Original article

A randomized trial of exercise and quality of life in colorectal cancer survivors

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We conducted a randomized controlled trial to determine the effects of a home-based exercise intervention on change in quality of life (QOL) in recently resected colorectal cancer survivors, most of whom were receiving adjuvant therapy. Participants were randomly assigned in a 2 : 1 ratio to either an exercise ($n = 69$) or control ($n = 33$) group. The exercise group was asked to perform moderate intensity exercise 3–5 times per week for 20–30 min each time. The primary outcome was change in QOL as measured by the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) scale. Adherence in the exercise group was good (75.8%) but contamination in the control group was problematic (51.6%). Intention-to-treat analysis revealed no significant differences between groups for change in the FACT-C (mean difference, –1.3; 95% CI, –7.8 to 5.1; $P = 0.679$). In an 'on-treatment' ancillary analysis, we compared participants who decreased versus increased their cardiovascular fitness over the course of the intervention. This analysis revealed significant differences in favour of the increased fitness group for the FACT-C (mean difference, 6.5; 95% CI, 0.4–12.6; $P = 0.038$). These data suggest that increased cardiovascular fitness is associated with improvements in QOL in colorectal cancer survivors but better controlled trials are needed.

Keywords: adherence, anxiety, contamination, depression, fatigue, physical fitness.

INTRODUCTION

Cancer and its treatments often produce significant morbidities that undermine quality of life (QOL) in survivors (Shapiro & Recht 2001). Research has accumulated to suggest that physical exercise may be one strategy to enhance QOL both during and after cancer treatments (see Courneya 2001; Courneya *et al.* 2003c for reviews). Almost all intervention studies to date have focused on breast cancer or bone marrow transplant survivors. Yet, any cancer that is associated with QOL decrements from the disease or its treatment may potentially benefit from exercise (Courneya & Friedenreich 1997). It may be unwise, however, to generalize the results from one group of cancer survivors to another because each cancer is unique in terms of the natural history and pathology of the disease, the treatment protocols used to manage the disease, the side-effects of the disease and treatment, and the characteristics of the survivors including their demographic profile, medical history and lifestyle.

Colorectal cancer is the third most common cancer in the US for both men and women (American Cancer Society 2002). It is estimated that 135 400 new cases of colorectal cancer will be diagnosed in the US in 2001,

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representing 11% of all new cancer diagnoses. Moreover, the relative survival rate for colorectal cancer is quite favourable with 1-, 5- and 10-year rates of 82%, 61% and 55%, respectively. Furthermore, colorectal cancer differs from breast cancer in a variety of meaningful ways that preclude the generalizing of research results. Some of the more relevant differences are that colorectal cancer survivors tend to be older, include equal numbers of men and women, present with more advanced disease, and undergo different surgical and medical procedures (Skibber *et al*. 2001a, b).

To date, only two observational studies have examined exercise in colorectal cancer survivors (Courneya & Friedenreich 1997; Courneya *et al*. 1999). In one study, a retrospective design was used wherein 130 colorectal cancer survivors recalled their exercise levels at pre-diagnosis, during treatment and post-treatment, and reported their current QOL (Courneya & Friedenreich 1997). In the other study, 63 recently resected colorectal cancer survivors reported their exercise levels and QOL over a 4-month period (Courneya *et al*. 1999). In both studies, evidence was found for a positive association between exercise and QOL but the observational designs preclude definitive conclusions from being drawn.

Here we report the first randomized controlled trial (RCT) designed to compare exercise to usual care in colorectal cancer survivors. The primary hypothesis was that the exercise group would experience significant improvements in QOL compared to the control group. We expected the exercise group to also show greater improvements in satisfaction with life, fatigue, anxiety, depression and physical fitness.

METHODS

Setting and participants

Participants were 102 colorectal cancer survivors from the Cross Cancer Institute (CCI) in Edmonton, Alberta, Canada. Eligibility criteria for the study were: (i) surgery for colorectal cancer within the past 3 months, (ii) recovery from surgery as indicated by an attending physician, (iii) ability to understand and provide written informed consent in English, (iv) passed the revised Physical Activity Readiness Questionnaire (rPAR-Q; Thomas *et al.* 1992), and (v) no contraindications to exercise as determined by a submaximal cardiorespiratory fitness test. The Alberta Cancer Board Research Ethics Committee and the University of Alberta Health Research Ethics Board provided ethical approval for the study. Written informed consent was obtained for all procedures.

Experimental design and procedures

The study was a two-group, prospective RCT. Eligible participants were identified by oncologists at the weekly meeting of the Gastro-Intestinal Tumor Group at the CCI. A research nurse approached all eligible participants in the clinic and briefly explained the study and gave interested participants an information package. The information package contained a 'Notice of Research Study' brochure, two copies of an informed consent, and the baseline questionnaire. Participants who were given an information package received a recruitment telephone call from the project director. The project director further explained the purpose and protocol of the study, answered any questions, and determined final eligibility using the rPAR-Q. All participants who were still interested and passed the rPAR-Q were scheduled for a physical fitness test at the CCI. They were asked to bring their completed questionnaire and informed consent to the fitness test.

