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Effects of a Home-based Exercise Program on Anxiety and Mood Disturbances in Older Adults with Cancer Receiving Chemotherapy

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Abstract

BACKGROUND/OBJECTIVE—Exercise interventions improve anxiety and mood disturbances in patients with cancer. However, studies are limited in older adults with cancer. We assessed the effects of exercise on anxiety, mood, and social and emotional well-being in older patients with cancer during their first 6 weeks of chemotherapy.

DESIGN—Exploratory secondary analysis of a randomized controlled trial (RCT).

SETTING—Community oncology practices.

PARTICIPANTS—Older patients (aged 60 years or older) undergoing chemotherapy (N = 252).

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INTERVENTION—Patients were randomized to Exercise for Cancer Patients (EXCAP) or usual care (control) for the first 6 weeks of chemotherapy. EXCAP is a home-based, low- to moderate-intensity progressive walking and resistance training program.

MEASUREMENTS—Analysis of covariance, with study arm as the factor, baseline value as the covariate, and study arm $\times$ baseline interaction, was used to evaluate arm effects on postintervention anxiety (State Trait Anxiety Inventory [STAI]), mood (Profile of Mood States [POMS]), and social and emotional well-being (Functional Assessment of Cancer Therapy—General subscales) after 6 weeks.

RESULTS—Median age was 67 years; 77% had breast cancer. Statistically significant group differences were observed in the STAI score ($P = .001$), POMS score ($P = .022$), social well-being ($P = .002$), and emotional well-being ($P = .048$). For each outcome, EXCAP patients with worse baseline scores had larger improvements at 6 weeks; these improvements were clinically significant for STAI score and social well-being.

CONCLUSIONS—Among older cancer patients receiving chemotherapy, a 6-week structured exercise program improved anxiety and mood, especially among those participants with worse baseline symptoms. Additional RCTs are needed to confirm these findings and evaluate the appropriate exercise prescription for managing anxiety, mood, and well-being in this patient population.

Keywords

anxiety; exercise; mood; older adults with cancer; social and emotional well-being

The majority of new cancer diagnosis occurs in adults aged 60 years or older.¹ A diagnosis of cancer increases the likelihood of experiencing anxiety and mood disturbance, which can affect emotional and social well-being, ultimately leading to treatment interruptions and decreased survival.^{2–5} Older patients can derive benefits from chemotherapy, but they frequently experience higher rates of toxicities.^{6–8} Pharmacologic interventions for anxiety and mood disturbances often result in significant adverse effects in older adults. Many of these medications, such as the benzodiazepines and antidepressants, are listed in the American Geriatrics Society Beers Criteria® for potentially inappropriate medication use in older adults.⁹ Therefore, behavioral interventions to improve anxiety, mood disturbances, and emotional and social well-being are desirable.

Several studies have been conducted to examine the relationship between exercise and psychological outcomes in cancer survivors.^{10–17} For example, a randomized controlled trial (RCT), conducted among 116 patients with lung cancer, found improvement in anxiety after a home-based walking exercise program.¹⁵ In a systematic review by Craft and colleagues, exercise was found to have positive effects on mood disturbances in cancer survivors; most of the programs were conducted in community facilities, laboratories, or gyms.¹⁴ However, many of these studies were not conducted specifically among older adults, and existing studies have small to moderate sample sizes.¹⁴

In this study, we conducted a secondary analysis of a nationwide RCT to assess the effects of exercise on anxiety, mood, and social and emotional well-being in older patients with cancer receiving active chemotherapy.

METHODS

Study design and setting

This is an exploratory secondary analysis of a nationwide RCT conducted within the University of Rochester Cancer Center (URCC) National Cancer Institute Community Oncology Research Program (NCORP; NCT00924651).¹¹ The primary aim of the RCT was to assess the effects of exercise on cancer-related fatigue in patients receiving active chemotherapy.¹¹ Patients were recruited from 19 community oncology practices between November 2009 and July 2014.

