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Physical Activity and Obesity in Endometrial Cancer Survivors: Associations with Pain, Fatigue, and Physical Functioning

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Abstract

OBJECTIVE—This study aims to determine the prevalence of physical activity and obesity and their relationship to physical functioning, fatigue, and pain in endometrial cancer survivors.

STUDY DESIGN—Surveys were mailed to 200 survivors of endometrial cancer diagnosed within the last five years; 61% were returned. Surveys assessed physical activity, height and weight, comorbid health problems, physical functioning, fatigue, and pain.

RESULTS—Twenty-two percent exercised in the past month at the level of current public health recommendations; 41% reported no physical activity, and 38% reported some activity. Sixteen percent were overweight and 50% were obese. Both lower BMI and higher physical activity were related to better physical functioning. Higher physical activity was related to less fatigue, primarily for patients of normal BMI.

CONCLUSIONS—Results suggest endometrial cancer survivors' obesity and inactivity contributes to poorer quality of life. This population could benefit from quality of life interventions incorporating physical activity.

Keywords

Endometrial cancer; exercise; fatigue; obesity; pain; physical functioning

INTRODUCTION

Endometrial cancer is the most common gynecologic malignancy; in 2006 an estimated 40,200 women in the United States were affected,¹ and U.S. women have a 2.6% lifetime risk of being diagnosed with the disease.² Because endometrial cancer is often diagnosed at an early stage² and has a high cure rate,³ enhancing the quality of life of survivors is a high priority.

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Obesity is a risk factor for endometrial cancer,^{4–6} which explains its high prevalence among survivors of the disease.⁷ Sedentary lifestyle, diabetes, and hypertension have also been implicated as risk factors.⁶ These risk factors put endometrial cancer survivors at increased risk for health problems such as heart disease, diabetes, osteoarthritis, stroke, and respiratory problems, as well as other cancers.^{8,9} Physical inactivity and obesity also affect survivors' quality of life, either independently or through their association with chronic diseases. Courneya and colleagues⁷ recently published a study reporting a high prevalence of obesity and low physical activity among endometrial cancer survivors. They also found that physical activity was associated with better quality of life, and that obesity was related to higher fatigue and lower quality of life.

Given the risk factors for endometrial cancer and reports of obesity and lack of physical activity among endometrial cancer survivors, we aimed to estimate the prevalence of obesity and physical activity in a hospital-based sample of endometrial cancer survivors and to study the effects of obesity and physical activity on survivors' physical functioning, fatigue, and pain. In particular, because a large percentage of cancer survivors engage in physical activity at levels below the recommended 30 minutes of moderate-intensity activity on most days of the week,¹⁰ we wanted to explore whether physical activity at a level below recommended guidelines might still have a beneficial effect on physical functioning, fatigue, and pain. If we could show that even small increases in activity provide some benefits, this could encourage sedentary cancer survivors to begin to increase their activity levels, even if they feel they cannot attain levels recommended by public health guidelines. Finally, we explored whether survivors reported co-morbidities that might interfere with adopting a more physically active lifestyle.

MATERIALS AND METHODS

Design and Sample

The research protocol was approved by the M. D. Anderson Cancer Center Institutional Review Board. We conducted a cross-sectional survey of endometrial cancer survivors from the M. D. Anderson Tumor Registry. We focused on survivors of early stage cancer, because they have the highest survival and lowest risk of recurrence, justifying a shift in emphasis from cancer treatment to lifestyle behaviors and chronic disease risk. All of the women met the following criteria: (1) diagnosed within the past 5 years with endometrial cancer that was either confined to the uterine corpus or extended only to the cervix (FIGO [International Federation of Gynecology and Obstetrics] stage I or II or SEER [Surveillance Epidemiology and End Results] stage 2 or 3), (2) received treatment at M. D. Anderson, (3) treated with surgery and/or radiation, (4) age 18 years or older, and (5) residing within the U.S. Of the 259 eligible women identified, 200 were chosen using simple random sampling. Three additional women had to be selected to replace patients with bad addresses.

