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Article

ARTICLE

Randomized Trial of Exercise on Quality of Life in Women With Ovarian Cancer: Women's Activity and Lifestyle Study in Connecticut (WALC)

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Abstract

Background: Ovarian cancer survivors experience a wide range of treatment side effects that can negatively affect health-related quality of life (HRQOL). Physical activity has been shown to improve HRQOL and cancer-related fatigue (CRF) for other cancer survivors; however, no large randomized controlled trial (RCT) has been conducted for ovarian cancer.
Methods: This study examined the impact of a six-month RCT of exercise vs attention control on change in HRQOL (Short Form Health Survey-36) and CRF (Functional Assessment of Cancer Therapy-Fatigue Scale) in ovarian cancer survivors. Women (n = 144) were randomly assigned to study arms between May 1, 2010, and March 20, 2014. All statistical tests were two-sided.
Results: A total of 74 women were randomly assigned to exercise and 70 to attention control. A total of 113 (78.5%) of the participants completed the six-month assessment. Adherence to the exercise intervention was excellent (166.0±66.1 minutes/week in the exercise arm). At six months, women in the exercise arm had improved physical HRQOL (SF-36 Physical Component Summary Score) compared with the control arm, 1.8 (SD = 1.1) vs –2.0 (SD = 1.2) , respectively (group difference = 3.7, SD = 1.2, 95% confidence interval [CI] = 0.7 to 6.8, $P = .02$). No group differences were seen for change in mental HRQOL. There was a statistically significant improvement in the fatigue score (Functional Assessment of Cancer Therapy–Fatigue) for exercisers (4.0, SD = 1.1, 95% CI = 1.8 to 6.2, $P < .001$) but not for controls (1.2, SD = 1.2, 95% CI = –1.1 to 3.5, $P = .31$), with a between-group difference of 2.8 (SD = 1.5, 95% CI = –0.2 to 5.7, $P = .06$).
Conclusions: We found a six-month home-based, telephone-delivered exercise intervention of primarily brisk walking to be associated with improved physical HRQOL in women with ovarian cancer. Given that higher HRQOL and exercise have both been associated with overall survival in women diagnosed with ovarian cancer, oncologists and primary care providers should recommend and refer women diagnosed with ovarian cancer to clinic- or community-based exercise programs.

Ovarian cancer is the fifth leading cause of cancer death in women in the United States (1). While over 90% of women with localized disease will survive five years or more, survival of this duration for those with late-stage disease is only 28% (1). Health-related quality of life (HRQOL) is adversely impacted by ovarian cancer treatment (2), with fatigue a commonly reported

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side effect. Cancer-related fatigue (CRF) is different from normal fatigue and is characterized as "an unusual, persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning" (3). CRF can impact the ability to perform activities of daily living and is negatively associated with HRQOL (4).

Favorable associations of exercise on HRQOL and CRF have been observed in cancer survivors, but few studies have included women diagnosed with ovarian cancer (5). Four small pilot exercise interventions (40 survivors or fewer per study) in ovarian cancer survivors have been published, with three observing an effect of exercise on improving HRQOL (6–9). An ongoing trial, the Lifestyle Intervention for Ovarian Cancer Enhanced Survival, will examine the impact of diet and exercise intervention on progression-free survival in women with ovarian cancer. However, given that few studies examine physical activity among ovarian cancer survivors and that those have limited size and study duration, definitive results of the effect of exercise on HRQOL and CRF are lacking.

The purpose of the Women's Activity and Lifestyle Study in Connecticut (WALC) was to examine the effect of a six-month aerobic exercise intervention vs attention control on change in HRQOL and CRF in women diagnosed with ovarian cancer. To our knowledge, this study is the largest randomized controlled trial of exercise in ovarian cancer survivors to date. We hypothesized that women randomly assigned to exercise would experience improvements in HRQOL and CRF compared with women randomly assigned to attention-matched control.

