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CLINICAL TRIAL

Effect of air travel on lymphedema risk in women with history of breast cancer

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Abstract To assess the impact of air travel on swelling of the 'at risk' arm of women treated for breast cancer. Women treated for breast cancer from Canada ($n = 60$) and from within Australia ($n = 12$) attending a dragon boat regatta in Queensland, Australia participated. Women were measured within 2 weeks prior to their flight, on arrival in Queensland and, for 40 women travelling from Canada, measured again 6 weeks following return to Canada. Changes to extracellular fluid were measured using a single-frequency bioimpedance device (BIA). Each arm was measured separately using a standardized protocol to obtain the inter-limb impedance ratio. An increase in the ratio indicates accumulated fluid. Information regarding medical management of participants' breast cancer, use of compression garment and history of exercise were also obtained. For most women (95%), air travel did not adversely affect the impedance ratio. The BIA ratio of long-haul travellers was 1.007 ± 0.065 prior to the flight and 1.006 ± 0.087 following the flight. The ratio of short-haul travellers was 0.994 ± 0.033 and following the flight was 1.001 ± 0.038. Air travel did not cause significant change in BIA ratio in the 'at-risk' arm for the majority of breast cancer survivors who participated in dragon boat racing. Further research is required to determine whether these findings are generalizable to the population of women who have been treated for breast cancer.

Keywords Lymphedema · Breast cancer · Airplane travel

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Introduction

One adverse outcome of treatment for breast cancer is lymphedema. The inability to identify reliably the precipitating factors that cause lymphedema to appear or worsen has served to foster fear and frustration in women who may be at risk by virtue of prior breast cancer [1, 2]. Many patient education materials continue to promulgate behavioural and lifestyle adaptations purported to limit or minimize risk of lymphedema [3]. Much of this information is, however, unsubstantiated or anecdotal, lacking any evidence-base, thereby providing little guidance for the clinician. One issue for which women seek guidance but for which there is no evidence is whether air travel will cause or exacerbate lymphedema [4].

It is conjectured that air travel will exacerbate or cause lymphedema due to the relatively rapid change in pressure and the sustained lower cabin pressure [5]. There are, however, only two published studies, excluding a single case study [6], on air travel and lymphedema [4, 7]. Both were retrospective and used only self-report. No prospective studies have been conducted to date.

The aim of this study was to describe prospectively the effect of air travel on extracellular fluid (ECF), measured by impedance analysis, in the 'at risk' upper limb of women treated for breast cancer. We took advantage of Dragons Abreast International Dragon Boat Regatta, held in Caloundra, Queensland, Australia to assess prospectively the effect of air travel on lymphedema risk in the upper limbs of women treated for breast cancer.

Methods

Participants

Women who had been treated for breast cancer and were attending the Dragon Boat Regatta in Caloundra, Queensland were eligible to participate. Women were excluded if they were pregnant or fitted with a pacemaker. Data were obtained from 60 women travelling internationally from Canada, and from 12 women travelling domestically within Australia. Forty women from Canada were available for follow-up measures approximately 6 weeks following their return to Canada. Flights from Canada to Queensland were approximately 18 h duration whereas the domestic flights were <4 h duration. The women ranged in age from 44 to 69 years. Forty-seven women had undergone mastectomy and 25 had undergone wide local excision. Fifty-three women had undergone axillary node dissection, eight had undergone sentinel node biopsy, four had undergone no axillary surgery and seven were unsure of surgery to the axilla. Participant characteristics are shown in Table 1. Notably, this group of women was unique as all were training, albeit at different intensities, in dragon boat racing. Women rated their training intensity on a three-point scale in which one was equivalent to low intensity, two was equivalent to moderate intensity and three was equivalent to high intensity. The mode on a three-point scale of self-reported intensity of training was 3, i.e. high intensity. Data from three women travelling from Canada who had undergone bilateral breast surgery and from five women in whom two of three measures of lymphedema or details regarding breast surgery were missing were excluded from any analysis. Ethical approval for this study was obtained from the University of Sydney and from the Alberta Cancer Board and all women provided written informed consent before assessment commenced.