Procedures

Each of the 200 women was mailed a packet that included a letter describing the study, a questionnaire, a refusal form, and a postage-paid return envelope. Each woman was assigned an identification number to identify who returned the questionnaires. Follow-up of non-respondents was done using procedures based on those described by Dillman.¹¹ One week after the initial packet was mailed, a reminder/thank you letter was sent. At three and six weeks after the initial mailing, replacement questionnaires, refusal cards, and postage-paid envelopes were mailed to non-respondents.

Measures

The questionnaires assessed physical activity, physical functioning, pain, fatigue, height, weight, age, and medical problems interfering with physical activity. Participants completed

the physical functioning (PF) subscale of the Medical Outcome Study Short Form-36 (SF-36) quality of life questionnaire.^{12, 13} The PF subscale consists of 10 items designed to assess the ability to conduct activities of daily living requiring large motor skills; a higher score indicates better physical functioning. The internal consistency of the subscale is excellent (Cronbach's alpha = 0.89 to 0.92),¹³ and it correlates with other physical functioning measures and distinguishes between serious and mild medical conditions.¹⁴ Each survivor's PF subscale score was compared with the mean for women of the survivor's age, as presented in the published SF-36 norms.¹³

Fatigue and pain were assessed using two items from the Brief Pain Inventory and the Brief Fatigue Inventory,^{15–17} which rates usual and worst pain and fatigue levels during the previous week on an 11-point scale (0 = no pain/fatigue to 10 = pain/fatigue as bad as you can imagine).^{15–17} We found high correlations between the "usual" and "worst" ratings of both symptoms (0.93 and 0.81 for pain and fatigue, respectively), so these ratings were averaged for analyses comparing the symptoms of respondents with differing levels of obesity or physical activity.

The 2000 Behavioral Risk Factor Surveillance System (BRFSS)¹⁸ interview was adapted to measure physical activity. Respondents indicated whether they participated in any physical activities during the past month, and what they did, the number of days per week, and the number of minutes each day. Participants who reported that they did not participate in any physical activity or exercise in the past month were categorized as sedentary. Activities were coded as moderate or vigorous depending on their MET (metabolic equivalent) value.¹⁹ Moderate intensity activities were defined as those between 3 and 6 METs, while vigorous activities were defined as >6 METs. Those who engaged in moderate-intensity activity 5+ days/week for 30 minutes or more or vigorous activity 3+ days/week for 20 minutes or more were categorized as meeting public health guidelines for physical activity. Respondents reporting physical activity at a level lower than the public health recommendation were coded as somewhat active.

Comorbid health problems were assessed by asking respondents if they had health problems that interfered with exercising and, if so, to describe them. Descriptions of health problems were coded into the categories described in the Results. They also reported their age, as well as height and weight, from which we calculated body mass index (BMI: weight in kg/height in meters²).

Other medical and demographic variables were abstracted from the tumor registry records and the survivors' medical records.

Analysis

Descriptive statistics were used to characterize the sample with regard to physical activity, BMI, fatigue, pain, and physical functioning. Relationships between the independent variables of physical activity and BMI and the dependent variables of fatigue, pain, and physical functioning were tested using analysis of variance (ANOVA). Because there were very few participants in the highest BMI categories who were physically active, the obese categories (BMI 30–35, BMI 36–40, and BMI 41–45) were collapsed for this analysis to create a 3 (normal weight, overweight, obese) × 3 (sedentary, somewhat active, active) ANOVA. Planned comparisons of the main effects were included in the analysis: overweight and obese groups were compared to normal weight women, and sedentary and somewhat active women were compared to the active group. The analyses were repeated, controlling for potentially confounding variables (age, disease stage, years since diagnosis, treatment, and having a musculoskeletal condition).

RESULTS

Description of Respondents

Sixty-one percent of the sampled survivors (121/200) responded to the survey. However, upon final review of the medical records, one respondent and two non-respondents were found to be ineligible—one did not have invasive cancer and two had uterine sarcomas. The final response rate was thus 120 out of 197 (61%). Table 1 provides the demographic and medical characteristics of the respondents and non-respondents. It should be noted that these data are from the medical records and thus reflect variables at the time of treatment at M. D. Anderson. The only significant difference between the two groups was in marital status ($p=0.040$; respondents were more likely to be married).