Participants

In the primary study, adult patients, aged 21 years or older, were eligible to participate if they had a primary diagnosis of cancer other than leukemia, had no distant metastasis, had not previously received chemotherapy, were planning to initiate chemotherapy without concurrent radiation for at least 6 weeks (2- vs 3-week cycles of chemotherapy), a Karnofsky performance status of 70 or above, and were able to read English. Patients were excluded if they had physical limitations that precluded them from participating in a low- to moderate-intensity home-based progressive walking and resistance exercise program. Patients who were in the active or maintenance stage of exercise behavior, as assessed by the one-item Exercise Stages of Change Short Form, were also excluded.¹⁸ For this exploratory secondary analysis, we included patients who were aged 60 years or older at the time of enrollment and had completed data on the outcomes of interest at baseline and postintervention. The study was approved by the Institutional Review Boards at University of Rochester and all the individual NCORP affiliate sites prior to enrollment of participants.

Study procedures

Once informed consent was obtained, participants completed baseline assessments, including standard demographic and clinical information, the State Trait Anxiety Inventory (STAI), the Profile of Mood States (POMS), and the Functional Assessment of Cancer Therapy-General (FACT-G) emotional and social well-being.^{19–21} Participants were provided a pedometer and daily diary to record their baseline daily walking steps for 4 days (day –4 to day –1) before the intervention was initiated (day 0).

For randomization, participants were stratified by NCORP site, chemotherapy cycle length, sex, and degree of fatigue (two levels: 5 or less or greater than 5 on a 0–10 clinical symptom inventory); and they were randomly assigned to receive chemotherapy alone (control) or chemotherapy and a 6-week home-based progressive walking and resistance band exercise program (Exercise for Cancer Patients [EXCAP]). Group assignment was determined by a computer-generated random numbers table in random blocks of four or six and an allocation ratio of 1:1. At the end of the 6-week intervention, all participants completed the same assessments as at baseline.

Intervention

Details about the intervention have been described previously.²² Briefly, EXCAP is a home-based, progressive, low- to moderate-intensity aerobic and resistance exercise program. Participants who were randomized to the EXCAP arm were provided with the EXCAP exercise kit, containing a pedometer, three therapeutic bands (medium, heavy, and extra heavy), and an instruction manual. For each of the NCORP sites, a designated clinical research associate was trained by an American College of Sports Medicine-certified exercise physiologist from the URCC Research Base to teach the EXCAP program to participants and conduct assessments. The aerobic component involved walking, and participants received individually tailored, progressive walking prescriptions based on their baseline number of steps. They were instructed to wear a pedometer and record their daily steps over a 6-week period, starting on their first day of chemotherapy treatment. Participants were encouraged to progressively increase their steps by 5% to 20% every week (60%–85% of heart rate reserve as the target heart rate for participants). For resistance exercise, participants performed exercises with therapeutic bands (3–5 rating perceived exertion [RPE] scale).²³ Participants were encouraged to perform 10 required exercises (eg, squat or chest press) and four optional exercises daily with an individually tailored set/repetition scheme. Participants were encouraged to progressively increase the intensity, sets, and/or number of repetitions of resistance band exercises over the course of the program.

Participants who were randomly assigned to the control arm did not receive the EXCAP kit and instruction manual during the intervention period, but they were provided the kit *au gratis* at the end of the study. They were given a pedometer for 4 days at baseline (day –4 to day –1) and 4 days before the end of the study (day 38 to day 41) to record their daily steps. These participants were not asked to record their daily steps from day 0 to day 37 of the study.

Measures

Exercise adherence—Participants were asked to record exercise adherence daily on a diary. This information included daily steps from the pedometer, minutes of resistance exercise, and RPE (1 being no exertion, and 10 being maximal exertion).²⁴

Outcome measures: anxiety, mood, and social and emotional well-being—

Anxiety symptoms were assessed using the validated and reliable STAI form Y-1.^{19,25,26} The STAI is a self-reported questionnaire on the presence and severity of anxiety symptoms (range = 20–80, with a higher score indicating higher anxiety). Mood was assessed using the validated and reliable 30-item POMS (range = –20 to 100, with a higher score indicating a higher level of impairment).^{21,27,28} Social and emotional well-being were assessed using the validated and reliable FACT-G version 4 social and emotional subscales (range = 0–28 and 0–34, respectively, with a higher score indicating better well-being).²⁰

