Breast cancer-related arm lymphoedema: a critical unmet need

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One in five women treated for breast cancer develop breast cancer-related lymphoedema (BCRL),[1] with subsequent profound impact on individuals and the healthcare system. Further, there is no known cure for lymphoedema, and it is costly to manage, imposing inequitable financial burdens. Contemporary management seeks to reduce impact and prevent progression. Unfortunately, advancement in lymphoedema care has been constrained by a lack of investment in lymphoedema services, underpinned by a limited research base, misunderstanding of lymphoedema prevalence and failure to recognise its associated morbidity. We appreciate the focus by the recently published MASCC clinical practice guidance for the prevention of BCRL as a critical unmet need.[2]

The BCRL prevention guidance identified by Wong et al.[2] was derived through the use of a Delphi consensus process, which is useful for those areas with limited research.[3] However, for over 50 years, international and national lymphoedema organisations have supported and disseminated lymphology research, stimulated and strengthened cross-disciplinary lymphology collaborations and networks, upskilled the workforce and educated consumers (people at risk or living with lymphoedema). These organizations have used the growing evidence base to guide, revise, update, and publish lymphoedema measurement, prevention, and management guidelines.[4–8] While the newly published MASCC guidance largely support existing recommendations by lymphology associations, there are some notable points in the Wong et al. paper worthy of further discussion.

Through epidemiological, as well as clinical trial research, understanding of potential BCRL risk factors and prevention strategies has improved considerably over the past decade. This evidence has been included in systematic reviews and meta-analyses, which in turn enables high-quality research evidence rather than consensus to guide identification of characteristics associated with the greatest increased (or decreased) risk of BCRL.[1,9] Treatment characteristics, in particular more extensive lymph node removal, continue to dominate as risk factors. Access to prophylactic lymphatic reconstruction or axillary reverse mapping to counteract treatment-induced increased risk is limited - typically only available to those who can access and afford these specialist services. Further, the known risk factors (individually or collectively of all types) cannot accurately predict who will develop BCRL and who will not. Yet, the MASCC guidance states that when there are resource limitations, interventions to prevent BCRL should be prioritised according to body mass index, type of radiotherapy and when 15 lymph nodes or more are removed as part of breast cancer treatment. This recommendation does not consider variance explained by this specific group of risk factors (which is likely <35%),[1] nor does the recommendation consider the potential for more cost-effective and feasible strategies particularly in fiscally-, workforce-, or resource-restrained settings. Other strategies with potential high impact could include, but are not limited to, improved patient education on the signs and symptoms of BCRL requiring follow-up, workforce education on lymphology and related disorders, or the integration of a symptom screening tool among patient follow up.

Over the past 20 years, research advancements have occurred in BCRL assessment (timing and method), and diagnostic thresholds.[4–6] This research has informed best practice guidelines by lymphoedema societies, which have endorsed prospective surveillance of lymphoedema and potential modes of treatment

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(in particular compression). While there is emerging evidence to support compression as a potential prevention strategy, there is also research that does not demonstrate benefit.[10] Future research needs to establish the effect in an adequately-powered trial, as well as acceptability, feasibility and duration of using compression in the prevention setting before use of prophylactic compression can be recommended for integration among clinical practice. In addition, we need to be certain that the potential for harm from prophylactic compression (e.g., through the use of ill-fitting garments, adverse psychological impact of increased attention to the at-risk limb and associated costs) does not outweigh any potential benefit. Thus, the guidance around use of compression for the prevention of BCRL may be premature. Concurrently, it is unclear why the MASCC guidance did not endorse (or explore consensus) use of exercise therapy in the prevention of BCRL. Strong evidence is available to support the safety and feasibility of exercise therapy post-breast cancer, as well as its efficacy in reducing risk of lymphoedema for those who have had five + nodes removed as part of breast cancer treatment (RR, 0.49; 95% CI, 0.28–0.85).[11]

There is much work to be done to inform practical, sustainable, equitable, cost-effective, and research-supported lymphoedema prevention and management strategies to improve lives of those with breast cancer. This research needs to involve all relevant stakeholders – consumers, healthcare professionals, lymphoedema societies and advocates, researchers, educators and policy-makers – to produce the most collaborative, meaningful advancements. We applaud the efforts of Wang et al., and welcome all who strive to improve the field of lymphology.

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Declaration of interests

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References

1 DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol*. 2013;14(6):500–515. https://doi.org/10.1016/S1470-2045(13)70076-7.
2 Wong HCY, Wallen MP, Chan AW, et al, MASCC BCRAL Expert Panel and the Oncodermatology and Survivorship Study Groups. Multinational Association of Supportive Care in Cancer (MASCC) clinical practice guidance for the prevention of breast cancer-related arm lymphoedema (BCRAL): international Delphi consensus-based recommendations. *EClinicalMedicine*. 2024;68:102441. https://doi.org/10.1016/j.eclinm.2024.102441.
3 Nasa P, Jain R, Juneja D. Delphi methodology in healthcare research: how to decide its appropriateness. *World J Methodol*. 2021;11(4):116–129. https://doi.org/10.5662/wjm.v11.i4.116.
4 Executive Committee of the International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2020 consensus document of the international society of lymphology. *Lymphology*. 2020;53(1):3–19.
5 Martínez-Jaimez P, Fuster Linares P, Piller N, et al. Multidisciplinary preventive intervention for breast cancer-related lymphedema: an international consensus. *Eur J Cancer Care*. 2022;31(6):e13704. https://doi.org/10.1111/ecc.13704.
6 Armer JM, Ostby PL, Ginex PK, et al. ONS Guidelines™ for cancer treatment-related lymphedema. *Oncol Nurs Forum*. 2020;47(5):518–538. https://doi.org/10.1188/20.ONF.518-538.
7 Lymphoedema Framework. Best practice for the management of lymphoedema. In: *International consensus*. London: MEP Ltd; 2006. https://www.lympho.org/uploads/files/files/Best_practice.pdf. Accessed February 22, 2024.
8 Australasian lymphology association position statements and guidelines. https://www.lymphoedema.org.au/about-lymphoedema/position-statements/.
9 Shen A, Lu Q, Fu X, et al. Risk factors of unilateral breast cancer-related lymphedema: an updated systematic review and meta-analysis of 84 cohort studies. *Support Care Cancer*. 2022;31(1):18. https://doi.org/10.1007/s00520-022-07508-2. PMID: 36513801.
10 Bundred NJ, Barrett E, Todd C, et al, Investigators of BEA/PLACE studies. Prevention of lymphoedema after axillary clearance by external compression sleeves PLACE randomised trial results. Effects of high BMI. *Cancer Med*. 2023;12(5):5506–5516. https://doi.org/10.1002/cam4.5378. Epub 2022 Dec 12. PMID: 36507561; PMCID: PMC10028125.
11 Hayes SC, Singh B, Reul-Hirche H, et al. The effect of exercise for the prevention and treatment of cancer-related lymphedema: a systematic review with meta-analysis. *Med Sci Sports Exerc*. 2022;54(8):1389–1399. https://doi.org/10.1249/MSS.0000000000002918.