Prior to the physical fitness test, participants were randomly assigned to an exercise group or wait-list control group using a random-numbers table. The specified allocation ratio for the exercise and control groups was 2 : 1. We used a 2 : 1 ratio because we anticipated a 50% non-adherence rate in the exercise group similar to research in well populations. This rate of drop out would allow us to maintain equal numbers in the groups for the final analysis. The fitness test was conducted by a certified fitness consultant (blinded to the experimental group) under the supervision of the project director (not blinded to the experimental group). After completing the physical fitness test, the fitness consultant provided the results to the project director and left the testing facility. At that time, participants in both groups received feedback on their test results.

Participants assigned to the control group were then asked not to begin a structured exercise programme and were not given an exercise prescription. They were reminded, however, that after their second fitness test (in about 16 weeks), they would be given an appropriate exercise prescription. Participants assigned to the exercise group were given a fitness consultation lasting about 30 min that included a personalized exercise prescription for the next 16 weeks. The fitness consultation was based on a booklet developed by the authors entitled 'Guide to Physical Exercise Following a Cancer Diagnosis'. This booklet contained the participants' individualized exercise prescription, basic information on exercise prescription guidelines, and strategies for maintaining the exercise programme.

On a weekly basis, the project director made telephone calls to all participants to report their level of exercise for

the previous week and to answer any questions. Modifications were made to the prescribed exercise programmes for those in the exercise group if necessary. The weekly exercise reports were used to determine the adherence and contamination rates for the exercise and control groups, respectively. One to two weeks prior to the 16 week post-test assessment, participants were mailed the follow-up questionnaire and booked for a second fitness test. Participants were asked to bring their completed questionnaire to the second fitness test. Following the fitness test, all participants received an appropriate exercise prescription and a T-shirt for their participation in the study.

Intervention

Exercise group

Participants assigned to the exercise group were prescribed a home-based, personalized exercise programme that took into account their baseline fitness test results, exercise history, performance status, adjuvant therapy and personal preferences (Courneya *et al*. 2003a). The focus of the programme was on improving functional well-being through cardiovascular and flexibility exercises. Participants were allowed to choose the mode of exercise they preferred (e.g. swimming, cycling) but if they had no preference they were prescribed walking. The goal was to have participants exercising at least 3–5 times per week, for 20–30 min, at 65% to 75% of the predicted heart rate maximum (American College of Sports Medicine 1998). Progression towards this goal varied depending on motivation and capability. For some participants, early weeks were characterized by shorter duration (e.g. 10–15 min) and lower intensity (e.g. 50% to 60% maximum heart rate) that gradually increased to the desired goal.

Control group

Participants assigned to the control group were not prescribed a home-based, personalized exercise programme and were asked not to initiate any structured exercise over the course of the intervention.

Outcome measures

The primary outcome was QOL as assessed by the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) scale (Ward *et al*. 1999). The FACT-C includes subscales for physical, functional, emotional and social/family well-being, and a colorectal cancer subscale. We also computed the FACT-General (FACT-G) score by excluding the colorectal cancer subscale and the trial outcome index (TOI) score by summing the physical and functional well-being scales and the colorectal cancer subscale. The FACT-C and FACT-G have been well-tested in cancer survivors and found to be reliable, valid and responsive (Cella *et al*. 1993; Ward *et al*. 1999).

Secondary outcomes were satisfaction with life, depression, anxiety, fatigue, cardiovascular fitness, body composition and flexibility. Satisfaction with life was assessed by the Satisfaction With Life Scale (SWLS) developed by Diener & associates (1985). The SWLS contains five items that are rated on seven-point scales and summed for an overall score (ranging from 5 to 35) and has been shown to be a reliable, valid and responsive measure of overall QOL (Pavot & Diener 1993). Depression was assessed by the Centre for Epidemiological Studies Depression scale which is a well-validated, 20-item scale that measures the frequency of depressive symptoms over the past week (Radloff 1991). Items are scored from 0 (<1 day) to 3 (5–7 days) and summed to provide an overall score (ranging from 0 to 60). Anxiety was assessed by the state version of the State-Trait Anxiety Inventory (Spielberger *et al.* 1970). The version used in the present study asked participants how they felt 'during the past week'. The scale has 20 items that are rated on a 1 (not at all) to 4 (very much so) scale and summed for an overall score (ranging from 20 to 80). Fatigue was assessed by the 13-item Fatigue Scale of the FACT measurement system developed specifically for the cancer population (Yellen *et al*. 1997).

Cardiovascular fitness was assessed by the Modified Balke Treadmill Test. The test is terminated when participants reach 70% of their age-predicted maximum or when they voluntarily terminate the test. The score is the number of seconds to reach 70% of age-predicted maximum heart rate. This test has been shown to have a high correlation with predicted oxygen uptake (American College of Sports Medicine 1991). Body composition was assessed by Harpenden calipers (British Indicators LTD, London, UK) to measure skinfolds at five standard sites (triceps, biceps, subscapula, suprailiac and medial calf). The five sites were then summed for an overall score in millimetres. This method for body fat determination has been shown to yield predicted values within 3–5% of those obtained by hydrostatic weighing (McArdle *et al.* 1991). Flexibility of the lower back and posterior thighs (hamstrings) was assessed with the sit-and-reach test. This test requires participants to place their feet flat against a specially constructed box with knees fully extended and feet shoulder width apart. The participants extend forward to push a measuring scale that is on top of the box and hold this position for 1 s. The score is the farthest point

reached in centimetres out of two trials. The validity and reliability of this test have been established (Baumgartner & Jackson 1995).

