Six-Month Follow-up of Patient-Rated Outcomes in a Randomized Controlled Trial of Exercise Training during Breast Cancer Chemotherapy

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Abstract

Background: **Few exercise trials in cancer patients have reported longer-term follow-up. Here, we report a 6-month follow-up of exercise behavior and patient-rated outcomes from an exercise trial in breast cancer patients.**
Methods: **Breast cancer patients initiating adjuvant chemotherapy (n = 242) were randomly assigned to usual care (n = 82), resistance exercise training (RET; n = 82), or aerobic exercise training (AET; n = 78) for the duration of their chemotherapy. At 6-month follow-up, participants were mailed a questionnaire that assessed quality of life, self-esteem, fatigue, anxiety, depression, and exercise behavior.**
Results: **Two hundred one (83.1%) participants provided 6-month follow-up data. Adjusted linear mixed-model analyses showed that, at 6-month follow-up, the RET group reported higher self-esteem [adjusted mean difference, 1.6; 95% confidence interval (95% CI), 0.1-3.2; P = 0.032] and the AET group reported lower anxiety (adjusted mean difference, −4.7; 95% CI, −0.0 to −9.3; P = 0.049) compared with the usual care group. Moreover, compared with participants reporting no regular exercise during the follow-up period, those reporting regular aerobic and resistance exercise also reported better patient-rated outcomes, including quality of life (adjusted mean difference, 9.5; 95% CI, 1.2-17.8; P = 0.025).**
Conclusions: **Improvements in self-esteem observed with RET during breast cancer chemotherapy were maintained at 6-month follow-up whereas reductions in anxiety not observed with AET during breast cancer chemotherapy emerged at 6-month follow-up. Moreover, adopting a combined aerobic and resistance exercise program after breast cancer chemotherapy was associated with further improvements in patient-rated outcomes. Exercise training during breast cancer chemotherapy may result in some longer-term and late effects for selected patient-rated outcomes.** (Cancer Epidemiol Biomarkers Prev 2007;16(12):2572–8)

Introduction

Previous research (1, 2), including our own (3), has shown that exercise training during adjuvant breast cancer therapy improves physical fitness, body composition, and some aspects of psychosocial functioning and quality of life (Qol). In our Supervised Trial of Aerobic versus Resistance Training (3), we compared the effects of aerobic exercise training (AET) and resistance exercise training (RET) to usual care (UC) in 242 breast cancer patients initiating adjuvant chemotherapy. We previously reported that, at postintervention, AET was superior to UC for improving self-esteem, preserving aerobic fitness, and maintaining body fat levels, whereas RET was superior to UC for improving self-esteem, muscle strength, lean body mass, and chemotherapy completion rate (3). All other patient-rated outcomes—including fatigue, anxiety, depression, and the primary end point

Received 5/4/07; revised 9/10/07; accepted 9/17/07.

Grant support: This research study was funded by the Canadian Breast Cancer Research Alliance. Canada Research Chairs Program (K.S. Courneya and Y. Yasui); Research Team Grant from the National Cancer Institute of Canada with funds from the Canadian Cancer Society and the National Cancer Institute of Canada/Canadian Cancer Society Sociobehavioral Cancer Research Network (K.S. Courneya, R.J. Segal, D.C. McKenzie, J.R. Mackey, and C.M. Friedenreich); New Investigator Award from the Heart and Stroke Foundation of Canada (R.D. Reid); New Investigator Award from the Canadian Institutes of Health Research and a Health Scholar Award from the Alberta Heritage Foundation for Medical Research (C.M. Friedenreich); Canada Graduate Scholarship from the Canadian Institutes of Health Research and an Incentive Award from the Alberta Heritage Foundation for Medical Research (J.K. Vallance); and Senior Health Scholar Award from the Alberta Heritage Foundation for Medical Research (Y. Yasui).

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Note: K.S. Courneya had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Courneya, Segal, McKenzie, Mackey, Friedenreich, Gelmon, Reid. Analysis and interpretation of data: Courneya, Liu, Yasui, Segal, McKenzie, Mackey, Friedenreich, Gelmon, Reid, Ladha, Proulx, Vallance, Lane. Drafting of the manuscript: Courneya. Critical revision of the manuscript for important intellectual content: Segal, McKenzie, Mackey, Friedenreich, Gelmon, Reid, Ladha, Proulx, Vallance, Lane, Liu, Yasui. Statistical analysis: Liu, Yasui, Courneya. Obtained funding: Courneya, Segal, McKenzie, Mackey, Friedenreich, Gelmon, Reid. Administrative, technical, or material support: Courneya, Segal, McKenzie, Mackey, Gelmon, Yasui.