Statistical analysis—Data analyses were conducted using SAS statistical software, version 9.3 (SAS Institute), and the testing was performed at a two-tailed 5% level of significance. We used descriptive statistics (counts and percentages, medians, mean change scores, and SDs) to describe the two study arms. The χ^2 and Fisher's exact analyses as well

as independent *t*-tests were used to examine the group differences. Analysis of covariance was used to evaluate the effects of EXCAP on exercise adherence, anxiety, mood, and emotional and social well-being compared to the controls. For the outcomes, the initial model included study arm and baseline value as covariates. Then, the study arm $\times$ baseline value interaction was tested. If the interaction was significant ($P < .05$), we evaluated the mean difference between arms at five levels (5th, 25th, 50th, 75th, and 95th percentile of the baseline score). For these models, an F-test was used to evaluate the overall effect of the intervention and study arm $\times$ baseline value interaction. Given our study is exploratory in nature and hypothesis generating, we did not adjust for multiple comparisons.²⁹ Only complete cases were analyzed because sensitivity analyses using multiple imputation³⁰ did not show significant differences when reporting data from those who had complete data vs those who had estimated data with imputation.

RESULTS

Baseline characteristics

Figure SS1 shows the Consolidated Standards of Reporting Trials diagram of the study participants. A total of 252 older patients with cancer were included in this secondary analysis. The median age was 67 years (range = 60–89 years), and 92% were female (Table 1). Demographic and clinical characteristics were well balanced between the groups, except patients in the EXCAP group were slightly older: mean age = 68 years (SD = 5.7 years) vs 66 years (SD = 4.5 years) in the control group ($P = .001$) (Table 1).

Exercise adherence

At baseline, none of the participants reported performing regular resistance training. At postintervention, 71% (92/130) of participants in the EXCAP group reported performing resistance training over the 6-week study period. On average, participants in the EXCAP group reported performing resistance training for a mean duration of 22 minutes, 2.3 days/week, with a mean RPE of 2.6 (low intensity). Only 3 of 122 participants in the control group reported participating in resistance exercise during the study period. In terms of aerobic exercise, participants in the EXCAP group had an increased number of average daily steps walked from baseline to postintervention (267 steps; $P = .466$), whereas participants in the control group had a decreased number of average steps walked from baseline to postintervention (–284 steps; $P = .194$), but the change was not significant ($P = .238$; Table 2).

Effects of exercise on anxiety, mood, and social and emotional well-being

At baseline, no significant difference was noted in the STAI score between participants in the EXCAP and control groups ($P = .276$). A statistically significant change in anxiety levels was noted between the EXCAP and control groups ($P = .001$; Figure 1, Table SS1). Participants with higher levels of anxiety had improved anxiety with EXCAP compared to the control ($P = .001$ for interaction). For example, among patients who had a STAI score in the 75th percentile (higher score is worse), the EXCAP group had greater improvement in anxiety (mean difference between arms [EXCAP minus control] = –5.39; $P = .001$).

At baseline, no significant differences were noted in the POMS total score ($P = .471$) as well as social ($P = .173$) and emotional ($P = .324$) well-being between the EXCAP and control groups. Statistically significant changes in POMS total score ($P = .022$) and social ($P = .002$) and emotional ($P = .002$) well-being were noted between the EXCAP and control groups (Figure 1, Table SS1). Participants with higher levels of mood disturbances ($P = .032$ for interaction), lower social well-being ($P = .006$ for interaction), and lower emotional well-being ($P = .026$ for interaction) had improved mood and social and emotional well-being from EXCAP compared to control.

DISCUSSION

Our study supports the benefits of a low- to moderate-intensity, home-based exercise program in anxiety, mood, and social and emotional well-being in older patients with cancer receiving chemotherapy in community oncology practices across the United States. It is possible that the benefits were derived mainly from the resistance training component of the exercise intervention, given the nonsignificant change in number of average daily steps walked between the intervention and control groups. Nonetheless, results from this study support findings from previous studies demonstrating that exercise improved anxiety and mood in patients with cancer and the geriatric population.