Other measures

Exercise behaviour was assessed by the leisure score index (LSI) of the Godin Leisure-Time Exercise Questionnaire (Godin & Shephard 1985; Godin *et al.* 1986). The LSI consists of three questions that assess the average frequency of mild, moderate and strenuous exercise during free time in a typical week. We modified the LSI so that average duration for each intensity was also provided. An independent evaluation of this measure found its reliability and validity to compare favourably to nine other self-report measures of exercise based on various criteria including test-retest scores, objective activity monitors and fitness indices (Jacobs *et al.* 1993). In the present study, participants completed the LSI at baseline (referring to the past month) and on a weekly basis over the 16-week intervention (referring to the past week). Demographics were collected using self-report scales and included age, sex, marital status, education, income and employment status. The medical variables were abstracted from medical records and consisted of cancer site, stage of disease, and dates and types of cancer treatments.

Statistical analyses

All analyses were performed using the SPSS version 10.0 for Windows package (SPSS, Inc., Evanston, IL, USA). We examined retention biases by comparing retention rates between the experimental groups and also by comparing those who completed our study ($n = 93$) with those who dropped out ($n = 9$). We compared baseline characteristics of the two groups and adherence of participants to their experimental assignments using independent *t*-tests for continuous variables and chi-square tests for categorical variables. Our primary analysis utilized independent-samples *t*-tests to compare changes between groups in outcomes from baseline to post-intervention. Data were also analysed using analysis of covariance procedures in which groups were compared on the post-intervention value with the baseline value as the covariate.

RESULTS

Flow of participants through the study

Figure 1 presents the flow of participants through the study. Recruitment took place between October 1998 and April 2001. We recruited 34.6% of eligible participants to our study. The retention rate was 91.2% and did not differ between the control (93.9%) and exercise (89.9%) groups ($P = 0.496$). Participants who dropped out of our study were not significantly different from those who completed the study in any demographic variables, medical characteristics, past exercise or baseline QOL. All remaining analyses were based on the 93 participants who completed the QOL assessments or the 88 participants who completed the fitness tests at post-test.

Baseline characteristics

Table 1 shows the baseline demographic, medical and past exercise characteristics. No significant differences were found between experimental groups for any variable.

Adherence of participants to experimental groups

Table 2 presents data on the adherence of participants to their assigned experimental group. The exercise group did not perform appreciably more moderate/strenuous exercise compared to the control group.

Intention-to-treat analyses

Table 3 presents the intention-to-treat analyses for the QOL and physical fitness outcomes. No significant differences between groups were observed. Analyses of covariance did not change the results.

Exploratory ancillary analyses

Table 4 presents an unplanned ancillary analysis for the QOL outcomes. In this analysis, we compared those who improved in treadmill time over the course of the intervention ($n = 58$) to those who decreased or showed no change ($n = 35$). This approach has been used in previous research on exercise and cancer survivors when significant adherence and/or contamination problems have been encountered (Schwartz 1999; Mock *et al.* 2001; Schwartz *et al.* 2001). We selected the fitness measure as our grouping variable over the self-report exercise measure because of concerns of the fallibility of self-reports of moderate intensity exercise (Jacobs *et al.* 1993). Moreover, the RCT design of the study may be particularly problematic for self-report measures because it may invite differential reporting error between the arms. That is, participants in the exercise arm may over-report exercise because they know they are expected to exercise whereas participants in the control arm may under-report exercise because they