Methods

Study Population

Ovarian cancer survivors were randomly assigned between May 1, 2010, and March 20, 2014. Women deemed eligible after baseline assessments were randomly assigned in a 1:1 ratio to a six-month exercise program or to an attention control arm. Random assignment was block-stratified by disease stage (stage I and II vs III and IV) and age (55 years), and sequentially numbered envelopes within each strata were created and sealed until random assignment. Eligibility criteria included: English-speaking, between age 18 and 75 years, diagnosed with ovarian cancer within the past four years, and completion of chemotherapy at least one month prior to random assignment. Women had to be exercising fewer than 90 minutes per week and had to have received physician consent to start an exercise program.

Recruitment and Study Visits

Women from Connecticut were recruited using the Rapid Case Ascertainment (RCA) Shared Resource of the Yale Cancer Center, a Connecticut Tumor Registry field arm that identified women from all hospitals in Connecticut. Recruitment letters were sent to ovarian cancer survivors identified through RCA, with each participant telephoned to solicit interest and eligibility. Additionally, women were recruited by physicians at two additional study sites, Dana-Farber Cancer Institute (Boston, MA) and Geisinger Health Systems (Danville, PA).

The majority of women who lived outside of Connecticut learned about the study through national support groups, physicians, or brochures in clinic waiting rooms. These survivors were screened via telephone, and after receipt of the baseline questionnaires they were randomly assigned to exercise or attention control.

The study was approved by the Connecticut Department of Public Health and the Yale Human Investigation Committees, Dana-Farber/Harvard Cancer Center Institutional Review Board (IRB), Geisinger Health Systems IRB, and all 21 Connecticut hospital IRBs. The trial is registered at ClinicalTrials.gov: NCT02107066 (https://clinicaltrials.gov/ct2/show/NCT02107066). All participants gave written informed consent.

Measures

Self-reported sociodemographic variables were ascertained at baseline. Disease stage, time since diagnosis, chemotherapy treatment status, smoking history, family history of ovarian cancer, and history of recurrence were obtained via self-report, with an additional questionnaire completed by the participants' physicians to obtain physician-verified treatment information and review of medical records. Height and weight were measured using standard procedures. Participants were weighed in light clothing without shoes. Measurements were rounded up to the nearest 0.1 kg. Height without shoes was measured using a stadiometer, with measurements rounded up to the nearest 0.5 cm. Physical activity levels were assessed using the Modifiable Physical Activity Questionnaire (10), which asked about the duration and frequency of 20 recreational activities performed during the previous six months.

The main study outcomes of interest were HRQOL and CRF. The Short Form 36 (SF-36) health survey, version 1, was completed as a measure of HRQOL (11). The SF-36 survey was interpreted using eight subscales that can be combined into physical (PCS) and mental (MCS) component summary scores. The PCS score describes physical health and is comprised of the general health, bodily pain, physical functioning, and role-physical subscales. The MCS score describes mental health and is comprised of mental health, role-emotional, social functioning, and vitality subscales. Higher PCS and MCS scores indicate better HRQOL. The PCS and MCS are standardized using the 1998 US general population survey, so that a score of 50 represents the population average with a standard deviation of 10. The SF-36 is a reliable measure that has been broadly used in cancer populations and has a Cronbach's alpha coefficient ranging from .78 to .91 (12). CRF was assessed using the Functional Assessment of Cancer Therapy–Fatigue (FACT-F) questionnaire, comprised of 13 fatigue-related items and a test-retest r ranging from 0.84 to 0.90 (13). Each item on the FACT-F is answered on a four-point scale and summed, with scores ranging between 0 and 52. Lower scores indicate greater CRF (14,15). A three-point difference is considered to be a clinically important difference in physical function and CRF (15–17).

Intervention

The exercise intervention consisted of a six-month home-based moderate-intensity aerobic exercise program that was facilitated by weekly telephone calls to each participant from an American College of Sports Medicine (ACSM)–certified cancer exercise trainer. Women in the exercise arm were asked to participate in 150 minutes per week of moderate-intensity aerobic exercise, mainly brisk-walking, as recommended for cancer survivors by the ACSM and the American Cancer Society. The seven-day daily activity log (DAL) was used as the primary adherence measure of exercise. Women wore heart rate monitors and were given a targeted heart rate range (based on the

Karvonen method for moderate to vigorous intensity) (18). Participants recorded their exercise and heart rate in their daily activity log, and then reported this information to the exercise trainer during the weekly phone calls.

