

# Systematic Review of the Surgical Treatment of Extremity Lymphedema

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## Abstract

**Background** Although conservative management of lymphedema remains the first-line approach, surgery is effective in select patients. The purpose of this study was to review the literature and develop a treatment algorithm based on the highest quality lymphedema research.

**Methods** A systematic literature review was performed to examine the surgical treatments for lymphedema. Studies were categorized into five groups describing excision, liposuction, lymphovenous anastomosis (LVA), vascularized lymph node transfer (VLNT), and combined/multiple approaches. Studies were scored for methodological quality using the methodological index for nonrandomized studies (MINORS) scoring system.

**Results** A total of 69 articles met inclusion criteria and were assigned MINORS scores with a maximum score of 16 or 24 for noncomparative or comparative studies, respectively. The average MINORS scores using noncomparative criteria were 12.1 for excision, 13.2 for liposuction, 12.6 for LVA, 13.1 for VLNT, and 13.5 for combined/multiple approaches. Loss to follow-up was the most common cause of low scores. Thirty-nine studies scoring > 12/16 or > 19/24 were considered high quality. In studies measuring excess volume reduction, the mean reduction was 96.6% (95% confidence interval [CI]: 86.2–107%) for liposuction, 33.1% (95% CI: 14.4–51.9%) for LVA, and 26.4% (95% CI: – 7.98 to 60.8%) for VLNT. Included excision articles did not report excess volume reduction.

**Conclusion** Although the overall quality of lymphedema literature is fair, the MINORS scoring system is an effective method to isolate high-quality studies. These studies were used to develop an evidence-based algorithm to guide clinical practice. Further studies with a particular focus on patient follow-up will improve the validity of lymphedema surgery research.

## Keywords

- ▶ lymphedema
- ▶ lymphovenous anastomosis
- ▶ vascularized lymph node transfer

Lymphedema is a chronic, progressive condition that affects up to 3 million people in the United States.<sup>1</sup> The etiology is abnormal lymphangiogenesis during embryological development (primary) or injury to lymphatics (secondary). Secondary lymphedema frequently is associated with

oncological treatment. Although most common among breast cancer patients, lymphedema also develops after radiotherapy or lymph node dissection in gynecologic, melanoma, genitourinary, and head and neck cancer patients.<sup>2–4</sup> Limb swelling is caused by the accumulation of protein-rich

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**Table 1** ISL and Campisi staging for lymphedema severity

ISL stage and description		Campisi stage and description	
I	Accumulation of tissue fluid with higher protein content, which subsides with limb elevation	Ia	No overt swelling despite impaired lymph drainage
		Ib	Reversible swelling with limb elevation
IIa	Limb elevation alone rarely reduces swelling and pitting is manifest	II	Mild persistence of swelling with elevation
IIb	Limb may or may not pit as fat and fibrosis supervenes	III	Persistent swelling with recurrent lymphangitis
III	Lymphostatic elephantiasis: tissue is fibrotic and pitting is absent. Skin thickening, hyperpigmentation, increased skin folds, fat deposits, and warty overgrowth develop	IV	Fibrotic changes with column-like limb
		V	Elephantiasis with limb deformation including widespread lymphostatic warts

Abbreviation: ISL, International Society of Lymphology.

fluid in interstitial spaces, adipose deposition, and inflammation resulting in fibrosis.<sup>5</sup> The progressive enlargement and lymphatic stasis may cause recurrent infections and have been shown to significantly diminish patients' quality of life (QoL) and increase health care costs.<sup>2,6,7</sup> The varying degrees of clinical features are characterized by the lymphedema staging system from the International Society of Lymphology (ISL) or the Campisi scale (→ **Table 1**).<sup>8,9</sup>

There is no cure for lymphedema. Management is categorized as conservative or surgical. Nonsurgical management includes complete decongestive therapy (CDT), which is typically administered by a certified lymphedema therapist.<sup>8</sup> CDT consists of an initial reductive phase followed by an ongoing maintenance phase. The initial phase consists of manual lymph drainage, multilayer compression bandaging, therapeutic exercise, diligent skin care, education in self-management, and elastic compression. The maintenance phase is typically lifelong and includes lymph drainage, exercise, skin care, and compression garments.<sup>10,11</sup> High costs, variability in the quality of therapy, and patient compliance can hinder the efficacy of CDT.<sup>2,12</sup>

For patients with late-stage, nonpitting lymphedema, conservative therapy often is ineffective. Surgical management is used for advanced lymphedema as well as in conjunction with conservative treatment for earlier stages.<sup>13,14</sup> Surgical approaches can be divided into reductive (e.g., liposuction, skin/subcutaneous excision) or physiological (e.g., lymphovenous anastomosis [LVA], vascularized lymph node transfer [VLNT]). Liposuction, introduced as a method of lymphedema management by O'Brien et al (1989), directly removes adipose tissue and fibrosis, thereby significantly reducing limb volume in both upper and lower extremities.<sup>15-18</sup> The Charles procedure, first described in 1912, is an aggressive resection of skin and subcutaneous tissue of the extremity to the deep fascia followed by skin grafting.<sup>19</sup> Staged skin/subcutaneous excision removes excess fat, fibrous tissue, and skin allowing for primary closure. Similarly, suction-assisted protein lipectomy involves the removal of proteinaceous fatty tissue from the affected limb.<sup>20</sup> LVA aims to restore lymphatic circulation and bypass obstructions in lymphatics by connecting functioning lymphatic channels and similarly sized, subdermal venules to allow unidirectional

flow of lymphatic fluid directly into the venous system. VLNT is a free tissue transfer of lymph node-containing soft tissue to the affected limb.

Although surgical treatment of lymphedema is becoming common, outcomes literature assessing the approaches consists mainly of observational studies with few randomized controlled trials. Existing reviews of the surgical management of lymphedema describe nonvalidated strategies. Due to the lack of high-level evidence, no consensus exists for indications for specific procedures; comparative effectiveness of the approaches is unclear. The purpose of this study is to systematically review the literature describing surgical management of lymphedema to create a treatment algorithm based on the highest quality studies available. Secondary aims include examining complications associated with each surgical approach and summarizing QoL outcomes.