Role of the funding source: The Canadian Breast Cancer Research Alliance had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

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doi:10.1158/1055-9965.EPI-07-0413

of QoL—favored the exercise groups at postintervention but did not reach statistical significance. To date, no exercise trial in breast cancer patients receiving adjuvant chemotherapy has reported longer-term follow-up of outcomes beyond the immediate postintervention time point. It is unknown, therefore, if any of the benefits of exercise training during breast cancer chemotherapy are maintained into survivorship (i.e., longer-term effects) or if any new benefits emerge (i.e., late effects). It is also unknown if participants continue with exercise after such a trial and whether such continuation provides further improvements in outcomes.

Here, we report a 6-month follow-up of the patient-rated outcomes from the Supervised Trial of Aerobic versus Resistance Training. We hypothesized that improvements observed in self-esteem with exercise training during chemotherapy would be maintained at 6-month follow-up. We did not expect any late effects to emerge at 6-month follow-up for the other patient-rated outcomes of QoL, fatigue, anxiety, or depression. Finally, we hypothesized that participants reporting regular exercise during the follow-up period would also report better patient-rated outcomes at 6-month follow-up.

Materials and Methods

Setting and Participants. Our trial methods have been reported elsewhere (3). Here, we briefly summarize the main methods with additional attention to the 6-month follow-up assessment. Participants were recruited from the Cross Cancer Institute in Edmonton, Alberta; the Ottawa Hospital Integrated Cancer Program in Ottawa, Ontario; and the British Columbia Cancer Agency in Vancouver, British Columbia. Ethical approval was obtained from all three centers and written informed consent was obtained from all participants. Eligibility criteria included women ≥18 years old with stage I to IIIA breast cancer initiating adjuvant chemotherapy. Women were excluded if they had incomplete axillary surgery, transabdominal rectus abdominus muscle reconstructive surgery, uncontrolled illnesses, or were not approved by their oncologist.

Design and Procedures. The study was a prospective, three-armed, randomized controlled trial. Eligible participants were identified by their treating oncologist and, if interested, completed a baseline questionnaire, physical fitness tests, and dual X-ray absorptiometer scan before randomization. Participants were stratified by cancer center (Edmonton, Ottawa, and Vancouver) and chemotherapy regimen (taxane based versus nontaxane based) and randomly assigned within each stratum to either AET, RET, or UC in a 1:1:1 ratio using a computer-generated program. The allocation sequence was generated centrally in Edmonton and concealed from the project directors who assigned participants to groups.

Exercise Training Interventions. All exercise training sessions were supervised by qualified staff at fitness facilities associated with each cancer center. Participants assigned to AET or RET were asked to exercise for the duration of their chemotherapy, defined as beginning 1 to 2 weeks after their first chemotherapy administration and ending 3 weeks after the final chemotherapy administration. The AET group were asked to exercise thrice per week on a cycle ergometer, treadmill, or elliptical trainer beginning at 60% of VO_{2peak} for 15 min and progressing to 80% of VO_{2peak} for 45 min. The RET group were asked to exercise thrice per week performing two sets of 8 to 12 repetitions of nine different exercises at 60% to 70% of their estimated one repetition maximum and to progress the weight by 10% when they could complete >12 repetitions. The UC group were asked not to start an exercise training program during chemotherapy but were offered a 1 month supervised exercise program after postintervention assessments. The exercise groups did not have access to the fitness facilities after the intervention and neither did the UC group except for the initial 1 month supervised program if desired. At postintervention (or post 1 month training for the UC group), no specific instructions were provided concerning exercise behavior during follow-up.

Assessment of Endpoints at 6-Month Follow-up. All patient-rated outcomes were assessed at baseline (within 1-2 weeks after starting chemotherapy), midpoint (middle of chemotherapy/intervention), postintervention (3-4 weeks after chemotherapy/intervention), and at 6-month follow-up (6 months after the postintervention assessment). Objective outcomes (i.e., physical fitness and body composition) were only assessed at baseline and postintervention. Our primary end point in the trial was QoL. Our secondary patient-rated outcomes were self-esteem, fatigue, anxiety, and depression. These outcomes were selected for follow-up assessment because of their importance to cancer survivors and the fact that they could be measured with reliable and valid self-administered questionnaires delivered through the mail. Cancer-specific QoL and fatigue were assessed by the Functional Assessment of Cancer Therapy-Anemia (FACT-An) scales (4). Psychosocial functioning was assessed by the Rosenberg Self-Esteem Scale (5), the Center for Epidemiological Studies-Depression Scale (6), and the Spielberger State Anxiety Inventory (7).