Specifically, we demonstrated that older patients receiving chemotherapy who had worse anxiety, mood, and social and emotional well-being benefited most from the exercise program. One possibility is that these patients may have more room to gain an improvement in anxiety and mood symptoms. Of note, for the STAI measure, a cut point of 39 to 40 represents clinically significant anxiety symptoms,³¹ and a change in the score of 10 points or more is considered clinically meaningful.³² In this study, the subgroup of patients with a STAI score of 55 and above achieved the greatest improvements from the exercise intervention, which were clinically meaningful. For the POMS measure, no minimal important difference has been established, but similar to STAI, those with a worse POMS score (28 and above) achieved the greatest improvements from the exercise intervention. For social and emotional well-being, the minimal important differences are between 2 and 3 points.³³ In the context of the geriatric noncancer population, one RCT showed an exercise counseling intervention only benefited those with minor depressive symptoms vs major depressive symptoms.³⁴ While it is challenging to compare our findings due to the different populations and intervention, our study underscores the need to further evaluate the relationships between severity of anxiety and mood symptoms and the benefits of exercise in older adults with cancer.

Several mechanisms may explain the beneficial effects of exercise on mood and emotional well-being. First, exercise reduces chronic inflammation,³⁵ and there is growing evidence that this reduction of inflammation is an important way that exercise ameliorates mood disturbances.³⁶ Second, anxiety and mood disturbances have been linked to altered function of brain circuitry that processes sensations from the body³⁷ (ie, interoceptive brain circuitry).^{37–39} Exercise changes this brain circuitry and how the brain processes somatic sensations,⁴⁰ thereby suggesting another mechanism by which exercise ameliorates anxiety and mood disturbances.

On a broader scale, our findings suggest that low- to moderate-intensity exercise may be sufficient to improve psychological outcomes. Current exercise guidelines for healthy adults and cancer survivors primarily focus on improving physical fitness and cardiopulmonary function and recommend a one-size-fits-all approach.^{41–43} However, the recommended amount of activity should be tailored to a specific patient for a specific outcome, especially in older adults with cancer who may not be able to achieve the guideline-recommended level of exercise. Therefore, there is a need for RCTs to evaluate the specific exercise types, durations, and frequencies appropriate for specific outcomes.

There are several strengths in our study. Our data were derived from a nationwide RCT with a relatively large sample size, performed in older patients seen in community oncology clinics. These settings provide high generalizability of our data to other older patients in the United States. The exercise intervention was administered by clinical research associates and, therefore, could be easily implemented in other clinics across the country. In addition, we used validated scales (STAI, POMS, and FACT-G) to assess outcomes of interest in our study.

There are several limitations in our study. First, a large proportion of our patients were women, were white, had a high school education, had breast cancer, and had minimal comorbidities; therefore, our results may not be generalizable to men, patients with other types of cancer, patients of other racial/ethnic minorities, patients with lower than a high school education, and those with multiple comorbidities. Second, our population was a relatively “young” old population, and patients aged 75 or 80 years and older may respond differently to a physical activity intervention than patients aged 65 to 75 years. Third, the duration of the exercise intervention was only 6 weeks, and we did not collect longer-term outcomes; future studies are needed to evaluate the lasting effects of an exercise intervention during chemotherapy in this population. Fourth, this was an exploratory secondary data analysis, and we did not adjust for multiple comparisons; these hypothesis-generating findings will need to be tested for replication in a study that is specifically designed to test the effects of exercise on anxiety and mood in an older population of cancer patients. Finally, the control group received standard of care instead of an active placebo (ie, we did not control for attention), and, therefore, our observations are more susceptible to placebo effects.