Body Mass Index and Physical Activity

BMIs of the respondents are reported in Table 2. Because there were so few respondents in the underweight category ($BMI < 20$), it was combined with the normal weight category. A high proportion of the sample (66%) was either overweight or obese.

Only 22% ($n=26$) of the sample reported physical activity that met the public health guidelines. Thirty-eight percent ($n=45$) reported being somewhat active, and 41% ($n=49$) were sedentary. The most common form of activity was walking (48 women). Other common forms of activity were gardening/yardwork ($n=19$), resistance training ($n=8$), housework ($n=6$), general exercise or calisthenics ($n=7$), and swimming/water aerobics ($n=6$).

Table 3 displays respondents' BMI and physical activity level by the type of surgery and/or radiation treatment they received. There were no significant associations between BMI ($p=0.865$, 0.368 and 0.146, respectively) or physical activity level ($p=0.210$, 0.198 and 0.283, respectively) and type of surgery, radiation treatment, or time since diagnosis.

Comorbid Health Problems

Half of the women said they had a health problem that interfered with exercise. Musculoskeletal problems dominated their health concerns, including arthritis ($n=13$), knee pain/problems ($n=13$), back pain/problems ($n=11$), foot problems ($n=6$), hip pain ($n=4$), leg pain ($n=3$), sciatica ($n=3$), problems walking (e.g., had to use walker or wheelchair, $n=3$), bursitis ($n=1$), hand pain ($n=1$), and joint pain ($n=1$). Other common problems reported by the respondents were fatigue ($n=6$), recent surgery ($n=4$), being overweight ($n=4$), and hernia ($n=3$). Because of the high prevalence of musculoskeletal conditions (37%), we controlled for whether the respondent had such a condition in the analysis of obesity, physical activity, and outcomes.

Physical Functioning, Fatigue, and Pain

Mean scores for physical functioning, fatigue (worst and usual), and pain (worst and usual) are reported in Table 2. The mean difference between survivors' physical functioning scores and those of gender- and age-matched norms was -8.4 , with survivors scoring below the norm on average. The mean pain and fatigue scores by physical activity level and BMI are shown in Figures 1a and 2a. The symptoms of fatigue and pain show a clear downward trend with increasing levels of activity; the difference between sedentary respondents and those meeting public health activity recommendations was 2.4 points for fatigue and 2.7 for pain (on a 0–10 scale). As can be seen in Figure 1b, the level of physical functioning increases with increasing activity, regardless of whether it is expressed as the scale score or the difference between the individual respondent's score and the age- and gender-based norm. The descriptive data comparing fatigue, pain, and physical functioning between the BMI groups showed a similar gradient (Figures 2a and 2b), but the relationships appear to be weaker than those for physical activity.

Table 4 shows the mean scores for physical functioning, averaged worst and usual pain, and averaged worst and usual fatigue by BMI and physical activity level. For physical functioning, there were significant main effects for both BMI and physical activity. Participants with lower BMIs and higher levels of activity reported better physical functioning. The interaction (BMI $\times$ physical activity level) was not significant. Planned comparisons demonstrated significant differences in physical functioning between normal-weight and obese individuals ($p=0.005$) and between the sedentary group and those who met activity guidelines ($p=0.000$). These differences remained significant after controlling for medical and demographic covariates. Differences between normal-weight and overweight respondents and between active respondents and those who were somewhat active were not significant ($p=0.772$ and $p=0.212$, respectively).

For fatigue, the main effect was significant for physical activity but not for BMI. Both the sedentary group and the somewhat active group had higher fatigue than the respondents who were active at recommended levels ($p=0.005$ and $p=0.046$, respectively). The interaction between BMI and physical activity level was highly significant for fatigue. Exploring the interaction showed that physical activity had the strongest relationship to fatigue for participants with normal BMI; there was very little relationship between physical activity and fatigue for obese participants. After controlling for medical and demographic covariates, the interaction remained significant and the physical activity main effect was of borderline significance ($p=0.069$).