Assessment of Exercise during 6-Month Follow-up. At 6-month follow-up, participants were asked to recall their exercise over the past 6 months using the Godin Leisure Time Exercise Questionnaire (8). The Godin Leisure Time Exercise Questionnaire contains three questions that assess the average frequency of light (e.g., easy walking, bowling), moderate (e.g., fast walking, folk dancing), and vigorous (e.g., running, cross-country skiing) exercise during free time in a typical week in the past month. We modified the Godin Leisure Time Exercise Questionnaire to include the average duration of exercise and to refer to a typical week over the past 6 months (i.e., since the time the postintervention assessment was completed). We also included a separate question asking about resistance exercise (e.g., free weights or universal equipment at home or at a fitness club). Participants were then categorized into meeting or not meeting current guidelines for aerobic exercise (≥60 min of vigorous or 150 min of moderate-to-vigorous exercise per week; ref. 9) and resistance exercise (≥2 resistance training sessions per week; ref. 10). An independent evaluation of the Godin Leisure Time Exercise Questionnaire found its reliability and validity to compare favorably to nine other self-report measures of exercise based on various criteria,

including test-retest scores, objective activity monitors, and fitness indices (11).

Statistical Analyses. Our study was originally powered to detect a difference in change scores of 7 points (SD, 16) on the FACT-An from baseline to postintervention with a loss-to-follow-up of 10%, a two-tailed $\alpha < 0.05$, and no adjustment for multiple testing (3). We did not originally power the study for any additional loss to follow-up that may have occurred at the 6-month follow-up. We used linear mixed-model analysis to examine the differences in the two intervention groups (AET and RET) compared with the UC group in changes over time from baseline to 6-month follow-up for the five patient-rated outcomes (resulting in 10 comparisons). We used intention-to-treat analysis based on all available data from all randomized participants in their original group assignment regardless of nonadherence during the supervised intervention or any crossover during the 6-month follow-up (12). We used the same analytical approach to assess differences across three self-reported exercise groups (meeting ''neither,'' ''either,'' or ''both'' the aerobic and resistance exercise guidelines) but modeled the changes over time from postintervention (3-4 weeks after chemotherapy) to 6-month follow-up (resulting in 15 comparisons for the five patient-rated outcomes). We also explored potential interactions between group assignment and self-reported exercise group at follow-up in changes over time from baseline to 6-month follow-up using the same models that included the main effects and the interaction term (12). Our primary analyses were adjusted for initial value of the outcome (baseline or postintervention), age, marital status, employment status, disease stage, type of chemotherapy, and baseline (pretrial) exercise using baseline or postintervention propensity scores (13), consistent with our analysis of the postintervention effects (3). Interclass correlation coefficient estimates for cancer centers were obtained for each outcome based on the mixed model analysis. The estimates were 0.08 for QoL, 0.004 for self-esteem, 0.07 for fatigue, 0.04 for anxiety, and 0.03 for depression. Incorporation of interclass correlation coefficients did not alter our results or conclusions for any outcomes and so we present the results without the interclass correlation coefficients to be consistent with the analyses of our postintervention effects (3). For participants with missing data at postintervention or follow-up, we included all available data under the missing-at-random assumption of the mixed-model analysis.

Results

Flow of participants through the trial has been reported elsewhere (3). Briefly, we recruited 242 of 736 (33%) eligible participants and obtained postintervention data on 223 (92.1%) and 6-month follow-up data on 201 (83.1%). The 6-month follow-up rate differed by original group assignment ($P = 0.013$) with 73.2% (60 of 82) of UC, 89.0% of RET (73 of 82), and 87.2% of AET (68 of 78) providing follow-up data. The groups were balanced on all variables at baseline (3). Age ranged from 25 to 78 years (mean 49 years); 21% were obese, 25% had stage I disease, 61% had disease stage II, 59% received breast conservation surgery, 31% received a taxane-based chemotherapy, and 25% reported recent exercise. We previously reported two adverse events related to exercise after baseline maximal treadmill testing (3). One participant became light-headed, hypotensive, and moderately nauseous. A second experienced dizziness, weakness, and mild diarrhea. Both participants recovered quickly.