## Methods

A systematic review of contemporary peer-reviewed literature was performed to evaluate the surgical treatment of lymphedema. PubMed-MEDLINE, Cochrane Library databases, EMBASE, Scopus, and Web of Science were searched from January 2000 to May 2016 using terms to capture literature relating to all aspects of the surgical treatment of extremity lymphedema. Reference lists of relevant articles were searched for additional studies. Two reviewers independently reviewed 4,144 abstracts after removal of duplicates and 137 full texts. Clinical studies describing the surgical treatment of extremity lymphedema with a minimum sample size of eight patients were included in our study. Nonreferenced articles, case reports, and review articles were excluded. A total of 69 studies matched inclusion criteria. Studies were categorized into five groups describing excision ( $n = 9$ ), liposuction ( $n = 5$ ), LVAs ( $n = 27$ ), VLNT ( $n = 17$ ), and combined/multiple surgical approaches ( $n = 11$ ).

## Quality Control

The methodological index for nonrandomized studies (MINORS) scoring system is a validated instrument used to assess the methodological quality of nonrandomized surgical studies.<sup>21</sup> Due to the large number of observational

studies in surgery, the MINORS scores are important in assessing the quality and validity of published data. The MINORS scoring system is based on an 8-item index (global ideal score of 16) for noncomparative studies and a 12-item index (global ideal score of 24) for comparative studies.<sup>21</sup> Each article was assigned a MINORS score by averaging scores from two authors to identify the highest scoring (most validated) ones. Highly validated articles (> 12/16 or > 19/24 for noncomparative or comparative studies, respectively) were reviewed and the following data were extracted: number of patients, ISL or Campisi stage of patients, surgical procedure, length of follow-up, volume or circumference reduction, measurement technique, reported complications, QoL measures, and additional interventions. Only studies scoring > 12/16 or > 19/24 were considered valid for use in creating a management algorithm.

**Statistical Analysis**

For liposuction, LVA, VLNT, and combined VLNT and liposuction procedures outcomes for improvement of lymphedema were compared in forest plots and summarized with mean reduction, and the confidence interval (CI) was set to 95%. Separate comparisons were made for limb reduction in studies reporting circumferential change and volumetric change. Standard deviations (SD) were used to compute weighted averages using Stata/MP version 14.0 (StataCorp Inc.). In studies that did not report a SD, it was imputed using the Cochrane Handbook’s recommendation of dividing the width of the range by 4. The random effects model was used due to the high heterogeneity of the patient population, setting, and surgical procedures used in the studies.<sup>22</sup>

Studies reporting excisional procedures and combined approaches besides VLNT and liposuction were not quantitatively analyzed due to differences in surgical techniques and reported outcomes.

**Results**

**Quality Assessment**

For the 69 articles that met inclusion criteria, the average MINORS scores using noncomparative criteria were 12.1 (range: 8–15) for excision, 13.2 (range: 9–15) for liposuction, 12.6 (range: 8–16) for LVA, 13.1 (range: 9–16) for VLNT, and 13.5 (range: 10–16) for combined/multiple surgical approach studies. Of these 69 articles, 39 studies (5 excision, 4 liposuction, 12 LVA, 10 VLNT, and 8 combined/multiple surgical approaches) were found to be high quality through MINORS criteria, scoring > 12/16 or > 19/24. Reporting an aim, an end point, and an unbiased method for evaluating outcomes were three criteria that most commonly increased MINORS scores. Lack of appropriate follow-up and loss to follow-up were the most common reasons for low MINORS scores.

**Excisional Procedures**

A total of five high-quality studies including 76 patients with lower extremity (n = 65) or upper extremity (n = 11) lymphedema were identified reporting excisional procedures to treat advanced stage lymphedema (► **Table 2**).

**Table 2** Overview of excisional procedures for lymphedema

Study	Number of patients	ISL/Campisi stage	Lymphedema site	Surgical procedure	Follow-up time (mo)	Volume or circumference reduction	Measurement technique	Complications	QoL	Additional interventions
Salgado et al (2009) <sup>23</sup>	11	IIb (ISL)	UE	Excision with preservation perforators	17.8	21%	Circumference	Hyperesthesia (n = 1) Numbness (n = 4) Cellulitis (n = 3)	Not reported	Compression garments
Lee et al (2008) <sup>26</sup>	22	Not reported	LE	Excision	48	Not reported	Infrared optometric volumetry and circumference	Infection (n = 1) Delayed healing with wound disruption (n = 1)	Improved QoL in 93%	CDT and compression garments
van der Walt et al (2009) <sup>27</sup>	8	Not reported	LE	Modified Charles procedure	27.3	Percentage not reported; average 8.5 kg resected	Weight	Additional grafting (n = 3) Wound breakdown (n = 2)	Improved overall QoL, 45% improvement in LE function	Compression garments
Kim et al (2004) <sup>24</sup>	20	III, IV (Campisi)	LE	Excision	17.8	16%	Not reported	None	Not reported	Complex physical therapy or complex decongestive therapy, compression garments
Salgado et al (2007) <sup>25</sup>	15	Not reported	LE	Excision with preservation perforators	13	52%	Circumference	Cellulitis (n = 3) Seroma (n = 1) Hematoma (n = 1) Prolonged numbness (n = 2)	Not reported	Compression garments

Abbreviations: CDT, complete decongestive therapy; ISL, International Society of Lymphology; LE, lower extremity; QoL, quality of life; UE, upper extremity.

The weighted average for limb reduction could not be calculated due to the different primary outcome measures of the studies. One study reported a 21% absolute circumference reduction,<sup>23</sup> one study reported a 16% absolute volume reduction,<sup>24</sup> and one study reported a 52% excess circumference reduction.<sup>25</sup> Procedures included direct excision ( $n = 2$ ), excision with preservation of perforators ( $n = 2$ ), and modified Charles procedure ( $n = 1$ ). Two studies reported lymphedema staging of patients: one study included ISL stage IIb patients and one study included Campisi stages III to IV patients.<sup>23,24</sup> Thus, excisional procedures were only performed in patients with the most advanced stages of disease who were experiencing persistent swelling and fibrosis. Four of the five studies reported complications.<sup>23,25–27</sup> The most common complications were prolonged numbness, cellulitis, wound breakdown, and the need for additional grafting. Other complications included infection, seroma, hematoma, and hyperesthesia. All studies recommended use of compression garments postoperatively. In addition, two studies recommended continuation of CDT after the excisional procedure.<sup>24,26</sup> The two studies reporting QoL outcomes both showed improvements in well-being and function after the procedure.<sup>26,27</sup> The five high-quality excision studies had a mean  $\pm$  SD MINORS score of  $14.0 \pm 0.7$ .

