Early detection of breast cancer-related lymphoedema

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Position

The Australasian Lymphology Association (ALA) endorses the need for all patients treated for breast cancer to have access to:

1) an educational program informing them about lymphoedema, and
2) a prospective monitoring program for changes indicative of developing breast cancer-related lymphoedema.

Early detection of changes indicative of developing lymphoedema, and immediate conservative treatment, may reduce the long-term physical and functional impacts caused by progression and establishment of the condition.

All patients treated for breast cancer should undergo pre-operative measurements of their arm as well as receive education on lymphoedema, its risk factors, early signs of its development and a point of contact for clinical assessment if needed. For those who are at higher risk of developing breast cancer-related lymphoedema, monitoring should begin post-operatively and continue at regular intervals for at least two years.

Context and overview

Lymphoedema is a possible outcome from necessary, curative treatment for breast cancer. Lymphoedema manifests as a chronic swelling of a limb or body region, for which the complete underlying causes are not yet clear. Secondary to breast cancer treatment, lymphoedema can develop, in part, due to the disruption to the lymphatic system or an increase in lymphatic fluid beyond the capacity of the lymphatic system. In its early stages, lymphoedema presents as a soft, fluid-filled increase in limb size or volume. For some patients, the disease progresses, resulting in changes in the tissue architecture with the infiltration of fatty tissue and fibrosis. Conservative management of lymphoedema once it has progressed to these later stages is challenging.

Approximately 20% of patients who undergo an axillary lymph node dissection and 5% of those who undergo a sentinel node biopsy will develop breast cancer-related lymphoedema of the arm. Hand, breast and truncal lymphoedema may also develop, in combination with, or independently from arm lymphoedema. Most patients who develop lymphoedema will do so within the first two years post-surgical intervention for breast cancer. However, the risk of developing breast cancer-related lymphoedema is lifelong.

Breast cancer-related lymphoedema inflicts a significant cost to both the individual and health care system. Costs to the individual include reductions in quality of life, increases in anxiety/depression, decreases in physical function as well as an economic impact. For the patient, ongoing treatment is required to prevent worsening of the condition but is frequently minimally subsidised, requiring large out of pocket expenditures. For the health care system, those with lymphoedema are at a higher risk of cellulitis, a skin infection that may require costly, in-patient antibiotic treatment (for more information, see the ALA position statement on cellulitis).

Early detection of small changes in lymph fluid levels and limb size, indicative of developing lymphoedema, allows treatment to begin while the disease is potentially reversible. There is growing evidence that commencing conservative treatment at the first signs of the development of swelling may prevent the progression of lymphoedema to a later, established and less treatable, stage. Monitoring or surveillance programs, commenced before surgery, improve the ability to detect early signs of developing breast cancer-related lymphoedema.

Considerations in the development of prospective monitoring programs for breast cancer-related lymphoedema

Who should be monitored for breast cancer-related lymphoedema? Risk factors for developing breast cancer-related lymphoedema

It is currently unclear who is at the greatest risk for the development of breast cancer-related lymphoedema. Identification of high-risk groups could lead to targeted education and screening programs for those patients, while reducing the burden of worry for those at lower risk of development.
Some risk factors for the development of lymphoedema have been identified repeatedly, while for others, the findings are less clear.

Clearly identified risk factors for the development of breast cancer-related lymphoedema include:

- The extent of lymph node dissection. Those who undergo axillary lymph node dissection are at higher risk of developing breast cancer-related lymphoedema than those who undergo sentinel node biopsy.4, 6
- Radiotherapy, particularly when targeted to the axilla. Those who have radiotherapy targeted at the axillary lymph nodes or their approximate location are at higher risk than those who have radiotherapy to other regions;13, 16
- Increased body mass index (BMI) at the time of surgery. A higher BMI at the time of diagnosis or surgery for breast cancer increases risk of developing lymphoedema, regardless of the extent of axillary surgery.4, 15, 17

For those who undergo axillary lymph node dissection, taxane-based chemotherapy,17 and early swelling4 after surgery appear also to be predictive of the development of lymphedema. Other risk factors for development of lymphoedema, particularly for those who have a sentinel node biopsy are not clear. The risk factors identified to date do not fully explain who will develop lymphoedema.6

Risk assessment tools, calculators as well as machine learning platforms are currently being trialed and appear to have good initial discriminatory abilities to assist in determining an individual’s risk of developing lymphoedema.4, 12, 13 With future development, these tools will improve clinicians’ ability to give targeted risk information to patients in the future.

At this time, all patients at risk of lymphoedema should be, at minimum, informed of the risk of developing lymphoedema, what changes they may experience if lymphoedema is developing as well as who to contact if they are concerned.6

**How should breast cancer-related lymphoedema be screened?**

**Assessment of breast cancer-related lymphoedema in screening and detection.**

Currently there is little agreement on which measurement tool(s), or diagnostic thresholds for those tools, should be used to both screen for or diagnosis a patient with developing breast cancer-related lymphoedema.20 A differentiation should be made between a screening assessment and a diagnostic assessment.