For pain, there was a significant main effect for physical activity but not for BMI. The most active group reported significantly less pain than the sedentary group ($p=0.009$). The difference between the most active group and the somewhat active group was not significant. The interaction term was not significant. In adjusting for covariates, musculoskeletal conditions was significantly related to pain, and when this and other covariates were included in the analysis, the relationship between physical activity and pain was attenuated ($p=0.107$).

COMMENT

The results of this survey indicate a high prevalence of obesity and a low prevalence of physical activity among endometrial cancer survivors. In our sample, 16% of the respondents were overweight (BMI between 25 and 30), and 50% were obese (BMI ≥ 30). Comparing this the National Health and Nutrition Examination Survey (NHANES),²⁰ this sample of survivors has a higher prevalence of obesity than women in the general U.S. population. Given the age distribution in our sample, we would expect that approximately 32% of the women would be overweight and 35% would be obese. Given the importance of obesity as a risk factor for endometrial cancer, this is not surprising, but it does indicate a need for interventions to manage weight and related co-morbidities in this population.

Only 22% of the sample was physically active at the level of current public health recommendations, compared to 46% in the general U.S. population.²¹ This difference might be partly explained by the older age of our sample. National data show that older adults have lower rates of physical activity (41% for women age 65–74 and 33% for women 75 and older²²). Other surveys of cancer survivors have also found a higher prevalence of physical activity.^{7, 23} Lower physical activity in our sample also might be explained by the high prevalence of co-morbid conditions, particularly musculoskeletal complaints.²²

Physical activity was associated with physical functioning, fatigue, and pain, although the relationship with pain was attenuated after adjusting for musculoskeletal conditions. This mirrors the findings by Courneya et al.,⁷ who found that endometrial cancer survivors who exercised at recommended levels had better overall quality of life, physical well-being,

functional well-being, and social well-being and less fatigue. However, that study did not separate individuals who exercised at levels below public health recommendations from those who did not exercise at all. In examining this group separately, we found no significant differences in physical functioning and pain between the somewhat active group and participants whose physical activity met public health guidelines. This result is similar to findings from the BRFSS, which showed that any activity at all is associated with better physical and mental health.²⁴ For fatigue our results indicate that the somewhat active group had higher fatigue than the active group. Furthermore, there was a significant BMI $\times$ physical activity interaction, showing that the expected positive relationship between physical activity and fatigue occurred primarily among participants with a normal BMI. This suggests that although even modest increases in activity could have a positive effect on functioning and pain, activity sufficient to produce fitness improvements and/or weight loss may be needed to decrease fatigue.

BMI and physical functioning were related, as hypothesized, but the associations between BMI and pain and fatigue were not significant when physical activity was included in the model. This is at odds with the study by Courneya et al,⁷ which found a strong relationship between fatigue and BMI, but no relationship between BMI and overall quality of life, physical well-being, functional well-being, emotional well-being, or social well-being. Such differences could be due to differences in the measures used.

Several observational studies have shown associations between physical activity and colon and breast cancer recurrence.^{25–27} A relationship with endometrial cancer recurrence has not been studied, although such a link is biologically plausible. The insulin pathway is one possible mechanism. High levels of insulin can stimulate tumor development in the endometrial tissues by reducing levels of insulin growth factor binding protein-1. This increases levels of insulin growth factor-I (IGF-I) activity, which has been linked to proliferative activity in the endometrial tissue.⁵ Physical activity could assist endometrial cancer survivors with insulin regulation. A study of the effects of exercise training on insulin, insulin resistance, insulin-like growth factors, and insulin-like growth factor binding proteins in breast cancer survivors found that exercise decreased IGF-I,²⁸

Efforts to increase physical activity and address obesity face a number of challenges, several of which are highlighted in this study. Endometrial cancer survivors' co-morbid health problems complicate the adoption of physical activity and require tailored intervention approaches, including adaptation of activities to accommodate comorbid health problems such as musculoskeletal conditions. The cancer diagnosis has been identified as a 'teachable moment' by other research.^{23, 29} Indeed, in our study survivors further from diagnosis appear to be slightly less likely to be sedentary and obese, indicating that they may change their behavior in response to cancer diagnosis and treatment and may be receptive to programs to help them change health behavior and manage weight if warranted.