In conclusion, the results of our secondary data analysis suggest that older patients with cancer receiving active chemotherapy who have worse anxiety, mood, and social and emotional well-being at baseline may benefit from exercise. Further RCTs are needed to confirm these findings and identify optimal exercise prescriptions to improve psychosocial measures and elucidate potential biological mechanisms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Changes in anxiety, mood, and social and emotional well-being scores in the exercise and control groups. ^aPostintervention scores are adjusted for baseline scores and estimated as marginal means from analysis of covariance models. Values and 95% confidence intervals are presented. ^bHigher scores indicate worse anxiety or mood. ^cHigher scores indicate better social or emotional well-being. POMS indicates Profile of Mood States; STAI, State Trait Anxiety Inventory. * $P < .05$.

Table 1.

Baseline demographics of the study population

Characteristics	All (n = 252)	Exercise group (n = 130)	Control group (n = 122)	P-value
Age, mean (SD, range), y	66.7 (5.4, 60–89)	67.7 (5.7, 60–89)	65.5 (4.8, 60–89)	.001
Sex, No. (%)				
Female	231 (91.7)	120 (92.3)	111 (91.0)	.704
Male	21 (8.3)	10 (7.7)	11 (9.0)	
Marital status, No. (%) ^a				
Married	159 (63.4)	84 (64.6)	75 (62.0)	.666
Other	92 (36.7)	46 (35.4)	46 (38.0)	
Race, No. (%)				
White	229 (90.9)	117 (90.0)	112 (91.8)	.619
Other	23 (9.1)	13 (10.0)	10 (8.2)	
Education, No. (%) ^b				
More than college	42 (16.8)	24 (18.5)	18 (15.0)	.872
College	110 (44.0)	57 (43.9)	53 (44.2)	
High school/GED	87 (34.8)	44 (33.9)	43 (35.8)	
Less than high school/GED	11 (4.4)	5 (3.9)	6 (5.0)	
Comorbidities ^a				
Anemia ^a	21 (8.4)	12 (9.2)	9 (7.4)	.61
Hypertension ^a	129 (51.4)	68 (52.3)	61 (50.4)	.76
Congestive heart failure ^a	4 (1.6)	3 (2.3)	1 (0.8)	.62
Chronic obstructive pulmonary disease ^a	12 (4.8)	6 (4.6)	6 (5.0)	.90
Fibromyalgia ^a	11 (4.4)	7 (5.4)	4 (3.3)	.42
Hypothyroidism	41 (16.3)	23 (17.7)	18 (14.8)	.53
Hyperthyroidism	4 (1.6)	3 (2.3)	1 (0.8)	.62
Cancer site, No. (%) ^a				
Breast	194 (77.0)	103 (79.2)	91 (74.6)	.823
Colon	19 (7.5)	9 (6.9)	10 (8.2)	

Characteristics	All (<i>n</i> = 252)	Exercise group (<i>n</i> = 130)	Control group (<i>n</i> = 122)	<i>P</i> -value
Lung	12 (4.8)	5 (3.9)	7 (5.7)	
Other	27 (10.7)	13 (10.0)	14 (11.5)	
Previous cancer surgery, No. (%)	226 (89.7)	120 (92.3)	106 (86.9)	.157
Previous chemotherapy, No. (%)	3 (1.2)	0	3 (2.5)	.112
Previous radiation, No. (%)	7 (2.8)	4 (3.1)	3 (2.5)	.766
Previous hormone therapy, No. (%)	12 (4.8)	7 (5.4)	5 (4.1)	.632

Abbreviation: GED, General Educational Development.

^aOne missing.

^bTwo missing.

Table 2.

Exercise adherence

Exercise type	EXCAP group (n = 130)		Control group (n = 122)		P-value ^a
	Baseline	Postintervention	Baseline	Postintervention	
Aerobic exercise					
Average No. of daily steps	3598	3867	3903	3619	.238
RPE	2.5	3.8	2.9	2.9	
Resistance training					
Frequency, d/wk	0	2.3	0	0	<.001
Duration, min	0	22	0	0	
RPE	0	2.6	0	0	

Abbreviations: EXCAP, Exercise for Cancer Patients; RPE, rating of perceived exertion.

^aP-value testing the difference between the exercise and control groups.