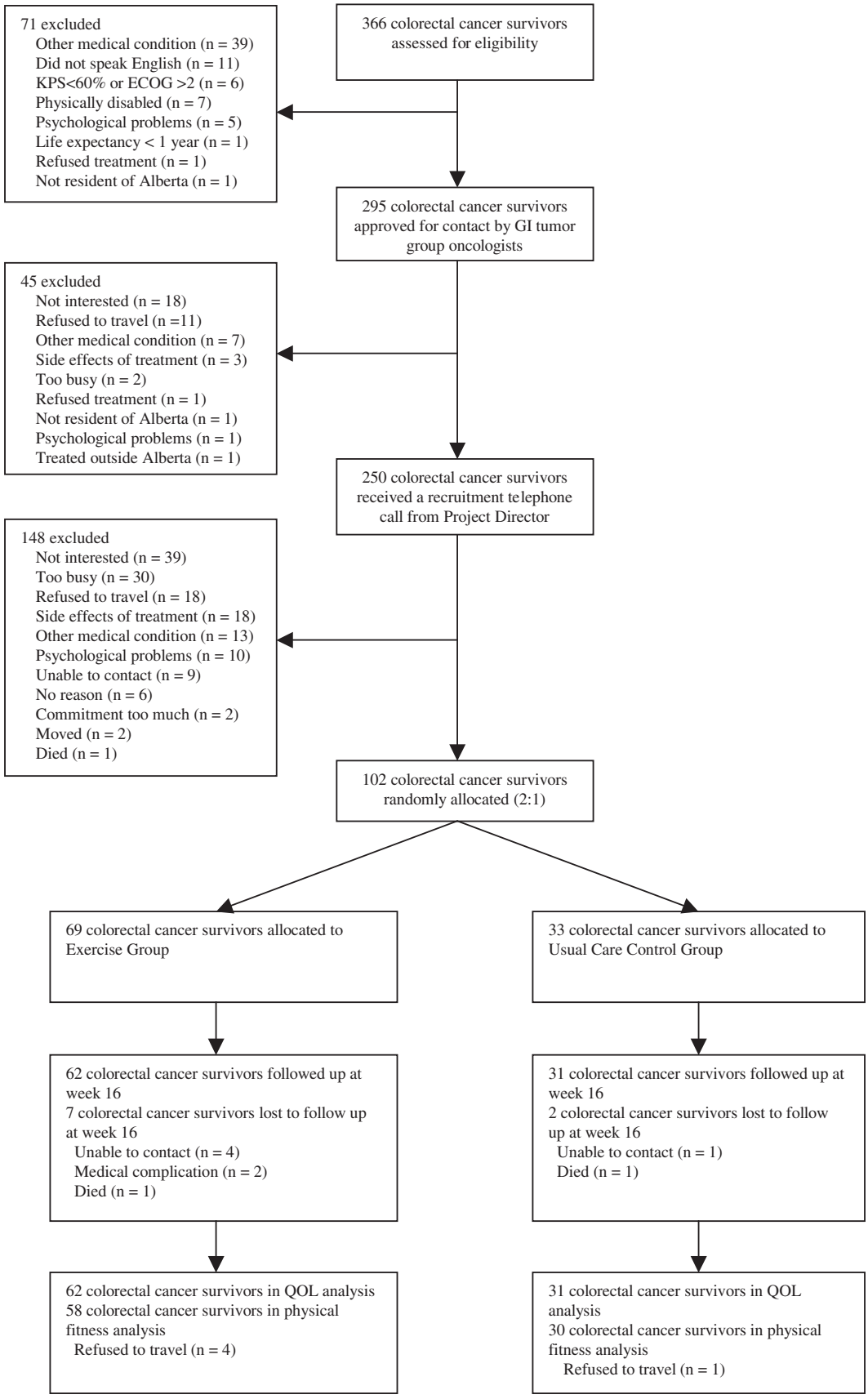

Figure 1. Flow of participants through the study.

Table 1. Baseline characteristics

Variable	Control group ($n = 31$)	Exercise group ($n = 62$)	P-value
Demographic data			
Age (mean; SD)	61.13 (9.93)	59.92 (10.73)	0.601
% Male	64.5	54.8	0.373
% Married	67.7	80.6	0.167
% Completed university	46.4	35.0	0.305
% Family income > $40 000 per year	53.6	65.5	0.286
% Full-time employed	30.0	29.5	0.961
Medical data			
Days post-surgery (mean; SD)	71.65 (18.08)	74.65 (34.02)	0.580
% Colon cancer	74.2	77.0	0.761
% Tumour stage 3/4	87.1	77.6	0.277
% Node stage 0	61.3	58.6	0.807
% Metastatic	0	6.9	0.135
% Surgery	100.0	100.0	1.00
% Colostomy	9.7	9.7	1.00
% Radiotherapy (RT)	16.1	23.0	0.445
% Chemotherapy (CT)	67.7	63.9	0.717
% Surgery alone	32.3	34.4	0.847
% Surgery plus RT	0	1.6	0.816
% Surgery plus CT	51.6	42.6	0.689
% Surgery plus RT and CT	16.1	21.3	0.757
Past exercise data (min week^{-1})			
Mild exercise (mean; SD)	164.03 (295.10)	121.45 (214.60)	0.430
Moderate exercise (mean; SD)	68.87 (97.57)	77.98 (137.01)	0.742
Strenuous exercise (mean; SD)	27.74 (57.43)	13.47 (69.36)	0.220
Moderate/strenuous exercise (mean; SD)	96.61 (126.39)	91.45 (148.42)	0.869
Total exercise (mean; SD)	260.65 (323.77)	212.90 (248.04)	0.433
% >60 Moderate/strenuous exercise	41.9	40.3	0.881
% >150 Moderate/strenuous exercise	32.3	27.4	0.628

Table 2. Adherence of participants to experimental conditions*

Variable	Control group ($n = 31$)	Exercise group ($n = 62$)	t (91)	P-value	d
Mild exercise	56.53 (65.18)	43.30 (103.41)	0.65	0.518	0.20
Moderate exercise	116.21(181.50)	145.24 (106.50)	0.97	0.334	0.16
Strenuous exercise	7.38 (36.33)	4.99 (20.23)	0.41	0.684	0.07
Moderate/strenuous exercise combined	123.59 (182.73)	150.23 (109.67)	0.88	0.383	0.15
Total exercise	180.12 (185.82)	193.52 (146.36)	0.38	0.705	0.07
% >60 Moderate/strenuous exercise	51.6	75.8	5.54	0.019	NA
% >150 Moderate/strenuous exercise	32.3	41.9	0.82	0.366	NA

d, standardized measure of effect size (calculated as the difference in means between the two groups divided by the standard deviation of the control group); NA, not applicable.
*Continuous data are presented as the mean (standard deviation) and categorical data are presented as the percentage. The units for all data are average minutes per week.

know they are not suppose to exercise. Changes in treadmill time are not susceptible to this differential reporting.