A screening program should involve a concise assessment using measurement tools and thresholds that have high sensitivity for the assessment of developing swelling. High sensitivity means that the tool or threshold is more capable of determining who does not have the condition.21 The screening assessment should also be brief to avoid burdening the patient and health system. In contrast, diagnosing lymphoedema, a more complete clinical assessment is usually required. This should focus on using tools or thresholds for diagnosis that demonstrate good specificity, meaning, they are stronger at determining who has the condition.21 Not all tools or thresholds do, or should, have both high sensitivity and specificity.20

The most commonly used clinical measurement tools and methods in Australasia that could be appropriate in a screening program include:

- **Circumference-based assessment**: determines the size or volume of an areas of the limb using a non-stretch tape measure or light (Perometer®). Measurements are made at a single site, for example a point perceived to have swelling, or at pre-defined points along the arm. The ALA provides a standardised assessment form and measurement guidelines. Circumference measurements may then be converted into a volume using a geometric formula. Outcomes may be presented in numerous forms but most frequently used include the inter-limb circumference or volume difference, or percent change from a previous measurement.22
  - Circumference/volume assessments may be undertaken with a tape measure or using a Perometer®.

- **Bioimpedance spectroscopy (BIS)**: provides a measurement of the volume of extracellular fluid, of which lymphatic fluid is a component. To complete the measurement, a small, harmless current is passed through the tissues.23 At a low frequency, the current is unable to pass through the cells, resulting in passage through the extra-cellular fluid. The resistance the current faces is inversely proportional to the amount of fluid present. Outcomes are traditionally presented as a ratio of the unaffected limb to affected limb.24 The most commonly used bioimpedance tools in Australia have normalized this ratio to a scale (LDex™ by Impedimed®).

Recent prospective monitoring studies have used a range of thresholds to trigger commencement of lymphoedema treatments.25, 12, 13, 25 When pre-operative measurements are available, a threshold related to the change in size or impedance is likely more sensitive to small changes than an absolute threshold. If pre-operative measurements are not available, normatively-determined thresholds, statistically determined from a population without breast cancer or lymphoedema, should be used20 and have been determined for both circumference measurements and BIS and are available.24, 26
Other assessment methods, including tissue dielectric constants (TDC)\textsuperscript{27}, palpation for pitting oedema, imaging such as lymphoscintigraphy\textsuperscript{28} or indocyanine green (ICG) lymphography\textsuperscript{29}, or patient reported symptoms,\textsuperscript{30} may also provide useful information in a screening assessment; however when and how these tools and their outcomes are best utilized is currently unknown.

**What should a prospective monitoring program encompass?**

*Evidence for the structure of a prospective monitoring program*

Numerous models of prospective screening programs have been investigated.\textsuperscript{10, 31, 32} Common features among investigated programs include:

1. Pre-operative assessment of all patients using circumference/volume and/or bioimpedance measurements
2. Regular post-operative assessments for patients at higher risk of lymphoedema development, such as patients who have undergone axillary lymph node dissection. While the optimal schedule is not yet known, most programs studied include more frequent assessments in the first 12 months post-operatively, with reducing frequency out to at least two years post-operation.
3. Once developing lymphoedema is suspected, either due to patient concern or the objective assessment outcome crossing a pre-determined threshold, there should be a referral pathway for specialist lymphoedema care. Optimal initial care is unknown; however, recent studies involving ready to wear compression garments and/or home exercise programs show promise.

**ALA recommendations**

Based on the currently available evidence, at this time, the ALA recommends that:

- All patients be pre-operatively assessed using circumference (volume) measurements and/or bioimpedance spectroscopy.
- These measurements should be provided to the patient for ongoing monitoring where available/convenient.
- All patients should receive information about the possibility of developing lymphoedema as well as the early signs and symptoms and the known risk factors.\textsuperscript{6}
- Patients who are deemed to be at high risk for the development of breast cancer-related lymphoedema should be monitored more regularly during the first year, and then at regular intervals for one more year.
- Patients who are deemed to be at lower risk for the development of breast cancer-related lymphoedema should be provided with information about who to contact if they have concerns about lymphoedema.

**Barriers to implementing these recommendations**

Major barriers currently exist in Australasia to allow the implementation of these recommendations including: lack of lymphoedema services in public hospitals; low awareness of lymphoedema among health care professionals; insufficient training of health care professionals to educate patients and/or monitor and subsequently treat patients who do develop lymphoedema.

**The questions that remain**

Currently, there is a lack of evidence to support optimal clinical decision making in the prevention and early management of lymphoedema. Future research into these, and other areas, could influence the recommendations in the future. Particular areas of future research should include:

1. What is the optimal schedule for monitoring for lymphoedema and how long should this period continue?
2. What is the role of prophylactic treatment during high-risk periods in preventing development of lymphoedema?
3. What are other modifiable risk factors for the development of lymphoedema?
4. What is the optimal threshold for detection of developing lymphoedema, particularly when a pre-operative measurement is completed?
5. What is the optimal initial treatment for developing lymphoedema?

Funding of future research into these areas should be prioritised to ensure development of best practice in the prevention, detection and initial treatment of breast cancer-related lymphoedema.

Disclaimer: This Position Paper replaced the previous Position Statement: Monitoring for the early detection of breast cancer-related lymphoedema – October 2012.
References