We compared participants that completed the 6-month follow-up ($n = 201$) with those that did not ($n = 41$) and found no differences in age; marital status; education; employment status; pretrial exercise; disease stage; surgical procedure; chemotherapy protocol; or baseline QoL, self-esteem, fatigue, or depression. Completers had slightly higher anxiety at baseline (42.5 ± 12.5 versus 37.6 ± 14.2; $P = 0.027$). The median length of the intervention was 17 weeks [95% confidence interval (95% CI), 9-24] and adherence to the supervised exercise training during chemotherapy was 72.0% and 68.2% in the AET and RET groups, respectively ($P = 0.411$).

At postintervention, 25 of 82 (30.5%) UC group participants attended the fitness center for their 1 month supervised exercise sessions. Of the 201 participants providing 6-month follow-up data, 42 (20.9%) reported meeting both the aerobic and resistance exercise guidelines, 16 (8.0%) reported meeting only the resistance exercise guideline, 58 (28.9%) reported meeting only the aerobic exercise guideline, and 85 (42.3%) reported meeting neither exercise guideline (Table 1). The percentage of participants meeting guidelines varied by original group assignment with fewer in the AET group reporting that they met the exercise guidelines during follow-up ($P = 0.034$). Given the small number of participants reporting that they met only the resistance exercise guideline, this group was combined with the group meeting only the aerobic exercise guideline to form a group meeting ''either'' exercise guideline for the purpose of analyses.

Effects of Exercise Training during Breast Cancer Chemotherapy on Patient-Rated Outcomes at 6-Month Follow-up. At 6-month follow-up, the RET group reported significantly higher self-esteem than the UC group (adjusted mean difference, 1.6; 95% CI, 0.1-3.2; $P = 0.032$) and the AET group showed a trend toward higher self-esteem compared with the UC group (adjusted mean difference, 1.0; 95% CI, -0.5 to 2.5; $P = 0.187$). The AET group also reported significantly lower anxiety than the UC group at 6-month follow-up (adjusted mean difference, -4.7; 95% CI, -9.3 to -0.0; $P = 0.049$) and a trend toward lower depression (adjusted mean difference, -2.7; 95% CI, -6.3 to 1.0; $P = 0.154$). All other changes in patient-rated outcomes at 6-month follow-up favored the exercise groups but did not reach statistical significance (Table 2).

Associations between Self-Reported Exercise during Follow-up and Patient-Rated Outcomes at 6-Month Follow-up. At 6-month follow-up, compared with participants reporting that they did not meet either exercise guideline, those reporting that they met both exercise guidelines reported significantly higher QoL (adjusted mean difference, 9.5; 95% CI, 1.2-17.8; $P = 0.025$) and less fatigue (adjusted mean difference, 4.5; 95% CI, 0.9-8.1; $P = 0.013$); and borderline significantly higher self-esteem (adjusted mean difference, 1.5; 95% CI, -0.2 to

Table 1. Self-reported exercise behavior at 6-month follow-up, overall and by group assignment

Variable	Randomized group assignment at baseline				*P*
	Overall (*N* = 201)	UC (*n* = 60)	RET (*n* = 73)	AET (*n* = 68)	
Self-reported exercise during follow-up					
Neither guideline, *n* (%)	85 (42.3%)	22 (36.7%)	29 (39.7%)	34 (50.0%)	0.034
Resistance only, *n* (%)	16 (8.0%)	9 (15.0%)	6 (8.2%)	1 (1.5%)	
Aerobic only, *n* (%)	58 (28.9%)	20 (33.3%)	17 (23.3%)	21 (30.9%)	
Both guidelines, *n* (%)	42 (20.9%)	9 (15.0%)	21 (28.8%)	12 (17.6%)	

NOTE: Data are presented as the number (percentage).Cut points for meeting guidelines on self-reported exercise during follow-up were ≥2 per week frequency for resistance exercise and ≥150 min of moderate-to-vigorous exercise per week or 60 min of vigorous exercise per week for aerobic exercise.