**Liposuction Procedures**

A total of four high-quality studies that included 105 patients with lower extremity ( $n = 6$ ) or upper extremity ( $n = 99$ ) lymphedema were identified reporting use of liposuction to treat advanced stage lymphedema (**►Table 3**). All four studies reported excess volume reduction, which is the percent decrease in additional volume of the lymphedematous extremity compared with the contralateral side. The weighted average of excess volume reduction was 96.6% (95% CI: 86.2–107%,  $I^2$ : 0.0%). Forest plots are presented in **►Fig. 1**. Of the two studies reporting ISL staging of patients, all patients were stage II or III.<sup>28,29</sup> No operative or postoperative complications were reported. Patients in all four studies were encouraged to continue wearing compression garments after the procedure. Three studies reported QoL outcomes showing improved overall well-being and decreased depression and anxiety postoperatively.<sup>28–30</sup> The four high-quality liposuction studies had a mean  $\pm$  SD MINORS score of  $14.25 \pm 0.5$ .

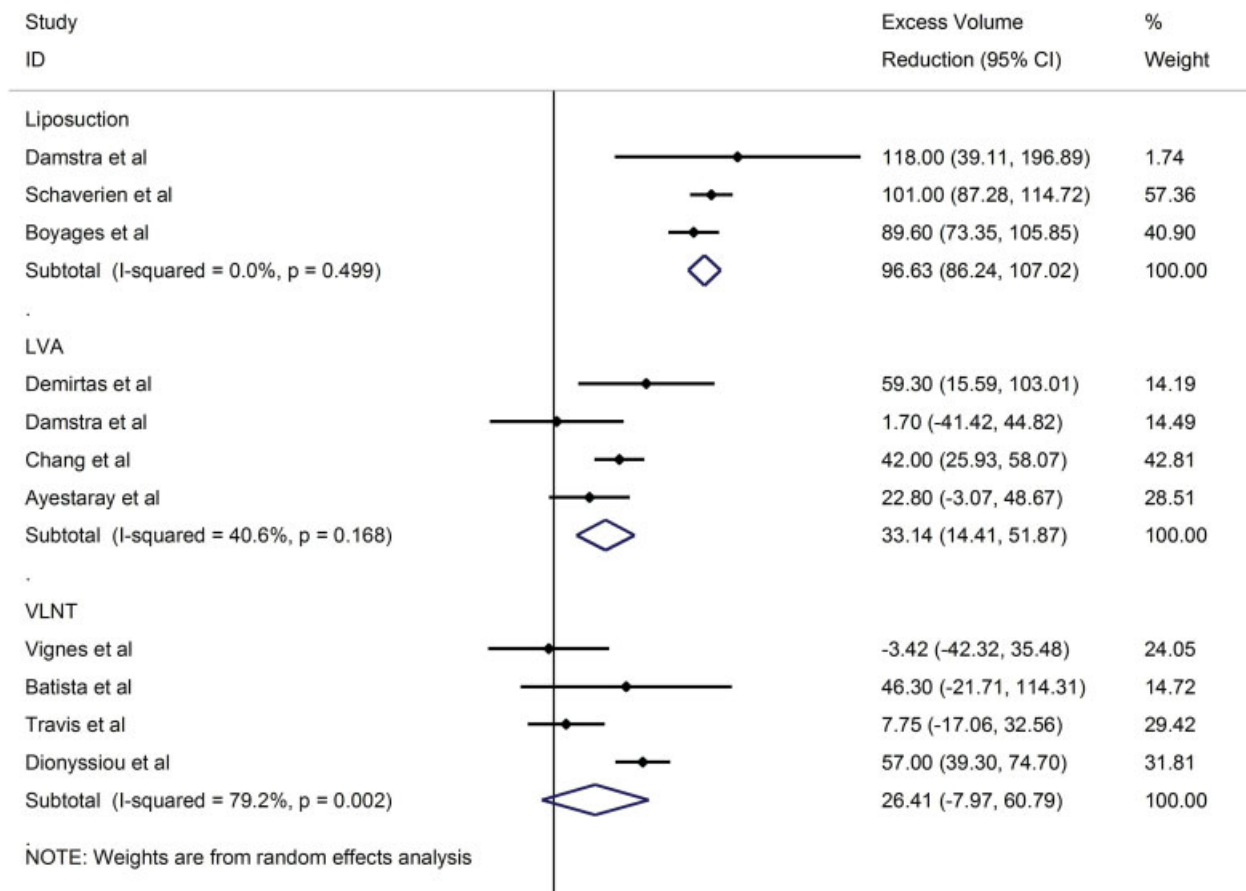
**Lymphatic Reconstructive Procedures**

A total of 12 high-quality studies that included 3,074 patients were identified reporting outcomes after lymphatic reconstructive procedures for lymphedema (**►Table 4**). The weighted average for limb reduction was 5.8% (95% CI: 0.066–11.5%,  $I^2$ : 62.3%) for absolute circumference reduction, 16.1% (95% CI: 2.59–29.6%,  $I^2$ : 0.0%) for excess circumference reduction, and 33.1% (95% CI: 14.4–51.9%,  $I^2$ : 40.6%) for excess volume reduction. Forest plots are presented in **►Figs. 1 to 3**. The studies included 164 patients with lower extremity lymphedema and 310 patients with upper extremity lymphedema. The largest series by Campisi et al included 2,600 patients with either upper or lower extremity

**Table 3** Overview of liposuction procedures for lymphedema

Study	Number of patients	ISL/Campisi Stage	Lymphedema site	Surgical procedure	Follow-up time (mo)	Volume reduction	Measurement technique	Complications	QoL	Additional interventions
Boyages et al (2015) <sup>28</sup>	21	II–III (ISL)	LE ( $n = 6$ ) UE ( $n = 15$ )	Liposuction	12	LE: 88.2% UE: 90.2%	Circumference	None	All patients reported improvements on an index of personally important activities	Compression garments
Schaverien et al (2012) <sup>30</sup>	12	Not reported	UE	Liposuction	38.4	101%	Circumference	None	Reduced anxiety and depression scores and improved overall well-being	Compression garments
Brorson et al (2006) <sup>29</sup>	35	II (ISL)	UE	Liposuction	12	103%	Water displacement	None	Improved overall well-being	Compression garments
Damstra et al (2009) <sup>66</sup>	37	Not reported	UE	Suction-assisted lipectomy	12	118%	Water displacement	None	Not reported	Compression garments

Abbreviations: ISL, International Society of Lymphology; LE, lower extremity; UE, upper extremity.



