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Quality of Life, Body Mass Index, and Physical Activity among Uterine Cancer Patients

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Abstract

Objective—The purpose of this study was to assess the independent and joint effects of body mass index (BMI) and physical activity (PA) on overall quality of life (QoL) in survivors of uterine cancer.

Methods—We conducted a survey among uterine cancer patients who received curative therapy at the University of Pennsylvania between 2006 and 2010. Surveys assessed weight, height, PA (college alumnus survey), and QoL (Functional Assessment of Cancer Therapy – Gyn).

Results—The response rate to the survey was 43%. Among 213 patients, the mean BMI was 31.1 ± 8.9 kg/m², and 48% reported ≥ 150 min·wk⁻¹ of PA. Higher BMI was independently associated with poorer overall QoL ($P=.050$), including physical ($P=.002$) and functional well-being ($P=.008$). Higher min·wk⁻¹ of PA was not independently associated with any QoL outcome. However, among patients who engaged in ≥ 150 min·wk⁻¹ of PA, the negative association between BMI and overall QoL was attenuated ($P=.558$), whereas among patients who engaged in <150 min·wk⁻¹ of PA, the negative association between BMI and overall QoL persisted ($P=.025$). Among patients who engaged in ≥ 150 min·wk⁻¹ of PA, the negative association between BMI, and physical and functional well-being was attenuated ($P=.765$ and $P=.284$), whereas among patients who engaged in <150 min·wk⁻¹ of PA, the negative association between BMI, and physical and functional well-being persisted ($P<.001$ and $P=.010$), respectively.

Conclusion—BMI is associated with poorer QoL among uterine cancer patients. The findings from this cross-sectional study are consistent with the hypothesis that endometrial cancer survivors who are able to perform 150 min/week of PA may be protected from the negative effects of BMI on QoL.

INTRODUCTION

Endometrial cancer is the most common gynecologic malignancy in the United States with an estimated 49,000 cases expected in 2013 [1]. The standard therapy is hysterectomy and bilateral salphingo-oophorectomy with adjuvant chemotherapy and/or radiation therapy

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depending on pathologic risk factors. The majority of women are diagnosed at an early stage when survival is over 90% at 5 years [2]. However, treatment (including, surgery, chemotherapy, and radiation therapy) can result in both acute and chronic side effects that can affect health related quality of life (QoL) [3, 4]. Concurrent medical co-morbidities in this population including diabetes, hypertension, obesity, cardiovascular conditions can also have a substantial impact on QoL. Furthermore, low quality of life is associated with prolonged length of hospital stay amongst gynecologic cancer patients undergoing surgery and consequently potentially higher health care costs [5]. As a result, focusing on methods to improve QoL in the survivorship period is a priority.

Prior research has observed that low physical activity (PA) negatively impacts QOL in patients with endometrial cancer [6]. Patients meeting guidelines for PA had significantly better QOL than those not meeting guidelines [7]. One of the potential co-morbidities influencing the level of PA in this population is the high prevalence of obesity; up to 90% of women with type 1 endometrial cancer are overweight or obese [8]. High rates of obesity and low levels of PA have been reported in uterine cancer patients while higher rates of PA and lower BMI were both independently associated with improved QoL and less fatigue in this population [6].

The purpose of our study was to estimate the levels of PA and BMI in a hospital based cohort of endometrial cancer survivors and to describe the association of BMI with PA level and overall health related quality of life. We were particularly interested in the physical and functional well-being aspects of QOL. Further, we were interested in determining whether the associations of BMI and QOL varied according to whether survivors are compliant with the PA at the levels recommended by the American Cancer Society, the American College of Sports Medicine, and the National Comprehensive Cancer Network.

METHODS

Patients and Methods

We conducted a mailed survey of patients with uterine cancer who received care at the Abramson Cancer Center at the University of Pennsylvania (Philadelphia, PA). Patients were women 20 years old with a diagnosis of uterine cancer. Patients were identified using surgical logs from 2008–2010, and ICD-9 codes 179.0, 182.0–182.8, from 2006–2010. Patients who met inclusion criteria were sent a letter signed by their oncologist explaining the purpose of the study. Potentially eligible patients were provided with the option to decline participation within two-weeks of receiving the letter from their oncologist. Those who did not decline participation were sent a survey to complete. After two-weeks, a second survey was sent to those who did not reply to the first mailed survey [9]. Disease recurrence or persistence was not an exclusion criteria for the study. The National Coalition for Cancer Survivorship defines cancer survivor as anyone from the time of diagnosis and for the balance of life including patients with metastatic disease. This protocol was approved by the University of Pennsylvania Institutional Review Board, and the University of Pennsylvania cancer center. Patients who provided their informed consent were those who mailed back the completed survey. Women who were unable to complete a written survey as they were non-English speaking, illiterate, or had cognitive impairments were excluded.