Using the weekly 26-chapter book that we developed, the trainer provided weekly individualized counseling via telephone to motivate participants to exercise. Each chapter contained information on a topic related to exercise as well as a topic relevant to ovarian cancer survivorship. The attention control arm received weekly phone calls from a WALC staff member, along with a 26-chapter book that only contained ovarian cancer survivorship–related information.

Statistical Analysis

The standardized SF-36 scales used in our trial have US national norm data of 50±10, thus, 140 subjects were needed to provide 80% power to detect a five-point difference (10% of norm) between the two arms with a statistical significance level of .05, after accounting for a 10% attrition rate. We used the longitudinal analysis method to achieve additional efficiency (19).

A mixed-model repeated measures analysis as proposed by Fitzmaurice et al. (19) was used to evaluate baseline to six-month differences in HRQOL and CRF scores between women randomly assigned to exercise vs attention control according to intention to treat. Baseline measures were included as part of the response profile, where the mean scores of the two arms at baseline were constrained to be equal within the regression model. Linear contrasts were used to obtain the change scores in each group and group difference as well. Least squares mean ± SD and 95% confidence intervals were reported. The maximum likelihood method was used to handle missing data (20). Study site, recurrence before and during study, and adjuvant treatment were included as covariates although there was little difference with or without adjustment therefore, we only present the adjusted results. Due to different percentages of missing values in the two arms, we conducted sensitivity analysis using multiple imputation under the missing not at random assumption with a tipping point approach. The treatment effect on PCS would lose statistical significance only if the missing women who were in the exercise group had a more than 1.2-point worse PCS at six months than controls (21).

Among women randomly assigned to exercise, we explored the dose effect of exercise on HRQOL and CRF and compliance to the weekly calls. Women who experienced a recurrence during the study continued with the study to the best of their ability and were included in the analyses. We examined effect modification of exercise on HRQOL and CRF by time since diagnosis, disease stage, baseline and during trial recurrence status, and baseline fatigue and HRQOL levels. Simple Bonferroni correction for multiple comparisons was used, such that a P value of less than .025 was set as statistical significance cut-point for the primary analysis. A two-sided .05 statistical significance level was applied for other analyses, including those for CRF and eight subdomains of HRQOL, as well as other exploratory analyses. All analyses were conducted using SAS, version 9.4 (SAS, Cary, NC). All statistical tests were two-sided.

Results

Trial Enrollment

Figure 1 describes the recruitment of 144 ovarian cancer survivors into the trial, with 74 randomly assigned to exercise and 70 randomly assigned to attention control. A total of 113 (78.5%) of the participants completed the six-month assessment (Figure 1). Reasons for loss to follow-up included withdrawal (12.9%), too ill (41.9%), and unknown (45.2%).

Baseline Characteristics

Participants were 57.3±8.6 (mean±SD) years of age, 1.7±1.0 years postdiagnosis, had a body mass index of 29.0±7.0, and were participating in 28.3±41.6 minutes per week of moderate- to vigorous-intensity exercise (Table 1). A majority of women were diagnosed with stage III or IV ovarian cancer (54.9%), and 93.1% reported having received chemotherapy. At baseline, 16.0% of the women reported having had disease recurrence prior to enrollment. There were no statistically significant differences in baseline characteristics between women randomly assigned to exercise vs attention control.

Intervention Adherence

Over the six-month intervention period, women randomly assigned to exercise participated in 166.0±66.1 minutes per week (mean±SD) of moderate-intensity exercise (Table 2). Average attendance to the 25 weekly telephone calls was 20.4±5.6 sessions and 21.7±5.5 sessions for the attention control and exercise arms, respectively (Table 2). No adverse events were reported by participants enrolled in this study.