**Fig. 1** Forest plots of excess volume reduction. CI, confidence interval; LVA, lymphovenous anastomosis; VLNT, vascularized lymph node transfer.

disease.<sup>31</sup> Nine studies reported either the ISL ( $n = 2$ ) or Campisi ( $n = 7$ ) staging of patients. Patients from stages I to III on the ISL staging system and from stages Ib to V on the Campisi scale were included in the studies. Thus, the patients who underwent LVA represent all stages of lymphedema severity, including patients with the earliest stages of disease.<sup>31–39</sup> Two studies reported complications involving partial skin ulceration ( $n = 1$ ) and wound dehiscence ( $n = 1$ ).<sup>35,37</sup> Ten studies recommended compression garments,<sup>31–38,40,41</sup> two studies encouraged physiotherapy,<sup>39,40</sup> and two studies used pumping, lymphatic drainage, or negative pressure therapy postoperatively.<sup>31,32</sup> Five studies reported QoL outcomes. Specifically, one study reported 91.7% symptom improvement, while two other studies reported an average satisfaction rate of 94.5%.<sup>33,34,40</sup> The two other studies reported improved QoL in 90% of patients and subjective improvement in 50%.<sup>35,41</sup> The 12 high-quality LVA studies had a mean  $\pm$  SD MINORS score of  $13.9 \pm 1.2$ .

### Tissue Transfer Procedures

A total of 10 high-quality studies that included 185 patients with lower extremity ( $n = 74$ ) and upper extremity ( $n = 111$ ) lymphedema were identified reporting use of VLNT to treat moderate to advanced staged lymphedema (**Table 5**). The weighted average for limb reduction was 39.5% (95% CI: 36.0–43.0%,  $I^2$ : 0.0%) for excess circumference

reduction,  $-4.04\%$  (95% CI:  $-23.6$  to  $15.5\%$ ,  $I^2$ : 74.2%) for absolute volume reduction, and  $26.4\%$  (95% CI:  $-7.98$  to  $60.8\%$ ,  $I^2$ : 79.2%) for excess volume reduction. Forest plots are presented in **Figs. 1, 2, and 4**. The four studies that report ISL staging include patients from stages IIa to III.<sup>42–45</sup> Thus, only patients with persistent swelling received VLNT. Seven studies reported complications of VLNT procedures.<sup>42–48</sup> The most common complications were cellulitis, lymphocele, and donor site pain, seroma, and lymphedema. Other complications included hematoma, wound dehiscence, wound infection, hydrocele, partial skin graft loss, and venous congestion. Additional interventions were used postoperatively in eight of the studies. Four suggested compression garments,<sup>43,44,46,49</sup> four encouraged CDT or physiotherapy,<sup>42,44,47,50</sup> and two also recommended lymphatic drainage.<sup>46,49</sup> Four studies reported QoL outcomes showing improved function, appearance, and mood along with decreased pain.<sup>43,45,50,51</sup> The 10 high-quality VLNT studies had a mean  $\pm$  SD MINORS score of  $14.1 \pm 0.9$ .

### Combined or Multiple Procedures

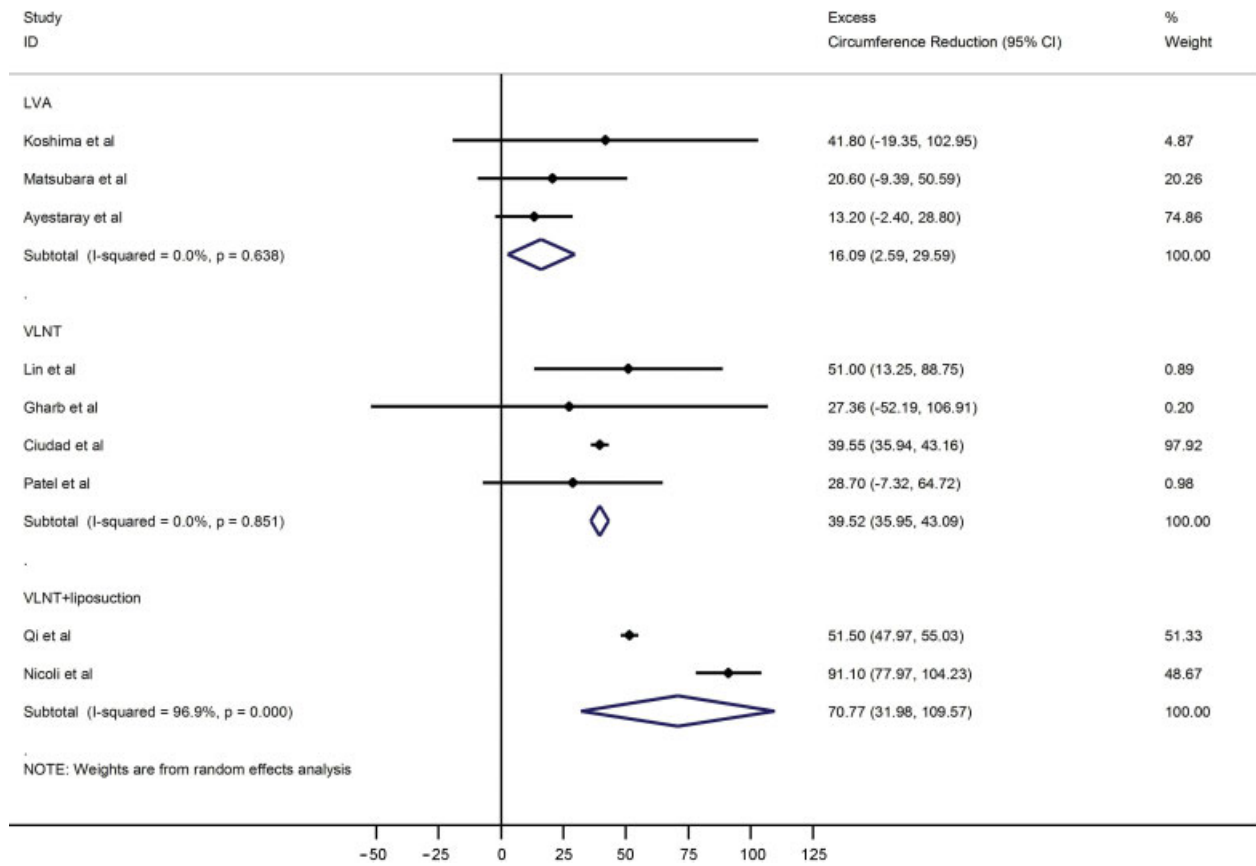
A total of eight high-quality studies that included 135 patients with lower extremity ( $n = 50$ ) or upper extremity ( $n = 59$ ) lymphedema were identified reporting use of multiple surgical approaches (**Table 6**). In addition, Granzow et al reported use of LVA, VLNT, and suction-assisted