In these analyses, baseline values for the QOL outcomes did not differ between groups. The FACT-C increased by 4.3 points in the increased fitness group and decreased by 2.2 points in the decreased fitness group ($P = 0.038$; Figure 2). Differences between groups in changes from baseline to post-intervention were also observed for anxiety ($P = 0.005$; Figure 3) and the TOI ($P = 0.044$; Figure 4). Borderline significant differences were observed for satisfaction with life ($P = 0.084$), depression ($P = 0.055$), the FACT-G ($P = 0.056$), physical well-being ($P = 0.076$), and the colorectal cancer subscale ($P = 0.063$). Analyses of covariance with baseline value as the covariate indicated significant differences between fitness groups at post-test on the FACT-C ($P = 0.024$), anxiety ($P = 0.001$), depression ($P = 0.004$), FACT-G ($P = 0.036$), TOI ($P = 0.023$), physical well-being ($P = 0.046$), emotional well-being ($P = 0.039$), and the colorectal cancer subscale ($P = 0.019$). Borderline significant differences were observed for satisfaction with life ($P = 0.078$), fatigue ($P = 0.069$), and functional well-being ($P = 0.057$).

To examine potential biases in our analysis, we compared the decreased and increased fitness groups on all demographic, medical, and past exercise variables and found no differences. These data indicate that these

Table 3. Effect of exercise intervention on quality of life (QOL) and physical fitness outcomes (intention-to-treat analyses)*

Variable	Baseline	*P*-value†	Post-intervention	Mean change	Difference between groups in mean change [95% CI]	*P*-value‡
Primary QOL outcome						
FACT-C (0–132)						
Exercise group	106.0 (14.0)		107.4 (16.5)	1.4 (15.7)		
Control group	107.0 (16.0)	0.756	109.8 (18.8)	2.7 (12.5)	–1.3 [–7.8 to 5.1]	0.679
Secondary QOL outcomes						
Satisfaction with life (5–35)	26.2 (5.6)		26.9 (6.0)	0.7 (5.0)		
Exercise group	26.3 (6.6)	0.973	27.8 (5.9)	1.5 (4.1)	–0.8 [–2.8 to 1.2]	0.427
Control group						
Anxiety (20–80)						
Exercise group	37.7 (11.3)		33.5 (11.5)	–4.3 (13.0)		
Control group	39.2 (14.5)	0.595	35.5 (12.6)	–3.7 (10.7)	–0.6 [4.8 to –6.0]	0.828
Depression (0–60)						
Exercise group	9.6 (8.1)		8.6 (8.7)	–1.0 (10.7)		
Control group	10.1 (12.0)	0.837	9.6 (10.9)	–0.5 (8.8)	–0.5 [3.8 to –5.0]	0.792
Fatigue (0–52)						
Exercise group	13.1 (10.1)		12.7 (10.9)	–0.4 (11.0)		
Control group	11.9 (10.8)	0.579	12.1 (10.8)	0.2 (12.1)	–0.6 [4.4 to –5.6]	0.810
FACT-G (0–104)						
Exercise group	84.7 (11.6)		85.6 (13.0)	0.9 (12.2)		
Control group	84.5 (14.1)	0.937	86.5 (15.0)	2.0 (9.7)	–1.1 [–6.1 to 3.8]	0.652
Trial outcome index (0–84)						
Exercise group	65.3 (11.3)		66.1 (13.5)	0.8 (13.5)		
Control group	66.1 (10.8)	0.737	67.2 (14.4)	1.2 (11.9)	–0.4 [–6.0 to 5.3]	0.903
Physical well-being (0–28)						
Exercise group	23.3 (4.3)		22.8 (5.2)	–0.5 (5.7)		
Control group	22.9 (4.5)	0.711	22.6 (5.9)	–0.3 (5.7)	–0.2 [–2.6 to 2.3]	0.898
Functional well-being (0–28)						
Exercise group	20.7 (5.1)		21.5 (5.1)	0.8 (5.3)		
Control group	20.6 (5.4)	0.968	21.4 (5.3)	0.7 (4.5)	0.1 [–2.2 to 2.2]	0.987
Emotional well-being (0–24)						
Exercise group	20.0 (3.9)		20.3 (3.8)	0.3 (3.4)		
Control group	19.4 (4.9)	0.499	20.7 (3.7)	1.3 (2.3)	–1.0 [–2.2 to 0.1]	0.082
Social/family well-being (0–24)						
Exercise group	20.8 (4.4)		21.0 (3.7)	0.3 (3.2)		
Control group	21.6 (2.8)	0.354	21.8 (3.0)	0.2 (5.4)	0.1 [–1.2 to 1.3]	0.933
Colorectal cancer subscale (0–28)						
Exercise group	21.3 (4.5)		21.8 (4.6)	0.5 (4.8)		
Control group	22.5 (3.3)	0.143	23.2 (4.4)	0.7 (4.3)	–0.2 [–2.2 to 1.8]	0.839
Secondary fitness outcomes						
Treadmill time (seconds)						
Exercise group	396 (291)		548 (300)	153 (267)		
Control group	314 (270)	0.207	406 (301)	93 (280)	60 [–62 to 181]	0.330
Resting heart rate (bpm)						
Exercise group	79.4 (12.2)		75.0 (9.6)	–4.4 (13.6)		
Control group	79.6 (15.0)	0.955	77.9 (12.5)	–1.7 (12.1)	–2.7 [3.2 to –8.6]	0.361
Sum of skinfolds (mm)						
Exercise group	90.2 (33.4)		92.1 (35.4)	1.9 (13.8)		
Control group	88.1 (43.5)	0.803	91.6 (40.8)	3.4 (13.4)	–1.5 [4.5 to –7.7]	0.607
Body mass index [weight (kg)/height (cm)^2]						
Exercise group	27.4 (5.4)		28.2 (5.7)	0.9 (1.1)		
Control group	27.8 (5.2)	0.731	28.6 (5.1)	0.8 (1.8)	0.1 [0.7 to –0.5]	0.803
Flexibility (cm)						
Exercise group	18.6 (10.0)		20.9 (9.6)	2.3 (5.0)		
Control group	20.5 (11.2)	0.405	21.8 (10.9)	1.3 (5.1)	1.0 [–1.2 to 3.3]	0.358

