

Title:

Prognostic significance of secondary lymphoedema following breast cancer

Abstract:

Background: While the adverse impact of lymphoedema on quality of life is clear, its potential relationship with survival has, to date, not been investigated. This work examines the effects of lymphoedema on overall survival (OS) following breast cancer (BC).

Methods: A population-based sample of Australian women (n=287) with diagnosed, invasive, unilateral BC, were prospectively observed for a median of 6.6 years. Lymphedema was assessed six months post-diagnosis using bioimpedance spectroscopy. OS was measured from date of diagnosis to date of death or date of last follow-up. The Kaplan-Meier method was used to calculate survival. Risk ratios (RR) and 95% confidence intervals (CI) for the association between lymphedema and OS were obtained using Cox proportional hazards survival models.

Results: A total of 27 (9.4%) women died during the follow-up period. Lymphedema was significantly associated with OS (log rank $P=0.024$), with the median survival for those with and without lymphedema being 78.1 and 83.6 months, respectively (RR=2.91; 95% CI: 1.10, 7.70; $P=0.031$). This association persisted following adjustment for established prognostic factors (such as age, tumour size and grade, extent of surgery and adjuvant therapy received), with the relative risk ranging between 2.84 (1.00, 8.18) and 4.25 (1.41, 12.84), depending on particular characteristics within the model.

Discussion: These represent compelling findings, demonstrating that lymphedema is crucial for *quantity* as well as *quality* of life following breast cancer treatment. Furthermore, findings highlight the potential importance of routine monitoring for lymphedema following BC treatment and the need for *evidence-based* prevention and treatment strategies.