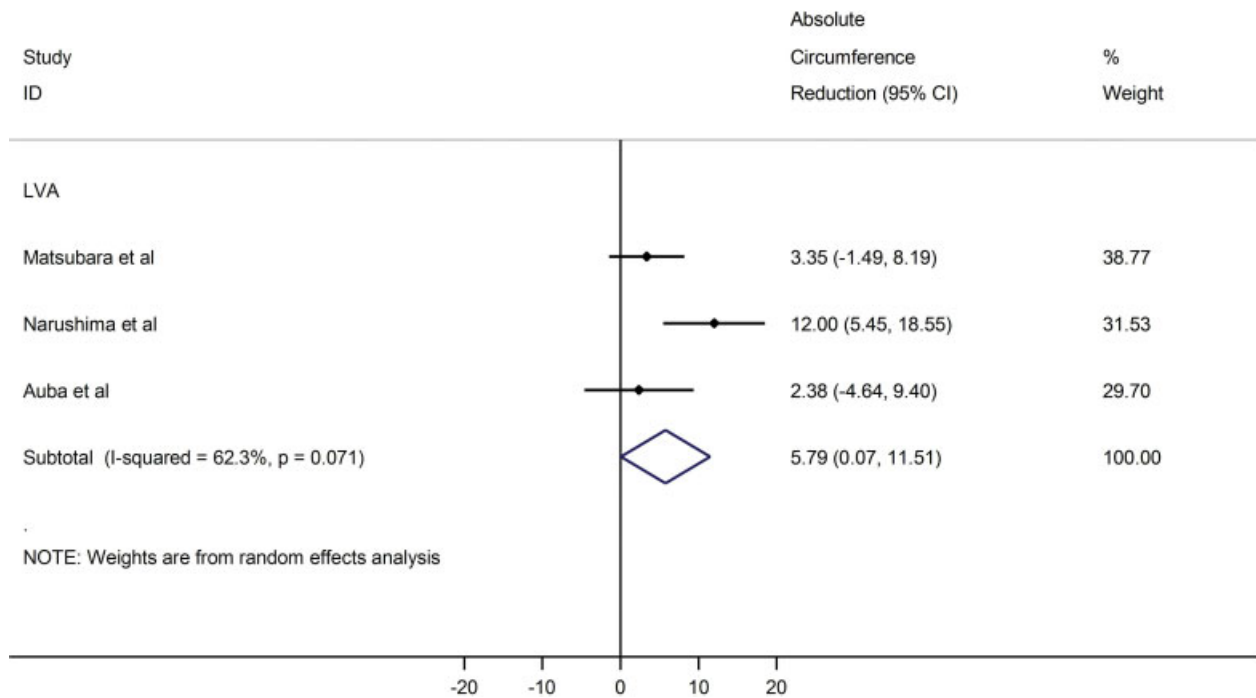
**Table 4** Overview of LVA procedures for lymphedema

Study	Number of patients	ISL/Campisi stage	Lymphedema site	Surgical procedure	Follow-up time (mo)	Volume or circumference reduction	Measurement technique	Complications	QoL	Additional interventions
Koshima et al (2004) <sup>32</sup>	52	III-IV (Campisi)	LE	LVA	14.5	41.8%	Circumference	Not mentioned	Not reported	Compression garments and pumping
Chang et al (2013) <sup>40</sup>	100	Not reported	LE (n = 11) UE (n = 89)	LVA	LE: 18.2 UE: 30.4	LE: Not reported UE: 42%	Circumference	None	LE: 57% symptom improvement 96% symptom improvement	Compression garments and physiotherapy
Demirtas et al (2009) <sup>33</sup>	42	II-IV (Campisi)	LE	LVA and/or lymphatocovenous implantation	11.8	59.3%	Circumference	Not mentioned	95.2% satisfaction	Compression garments
Auba et al (2012) <sup>34</sup>	10	II-V (Campisi)	LE (n = 4) UE (n = 6)	LVA	24	LE: 0.45 cm UE: 0.85 cm	Circumference	None	91.6% satisfaction	Compression garments
Ayestary et al (2013) <sup>35</sup>	20	II-V (Campisi)	UE	LVA	6	22.8%	Circumference	Partial skin ulceration (n = 1)	Improved QoL in 90%	Compression garments
Chen et al (2015) <sup>36</sup>	9	Ib-IV (Campisi)	LE (n = 3) UE (n = 6)	LVA	7.6	Not reported	Circumference	None	Not reported	Compression garments
Narushima et al (2010) <sup>37</sup>	14	II-IV (Campisi)	LE (n = 12) UE (n = 2)	LVA	8.9	11.3%	Circumference	Wound dehiscence (n = 1)	Not reported	Compression garments
Maegawa et al (2012) <sup>38</sup>	31	I-III (ISL)	LE	LVA	17.6	2%	Circumference	None	Not reported	Compression garments
Damstra et al (2009) <sup>41</sup>	10	Not reported	UE	LVA	96	1.7%	Water displacement and circumference	Not mentioned	Subjective relief in 50%	Compression garments
Campisi et al (2016) <sup>31</sup>	2,600	Ib-IIIb (Campisi)	LE and UE	LVA	120	69.0%	Water displacement and circumference	None	Not reported	Manual and mechanical lymphatic drainage, intermittent negative pressure therapy, and compression garments
Weiss et al (2015) <sup>59</sup>	177	Not reported	UE	Lymph vessel transplantation	32.1	62.8%	Circumference	None	Not reported	Not reported
Matsubara et al (2006) <sup>39</sup>	9	Ib (ISL)	LE	LVA	64.9	16.8%	Circumference	None	Not reported	Physiotherapy

Abbreviations: ISL, International Society of Lymphology; LE, lower extremity; LVA, lymphovenous anastomosis; QoL, quality of life; UE, upper extremity.



**Fig. 2** Forest plots of excess circumference reduction. CI, confidence interval; LVA, lymphovenous anastomosis; VLNT, vascularized lymph node transfer.