3.1; *P* = 0.083) and lower anxiety (adjusted mean difference, −4.3; 95% CI, −9.0-0.4; *P* = 0.070). Also, compared with participants reporting that they did not meet either exercise guideline, those reporting that they met either exercise guideline reported significantly lower fatigue (adjusted mean difference, 3.3; 95% CI, 0.2-6.4; *P* = 0.035) and trends toward higher QoL (adjusted mean difference, 5.9; 95% CI, −1.2-13.1; *P* = 0.104) and lower anxiety (adjusted mean difference, −3.3; 95% CI, −7.4-0.8; *P* = 0.110). All other changes in patient-rated outcomes at 6-month follow-up favored the exercise groups but did not reach statistical significance (Table 3). There were no interactions between group assignment and self-reported exercise during follow-up for any of the patient-rated outcomes (all *P* values >0.60).

Discussion

Our results indicate that improvements in self-esteem observed with exercise training during breast cancer chemotherapy were maintained at 6-month follow-up in the RET group and showed a trend toward being maintained in the AET group. Unexpectedly, AET during breast cancer chemotherapy showed a late effect on anxiety at 6-month follow-up and a trend toward a late effect on depression. Finally, participants reporting both aerobic and resistance exercise during the follow-up period reported better functioning at follow-up on most patient-rated outcomes, including QoL and fatigue. No previous exercise trials in breast cancer patients receiving chemotherapy have reported longer term follow-up beyond the immediate postintervention effects (1).

In a trial of 201 breast cancer patients receiving mixed chemotherapy and/or radiation treatments, Mutrie et al. (2) compared 12 weeks of combined aerobic and resistance exercise to UC and reported that immediate postintervention effects on aerobic fitness, shoulder mobility, breast cancer-specific symptoms, depression, and positive mood were largely maintained at 6-month follow-up. They also reported a borderline significant late effect for general QoL. Conversely, Daley et al. (14) examined 8 weeks of either aerobic exercise or flexibility exercise compared with UC in a trial of 108 breast cancer survivors 12 to 36 months posttreatment and reported that immediate postintervention effects on QoL, fatigue, self-worth, and aerobic fitness were not maintained at

Table 2. Effects of aerobic and resistance exercise during breast cancer chemotherapy on patient-rated outcomes at 6-month follow-up

	Baseline *M* (SD)	Follow-up *M* (SD)	Mean change *M* (95% CI)	Unadjusted group differences in mean change: *M* (95% CI); *P*	Adjusted group differences in mean change: *M* (95% CI); *P*
FACT-An					
UC	135.3 (28.1)	152.4 (26.4)	+18.2 (11.5-24.9)	RET vs UC: +2.3 (−6.9-11.5); *P* = 0.620	+2.7 (−6.6-12.1); *P* = 0.566
RET	132.2 (23.5)	152.9 (26.0)	+20.5 (14.2-26.8)	AET vs UC: +1.9 (−7.4-11.3); *P* = 0.686	+2.9 (−6.6-12.4); *P* = 0.546
AET	135.7 (29.0)	156.3 (24.0)	+20.1 (13.6-26.6)	RET vs AET: +0.4 (−8.6-9.4)	−0.2 (−9.5-9.1)
Self-esteem					
UC	34.1 (4.6)	33.9 (5.6)	−0.1 (−1.2-1.0)	RET vs UC: +1.2 (−0.3-2.7); *P* = 0.119	+1.6 (0.1-3.2); *P* = 0.032
RET	34.1 (4.2)	35.2 (4.6)	+1.1 (0.1-2.1)	AET vs UC: +1.0 (−0.5-2.5); *P* = 0.201	+1.0 (−0.5-2.5); *P* = 0.187
AET	34.0 (5.1)	35.0 (4.7)	+0.9 (−0.1-2.0)	RET vs AET: +0.2 (−1.3-1.7)	+0.6 (−0.8-2.1)
Fatigue					
UC	34.6 (11.1)	41.5 (9.8)	+7.0 (4.1-10.0)	RET vs UC: −0.6 (−4.6-3.4); *P* = 0.754	−0.1 (−4.1-3.9); *P* = 0.966
RET	34.3 (10.1)	40.8 (10.5)	+6.4 (3.7-9.1)	AET vs UC: −0.4 (−4.5-3.6); *P* = 0.831	+0.6 (−3.5-4.6); *P* = 0.779
AET	35.3 (12.1)	42.1 (10.5)	+6.6 (3.8-9.4)	RET vs AET: −0.2 (−4.1-3.7)	−0.7 (−4.6-3.3)
Anxiety					
UC	42.0 (13.7)	37.4 (12.0)	−5.3 (−8.6 to −1.9)	RET vs UC: −1.3 (3.3 to −5.8); *P* = 0.582	−2.5 (2.1 to −7.1); *P* = 0.279
RET	42.0 (12.0)	35.5 (13.0)	−6.5 (−9.7 to −3.4)	AET vs UC: −3.7 (0.9 to −8.4); *P* = 0.113	−4.7 (−0.0 to −9.3); *P* = 0.049
AET	40.9 (13.3)	32.2 (11.2)	−9.0 (−12.2 to −5.8)	RET vs AET: +2.5 (2.0 to −6.9)	+2.1 (2.4 to −6.7)
Depression					
UC	13.9 (9.7)	10.2 (9.5)	−4.0 (−6.6 to −1.3)	RET vs UC: −0.2 (3.5 to −3.8); *P* = 0.932	−1.3 (2.3 to −4.8); *P* = 0.493
RET	13.8 (10.1)	9.6 (10.4)	−4.1 (−6.6 to −1.7)	AET vs UC: −1.6 (2.1 to −5.3); *P* = 0.395	−2.7 (1.0 to −6.3); *P* = 0.154
AET	12.8 (9.8)	7.2 (7.5)	−5.6 (−8.2 to −3.0)	RET vs AET: +1.4 (5.0 to −2.1)	+1.4 (5.0 to −2.2)