HRQOL and CRF Scores

Table 3 presents the mean baseline scores, as well as change between baseline and six-month scores for HRQOL and CRF. Women randomly assigned to the exercise arm had a mean 1.8-point (SD = 1.1) improvement in physical functioning (95% confidence interval [CI] = –0.4 to 3.9) as measured by the PCS, compared with a 2.0-point (SD = 1.2) decline (95% CI = –4.3 to 0.3) in the attention control arm (between-group difference of 3.7±1.2, 95% CI = 0.7 to 6.8, P = .02, corresponding to a standardized effect size of 0.41). Statistically significant between-group differences were observed for changes in SF-36 subscales for physical functioning, social, and general health ($P \leq .02$). Change in mental HRQOL (MCS) was not statistically significantly different. There was a statistically significant improvement in the FACT-F for exercisers (4.0, SD = 1.1, 95% CI = 1.8 to 6.2, $P < .001$) but not for controls (1.2, SD = 1.2, 95% CI = –1.1 to 3.5, P = .31), with a between-group difference of 2.8 (SD = 1.5, 95% CI = –0.2 to 5.7, P = .06) (Table 3).

We were able to ascertain recurrence status for 136 participants during the study. Twenty-four women in the control arm had a recurrence during the study, compared with 17 in the exercise arm. Among women who did not have a recurrence of ovarian cancer during the study (n = 95, n = 53 exercisers, and n = 42 controls), women randomly assigned to exercise had a statistically significant improvement in PCS (3.4±1.1, 95% CI = 1.1 to 5.6, P = .004) compared with a statistically nonsignificant change in PCS in the control group (–0.3±1.3, 95% CI = –2.8 to 2.2, P = .81) (data not shown). The group difference was 3.7±1.6 (95% CI = 0.5 to 6.9, P = .03). However, both exercisers and controls who had a recurrence during the study experienced worsening PCS (–7.1±2.5, 95% CI = –12.1 to –2.1, P = .006, in exercisers, and –6.2±2.1, 95% CI = –10.4 to –2.1, P = .004, in controls; group difference –0.9±3.1, 95% CI = –5.4 to 7.1, P = .78) (data not shown).