FACT-C, Functional Assessment of Cancer Therapy-Colorectal; FACT-G, FACT-General.
Data are presented as the mean (standard deviation).
*Exercise group ($n = 62$), control group ($n = 31$) for QOL analyses; and exercise group ($n = 58$), control group ($n = 30$) for fitness analyses.
†*P*-value for difference between groups at baseline.
‡*P*-value for difference between groups in change from baseline to post-intervention.

Table 4. Association between change in fitness and change in quality of life (QOL) (ancillary analyses)*

Variable	Baseline	*P*-value†	Post-intervention	Mean change	Difference between groups in mean change [95% CI]	*P*-value‡
Primary QOL outcome						
FACT-C (0–132)						
Increased fitness group	106.9 (15.6)		110.9 (14.9)	4.3 (13.2)		
Decreased fitness group	105.9 (13.0)	0.796	103.7 (19.8)	–2.2 (16.1)	6.5 [0.4 to 12.6]	0.038
Secondary QOL outcomes						
Satisfaction with life (5–35)						
Increased fitness group	26.1 (5.6)		27.8 (5.3)	1.6 (4.3)		
Decreased fitness group	26.5 (6.5)	0.798	26.3 (6.9)	–0.1 (5.2)	1.7 [–0.2 to 3.7]	0.084
Anxiety (20–80)						
Increased fitness group	38.4 (11.5)		31.6 (10.0)	–6.8 (11.6)		
Decreased fitness group	37.9 (13.9)	0.850	38.3 (13.6)	0.4 (12.1)	–7.2 [–2.2 to –12.2]	0.005
Depression (0–60)						
Increased fitness group	9.1 (7.9)		6.7 (7.5)	–2.4 (10.1)		
Decreased fitness group	10.9 (11.8)	0.375	12.6 (11.3)	1.7 (9.6)	–4.1 [0.1 to –8.4]	0.055
Fatigue (0–52)						
Increased fitness group	11.9 (9.4)		10.7 (9.3)	–1.2 (9.8)		
Decreased fitness group	14.1 (11.6)	0.315	15.5 (12.5)	1.4 (13.5)	–2.6 [2.2 to –7.4]	0.290
FACT-G (0–104)						
Increased fitness group	84.8 (13.4)		87.8 (12.1)	3.0 (10.5)		
Decreased fitness group	84.4 (10.7)	0.873	82.8 (15.4)	–1.7 (12.3)	4.7 [–0.1 to 9.4]	0.056
Trial outcome index (0–84)						
Increased fitness group	65.8 (11.6)		68.9 (11.3)	3.1 (11.7)		
Decreased fitness group	65.0 (10.4)	0.733	62.5 (16.5)	–2.5 (14.3)	5.6 [0.2 to 11.0]	0.044
Physical well-being (0–28)						
Increased fitness group	23.2 (4.4)		23.6 (4.2)	0.4 (4.8)		
Decreased fitness group	23.1 (4.3)	0.959	21.4 (6.8)	–1.7 (6.7)	2.1 [–0.2 to 4.5]	0.076
Functional well-being (0–28)						
Increased fitness group	20.8 (5.6)		22.2 (4.9)	1.4 (5.1)		
Decreased fitness group	20.4 (4.7)	0.735	20.2 (5.4)	–0.2 (4.7)	1.6 [–0.5 to 3.7]	0.140
Emotional well-being (0–24)						
Increased fitness group	20.0 (3.9)		21.0 (3.2)	1.0 (2.9)		
Decreased fitness group	19.5 (4.8)	0.641	19.5 (4.4)	0.0 (3.4)	1.0 [–0.3 to 2.3]	0.124
Social/family well-being (0–24)						
Increased fitness group	20.9 (3.7)		21.1 (3.3)	0.2 (2.7)		
Decreased fitness group	21.3 (4.4)	0.620	21.6 (3.8)	0.3 (3.3)	–0.1 [–1.3 to 1.1]	0.850
Colorectal cancer subscale (0–28)						
Increased fitness group	21.8 (4.1)		23.1 (3.8)	1.3 (4.2)		
Decreased fitness group	21.5 (4.4)	0.669	20.9 (5.3)	–0.6 (5.0)	1.9 [–0.1 to 3.8]	0.063