This study has potential limitations that should be noted. One is that our response rate was only 61%. This compares favorably, however, with other cancer survivor surveys reported in the literature,^{7, 23} and our analysis of differences between respondents and non-respondents did not reveal any serious selection biases. A second limitation is that our question about comorbid health problems was open ended and relied on respondent recall. A structured questionnaire to query respondents about health problems may have been more accurate and provided additional information, such as the severity of the health problem. However, we recognized that survivors would be less likely to respond to a lengthy survey, and because our intent was to obtain only a brief description of the comorbid health problems rather than a detailed inventory, we sacrificed some precision in the reporting of health problems for a higher response rate. Future studies could be done to more clearly delineate the relationship between

the comorbid health problems and physical activity in this population. Third, we relied on self-reported weight and height to calculate BMI. Self-report data often underestimates BMI, especially among older and more overweight individuals.^{30, 31} If some respondents who are actually obese were misclassified as normal weight or overweight, this likely would have reduced the size of the relationship between BMI and outcomes. Finally, this is a cross-sectional study, and although the relationships we have found indicate associations, causality cannot be demonstrated. We found relationships between physical activity and functional outcomes, but one could speculate that either physical activity improves physical functioning, fatigue, and pain or poor physical functioning, fatigue, and pain causes cancer survivors to be less active. Indeed, both are probably true to some extent. However, exercise has been used successfully as an intervention for survivors of other types of cancer and has been shown in randomized studies to improve these outcomes.^{32–37} Such findings, along with the relationships uncovered in this survey of endometrial cancer survivors, indicate that exercise may be a helpful component of quality of life and disease prevention interventions for this population.

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Figure 1. Participants with higher levels of physical activity (PA) reported less fatigue and pain (figure 1a) and better physical functioning (figure 1b) than those who reported no PA.

Figure 2. Survivors with higher Body Mass Index reported higher levels of pain and fatigue (figure 2a) and lower levels of physical functioning (figure 2b).

Table 1

Characteristics of respondents and non-respondents

Variable	Respondents		Non-respondents		Significance <i>p</i>
	N	%	N	%	
SEER Stage					0.566
• Local	100	84.0	67	87.0	
• Regional	19	16.0	10	13.0	
Surgery ^a					0.399
• No Surgery	4	3.4	0	0.0	
• Open hysterectomy	105	88.2	71	92.2	
• Laparoscopic hysterectomy	10	8.4	6	7.8	
Radiation ^a					0.958
• No Radiation	68	57.1	43	56.6	
• External Beam Only	6	5.0	5	6.6	
• Vaginal Cuff Only	23	19.3	14	18.4	
• External Beam and Vaginal Cuff	19	16.0	13	17.1	
• Alto Only	1	.84	1	1.3	
• Alto and External Beam	2	1.7	0	0.0	
Chemotherapy ^a					0.168
• No	112	94.1	75	97.4	
• Yes	7	5.9	2	2.6	
Race or ethnicity					P=0.405
• White	88	74.0	50	64.9	
• African-American	10	8.4	10	13.0	
• Spanish Surname	16	13.5	15	19.5	
• Other	5	4.2	2	2.6	
Marital status					P=0.040
• Married	71	60.2	30	39.5	
• Widowed	23	19.5	22	29.0	
• Divorced	9	7.6	11	14.5	
• Single	15	12.7	13	17.1	
BMI at time of surgery (from medical record)					0.203
• <25	28	28.6	11	16.7	

Variable	Respondents		Non-respondents		Significance <i>p</i>
	N	%	N	%	
• 25 – <30	17	17.4	17	25.8	
• 30 – <35	17	17.4	7	10.6	
• 35 – <40	11	11.2	9	13.6	
• >=40	25	25.5	22	33.3	
	Mean	SD	Mean	SD	
Age	59.9	12.7	62.4	13.5	P=0.190
Years since diagnosis	2.9	1.6	2.8	1.4	P=0.472

^a Fisher exact test used

Table 2
Descriptive statistics for BMI, physical activity, physical functioning, fatigue, and pain.