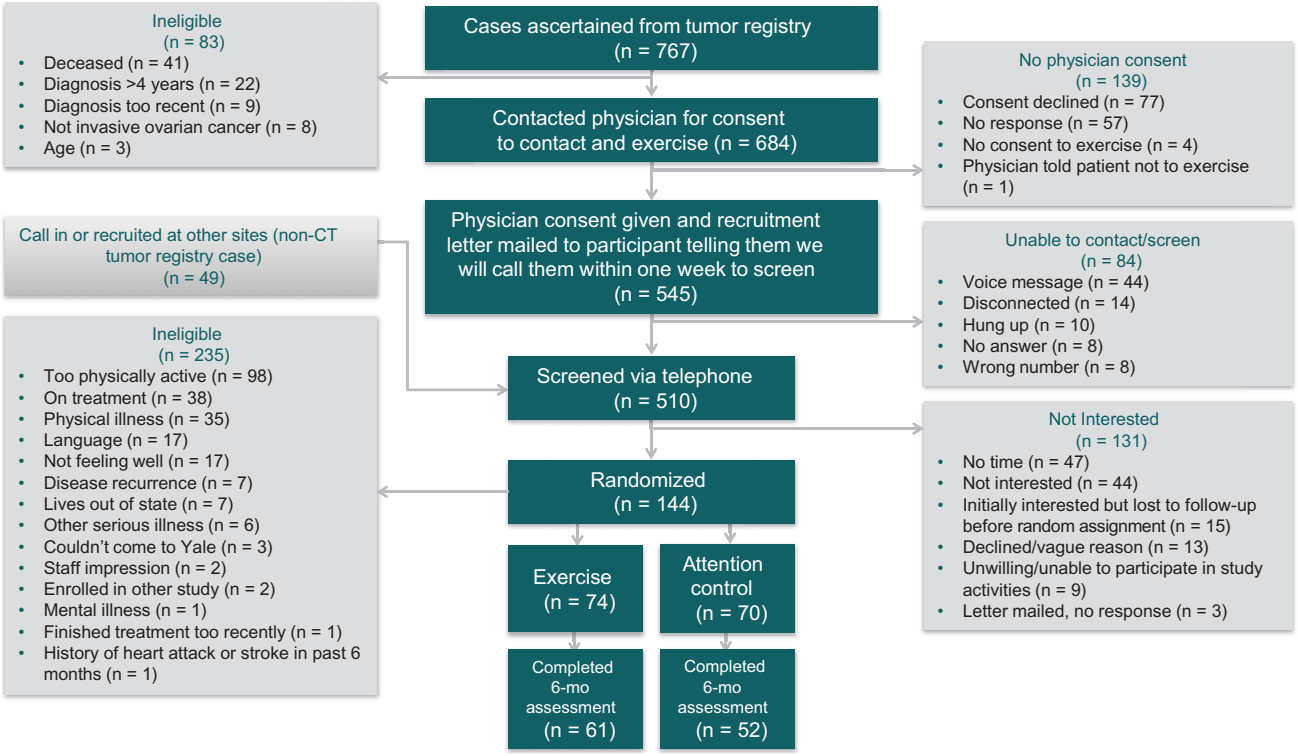

Figure 1. Flow of participants through the Women's Activity and Lifestyle Study in Connecticut study.

Table 4 shows the dose-response results for women randomly assigned to exercise and attendance to weekly phone calls for both groups, with a statistically significant improvement in physical HRQOL (3.8±1.4, 95% CI = 0.9 to 6.7, $P = .01$) and CRF levels (5.2±1.4, 95% CI = 2.3 to 8.0, $P < .001$) at the six-month time point in women randomly assigned to exercise who participated in exercise 150 or more minutes per week, but not among women randomly assigned to exercise who exercised fewer than 150 minutes per week. The change in physical HRQOL was statistically significantly greater in the group that exercised 150 or more minutes per week compared with those who exercised less (6.8-point difference in between-group change, 95% CI = 1.5 to 12.1, $P = .01$). The change in FACT-F was 5.8 points greater for those who exercised 150 or more minutes per week compared with those who exercised less (95% CI = 0.8 to 10.9, $P = .02$) after adjusting for study site, recurrence at baseline and during study, and chemotherapy at baseline. Women randomly assigned to exercise who attended 80% or more of the telephone calls had a statistically significant improvement in FACT-F (10.4 points, 95% CI = 2.0 to 18.9, $P = .02$) and PCS (9.6 points, 95% CI = 0.6 to 18.7, $P = .04$) compared with women randomly assigned to attention control who also attended 80% or more of the telephone calls (Table 4). Additionally, disease recurrence during the study did not have a statistically significant impact on adherence to telephone calls; it did impact levels of exercise among women randomly assigned to the exercise group (35.3% of women who recurred had average exercise level ≥150 minutes/week, compared with 77.4% of women who did not have a recurrence, $P = .003$) (data not shown).

Time since diagnosis modified the effect of exercise vs control on PCS (between-group difference of 5.0, 95% CI = 0.5 to 9.4, $P = .03$) (data not shown) among women who were diagnosed 18 or more months prior to study enrollment, but no between-group difference among women diagnosed less than 18 months prior to enrollment.

We examined the exercise effects on PCS and the SF-36 Physical Functioning (SF-PF) subscale and found that the effects varied according to baseline PCS and SF-PF level. Those who had worse baseline scores benefited more from exercise as compared with those with better baseline scores (exercise effect decreased by 0.3 points with every 1 point less in baseline score, 95% CI = –0.01 to 0.6, $P = .05$, for PCS, and 95% CI = 0.05 to 0.6, $P = .02$, for SF-PF) (data not shown).

Discussion

Our exercise intervention of 150 minutes per week of primarily brisk walking improved physical HRQOL in ovarian cancer survivors. A three-point difference in physical HRQOL was observed between the exercise and attention control groups. With a Cohen's effect size of 0.4 for physical HRQOL, this implies that 66% of the women in the exercise group experienced an improvement in physical HRQOL in relation to the control group. We had excellent adherence to exercise, with an average of 166.0±66.1 minutes per week in the exercise group. A dose-response association was observed, with exercise at recommended levels of 150 or more minutes per week associated with greater improvements in physical HRQOL. Our finding that exercise at the recommended levels can improve physical HRQOL is clinically important as there is some literature to suggest that HRQOL is associated with overall survival in women diagnosed with ovarian cancer (22). Thus, it could be that exercise could benefit not just HRQOL but survival as well. Oncologists should therefore implement exercise counseling in their practices for ovarian cancer patients and/or refer to community-based exercise programs, such as the LIVESTRONG at the YMCA exercise program (23).