FACT-C, Functional Assessment of Cancer Therapy-Colorectal; FACT-G, FACT-General.
Data are presented as the mean (standard deviation).
*Increased fitness group ($n = 58$); decreased fitness group ($n = 35$).
†*P*-value for difference between groups at baseline.
‡P-value for difference between groups in changes from baseline to post-intervention.

variables do not explain the differences we found in QOL between the two fitness groups.

DISCUSSION

We conducted an RCT to examine the effects of exercise on changes in QOL and physical fitness in recently resected colorectal cancer survivors. Our intention-to-treat analyses did not yield any significant differences between groups. Given our problems with exercise adherence and contamination, we conducted an exploratory ancillary analysis comparing participants who increased versus decreased their cardiovascular fitness. This analysis showed significant differences in favour of the increased fitness group for changes in the FACT-C, anxiety and the TOI.

The strengths and limitations of our trial merit comment. Strengths include the first RCT to examine exercise in colorectal cancer survivors, a good recruitment rate (35%), a decent sample size, inclusion of a fitness measure, validated measures of QOL, a good adherence rate (76%) and an excellent retention rate (91%). Limitations include a significant problem with exercise contamination in the control group (52%), an unsupervised exercise intervention, a self-report measure of exercise, a short exercise intervention, and a submaximal fitness test.

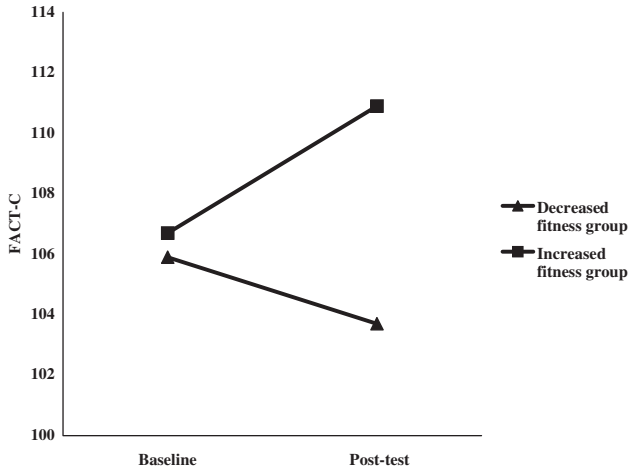

Figure 2. Significant change in quality of life as measured by the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) scale.

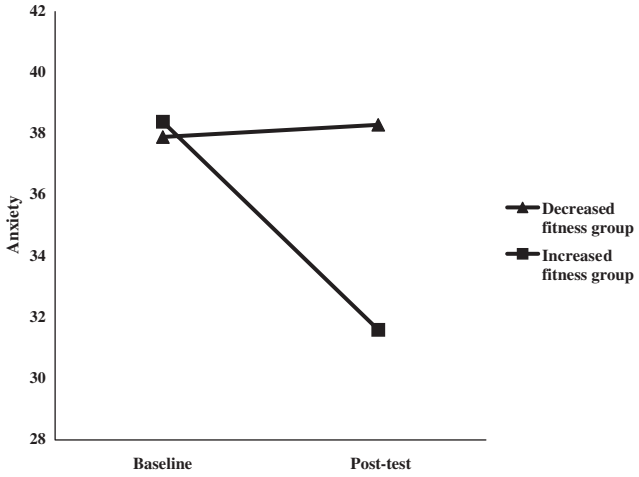

Figure 3. Significant change in anxiety.

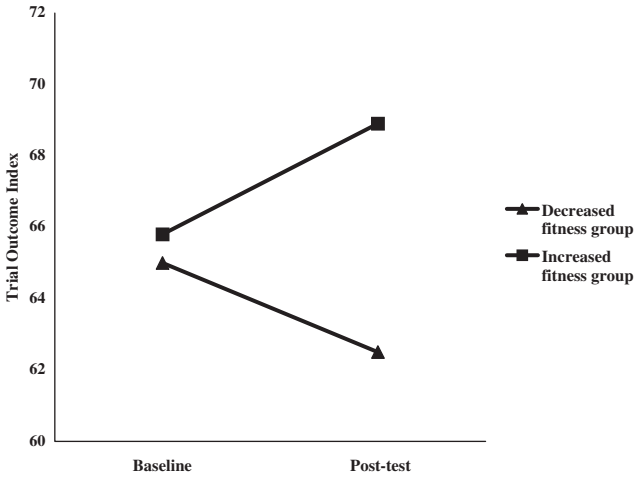

Figure 4. Significant change in the trial outcome index.

