TITLE: Lymphatic-Venous Anastomosis for Lymphedema: Clinical and Cost-Effectiveness

DATE: 2 December 2013

RESEARCH QUESTIONS

1. What is the clinical effectiveness of lymphatic-venous anastomosis for the treatment of lymphedema?

2. What is the cost-effectiveness of lymphatic-venous anastomosis for the treatment of lymphedema?

KEY MESSAGE

One systematic review and 13 non-randomized studies were identified regarding the clinical effectiveness of lymphatic-venous anastomosis for the treatment of lymphedema. No cost-effectiveness information was identified.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2013, Issue 11), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. The search was also limited to English language documents published between January 1, 2008 and November 15, 2013. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are
presented first. These are followed by randomized controlled trials, non-randomized studies, and economic evaluations.

One systematic review and 13 non-randomized studies were identified regarding the clinical effectiveness of lymphatic-venous anastomosis for the treatment of lymphedema. No health technology assessments, randomized controlled trials, or economic evaluations were identified. Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

The identified information regarding the clinical effectiveness of lymphaticovenous anastomosis (LVA) was obtained from non-randomized studies. Reductions in lymphedema volumes\textsuperscript{2,3,4,11,13} or reductions in lymphedema severity\textsuperscript{12} in patients with secondary lymphedema were observed using the following types of LVA manipulation:

- LVA\textsuperscript{3-4,10-11,13}
- modified LVA\textsuperscript{11}
- lymphaticovenous side-to-end anastomosis (LVSEA)\textsuperscript{7}
- modified LVSEA\textsuperscript{5}
- supermicrosurgical (SM) LVA\textsuperscript{12,14}
- pi-shaped SM LVA\textsuperscript{2}
- low invasive scarless LVA\textsuperscript{9}

These reductions in lymphedema volume\textsuperscript{2,3,4,11,13} or reductions in lymphedema severity\textsuperscript{2} were observed in the upper or lower extremities,\textsuperscript{3-9,12-14} head and neck,\textsuperscript{2} or genitalia\textsuperscript{11} in patients with:

- breast cancer\textsuperscript{12,13}
- other cancers\textsuperscript{3,4}
- unspecified initial conditions.\textsuperscript{2,5-7,9-10,14}

Patency was maintained after LVA\textsuperscript{3,8} and modified LVSEA.\textsuperscript{5} In one study, this patency lasted up to 42 months.\textsuperscript{3} It also appeared that compliance with continuing complex decongestive physiotherapy after LVA or LVSEA was an important factor in maintaining long-term results.\textsuperscript{8,10} In addition, the authors of some studies concluded that LVA was promising\textsuperscript{8} or that clinical improvement was observed.\textsuperscript{6} No information was identified on the five- to ten-year clinical effectiveness of LVA. Table 1 highlights the specifics of the populations, LVA treatment, and conclusions relating to the identified studies.

No conclusions regarding the microsurgical treatment of secondary lymphedema were provided by the authors of the systematic review due to the methodological shortcomings of the available evidence.\textsuperscript{1} However, they highlighted the need for high quality studies due to consistent positive findings with respect to limb volume reduction.
# Table 1: Summary of Included Studies Regarding LVA Treatment in Patients with Lymphedema