Quality of Life Questionnaire

Quality of life (QoL) was measured using the Functional Assessment of Cancer Therapy, Gynecologic Oncology Group (FACT-G) questionnaire [10, 11]. The FACT-G questionnaire has four subscales that measure physical well-being (PWB), social and family well-being (SFWB), emotional well-being (EWB), and functional well-being (FWB). These subscales can be aggregated to create a composite QoL outcome score. Patients were asked to consider how they felt in the previous seven days. Higher values denote better QoL.

Body Mass Index

Patients self-reported their height and current body weight. We then calculated body mass index (BMI) as weight divided by height squared (kg/m^2). For descriptive purposes we calculated categories of BMI, where <25.0 , $25.0\text{--}29.9$, $30.0\text{--}34.9$, $35.0\text{--}39.9$, and 40.0 represent healthy weight, overweight, moderately obese, severely obese, and very severely obese, respectively.

Physical Activity Questionnaire

The Paffenbarger Physical Activity Questionnaire was used to assess participation in PA [12]. The PA questionnaire is valid [13], correlates with objective measures of physical fitness [14], and has been used among other cancer sites for epidemiologic studies [15, 16]. Patients were asked to free-list any PA's they participated in on a regular basis in the past one year. For each PA, patients listed the average number of sessions per week and the duration of the activity in minutes. Total PA was generated by summing the number of minutes of PA reported each week ($\text{min}\cdot\text{wk}^{-1}$). We then dichotomized this variable between women who met (versus did not meet) the recommended dose of PA of $150\text{ min}\cdot\text{wk}^{-1}$, as recommended by the American College of Sports Medicine, American Cancer Society, and National Comprehensive Cancer Network.

Covariates

Information on covariates came from self-report or the electronic medical record. Age, race, BMI, and PA were self-reported. Variables collected from the electronic medical record included pathology type, stage of cancer, cancer treatment history, number of lymph nodes removed, and time since diagnosis. The Charlson Comorbidity Index was used to quantify number of comorbidities [17].

Statistical analysis

The response rate to our survey was calculated using methods described by the American Association for Public Opinion Research [9]. Continuous variables are reported as means \pm standard deviations (SD), and categorical variables are reported as counts with percentages (%). Normality of QoL outcomes were examined using the Shapiro-Wilk test, and graphically with histogram plots. All QoL outcomes were negatively skewed. QoL outcomes were transformed using a square transformation (i.e., QoL^2) to achieve Gaussian distribution. We used least squares regression to estimate the magnitude of association for each kg/m^2 increase in BMI or each $\text{min}\cdot\text{wk}^{-1}$ increase in PA, on the QoL outcome of interest. We then conducted regression analysis of BMI on QoL, stratified among those who

did (versus did not) meet recommended PA guidelines. All results presented herein are back transformed (i.e., using the square root) to ease interpretation of results. We examined unadjusted regression models, and then built multivariable regressions model adjusting for socio-demographic and clinical characteristics. Results were consistent in both adjusted and unadjusted models; therefore multivariable adjusted models are presented. Statistical tests were two-sided and $P < .05$ was the threshold for statistical significance. All statistical analyses were conducted using Stata 12.0 (College Station, TX).

RESULTS

Mailed survey results

Five hundred thirty one potentially eligible patients were identified using surgical case logs and ICD-9 codes. Among 531 mailed letters, 225 patients returned surveys. Twelve surveys were identified as not meeting inclusion criteria (i.e., 10 diagnosed with cancer before 2006, and two misclassified (diagnosed with other gynecologic cancers)), thus our response rate was 43% and included 213 patients.

Socio-demographic and clinical characteristics

Socio-demographic and clinical characteristics are depicted in Table 1. Age ranged from 29–94 years. Patients were commonly diagnosed with early stage endometrial adenocarcinoma, and treated surgically. Time since diagnosis ranged from 4–72 months.