NOTE: *M* (SD) at 6-month follow-up is based on available data. Mean change is based on 6-month follow-up score minus baseline score but may not precisely reflect this difference given that mean change is estimated based on mixed model analysis. Adjusted group difference in mean change was adjusted for baseline value of the outcome, age, marital status, employment status, disease stage, chemotherapy protocol, baseline exercise status, and smoking status. *P* values are presented only for hypothesized comparisons.

6-month follow-up. They did note, however, that immediate postintervention effects on depression were maintained at 6-month follow-up and a late effect on satisfaction with life emerged for the flexibility group. Finally, in a trial of mixed cancer survivors within 1 month of completing adjuvant therapy, Thorsen et al. (15, 16) examined 3 months of aerobic exercise training compared with UC and reported that immediate postintervention effects on aerobic fitness were maintained at 6-month follow-up but not at 12-month follow-up. Immediate postintervention effects on patient-rated outcomes that originally favored the UC group were not reported at follow-up (16).

Our results indicate that exercise training during breast cancer chemotherapy may have longer-term effects on self-esteem. We previously reported that both RET and AET improved self-esteem during breast cancer chemotherapy by 1.3 points or 0.28 SDs (3). These immediate improvements seem to have been largely maintained at 6-month follow-up although only the RET group maintained statistical superiority. At 6-month follow-up, the advantage in the RET group actually increased to 1.6 points (SD 0.35), whereas the advantage in the AET group was reduced to 1.0 points but still can be considered a small standardized effect size (SD 0.22). Improved self-esteem is an important outcome for breast cancer patients going through difficult treatments and it is promising that this benefit was maintained at 6-month follow-up. It is possible that the self-esteem benefits obtained from successfully completing a challenging exercise program during difficult chemotherapy treatments may have a longer-lasting effect. It is unclear, however, if the improvements in self-esteem would result in better day-to-day role functioning for these women. Future trials should include measures of role functioning to determine if the exercise benefits to self-esteem extend to day-to-day functioning.

Our results also indicate that aerobic exercise training during breast cancer chemotherapy may have late effects on markers of psychosocial distress. We previously reported that AET had trivial effects on anxiety and depression during breast cancer chemotherapy (3). At postintervention, the AET group was nonstatistically superior to the UC group by −1.7 points on anxiety (SD 0.13) and −0.3 points on depression (SD 0.03; ref. 3). At 6-month follow-up, however, the AET group was statistically superior to the UC group on anxiety by −4.7 points (SD 0.36) and showed a trend toward less depression by −2.7 points (SD 0.27). These findings are consistent with recent meta-analyses (1, 17) that have noted modest effects of exercise training on psychosocial distress during cancer therapy but more consistent effects posttherapy. It is unclear why AET may provide a late effect on psychosocial distress in this clinical setting. It is possible that the psychosocial distress associated with chemotherapy may overshadow any small benefit from AET during treatment, but once the short-term distress of chemotherapy is over, the small effect of AET on psychosocial distress may emerge. It is also possible that AET may reduce the psychosocial distress that can result after chemotherapy from chemotherapy-induced menopause, side effects of aromatase inhibitors, or not receiving any treatments at all. Again, however, the clinical significance of improved anxiety is unclear. For example, it is unknown if the improvements in anxiety reported here are sufficient to improve day-to-day role functioning or reduce the need for antianxiolytic medications.