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Initial Condition/Patient Population (n)</th>
<th>Lymphedema Location</th>
<th>LVA Type</th>
<th>Author Conclusions</th>
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<tbody>
<tr>
<td><strong>Systematic Reviews</strong></td>
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<td>Penha et al. 2013¹</td>
<td>Breast cancer/2⁰ lymphedema (n=NR)</td>
<td>Upper limbs</td>
<td>Unclear⁴</td>
<td>● Methodological shortcomings did not allow for conclusions</td>
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<td><strong>Non-Randomized Studies</strong></td>
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<td>Ayestaray et al. 2013²</td>
<td>JL/Chronic 2⁰ neck and head lymphedema (n=4)</td>
<td>Head and neck</td>
<td>pi-shaped SM LVSEA</td>
<td>● Effective at reducing skin tissue fibroids and lymphedema volume</td>
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</table>
| Boccardo et al. 2013³ | Melanoma in an extremity/2⁰ lymphedema (n=41) | Lower limbs | LVA | ● Significant reduction in leg lymphedema  
    ● Patency maintained at an average follow-up of 42 months in 35 patients  
    ● Lymphatic–venous multiple anastomoses was particularly successful when treating lymphedema early |
| Chang et al. 2013⁴ | Various cancers/2⁰ lymphedema (n=65) | Upper and lower limbs | LVA | ● Lymphovenous bypass may reduce lymphedema severity, particularly in early-stage upper extremity lymphedema |
| Yamamoto et al. 2013⁵ | Female patients with LEL (n=14 limbs) | Lower limbs | Modified LVSEA | ● Modified S-E anastomoses was not difficult and did not require revision  
    ● Modified S-E anastomoses showed good patency  
    ● LEL indices significantly decreased post-operatively  
    ● Modified S-E anastomoses efficaciously diverted lymph flow |
| Auba et al. 2012⁶ | NR/5 with LLL & 7 with ULL (n=12) | Upper and lower limbs | LVA | ● At 18 months follow-up:  
    ○ Some patients showed variable objective limb perimeter reduction  
    ○ Some patients showed subjective clinical improvement |
| Maegawa et al. 2012⁷ | NR/Pre-op CDP (n=31) | Lower limbs | LVSEA | ● LVSEA was able to reduce the volume  
    ● Volume reduction was not large  
    ● The need for postoperative CDP decreased in some patients |
| Maegawa et al. 2012⁸ | NR/Pre-op & post-op CDP (n=107) | Peripheral | LVSEA | ● LVSEA technique was found to be promising in treating lymphedema  
    ● Cumulative patency rates were 75% at 12 months and |
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| Mihara et al. 2012<sup>2</sup> | NR/ stage 0<sup>b</sup> in 3 patients; stage 1 in 3 patients (n=6) | Lower limbs | Low invasive scarless LVA | 36% at 24 months post-surgery
| Lee et al. 2011<sup>10</sup> | NR/ 2<sup>o</sup> lymphedema in clinical stage II and had received CDP for ≥1 year pre-op (n=32) | NR | LVA | ● LVAs more effective in 2<sup>o</sup> lymphedema vs 1<sup>o</sup> lymphedema in patients in earlier stages of lymphedema  
● Compliance with CDP was the most important factor in maintaining long-term results |
| Mukenge et al. 2011<sup>11</sup> | PRS following pelvic lymphadenectomy/External genital organ lymphedema (n=11) | Male genitalia | Modified LVA<sup>c</sup> | ● The modified LVA<sup>c</sup> resolved the lymphedema |
| Chang et al. 2010<sup>12</sup> | Breast cancer/2<sup>o</sup> lymphedema (n=16) | Upper limbs | SM LVA | ● SM LVA may be effective in reducing the severity of 2<sup>o</sup> lymphedema |
| Damstra et al. 2009<sup>13</sup> | Breast cancer/2<sup>o</sup> lymphedema (n=10) | Upper limbs | LVA | ● Minimal volume reduction of lymphedema after LVA |
| Demirtas et al. 2009<sup>14</sup> | NR/ NR (n=42) | Lower limbs | SM LVA + NOPT | ● SM LVA appeared highly beneficial in early stage lymphedema  
● Could be offered as the best option for certain patients |

<sup>2</sup> = secondary; CDP = complex decongestive physiotherapy; JL = jugular lymphadenectomy; LEL = lower extremity lymphedema; 
LVA = lymphaticovenular anastomosis/lymphatic-venous anastomoses; LVSEA = lymphaticovenous side-to-end anastomosis; 
NOPT = nonoperative physical therapy; NR = not reported; pre-op = preoperatively; post-op = postoperatively; PRS = pelvic radical surgery; S-E = side-to-end; SM = supermicrosurgical; vs = versus. 
<sup>a</sup> Unsure which procedure was performed. 
<sup>b</sup> Defined as subclinical. 
<sup>c</sup> “New microsurgical technique based on lymphovenous anastomosis between the collectors of the spermatic funiculus and the veins of the pampiniform plexus, allowing testicular lymphatic drainage.”<sup>11</sup>
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses


Randomized Controlled Trials
No literature identified.

Non-Randomized Studies


**Economic Evaluations**
No literature identified.

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APPENDIX – FURTHER INFORMATION:

Non-Randomized Studies – Lymphedema Prevention Studies


Review Articles


Case Studies


Additional References