The baseline CRF scores of our study participants fall between the published CRF scores of two other studies of ovarian

Table 1. Baseline characteristics by study arm

Characteristic	Total study population (n = 144)*	Study arm	
		Exercise intervention (n = 74)*	Attention control (n = 70)*
Mean age (SD), y	57.3 (±8.6)	57.3 (±8.8)	57.4 (±8.5)
Race/ethnicity, No. (%)			
Non-Hispanic white	137 (95.1)	72 (97.3)	65 (92.9)
Other	7 (4.9)	2 (2.7)	5 (7.1)
Education Level, No. (%)			
No GED or equivalent	4 (2.8)	3 (4.1)	1 (1.4)
GED and some college/Associates	60 (41.7)	32 (43.2)	28 (40.0)
College graduate or advanced degree	80 (55.6)	39 (52.7)	41 (58.6)
Employment status, No. (%)			
Unemployed/retired	69 (48.3)	34 (46.0)	35 (50.7)
Employed part-time (<35 h/wk)	29 (20.3)	18 (24.3)	11 (15.9)
Employed full-time (>35 h/wk)	45 (31.5)	22 (29.7)	23 (33.3)
Marital status, No. (%)			
Single	15 (10.4)	8 (10.8)	7 (10.0)
Divorced, separated, or widowed	24 (16.7)	16 (21.6)	8 (11.4)
Married or living with partner	105 (72.9)	50 (67.6)	55 (78.6)
Family history of ovarian cancer, No. (%)			
Yes	18 (12.7)	11 (14.9)	7 (10.3)
No	124 (87.3)	63 (85.1)	61 (89.7)
Cancer stage at diagnosis, No. (%)			
I	34 (23.6)	21 (28.4)	13 (18.6)
II	30 (20.8)	11 (14.9)	19 (27.1)
III	58 (40.3)	31 (41.9)	27 (38.6)
IV	21 (14.6)	10 (13.5)	11 (15.7)
Unknown	1 (0.70)	1 (1.4)	0 (0.0)
Mean time since diagnosis (SD), y	1.7 (±1.0)	1.7 (± 0.9)	1.7 (±1.1)
Chemotherapy prior to enrollment, No. (%)			
Yes	134 (93.1)	69 (93.2)	65 (92.9)
No	10 (6.9)	5 (6.8)	5 (7.1)
Cancer recurrence prior to enrollment, No. (%)			
Yes	23 (16.0)	13 (17.6)	10 (14.3)
No/unknown	121 (84.0)	61 (82.4)	60 (85.7)
Mean body mass index (SD), kg/m^2	29.0 (±7.0)	29.0 (±7.2)	29.1 (±6.8)
Mean physical activity (SD), min/wk	28.3 (±41.6)	26.0 (±44.2)	30.8 (±38.9)

*Numbers may not sum to total because of missing data, and percentages may not sum to 100% because of rounding. GED = General Education Diploma.

Table 2. Adherence to the exercise intervention and telephone calls from baseline to 6 mo

Adherence to exercise	Exercise arm (n = 74)	Adherence to calls	Attention control arm (n = 70)	Exercise arm (n = 74)	P*
Mean (SD), min/wk	166.0 ± 66.1	Mean (SD) attendance to calls	20.4 ± 5.6	21.7 ± 5.5	.18
% of goal (150 min/wk)	110.7	of goal (25 calls)	81.7	86.7	
% participants adhering to:		of subjects adhering to:			
≥150 min/wk (100% of goal)	64.9	25 calls (100 of goal)	19.1	47.3	
≥120 min/wk (80%)	83.8	≥20 calls (80)	73.5	79.7	
≥90 min/wk (60%)	91.9	≥15 calls (60)	86.8	89.2	
≥60 min/wk (40%)	91.9	≥10 calls (40)	94.1	94.6	
≥30 min/wk (20%)	98.6	≥5 calls (20)	97.1	98.6	
≥0 min/wk (0%)	100.0	≥0 calls (0)	100.0	100.0	