Protocol

Baseline assessments were performed within 2 weeks prior to flying to Australia for Canadian participants and within 1 week for Australian travellers. Information regarding their surgery, subsequent treatment (chemotherapy, radiotherapy and/or hormone therapy), training schedules, height and hand dominance were obtained from participants and verified with medical records where possible. The inter-limb difference in upper limb ECF was determined using a single frequency bioimpedance analysis (BIA) [8, 9]. As soon as practicable (i.e. within 24 h) after arrival in Caloundra, the participants completed their second assessment. This included confirming their flight details and determining their use of a compression garment during the flight. Information was also obtained on their training regimen prior to travel. A second BIA measure was then taken. Six weeks after returning home, the Canadian participants were reassessed with BIA. This time interval was chosen to minimize any acute effects of flying upon their 'at risk' arm.

Table 1 Participants' characteristics and medical management

	International $N = 60$	Domestic $N = 12$
Age[a]	58.9 ± 6.6	59.3 ± 4.0
Dominant side affected[b]	34 (57)	4 (33)
Breast surgery[b]		
Wide local excision	18 (30)	7 (58)
Mastectomy	17 (28)	4 (33)
Mastectomy + reconstruction	25 (42)	1 (8)
Axillary surgery[b]		
None	4 (6)	0 (0)
Sentinel node biopsy	7 (12)	1 (8)
Axillary node dissection	42 (70)	11 (92)
Unknown	7 (12)	0 (0)
Chemotherapy[b]—yes	33 (55)	5 (42)
Radiotherapy[b]—yes	44 (73)	9 (75)
Hormone therapy[b]—yes	29 (48)	4 (33)
Compression garment on flight[b]—yes	12 (20)	3 (25)
Exercise sessions/week[b]		
≤2	36 (60)	7 (58)
≥3	24 (40)	5 (42)
Exercise intensity[b]		
1. Nil-Low	5 (8)	0 (0)
2. Medium	16 (27)	4 (33)
3. High	39 (65)	8 (67)

[a] Mean ± standard deviation

[b] Number of participants (percentage of group)

Bioimpedance analysis (BIA)

BIA was used as our outcome measure for the effect of air travel on lymphedema status. BIA has previously been shown to be an accurate method for determination of accumulation of ECF characteristic of lymphedema [8, 9]. We have also shown that the intra-rater reliability is very

Table 2 Inter-arm BIA ratios at each time point and absolute change from baseline

	Baseline	Post	Follow-up	Δ Post-baseline	Δ Follow-up-baseline
Long haul ($n = 60$)	1.007 (0.990 to 1.024)	1.006[a] (0.983 to 0.029)	–	−0.01 (−0.033 to 0.013)	–
Short haul ($n = 12$)	0.994 (0.973 to 1.015)	1.001 (1.013 to 0.061)	–	0.007 (−0.025 to 0.039)	–
Long haul (subset measured at follow-up; $n = 40$)	1.009 (0.986 to 1.034)	1.010 (0.980 to 1.040)	1.015 (0.991 to 1.039)	−0.013 (−0.046 to 0.020)	0.005 (−0.011 to 0.021)

[a] Data missing on two participants

high ($ICC_{2,1} = 0.96$; 95% CI: 0.93–0.98) in a group of women with and without lymphedema ($n = 51$), measured on two occasions, 1 month apart [10].

BIA was performed using a single frequency impedance device specifically designed for lymphedema assessment (XCA, ImpediMed, Ltd.). BIA assessment of each arm, from the wrist to the axilla, was performed with the women in a supine, or for a few, in a relaxed sitting position, according to methods previously described [11]. Briefly, any jewellery was removed, the skin at the electrode sites was cleaned with an alcohol wipe and electrodes then applied. Placement of the electrodes was based on the equipotential principle, thereby standardizing limb length. Electrodes were placed on the dorsum of the wrists in line with the ulnar styloid, on the dorsum of the hands below the third digit, and on the dorsum of the right foot. Measurements were made first on the affected side and then on the unaffected side. Data are presented as a ratio of impedance.