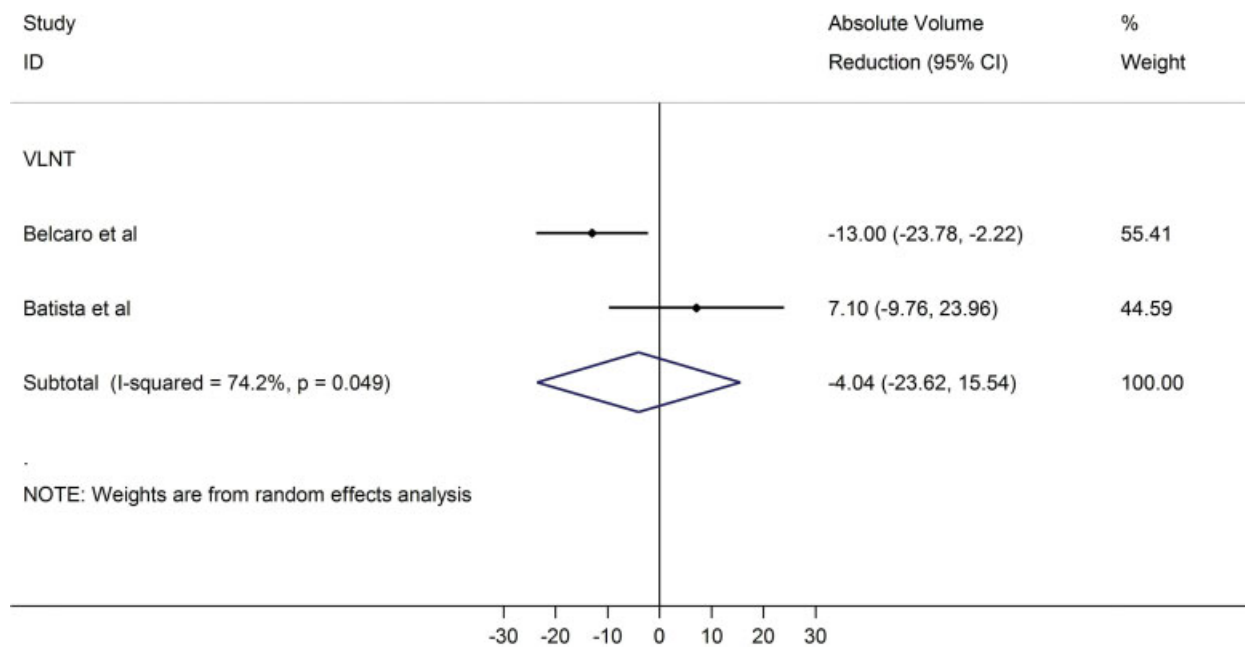
**Fig. 3** Forest plots of absolute circumference reduction. CI, confidence interval; LVA, lymphovenous anastomosis.

**Table 5** Overview of VLNT procedures for lymphedema

Study	Number of patients	ISL stage	Lymphedema site	Surgical procedure	Follow-up time (mo)	Volume or circumference reduction	Measurement technique	Complications	QoL	Additional interventions
Vignes et al (2013) <sup>46</sup>	26	Not reported	LE (n = 12) UE (n = 14)	Autologous lymph node transplantation	40	- 3.42%	Circumference	Donor-site pain (n = 4) Lymphocele (n = 4) lymphedema (n = 6) Hydrocele (n = 1)	Not reported	Compression garments, bandages, manual lymph node drainage
Dionyssiou et al (2016) <sup>44</sup>	18	II	UE	VLNT	18	57%	Circumference	Prolonged lymphorrhea at the donor area (n = 2) Donor-site pain (n = 2)	Not reported	Physiotherapy and compression garments
Ciudad et al (2015) <sup>45</sup>	10	II-III	LE (n = 5) UE (n = 5)	VLNT	14.7	LE: 39.6% UE: 39.5%	Circumference	Partial skin graft loss (n = 1)	2.6-fold improvement in QoL	Revision surgery (n = 5)
Batista et al (2017) <sup>47</sup>	38 (23 with reduction data)	Not reported	LE	VLNT	25.2	46.3% (n = 15) 7.1% (n = 8)	Circumference	Minor complications (n = 11) including hematoma, seroma, and wound dehiscence with skin graft	Not reported	CDT
Gharb et al (2011) <sup>42</sup>	21	Ila	UE	VLNT	46	27.4%	Circumference	Partial flap necrosis (n = 2) Inguinal seroma (n = 2) Forearm cellulitis (n = 3)	Not reported	Physiotherapy
Patel et al (2015) <sup>51</sup>	25	Not reported	LE (n = 10) UE (n = 15)	VLNT	LE: 16.1 UE: 25.4	LE: 35.2% UE: 24.4%	Circumference	Not mentioned	Improvement in function, appearance, symptoms, and mood	None
Hou et al (2008) <sup>50</sup>	15	Not reported	UE	Autologous bone marrow stromal transplantation	12	81%	Circumference	Not mentioned	Reduced overall pain	Complex decongestive physiotherapy
Travis et al (2015) <sup>43</sup>	10	II-III	UE	Microvascular lymph node transfer	3	7.7%	Circumference	Donor-site seroma (n = 1)	90% functional improvement	Compression garments
Belcaro et al (2008) <sup>49</sup>	9	Not reported	LE	Autologous lymphatic tissue transfer	120	- 13%	Water displacement	None	Not reported	Compression garments, lymphatic drainage
Lin et al (2009) <sup>48</sup>	13	Not reported	UE	VLNT	56	50.6%	Circumference	Venous congestion (n = 1) Wound infection (n = 1)	Not reported	Not mentioned

Abbreviations: CDT, complete decongestive therapy; ISL, International Society of Lymphology; LE, lower extremity; UE, upper extremity; VLNT, vascularized lymph node transfer.





**Fig. 4** Forest plots of absolute volume reduction. CI, confidence interval; VLNT, vascularized lymph node transfer.

lipectomy to treat lower and upper extremity lymphedema in 26 patients.<sup>20</sup> Of the seven remaining studies, two combined liposuction with flap transfers,<sup>52,53</sup> two combined VLNT with microvascular breast reconstruction,<sup>54,55</sup> one combined VLNT with LVA,<sup>56</sup> one combined a modified Charles procedure with VLNT,<sup>57</sup> and one compared LVA and VLNT.<sup>58</sup> The two studies combining liposuction and flap transfer had a weighted average reduction of excess circumference of 70.8% (95% CI: 32.0–110%) with an  $I^2$  of 96.9%, which is significantly higher heterogeneity than you would expect by chance.<sup>52,53</sup> The forest plot is presented in **Fig. 2**. Three studies reported the ISL stage of patients, which varied widely due to the range of procedures performed in this group. Patients with ISL stage II lymphedema were included in one of the VLNT + liposuction studies,<sup>52</sup> and patients with ISL stage III lymphedema underwent the VLNT + modified Charles procedure.<sup>57</sup> In the study comparing LVA with VLNT, patients with ISL stages I to IIa underwent LVA, while patients with stages IIb to III underwent VLNT.<sup>58</sup> Five studies reported complications.<sup>20,53,55,57,58</sup> The most common complications were partial skin graft/skin flap loss, delayed healing, and donor-site lymphedema. Other complications in the combined approach studies included numbness, wound dehiscence, congestion in the skin paddle, infection, and venous thrombosis. All studies recommended use of compression garments postoperatively. In addition, two studies recommended physiotherapy,<sup>54,55</sup> one encouraged lymph drainage procedures,<sup>58</sup> and one suggested massage therapy.<sup>55</sup> The only study that included QoL outcomes showed improved QoL in the two presented case studies of patients receiving flap transfer with liposuction.<sup>53</sup> The eight high-quality combined approach studies had a mean  $\pm$  SD MINORS score of  $14.3 \pm 1.3$ .

