Final Report to Breast Cancer Australia

Project Title: Randomised controlled trial of exercise in breast cancer patients with upper limb lymphoedema

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Brief Overview of Project, including Significance:

Although advances in the treatment for breast cancer have led to a reduction in side effects, there remains a subgroup of women who continue to experience significant treatment-related impairment. Furthermore, the impact of initial diagnosis and treatment continues into long-term survivorship. Of all the potential side effects women may experience following breast cancer treatment, arguably lymphoedema is considered the most problematic and dreaded complication. It has been estimated that at least one-third of women treated for breast cancer will develop upper limb lymphoedema (ULL). The presence of ULL brings with it a whole range of physical, emotional, social and practical issues, all of which contribute to adverse changes in quality of life.

Unfortunately, there is a paucity of methodologically sound research surrounding lymphoedema, making it difficult to give evidence-based recommendations to women regarding lymphoedema prevention, management or reduction. In contrast, there is a significant evidence-based supporting the role of exercise during and following breast cancer on facilitating recovery and improving quality of life. Exercise-based interventions for breast cancer survivors provide significant benefits including improved fitness, reduction of the weight gain commonly associated with treatment, reductions in fatigue, and improvement in sleep, body image, self esteem, mood and symptoms associated with menopause. However, those at risk, or who have, ULL have traditionally been advised to restrict activity, particularly of the lymphedematous arm, for fear of exacerbating the condition. Limiting exercise has the potential to deny women an important strategy to improve well-being, physical functioning and hence quality of life.

Therefore, the purpose of this project was to investigate the role of a mixed-type, moderate intensity exercise program in women with lymphoedema, including the effectiveness of the program in the management of lymphoedema, and improvements in fatigue, body image, body weight, mood, upper body function and quality of life. Furthermore, it was an objective to determine the acceptability of the program to women with lymphoedema, while at the same time contribute to the evidence-base regarding the efficacy and safety of the particular exercise program tested for women with lymphoedema.

Progress to date:

Study recruitment January to March, 2006

Patients who had completed treatment for unilateral breast cancer at least 6 months prior, had subsequently developed lymphoedema and who were prepared to travel to the Royal Brisbane and Women's Hospital (RBWH) on a regular basis for 12 weeks, were recruited into the study. Recruitment procedures involved:

- Advertisements in the Lymphoedema Association of Queensland newsletter
- Advertisements in the Breast Cancer Network of Australia newsletter (BEACON)
- Radio advertisements
- Email advertisements describing the study to staff at Royal Brisbane and Women's Hospital (RBWH), University of Queensland (UQ) and the Queensland University of Technology (QUT)
- Study information packs were sent to physiotherapists who specifically treat women with ULL:
  The information pack described the study and informed them that a Research Assistant will be phoning during the next 2 weeks to determine how many of their patients meet the eligibility criteria and would they be willing to send on the participant information packages to these patients on how behalf. This proved the most successful recruitment strategy.
- A study information pack was sent to past lymphoedema patients involved with a previous study of one of the chief investigators (SH).

Over 150 women responded to this recruitment approach. Only 32 of these women met all eligibility criteria, with the 'being able and willing to travel to the RBWH on a regular basis for the exercise intervention' being the most restrictive criteria. All 32 eligible women provided informed consent and were then randomly allocated to the exercise intervention or control group.

Testing phases April, August and November, 2006

The study group participated in three testing sessions scheduled at pre-intervention (April), immediately post-intervention (August) and at 12-week follow-up (November). During each testing session, lymphoedema status was assessed via standard objective measures, specifically perometery and bio-electrical impedance (BIA), while body weight and composition was assessed with scales and BIA. Measures of fatigue, body image, depression, self-report upper body function, and quality of life were also assessed, using standard validated questionnaires. Data were collected on various patient and treatment characteristics.

All three testing phases were successfully completed with all 32 women participating in all three sessions. Missing data were minimal with less than 10% for any item collected via the questionnaire and less than 10% of objective measures (lymphoedema status via perometry or BIA, and body composition).