*P value is for two-sided t test (continuous variables).

cancer survivors who had completed treatment (reported mean scores were approximately 27 [7] and 43 [24]), and published normative data for the FACT-F had a mean normative score of 40.1 (SD = 10.4) (17). Compared with the general population, our study participants reported greater fatigue at baseline. Similarly, at baseline, women in our study had average physical and mental HRQOL scores that were worse than the general population mean of 50. Baseline physical HRQOL modified the effect of exercise, indicating that women with lower physical HRQOL at baseline could benefit more from exercise compared

Table 3. Change in FACT-Fatigue, SF-36 summary, and subscale scores for exercise (n = 74) vs attention control (n = 70)*

Variables	Baseline		Change over 6 mo				
	Attention control arm Mean (SD)	Exercise arm Mean (SD)	Attention control arm Mean (95% CI)	Exercise arm Mean (95% CI)	Effect Mean (95% CI)	Cohen's effect size	P†
FACT-F	35.8 (10.8)	36.7 (11.1)	1.2 (–1.1 to 3.5)	4.0 (1.8 to 6.2)	2.8 (–0.2 to 5.7)	0.26	.06
SF-36 component summary							
Physical	45.6 (9.2)	46.3 (8.9)	–2.0 (–4.3 to 0.3)	1.8 (–0.4 to 3.9)	3.7 (0.7 to 6.8)	0.41	.02
Mental	48.9 (11.4)	47.5 (11.3)	0.5 (–1.9 to 2.9)	1.6 (–0.6 to 3.9)	1.2 (–1.8 to 4.2)	0.11	.44
Subscales							
Physical	45.8 (8.1)	45.3 (9.9)	–2.0 (–3.8 to –0.2)	2.3 (0.6 to 4.0)	4.3 (1.9 to 6.7)	0.48	<.001
Roles: physical	41.9 (11.1)	42.5 (10.9)	–0.4 (–3.3 to 2.5)	2.1 (–0.6 to 4.8)	2.5 (1.3 to 6.3)	0.23	.19
Bodily pain	51.0 (9.9)	51.8 (9.5)	–1.8 (–4.5 to 0.8)	0.1 (–2.4 to 2.6)	1.9 (–1.5 to 5.3)	0.20	.27
Vitality	48.3 (10.8)	48.4 (10.9)	0.0 (–2.2 to 2.3)	2.6 (0.6 to 4.7)	2.6 (–0.3 to 5.4)	0.24	.08
Social	48.2 (10.6)	46.8 (9.9)	–1.4 (–3.8 to 1.1)	2.4 (0.0 to 4.7)	3.7 (0.6 to 6.9)	0.36	.02
Roles: emotional	45.6 (11.5)	45.7 (12.5)	0.4 (–2.7 to 3.6)	1.8 (–1.1 to 4.8)	1.4 (–2.5 to 5.2)	0.12	.47
Mental health	49.2 (9.5)	47.1 (10.4)	0.8 (–1.2 to 2.8)	1.5 (–0.3 to 3.4)	0.8 (–1.8 to 3.3)	0.08	.56
General	45.4 (8.5)	46.4 (9.7)	–2.3 (–4.2 to –0.4)	1.6 (–0.2 to 3.4)	3.9 (1.3 to 6.5)	0.43	.004

*Covariates included: study site, recurrence prior to and during study, adjuvant treatment. CI = confidence interval; FACT-F = Functional Assessment of Cancer Therapy–Fatigue; MCS = mental component summary; PCS = physical component summary.
†P value from linear mixed-model analysis (two-sided).

