



Is immediate lymphatic reconstruction the future of lymphedema prevention?

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Breast cancer-related lymphedema is a type of secondary lymphedema that may occur as a long-term complication after tumor or lymph node resection, leading to lymphatic fluid accumulation and fibrosis, affecting approximately 29% to 49% of patients who undergo axillary lymph node dissection (ALND) and 5–7% after sentinel lymph node biopsy (SLNB) (1,2). As a result, clinicians continue to study ways to prevent the onset or even cure of lymphedema and improve the lives of those who develop it (3).

Several ongoing studies aim to address the risk factors that contribute to the disease before its onset. Immediate lymphatic reconstruction (ILR) is a direct shunting of the lymphatic drainage to the venous system immediately after ALND, aiming to prevent fluid backup (4). Authors like Boccardo *et al.* found that this kind of approach is safe with their study using the lymphatic microsurgical preventive healing approach (LYMPHA), however, there needs to be more evidence about long-term effects to back up the use of these procedures in clinical practice (5,6).

The study by Coriddi *et al.* focuses on ILR as a preventive measure (7). This study is a randomized controlled trial in

which the authors selected female patients between the ages of 18 and 75 years, treated at Memorial Sloan Kettering Cancer Center, who underwent unilateral ALND or SLNB with a high likelihood of needing ALND, and immediately after, they evaluated if the patients had transected lymphatic channels and had a suitable vein for bypass. The patients who fulfilled these criteria were randomized to undergo ILR by connecting the transected lymphatic channels to a vein, the ones who did not, underwent lymph channel clipping. Excluded patients were males with breast cancer and females with bilateral SLNB or treatment for recurrent disease in the axilla or the lack of a vein or unavailable lymph channel for the bypass. The authors also measured patient-reported outcomes using questionnaires for lymphedema quality of life, upper extremity lymphedema, and depression and anxiety related to it (7).

These types of studies are very important to advance in the prevention and treatment of lymphedema and to measure which interventions should be done to decrease the impact of lymphedema in breast cancer survivors. We congratulate the authors and appreciate their contribution

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to our field. To follow the future results of this study, we would like to emphasize some crucial points regarding the ILR approach mentioned in the paper.

First, we wonder if there are any differences among the surgeons in their rate of finding suitable veins and lymphatic channels intraoperatively and if they performed any tests on the lymphatic system to verify if they were functional before proceeding with the bypass. Additionally, we would like to know if they tested the anastomosis using any contrast agents before ending the procedure since it's important to make sure that despite finding the vessels and connecting them, the anastomosis was patent (8-10).

Secondly, it is important to consider the lack of blinding for both surgeons and patients. Due to the nature of the procedure, the surgeon cannot be blinded, which makes them susceptible to biases such as observer bias. As for the patients, they are susceptible to the Hawthorne effect, where patients change their behavior because they know they are being observed, this might explain why the patients who did not get the procedure were more diligent in their use of compression garments (11,12). Biases could be reduced if the person in charge of follow-ups is blinded to the patient's treatment.

Additionally, it wasn't stated what type of breast reconstruction was performed or if they had breast reconstruction at all. It is still controversial whether autologous reconstruction provides better lymphatic drainage than implant-based reconstruction. Nonetheless, in previous studies, patients who underwent any type of breast reconstruction had a lower rate of lymphedema than those who only had a mastectomy, and this could be a confounder as to whether the lymphedema rate is lower due to the ILR or the reconstruction (13).

As for the follow-up period, less than two years is still short-term, it is important to continue to follow the patients because it is still unclear if this procedure prevents lymphedema in the long term or if it just delays its onset, in the latter scenario it opens a debate about whether these immediate preventive interventions should be done or necessary.

Even with the challenges that lymphedema research faces, we are excited to have these contributions to our field and we hope that the future results from this RCT help unveil some of the questions that persist. We thank again the authors for their commitment to this rigorous and well-done study.

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