Given that our trial was not intended to promote longer-term behavior change, it was reassuring to

Table 3. Associations between self-reported exercise during 6-month follow-up and patient-rated outcomes at 6-month follow-up

	Postintervention	Follow-up *M* (SD)	Mean change *M* (SD)	Unadjusted group differences in mean change: *M* (95% CI); *P*	Adjusted group differences in mean change: *M* (95% CI); *P*
FACT-An					
Neither	137.3 (28.1)	146.9 (28.9)	+ 9.8 (5.2-14.3)	BT vs NT: +7.0 (−0.9-14.9); *P* = 0.083	+9.5 (1.2-17.8); *P* = 0.025
Either	142.6 (27.3)	157.2 (22.0)	+14.4 (9.6-19.3)	ET vs NT: +4.7 (−2.0-11.4); *P* = 0.169	+5.9 (−1.2-13.1); *P* = 0.104
Both	146.2 (22.3)	162.6 (19.5)	+16.8 (10.3-23.2)	BT vs ET: +2.3 (−5.8-10.4); *P* = 0.573	+3.6 (−4.7-11.8); *P* = 0.397
Self-esteem					
Neither	33.7 (5.2)	33.8 (5.4)	+0.1 (−0.8-1.0)	BT vs NT: +1.4 (−0.2-3.0); *P* = 0.083	+1.5 (−0.2-3.1); *P* = 0.083
Either	33.9 (5.1)	34.9 (4.7)	+0.9 (−0.1-1.9)	ET vs NT: +0.8 (−0.5-2.2); *P* = 0.230	+0.6 (−0.9-2.0); *P* = 0.454
Both	35.0 (4.7)	36.5 (4.1)	+1.5 (0.2-2.8)	BT vs ET: +0.6 (−1.0-2.2); *P* = 0.483	+0.9 (−0.8-2.6); *P* = 0.280
Fatigue					
Neither	33.5 (11.7)	37.8 (11.8)	+4.5 (2.5-6.5)	BT vs NT: +2.5 (−1.0-6.0); *P* = 0.155	+4.5 (0.9-8.1); *P* = 0.013
Either	36.8 (11.2)	43.3 (8.4)	+6.5 (4.3-8.6)	ET vs NT: +2.0 (−1.0-4.9); *P* = 0.185	+3.3 (0.2-6.4); *P* = 0.035
Both	38.6 (8.0)	45.6 (7.3)	+7.0 (4.2-9.8)	BT vs ET: +0.5 (−3.0-4.1); *P* = 0.767	+1.2 (−2.4-4.7); *P* = 0.512
Anxiety					
Neither	35.8 (12.6)	37.0 (12.9)	+1.1 (−1.4-3.7)	BT vs NT: −4.6 (−9.0 to −0.2); *P* = 0.040	−4.3 (−9.0-0.4); *P* = 0.070
Either	36.7 (11.3)	33.8 (11.1)	−2.9 (−5.6 to −0.1)	ET vs NT: −4.0 (−7.7 to −0.3); *P* = 0.036	−3.3 (−7.4-0.8); *P* = 0.110
Both	36.4 (11.0)	32.9 (12.4)	−3.5 (−7.1-0.1)	BT vs ET: −0.6 (−5.1-3.9); *P* = 0.784	−1.0 (−5.7-3.7); *P* = 0.677
Depression					
Neither	10.9 (9.9)	10.8 (10.6)	−0.1 (−2.2-2.1)	BT vs NT: −3.2 (−6.9-0.6); *P* = 0.095	−3.1 (−7.0-0.8); *P* = 0.122
Either	10.6 (9.8)	7.9 (7.7)	−2.6 (−4.9 to −0.3)	ET vs NT: −2.5 (−5.7-0.6); *P* = 0.115	−1.9 (−5.3-1.5); *P* = 0.273
Both	10.2 (9.4)	7.0 (8.3)	−3.2 (−6.3 to −0.2)	BT vs ET: −0.6 (−4.4-3.2); *P* = 0.743	−1.2 (−5.1-2.7); *P* = 0.552

NOTE: *M* (SD) at postintervention and follow-up are based on available data. Mean change is based on follow-up score minus postintervention score but may not precisely reflect this difference given that mean change is estimated based on mixed model analysis. Adjusted group difference in mean change was adjusted for postintervention value of the outcome, age, marital status, employment status, disease stage, chemotherapy protocol, and baseline exercise status.