Table 4. Change over 6 mo of HRQOL stratified by adherence to the exercise intervention and telephone calls

Variables	Change in FACT-F		Change in PCS		Change in MCS	
	Mean (95% CI)	P*	Mean (95% CI)	P*	Mean (95% CI)	P*
Average exercise, min/wk						
<150 (n = 26)	–0.7 (–4.8 to 3.5)	.75	–3.0 (–7.4 to 1.4)	.18	1.0 (–3.4 to 5.4)	.64
≥150 (n = 48)	5.2 (2.3 to 8.0)	<.001	3.8 (0.9 to 6.7)	.01	2.3 (–0.7 to 5.2)	.13
Difference of exercise effect by exercise level	5.8 (0.8 to 10.9)	.02	6.8 (1.5 to 12.1)	.01	1.2 (–4.1 to 6.5)	.64
Adherence to telephone calls						
Attended <80% calls						
Control (n = 20)	8.2 (2.5 to 13.8)	.005	0.9 (–5.0 to 6.7)	.77	2.6 (–3.5 to 8.7)	.40
Exercisers (n = 15)	2.0 (–4.0 to 8.1)	.51	–3.9 (–10.2 to 2.5)	.22	1.7 (–4.9 to 8.3)	.60
Effect of exercise	–6.1 (–14.0 to 1.7)	.13	–4.7 (–13.2 to 3.7)	.27	–0.9 (–9.4 to 7.6)	.84
Attended ≥80% calls						
Control (n = 50)	–0.3 (–2.8 to 2.3)	.82	–2.6 (–5.1 to –0.2)	.04	–0.1 (–2.8 to 2.6)	.96
Exercisers (n = 59)	4.0 (1.7 to 6.4)	.001	2.3 (0.1 to 4.6)	.05	1.4 (–1.1 to 3.9)	.27
Effect of exercise	4.3 (1.2 to 7.5)	.01	4.9 (1.7 to 8.1)	.003	1.5 (–1.8 to 4.7)	.38
Difference of exercise effect by attendance	10.4 (2.0 to 18.9)	.02	9.6 (0.6 to 18.7)	.04	2.3 (–6.8 to 11.5)	.61

*P value from linear mixed-model analysis (two-sided). CI = confidence interval; FACT-F = Functional Assessment of Cancer Therapy–Fatigue; MCS = mental component summary; PCS = physical component summary.

with women with relatively good HRQOL. Screening for ovarian cancer survivors with low physical HRQOL may help physicians identify women who may have greater benefit from starting an exercise program. In addition, statistically significant improvements in physical HRQOL were detected only among exercisers who did not have a recurrence during the study. Women who recurred during the study had declines in HRQOL and CRF over the six-month study period, regardless of arm. They were also less likely to meet the exercise goal of 150 minutes per week in the intervention arm. Treatment for a recurrence would likely impact CRF, physical HRQOL, and the ability to attain the study exercise goals. Because recurrence is common in women diagnosed with ovarian cancer, future studies need to explore how to improve HRQOL and decrease CRF levels in women who experience a recurrence of ovarian cancer.

Our study findings are consistent with the results from trials in breast cancer survivors (25,26) and with a recent meta-analysis looking at physical activity interventions in all cancer types (27). Our findings corroborate the recommendations put forth by the American College of Sports Medicine exercise guidelines for cancer survivors (28).

Strengths of our study included the population-based recruitment approach, randomized design, large sample size, and six-month study duration. Our study also had limited exclusion criteria and represents a broad sample of ovarian cancer survivors. In addition, the home-based, telephone-delivered approach to increasing exercise is cost-effective and allows for easier implementation in the clinic or community.

A potential weakness of our study was the use of self-reported physical activity; however, the prospective study design, daily exercise recording, and weekly phone calls with the exercise trainer minimized recall bias. Additionally, the generalizability of the results may be affected by the fact that only a portion of women invited to participate in the study did so and by the limited racial diversity in our study population.

In summary, we found a six-month home-based exercise intervention in ovarian cancer survivors is feasible and associated with improved physical HRQOL and physical functioning. Oncologists and primary care providers should recommend and refer women diagnosed with ovarian cancer to clinic- or community-based exercise programs. Given that higher HRQOL has been associated with overall survival in women with ovarian cancer (22,29,30), future studies should examine whether exercise can improve survival in this population and whether HRQOL is a mediating variable.

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