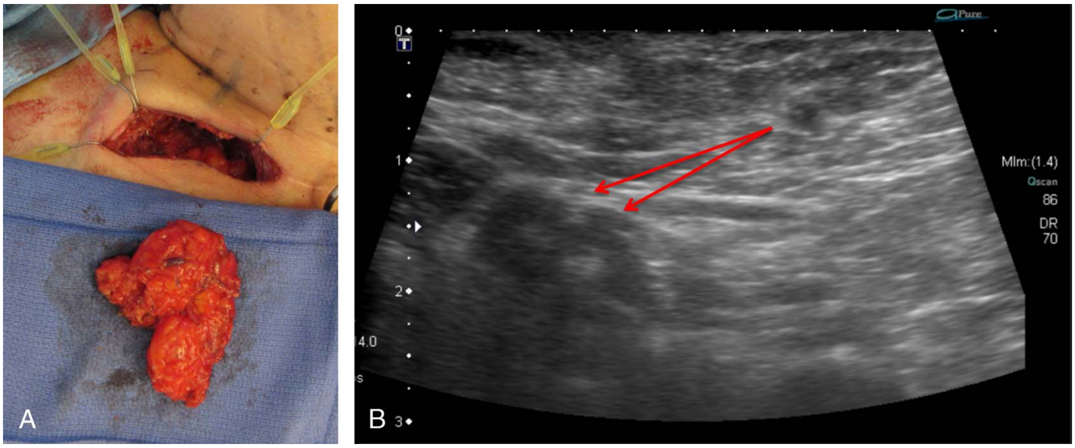

FIGURE 3. A, Harvested right TCA flap. B, IOUS demonstrating 2 of 4 total lymph nodes visualized in the flap (grey arrows).

TABLE 1. Baseline Demographics

Affected Region	Total n = 21
Left upper extremity	13
Right upper extremity	6
Left lower extremity	1
Right breast	1
Age, yr	58.7 (8.6)
BMI, kg/m^2	32.3 (5.5)
Duration of symptoms, yr	3.4 (4.1)
Campisi Staging[20]	Hung-Chi Chen Staging[21]
IB 7	II 6
IIA 7	IIIA 7
IIB 5	IIIB 7
IIIA 2	IVA 1
History of infection (patients)	3
Donor site	
SCIA	14
TCA	1
Omentum (gastroepiploic)	6
No. node identified and transferred	
SCIA	4.3 (1.3)
TCA	4
Omentum (gastroepiploic)	5.2 (1.5)

TABLE 2. Literature Review of Lymph Node Quantification Based on Flap Type

	Donor Site		
Study (Imaging Modality)	SCIA/DIEP	TCA	Omentum
Patel et al, 2014 (US)[14]	3.3	0.9	
Cheng et al, 2013 (cadaveric dissection)[4]	6.2		
Zeltzer et al, 2017 (CT)[15]	3.1		
Zhang et al, 2014 (CT)[22]	3.3		
Current study (IOUS)	4.3	4	5.2

with more lymph nodes being transferred, making the development of a precise method of quantification highly important.

Limitations

Although these results are telling, there are limitations to this study. First, the series is relatively small in size. Second, it is well known that, although US affords many advantages over other imaging modalities, results can be quite operator dependent. In this study, available attending radiologists performed the IOU. To minimize variability and ensure comparability of results, the primary surgeon (D.S.) was present for all of the studies to supervise and guide the IOU. Third, although we did note an increased number of lymph nodes compared with the percutaneous study by Patel et al, we did not actually acquire percutaneous data, so that limits a head-to-head comparison. However, given corollaries to intraoperative ultrasounds in other organ systems, we do believe this method provides greater sensitivity for identifying lymph nodes. Future studies with a larger cohort will be needed to further quantify the use of IOUS in VLNT and to find methods of improving outcomes via this method.

CONCLUSIONS

The number of lymph nodes identified using IOUS seems to be higher than those reported by percutaneous US and other imaging modalities in previous studies. Higher resolution with IOUS likely accounts for the improved accuracy of this technique. Moreover, IOUS allowed for localization of the lymph nodes within flaps and precise mapping which enhanced flap characteristics.

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