Previous research by Cornish et al. [9] established cut-offs for determination of lymphedema: a ratio $\geq$1.139 for women in whom the surgery was on their dominant side and a ratio $\geq$1.066 for those in whom the surgery was on the non-dominant side was indicative of lymphedema. Alternatively, a change in BIA ratio greater than 0.100 from a pre- to post-measurement may also be considered indicative of a change in status, i.e. a worsening of the condition in someone who has lymphedema or at risk of lymphedema in someone who previously was below the cut-offs [9, 10].

Data analysis

The effect of airplane travel on the BIA inter-limb impedance ratio was determined using analysis of covariance (ANCOVA). The dependent variable was the difference in BIA ratio (post-baseline), and the independent variable was 'group' (domestic and international travel); baseline BIA ratio, age, occurrence of axillary surgery, radiotherapy and use of sleeve during travel were entered into the analysis as covariates. In addition, a paired *t*-test was undertaken on the Canadian women in whom we had collected follow-up data: their pre-travel data were compared to their follow-up data. Analysis was undertaken with SPSS vs17 and significance was set at $P < 0.05$.

Results

The impedance ratios for baseline, post-measures and follow-up are reported in Table 2. The mean change in BIA was 1% in women travelling from Canada and <1% in women travelling within Australia. Seven women, all from Canada, exceeded the impedance ratio cut-off for early detection of lymphedema at the 'post-travel' measurement. Three of these women exceeded this ratio prior to travel indicating four new cases (shaded grey areas of Fig. 1a, b). Follow-up of three of these four new cases revealed that the ratio had decreased to below the cut-off again in two women, representing one (and possibly two) new cases of lymphedema (Fig. 1c, d).

Examination of the percentage change in the impedance ratio from pre to post flight revealed that the post-travel impedance ratio increased from baseline by <1% in 38 women (54%); between 1 and 5% in 19 women (27%); between 5 and 10% in ten women (14%); and >10% in three women (4%) (Fig. 1e, f). In the group of women in whom the ratio increased by $\geq$5%, this increase in ratio was indicative of worsening of lymphedema in two women and instigating lymphedema in four other women. For the other seven women, their impedance ratio increased but remained within the 'normal', non-lymphedematous range.

Univariate analysis revealed no significant difference in impedance change scores between the women who travelled from Canada and those who travelled within Australia when medical treatments, and use of compression garments were accounted for within the model ($F_{1,64} = 0.41$; $P = 0.53$). None of the covariates, including use of compression garments (Fig. 2), contributed significantly to the model. In addition, paired *t*-tests revealed no significant difference in the impedance ratio between follow-up and the baselines scores for the 40 women from Canada for whom we had follow-up data ($t_{40} = 0.714$; $P = 0.48$).