Study design and intervention Intervention: May-July, 2006

This was a randomised controlled trial of a specific exercise program designed by an experienced physiotherapist and exercise physiologist. Sixteen women were randomly allocated to the exercise intervention and control group, respectively. The intervention consisted of a 12-week moderate intensity, mixed-type exercise program, involving aerobic and resistance exercise. The aerobic component involved participation in floor-based aerobic exercise to music, water-based aerobic exercise, use of ergometers including treadmills, bikes, rowers and steppers, as well as other forms of aerobic exercise such as walking or swimming. During weeks 1-4, participants partook in aerobic exercise three

times/week, of which 2 sessions were supervised. The number of aerobic exercise sessions increased to 4 per week from week 5 onwards, two of which were supervised sessions throughout weeks 5-8, while only 1 session was supervised for weeks 9-12. A gradual increase in exercising intensity and duration occurred throughout the 12-week program to ensure controlled exercise progression. Resistance exercises were introduced during week 3, using water as resistance. The resistance program progressed to using machine weights that targeted large muscle groups during weeks 5-8, with the exercise prescription focusing on muscular endurance (light to moderate weight, high repetitions). The final four weeks of the program incorporated the use of free weights, with the prescription focusing more on improving muscular strength (increased weight, fewer repetitions).

Key issues and results regarding study design and intervention:

- The randomisation process was successful with the intervention and control group having no differences in key personal, treatment and lymphoedema status characteristics at baseline.

- Excellent study adherence was attained for both groups. In regard to the exercise intervention group:
    - 14 women participated in 80% or more of the supervised sessions.
    - Two women participated in less than 80% with extended sickness (week 6-11; several colds/flu in a row) and need for hysterectomy during week 9 being the reasons for non-attendance.
    - During the exercise sessions, all women successfully met the exercise prescription criteria.
    - High acceptability of the exercise program was reported by all intervention participants.

- There was no difference in lymphoedema status between the exercise intervention and control groups at each of the three testing phases. There was however some evidence suggesting improved lymphoedema status in 4 of the exercise intervention participants. Importantly, participation in the exercise intervention did not exacerbate lymphoedema status.

- With respect to other characteristics of interest:
    - Fatigued decreased in both groups.
    - Level of anxiety improved in the exercise group.
    - Weight (not accounting for body composition), degree of depression, and upper body function were found to remain stable overtime for all participants.
    - Short term improvement in body image for the exercise group was evident.
    - Quality of life was found to increase for both groups with data indicating an increasing trend and maintenance over the study duration for the exercise group and an increase between the second and third time-points for the control group.

It is important to highlight though that original sample size calculations indicated that 40 women per group would be needed to detect statistically significant differences between groups and across time.

- Self-report/subjective findings reported by the exercise group following the intervention included:
    - Feelings of empowerment – they were now doing something for themselves.
    - Reduced sense of fear regarding use of their lymphoedematous arm and improved knowledge about their personal capacities (whole body and arm).
    - Improved self-confidence and body image.
    - Reduced weight and/or clothes and compression garments feeling loose.

Other achieved and planned outcomes as a consequence of study completion

- All control and exercise intervention participants were invited to a presentation evening held on 9 November, 2006 at the RBWH, during which the preliminary findings of the study were reported and women were able to ask questions and have any issues clarified.

- Reports summarising the preliminary findings of the study have been sent to all participants, allied health professionals and organisations (Lymphoedema Association of Australia, BEACON, RBWH, UQ and QUT) involved with this work. Summaries of these results will likely be presented in the respective organisation's newsletters or monthly magazines. These reports, as well as the contact made with allied health professionals during the recruitment phase of the study have led to:
    - the establishment of relationships with key Brisbane-based health professionals working with women with ULL (this will aid future lymphoedema-related research), and
    - improved community awareness regarding ULL following breast cancer as well as the Cancer and Bowel Research Trust

- International conference presentations and planned submission of manuscript:
    - The 21st International Congress of Lymphology is scheduled 26-29 September, Shanghai, China – the results of this work will contribute to development of three abstracts to be submitted for oral presentation at this meeting, covering the following issues/results derived from the study:
        1. The role of an exercise program in women with lymphoedema, including the effectiveness of the program in the management of lymphoedema, and improvements in fatigue, body image, body weight, mood, upper body function and quality of life.
        2. The acceptability of an exercise program to women with lymphoedema – results from the women's perspective.
        3. The methodological implications of dealing with intervention studies involving women with lymphoedema.

- The results to be presented in three oral presentations will be brought together in one manuscript submitted to a peer-reviewed journal – planned submission date: July, 2007; Journal: Lymphology or Journal of Lymphology.

Future Plans

Much work is still required in the broad areas of lymphoedema prevention, detection and management. However, in regard to exercise as a potential intervention strategy, the completion of this work has improved the evidence-based in the lymphoedema arena. Consequently, current and future exercise-intervention work being undertaken by the chief investigators of this study, will no longer exclude women with lymphoedema from participating. Furthermore, work directly dealing with women with lymphoedema will continue, with the goal of improving the evidence-base and translating this into improved advice provided to women with, or at risk of developing, lymphoedema.