Abbreviations: NT, meeting neither exercise guideline; ET, meeting either exercise guideline; BT, meeting both exercise guidelines.

observe that almost 60% of participants reported meeting at least one exercise guideline at 6-month follow-up, and 20% reported meeting both. At baseline in our sample, only 26% were meeting the aerobic exercise guideline and only 8% were meeting the resistance exercise guideline (3). Moreover, previous surveys of postadjuvant therapy cancer survivors in Alberta, Canada, have shown that only about 30% are meeting aerobic exercise guidelines (18-21). It was also noteworthy that the UC group adopted exercise during the follow-up. Of the 60 participants in the UC group that provided follow-up data, 23 (38%) had attended the fitness center for their postintervention exercise sessions and many were exposed to both AET and RET. Overall, these data suggest that a supervised exercise training program during adjuvant chemotherapy may be an effective strategy for helping sedentary breast cancer patients transition to active breast cancer survivors. Physically active breast cancer survivors may have a lower rate of recurrence, breast cancer–specific mortality, and all-cause mortality (22). Training in self-regulation behavior change techniques during the supervised program may further enhance exercise maintenance at long term follow-up (23).

Self-reported exercise during follow-up was associated with several patient-rated outcomes at 6-month follow-up. In particular, meeting both aerobic and resistance exercise guidelines was associated with statistically and meaningfully better QoL and fatigue. The differences in QoL and fatigue of 9.5 and 4.5 points, respectively, exceed the minimally important differences on these scales of seven to eight points (FACT-An) and three to four points (FACT-F). It is possible, of course, that these associations indicate that better patient functioning after chemotherapy is associated with adopting or maintaining regular exercise. Only randomized controlled trials comparing a combined exercise program to a single exercise mode or to UC in the postadjuvant setting can answer this question. Although no trials have compared a combined exercise program to a single exercise mode, several have compared combined exercise to UC and reported compelling results (1). For example, Milne et al. (24) randomized 58 breast cancer survivors within 2 years of diagnosis to a combined supervised exercise program versus UC and reported substantial improvements in cancer-specific QoL and fatigue that were thrice the minimally important differences. Consequently, data are converging to suggest broader and more robust effects of exercise training on patient-rated outcomes in the postadjuvant setting compared with the adjuvant setting. It is possible that cancer survivors may be better able to respond physically and mentally to an exercise program after completion of difficult treatments. Randomized controlled trials that directly compare adjuvant and postadjuvant exercise interventions are warranted.

The overall strengths of our trial have been noted elsewhere (3). Additional strengths specific to the present report include the first exercise trial in breast cancer patients receiving chemotherapy to report longer-term follow-up of patient-rated outcomes, use of the intention-to-treat principle, inclusion of a follow-up exercise measure, and an acceptable follow-up rate of 83%. The overall limitations of our trial have also been noted elsewhere (3). Additional limitations of the present report include the reliance on a self-report measure of exercise during follow-up, differential loss to follow-up among the groups, failure to obtain follow-up measures of the objective end points, failure to obtain even longer-term follow-up data (e.g., 1 or 2 years), and the possibility of a chance finding due to multiple testing. Nevertheless, the consistency in the pattern of our findings—together with the fact that it was the UC group who had a higher loss at follow-up (which probably made our intervention-effect estimates more conservative) and the partial crossover of the UC group (38% started supervised exercise in our fitness facilities)—suggests a generally positive effect of exercise training on longer-term patient-rated outcomes.

In summary, our trial shows that exercise training during breast cancer chemotherapy may have a longer-term effect on self-esteem and a late effect on anxiety. Moreover, a supervised exercise program during breast cancer chemotherapy may be an effective strategy for facilitating the adoption and maintenance of exercise in the postadjuvant setting, which may further enhance patient-rated outcomes and possibly even improve survival. Cancer care professionals may recommend exercise training to breast cancer patients during chemotherapy to potentially enhance both shorter-term and longer-term patient-rated outcomes.

Acknowledgments

We thank Lisa Workman, M.A.; Neil Eves, Ph.D.; John McGavock, Ph.D.; Kristin Campbell, Ph.D.; Margaret McNeely, B.Sc.P.T., M.Sc.; Diana Jespersen, R.N.; Chris Scott, B.Sc.; Lianne Dolan, M.Sc.; Ben Wilson, B.Sc.; Christopher Sellar, M.S.; and Diane Cook, BPE; for their assistance in recruitment, exercise supervision, testing, data management, and manuscript preparation.

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