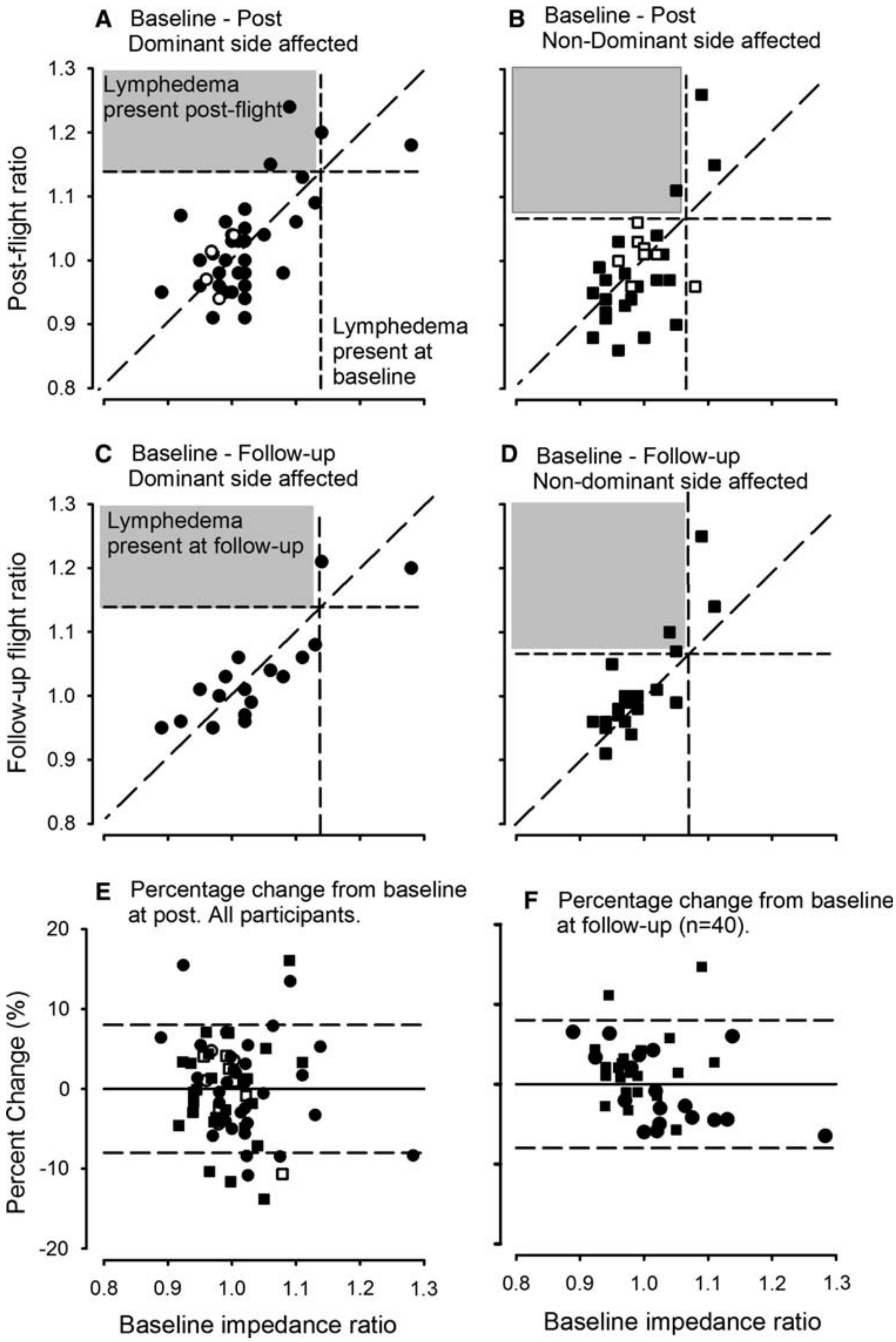

Fig. 1 Baseline impedance ratios plotted against post (**a**, **b**), follow-up (**c**, **d**) measures and respective percentage changes (**e**, **f**). *Filled symbols* long haul, *open symbols* short haul. **a**–**d** *Dashed lines* represent cut-offs for detection of lymphedema, *diagonal line* represents line of agreement. **e**, **f** *Solid horizontal line* represents no change, *dashed horizontal lines* indicate >10% change

Discussion

This is the first study to assess prospectively the short-term impact of air travel on lymphedema. For the majority of women we studied, the impedance ratio changed by less than 5%. Interestingly, few of the women in our study (7%) presented at the initial assessment with lymphedema, using an elevated bioimpedance ratio as the criterion. This is fewer than one might expect based on the reported incidence of lymphedema in breast cancer survivors. The reasons for this are unknown. Possibly, dragon boat racers are a self-selected cohort of those women who do not have lymphedema. Alternatively, it may be that this exercise provides a level of protection that would not be