The main finding of our trial is that there were no differences between groups in changes in QOL or fitness using an intention-to-treat analysis. In our view, the failure of the intervention to produce meaningful differences between groups in exercise levels prevented us from providing a definitive test of the effects of exercise on QOL and physical fitness in this cancer survivor population. This failure resulted primarily from the high contamination rate in the control group (51.6%) but also from the less than optimal adherence rate in the exercise group (75.8%).

Exercise adherence and contamination

The adherence problem in exercise RCTs has been established in the older adult literature (Martin & Sinden 2001) and is becoming apparent in the cancer literature. Adherence rates to home-based exercise interventions in cancer survivors appear to be 60–70% (Courneya *et al*. 2002). Consequently, our exercise adherence rate was comparable to that found in other studies. The problem of exercise contamination in the control group has received less attention (Courneya *et al*. 2002). Researchers rarely monitor contamination rates, presumably because it is assumed that participants in the control group will not exercise. A recent study, however, reported that 50% of breast cancer survivors assigned to the control group adopted the exercise programme (Mock *et al*. 2001). The result of that study is similar to our study and suggests that contamination may be a significant problem.

There are several possible explanations for the high contamination rates in these trials. First, cancer survivors can be very motivated for behaviour change after their diagnosis (Demark-Wahnefried *et al*. 2000; Jones & Courneya 2002). Participants join an exercise study because they want to exercise, not because they want to be controls. As pointed out by Mock *et al*. (2001), assignment to a control group may be disappointing to participants and, consequently, many may continue or begin an exercise programme despite their group assignment. One possible solution to this problem may be to screen out regular exercisers (Mock *et al*. 2001). Courneya *et al*. (2002) present data to show that this strategy should reduce contamination rates dramatically without unduly affecting adherence rates. A second possible solution, attempted in the present study, is to offer the intervention to the controls at the end of the study. Obviously this strategy was not sufficient to eliminate the contamination problem in the present study. A third possible solution is to ensure that participants understand the implications of random assignment and what is expected of them in each group

before joining the study. Some useful strategies to achieve this goal have been provided in the literature (Shumaker *et al*. 2000).

A second possible explanation for the contamination problem is the nature of the exercise intervention itself. That is, it is relatively easy for participants to adopt an exercise programme when it is home-based and requires little equipment or access to facilities (e.g. walking). In our other RCTs with cancer survivors, we have obtained higher adherence and lower contamination rates using supervised exercise programmes and expensive equipment (Courneya *et al*. 2003b; Segal *et al*. 2003). Of course, the disadvantage of this approach is that home-based walking programmes are typically preferred by cancer survivors and probably most likely to be adopted by this group (Jones & Courneya 2002).

A third possible cause of our contamination problem is the weekly telephone calls that we made to the control group to report their exercise. These calls were likely a constant reminder to control participants that they were in an exercise study and perhaps prompted them to exercise. We made the weekly telephone calls to the control group for two reasons: (i) to be able to measure the extent of the exercise contamination problem and (ii) to provide equal contact and attention for control group participants. We felt that recalling exercise on a weekly basis would be more accurate than at the end of a 16-week study. Nevertheless, there may be alternative strategies to the weekly telephone calls that could be considered.

Findings from exploratory ancillary analyses

In an 'on-treatment' ancillary analysis, we were able to show a significant association between change in fitness and change in QOL. We found that participants who increased their fitness over the course of the intervention showed improvements in the FACT-C, anxiety and the TOI compared to those who decreased fitness. The analysis of covariance results were even stronger. The magnitude of change in the FACT-C was 6.5 points and for the FACT-G was 4.7 points. A change of 4 or more points in the FACT-G is considered a minimal clinically important difference (Cella *et al*. 2002), but no such guideline is available for the FACT-C. Additional analyses of the subscales of the FACT-C indicated beneficial effects for the TOI, which contains items that mainly reflect physical and functional well-being.

Of course, such an ancillary analysis does not demonstrate that a change in exercise will cause a change in QOL or even that a change in fitness will cause a change in QOL. It does, however, suggest that exercise interventions that improve fitness *may* also enhance QOL in colorectal cancer survivors. This finding is consistent with a recent RCT in breast cancer survivors showing changes in fitness mediated some of the QOL changes (Courneya *et al*. 2003b). The only means of answering this question in colorectal cancer survivors, however, is to conduct an RCT that overcomes the problems experienced in the present study.

Summary

Our intention-to-treat analyses did not yield any significant effects of a home-based, moderate intensity exercise intervention in colorectal cancer survivors. Consequently, our data do not support the use of this exercise intervention in colorectal cancer survivors. Nevertheless, we feel that problems with exercise adherence and contamination prevented us from providing a definitive test of this question. Clearly, better controlled trials are needed to determine the effects of exercise in colorectal cancer survivors. In an exploratory ancillary analysis, we did find that increased cardiovascular fitness was associated with improvements in QOL. Given this finding, we suggest that additional research testing exercise interventions in this population is warranted, particularly exercise interventions designed to increase cardiovascular fitness.

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