## Discussion

Lymphedema is an incurable chronic disease associated with patient morbidity. Nonsurgical treatments, reductive, and physiologic procedures can decrease limb enlargement and improve QoL. The optimal treatment algorithm for lymphedema had been undetermined because of the difficulty in quantifying outcomes after an intervention. For example, an individual's limb diameter can fluctuate with changes in salt intake, fluid consumption, elevation, and use of compressive garments. Lymphoscintigraphy is a highly sensitive and specific study to diagnose but not quantify lymphedema.

The results of this study show that surgical management of lymphedema is effective for all clinical stages. LVA was found to be effective for ISL stages I to IIa or Campisi stages Ib to IIIb in which the lymphatic vessels are still able to transfer lymph fluid.<sup>31,58</sup> When reported, the rate of complications for LVA was 5.9%. Therefore, for early to mid-stages of lymphedema, LVA is the most appropriate choice due to its low complication profile and validated success. Although LVA requires at least partially functioning lymph connectors, VLNT can be performed with obstructed lymph channels. Ideally, this determination should be made at a preoperative visit via Tc-99m lymphoscintigraphy. Although VLNT improves lymphatic function in late-stage disease, there are considerable risks. When reported, the rate of complications for VLNT was 30.1%, suggesting that this invasive procedure should be reserved for only severe forms of lymphedema, typically ISL stages IIb to III.<sup>43,45,58</sup>

The effectiveness of lymphedema surgery is consistently enhanced in combined approaches. Given the varying degree of fibrosis and lymphatic damage in all stages of lymphedema, physiologic procedures to restore lymphatic fluid transit can

**Table 6** Overview of combined procedures for lymphedema

Study	Number of patients	ISL stage	Lymphedema site	Surgical procedure	Follow-up time (mo)	Volume or circumference reduction	Measurement technique	Complications	QoL	Additional interventions
Granzow et al (2014) <sup>20</sup>	26	Not reported	LE and UE	Suction-assisted lipectomy (n = 10) LVA (n = 8) VLNT (n = 8)	25	Suction-assisted lipectomy: 87% (LE) and 111% (UE) LVA/VLNT: subjective improvement in 88%	Circumference	Seroma drainage (n = 1) Delayed healing (n = 2)	Not reported	Compression garments
Nicoli et al (2015) <sup>52</sup>	10	II	UE	Liposuction with VLNT	6	91.5%	Circumference	None	Not reported	Compression garments
Qi et al (2009) <sup>53</sup>	11	Not reported	UE	Liposuction, myocutaneous flap transfer, and lymph-fascia grafting	26	51.5%	Circumference	Partial wound disruption (n = 2) Numbness (n = 2) Donor site lymphedema (n = 2)	Improved QoL reported in 2/2 case studies	Compression garments
Akita et al (2015) <sup>58</sup>	13	LVA: IIa VLNT: IIb-III (ISL)	LE	LVA or VNLT	LVA: 18.3 LVA: 15.1	Not reported	LEL index	VLNT: congestion in skin paddle (n = 3)	Not reported	Compression garments and lymph drainage procedures
Saaito et al (2012) <sup>54</sup>	9	Not reported	UE	VNLT and microvascular breast reconstruction	6	31.7%	Circumference	Not mentioned	Not reported	Physiotherapy, compression garments
Nguyen et al (2015) <sup>55</sup>	29	Not reported	UE	VLNT, microvascular breast reconstruction	11	48%	Circumference	Delayed wound healing (n = 3) Partial flap necrosis (n = 1) Venous thrombosis (n = 1) Donor site complications (n = 6)	Not reported	Physiotherapy, massage, compression garments
Koshima et al (2016) <sup>56</sup>	13	Not reported	LE	Lymphadiposal flaps/VLNT and LVA	28	Excellent response (n = 3) Good response (n = 6) No response (n = 4)	Not reported	None	Not reported	Compression garments
Sapountzis et al (2014) <sup>57</sup>	24	III (ISL)	LE	Modified Charles procedure with VLNT	14	100%	Circumference	Partial skin graft loss (n = 8) Partial skin flap loss (n = 1) Infection (n = 1)	Not reported	Compression garments

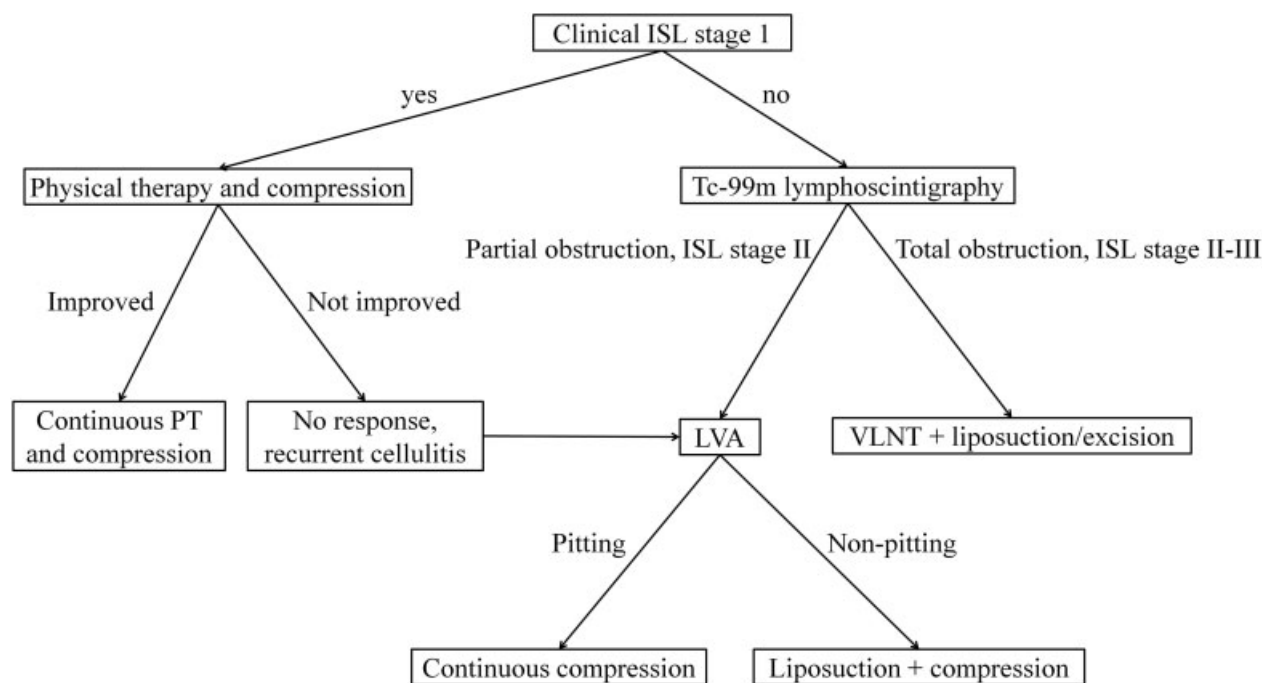
Abbreviations: ISL, International Society of Lymphology; LE, lower extremity; LVA, lymphovenous anastomosis; QoL, quality of life; UE, upper extremity; VLNT, vascularized lymph node transfer.