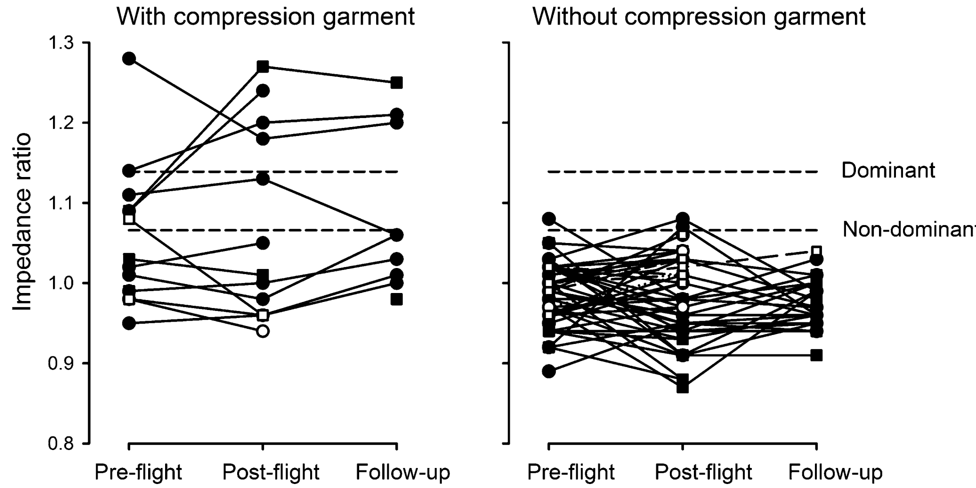

Fig. 2 Women categorized according to whether they used a compression garment during their flight to Queensland. Women above the 'cut-off' for their respective affected side (*dashed line*) are categorized as having lymphedema. *Circles* represent women in whom surgery was on the dominant side, *squares* represent women in whom surgery was on the non-dominant side. *Filled symbols* represent long-haul flights, *open symbols* represent short-haul flights

experienced by women who were not engaged in an upper-limb exercise programme [12, 13]. It has been theorized that exercise enhances lymph flow, improves protein resorption and generally improves flexibility of soft tissue thereby reducing the secondary impact on blood and lymph obstruction [14, 15]. To date, there is no evidence that exercise reduces lymphedema [12, 13] but it may protect against a worsening of the condition [16]. Vigorous training may have built up the tolerance of the lymphatics so that factors which impact on the lymphatics, e.g. change in airplane pressure and/or prolonged exposure to low cabin pressure, did not have a large effect. To determine the characteristics of women who are at risk for lymphedema in future studies, it will be important to include women who do and do not undertake vigorous upper-limb exercise.

There are only three other published studies on air travel and lymphedema [4, 6, 7], of which one was a single case study that examined the impact of multiple flights over a short period of time on the lymphedematous arm [6]. Graham [7] reported from a retrospective survey of 287 breast cancer survivors that there were no cases of permanent new or permanent increased swelling after flying and nine cases of temporary swelling. Casley-Smith and Casley-Smith [4] surveyed patients who were members of the Lymphedema Association of Australia. Six percent ($n = 27$) of the participants who presented with secondary lymphedema ($n = 490$) noted that it occurred during a flight. Findings from our study are similar to those from Casley-Smith and Casley-Smith [4] indicating that there is a small but identifiable risk to some women.

Overall the incidence of lymphedema was low: we noted four (6%) new cases at post, which dropped to one and possibly, two (5%) new cases at follow-up, all of whom had undergone axillary node dissection. Unfortunately, we do not have the ability to predict from our data in advance of flying which women are likely to develop lymphedema. Restriction of axillary surgery to a sentinel node biopsy may reduce the risk but women who undergo sentinel node biopsy can still develop lymphedema [17]. Prudent advice for women at risk of lymphedema contemplating air travel would be that the risk of precipitating or worsening pre-existing lymphedema is very low. On the basis of our findings, the wearing of a compression garment for women without lymphedema is unlikely to be advantageous but equally is unlikely to be harmful.

In conclusion, this was an opportunistic, observational study which took advantage of an event in Australia which attracted a large number of women from Canada. As such, variables like the use of a compression garment (although included as a covariate in the statistical analysis), the type and heaviness of the luggage which the women brought with them, the completion of exercises recommended during the flight [18], the cabin pressure, the participant's air travel history, and medications were not able to be controlled. The data from this study suggest that there was a small risk of development of lymphedema as a consequence of long-haul air travel for women treated for breast cancer. Notably, the majority of the breast cancer survivors in this study trained two or more times per week at moderate intensity for dragon boat racing. Further research is required to determine whether these findings are generalisable to all women treated for breast cancer.

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