Variable	Mean (SD) or n (%)
BMI at time of survey(self-reported	
<25	38 (33.6)
25 – <30	18 (15.9)
30 – <35	23 (20.4)
35–<40	15 (13.3)
>=40	19 (16.8)
No activity	49 (40.8)
Physical Activity	
Activity, not meeting guidelines	45 (37.5)
Activity, meeting guidelines	26 (21.7)
Physical functioning	63.6 (31.5)
Physical functioning, difference from norm	–8.1 (29.4)
Usual Fatigue	3.76 (2.59)
Worst Fatigue	4.59 (2.84)
Usual Pain	2.16 (2.51)
Worst Pain	2.89 (3.24)

Table 3
Previous treatment characteristics and time since diagnosis by physical activity levels and BMI of survivors

Treatment	Sedentary % (N)	PA level		Meeting guidelines % (N)	BMI	
		Somewhat active % (N)	Active % (N)		25–30 % (N)	>30 % (N)
Surgery						
Open hysterectomy	94 (46)	84 (37)		85 (22)	89 (16)	88 (49)
Laparoscopic Hysterectomy	2 (1)	14 (6)		12 (3)	11(2)	7 (4)
No surgery	4 (2)	2 (1)		4 (1)	0 (0)	5 (3)
Radiation therapy						
External beam alone or combined with vaginal cuff and/or ALTO	22 (11)	25 (11)		19 (5)	22 (4)	23 (13)
Vaginal cuff and/or ALTO only	29 (14)	9 (4)		19 (5)	39 (7)	16 (9)
No radiation therapy	49 (24)	66 (29)		62 (16)	39 (7)	61 (34)
Time since diagnosis						
< 2 years	41 (20)	41 (18)		28 (7)	50 (9)	36 (20)
≥ 2 years – < 4 years	35 (17)	25 (11)		48 (12)	28 (5)	42 (23)
≥ 4 years	24 (12)	34 (15)		24 (6)	22 (4)	22 (12)

Table 4
Physical functioning, fatigue, and pain by physical activity level and body mass index

	Physical Activity Level (PA)	Body Mass Index (BMI)			BMI			Significance (p)			BMI × PA	
		≤25 n=38	25–30 n=17	>30 n=57	Not adj	Adj ^a	Not adj	Not adj	PA	Adj ^a	Not Adj	Adj ^a
		Mean (SD)	Mean (SD)	Mean (SD)								
Physical Functioning	No exercise/PA, n=42	47.2 (30.7)	45.0 (29.4)	40.4 (25.9)	0.013	0.007	0.000	0.000			0.486	0.736
	Exercise/PA < guidelines, n=45	88.9 (15.7)	79.5 (12.0)	61.8 (28.9)								
	Exercise meeting guidelines, n=25	90.3 (25.5)	93.6 (6.3)	73.3 (25.8)								
Fatigue	No exercise/PA, n=41	6.6 (1.7)	4.3 (3.6)	4.7 (2.2)	0.275	0.402	0.018	0.069			0.001	0.002
	Exercise/PA < guidelines, n=45	3.8 (2.5)	6.2 (2.5)	4.1 (2.0)								
	Exercise meeting guidelines, n=25	1.6 (2.2)	2.9 (2.2)	5.5 (1.5)								
Pain	No exercise/PA, n=41	4.0 (3.8)	2.6 (3.6)	4.2 (3.0)	0.258	0.697	0.021	0.107			0.314	0.256
	Exercise/PA < guidelines, n=46	1.2 (2.1)	3.8 (2.9)	2.3 (2.5)								
	Exercise meeting guidelines, n=25	0.4 (0.5)	2.1 (3.6)	2.0 (2.2)								

^a Adjusted for age, disease stage, years since diagnosis, surgery, chemotherapy, radiation therapy, presence of musculoskeletal conditions..