be enhanced by reductive operations to remove chronic adipose and scar deposition. In the two studies examining a combined VLNT and liposuction approach, the weighted average reduction of excess circumference was 70.8%.<sup>52,53</sup> However, the large  $I^2$  of 96.9% suggests that additional studies that are more homogenous in terms of patient selection and specific surgical procedures are needed to further examine the effectiveness of this combined approach. In four other studies that used VLNT as the primary surgical approach, additional liposuction or radical reduction with preservation of perforators was needed in an average of 31.6% of patients to adequately remove lymphedematous and fibrotic soft tissue, especially in the proximal limb.<sup>42,46-48</sup> Likewise, in two of the LVA studies, an average of 16.0% of patients required liposuction after the LVA procedure to achieve optimal volume reduction.<sup>41,59</sup> Although a combined physiologic and reductive approach is most effective for late-stage lymphedema, when reported, the rate of complications for excisional procedures was 39.3%. Thus, like VLNT, excision should only be considered in late-stage disease. However, given the low risks associated with liposuction, it can be safely combined with LVA when physical examination findings such as lack of pitting in the limb reveal any fibrosis and fat deposition. For all of the aforementioned approaches, all but one study recommended compression garments or physiotherapy postoperatively to maintain or further reduce limb volume.<sup>51</sup> The summary of these findings is presented in our evidence-based management algorithm (→ Fig. 5).

Previous reviews on the role of surgery in the treatment of lymphedema support the conclusions of our algorithm. Cormier et al conducted a review of the lymphedema surgery

literature and concluded that excisional procedures most effectively reduce limb volume or circumference but are accompanied by a considerable risk of morbidity. In their review, none of the surgical procedures eliminated the need for ongoing compression therapy.<sup>60</sup> Likewise, in a recent review on the surgical management of breast cancer therapy-related upper limb lymphedema, the authors found that liposuction combined with compression garments resulted in a sustained reduction of arm lymphedema. In terms of LVA, the need for preoperative and intraoperative lymphatic mapping was emphasized as well as the superior results in earlier stages of lymphedema.<sup>61</sup> The consistent efficacy of physiological approaches has also been demonstrated by Basta et al, whose meta-analysis showed a 48.8 and 56.6% reduction in excess limb circumference and volume, respectively, following lymphovenous shunt or lymph node transplantation procedures.<sup>62</sup>

Obesity-induced lymphedema (OIL) is a recently described form of lymphedema that develops when a patient's body mass index (BMI) reaches a critical threshold of 50 to 60 kg/m<sup>2</sup>.<sup>63</sup> Hypotheses for the cause of lymphatic dysfunction in OIL include (1) normal lymphatic vessels that are overwhelmed by increased lymph from the enlarged extremity or (2) lymphatics that have been injured from inflammation associated with increasing adipose deposition and fibrosis.<sup>64,65</sup> No studies describing management of OIL met the inclusion criteria for our systematic review. Although most patients with OIL have ISL stages II to III, our proposed lymphedema treatment algorithm may not apply to these individuals because of the unique characteristics of OIL. Excessive weight is the etiology of the condition; the primary treatment is weight loss. These patients with lymphedema



**Fig. 5** Lymphedema treatment algorithm. ISL, International Society of Lymphology; LVA, lymphovenous anastomosis; PT, physical therapy; VLNT, vascularized lymph node transfer.

induced by obesity would have acquired lymphedema after their BMI had risen to 50 to 60 kg/m<sup>2</sup> and should be referred to a bariatric surgical weight loss center. Massive weight loss may possibly result in the resolution of lymphatic dysfunction in a subset of patients with OIL.<sup>64</sup> If individuals still have lymphedema after weight loss, reductive and physiologic procedures can be considered; the surgical risk would be more favorable because of the lower BMI.

The biggest limitation of our study is the heterogeneity of the included studies in terms of patients' lymphedema stage and etiology, method of assessing surgical outcomes, and inconsistent reporting of complications and QoL outcomes. Despite this limitation, the included studies nevertheless support our management algorithm. Although all of the studies reporting QoL outcomes showed an overall improvement in function, symptom severity, and aesthetics following surgery, lack of consistent quantitative reporting prevents a comprehensive conclusion regarding which surgical approaches are associated with the greatest subjective improvements. To better delineate indications for LVA versus VLNT and validate our proposed algorithm, more head-to-head comparison studies that adopt an accepted staging system, such as the ISL system, are needed. In addition, randomized controlled trials with homogenous patient populations in terms of etiology and stage that compare surgical treatments to conservative therapies would help further define the most appropriate interventions for patients according to their clinical stage. Finally, further studies with a particular focus on patient follow-up will help improve the validity of lymphedema surgery research.

## Conclusion

Although the overall quality of the lymphedema surgery literature is fair, using the MINORS criteria is an effective method to isolate the highest quality research studies. These studies were used to develop an evidence-based algorithm to guide clinical practice and identify patients who may benefit from surgical management. With ongoing compression treatment, both reductive and physiologic approaches can safely and effectively treat lymphedema.

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