Breast cancer-related lymphedema

Prevalence and prognostic significance six years after diagnosis

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▲ Background

Upper-body morbidity, including lymphoedema, is common after breast cancer and can persist well beyond the immediate treatment period, negatively impacting physical function and quality of life (1-2). The initial phase of lymphoedema is characteristed by abnormal swelling and occurs when the demand for lymphatic drainage surpasses the capacity of lymphatic flow (3). These areas of lymph congestion and alterations in lymph flow may be associated with changes in immunological profile and function (4), potentially influencing survival (5). However, the relationship between lymphoedema and survival has not previously received research attention. The aim of this study was to determine the prevalence of lymphoedema and related upper-body morbidity, six years following breast cancer diagnosis and to examine the prognostic significance of lymphoedema in relation to overall 6-year survival.

Methods and Results

A population-based sample of Australian women (n = 287) diagnosed with invasive, unilateral breast cancer in 2002 was followed for a median of 6.6 years and prospectively assessed for lymphoedema, upper-body symptoms and vital status. The baseline measure occurred at six months post-diagnosis and women were prospectively followed until six years post-diagnosis. Lymphoedema was assessed using bioimpedance spectroscopy (BIS), sum of arm circumferences (SOAC), and self-reported arm swelling. A woman was classified as having lymphoedema via BIS when the impedance ratio was more than three standard deviations above normative data or when the difference between the SOAC for the treated side was greater than 5cm of the SOAC for the untreated side. Data were available for 183 women at the six year follow-up. Overall survival for all 287 women was measured from the date of diagnosis to date of death or last follow-up (April 2009). Kaplan-Meier statistics were used to calculate overall survival and Cox proportional hazards models quantified the risk associated with the cumulative burden of lymphoedema (between 6 and 18 months post-diagnosis) and overall survival at follow-up. Model estimates were adjusted, one at a time, for known markers of breast cancer prognosis. Approximately 45 % of women reported at least one moderate to extreme upper-body symptom at the 6 year follow-up. Numbness and weakness were the most prevalent symptoms reported by 15.6 % and 13.8 % of women, respectively. The point prevalence of lymphoedema at 6 years was 6.5 % using BIS, with 22 % of women self-reporting arm swelling. Cumulatively, clinical evidence of lymphoedema was recorded in 34 % of women and 48 % reported arm swelling at least once since baseline assessment. Twenty-seven (9.4 %) women died during the follow-up period, and lymphoedema, assessed by BIS or SOAC between 6–18 months post-diagnosis, was associated with mortality (BIS: HR= 2.5; 95 % CI: 0.9, 6.8, p = 0.08; SOAC: 3.0; 95 % CI: 1.1, 8.7, p = 0.04). There was no association (HR = 1.2; 9 5% CI:

Lymphedema	n (%)[a]	Deaths (n)	Bivariate Cox Regression		
			HR	(95 % CI)	p-value
BIS					0,08
No	128 (67,4)	7	1,00	–	
Yes	62 (32,6)	8	2,48	(0,90; 6,83)	
SOAC					0,04
No	154 (79,0)	8	1,00	–	
Yes	41 (21,0)	6	3,03	(1,05; 8,73)	
selbst berichtet[b]					0,68
No	154 (55,2)	13	1,00	–	
Yes	125 (44,8)	12	1,18	(0,54; 2,58)	

a Sample sizes differ based on data available to determine lymphoedema status.
b Self-reported arm swelling.
Abbreviations: HR = hazard ratio; HR>1 indicates an increased risk of death; BIS, bioimpedance spectroscopy; SOAC, sum of arm circumferences.

Tab. 1. The relationship between cumulative burden of lymphoedema between six and 18 months following breast cancer diagnosis and overall 6-year survival.

0.5, 2.6, p = 0.68) between self-reported arm swelling and overall survival.

Conclusions

These preliminary findings suggest that lymphoedema may be associated with survival following breast cancer treatment and may be independent of other known indicators of disease such as stage of breast cancer, type of treatment or other personal characteristics. Although the statistical power of this work was limited, further investigation in other cancer cohorts and explication of the potential underlying biology is warranted.

References

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