BMI and Physical Activity Characteristics

Distribution of BMI among the study sample is depicted in Table 2. BMI ranged from 14–67 kg/m², and the mean BMI was 31.1 ± 8.9 kg/m². Categorically, 26%, 22%, 23%, 14%, and 15% of women were healthy weight, overweight, moderately obese, severely obese, and very severely obese, respectively. The median volume of PA was 90.0 min·wk⁻¹ [interquartile range: 0–240]. Categorically, approximately half (52%) reported <150 min·wk⁻¹ of PA, with 80 (38%) reporting being completely sedentary (i.e., 0 min·wk⁻¹ of PA). The most common PA's reported were walking (42%), aerobic gym-based activities including the recumbent bicycle and elliptical machine (11%), and swimming (8%). The distribution of BMI categories were similar among those who did (versus did not) meet recommended PA guidelines ($P = .847$). When treated as continuous variables, there was no correlation between BMI and min·wk⁻¹ of PA ($r = 0.02$, $P = .822$).

Quality of Life Scores

QoL scores are depicted in Table 3. We compared the QoL scores in our sample to those included in the validation study of the FACT-G questionnaire [11]. The composite FACT-G QoL outcome were similar between our sample and the validation sample ($P = .452$). QoL subscales were comparable between groups, with exception of SFWB where our sample reported lower scores, but this comparison did not reach statistical significance ($P = .088$).

Independent Effect of BMI on QoL

In multivariable analyses controlling for demographic, treatment, and patient related variables, higher levels of BMI were associated with significantly poorer overall QoL ($P=.050$; Table 4). Higher levels of BMI were associated with poorer PWB ($P=.002$) and FWB ($P=.008$). Higher levels of BMI were not associated with SFWB ($P=.603$) or EWB ($P=.899$).

Independent Effect of Physical Activity on QoL

In multivariable analyses controlling for demographic, treatment, and patient related variables, higher $\text{min}\cdot\text{wk}^{-1}$ of PA was not associated with any QoL outcome (Table 4).

Joint Effects of BMI and PA on QoL

In stratified analysis, among patients who engaged in $\geq 150 \text{ min}\cdot\text{wk}^{-1}$ of PA, the negative association between BMI and QoL was attenuated ($P=.558$), whereas among patients who engaged in $<150 \text{ min}\cdot\text{wk}^{-1}$ of PA, the negative association between BMI and QoL persisted ($P=.025$). This pattern was similar for PWB and FWB. Among patients who engaged in $\geq 150 \text{ min}\cdot\text{wk}^{-1}$ of PA, the negative association between BMI, and PWB and FWB were attenuated ($P=.765$ and $P=.284$), whereas among patients who engaged in $<150 \text{ min}\cdot\text{wk}^{-1}$ of PA, the negative association between BMI, and PWB and FWB persisted ($P<.001$ and $P=.010$), respectively.

DISCUSSION

Our results demonstrate that higher BMI is associated with inferior overall QoL, decreased physical and functional well-being in patients treated for endometrial cancer after controlling for standard patient demographic, treatment, and pathologic variables. The decreased QoL, PWB, and FWB associated with a higher BMI, however, were attenuated with levels of PA that met ACS, American College of Sports Medicine, and NCCN guidelines. Amongst those patients who did not reach the recommended PA level, the negative association between QoL, FWB, and PWB persisted with elevated BMI. Sustained weight loss is challenging in this patient population, however, our data is encouraging in that even amongst higher BMI women, those who do regular physical activity may be protected from the lower QoL observed among sedentary overweight or obesity survivors. The take home message for clinicians might be that overweight/obese endometrial cancer survivors who can tolerate exercise should be prescribed exercise, particularly if the patient reports poor quality of life.

Other groups have examined the interaction of BMI and PA on quality of life and have found that they contributed independently to QoL. Our analysis demonstrates that PA level in endometrial cancer patients who have a higher BMI may offer some protection from the negative effects of high BMI on QoL, PWB, and FWB. These findings are encouraging and suggest that programs aimed at improving levels of PA may have a significant impact on QoL and physical and functional well being particularly on those who have higher BMI and are at greatest risk of lower QoL. Our observation that PA attenuated the negative effects of increased BMI on QoL, PWB, and FWB are contrary to what was observed by Courneya et

al who found exercise and BMI independently improved QoL and PA and did not observe any interactions between BMI and PA and their association with QoL [3]. This may be due to the higher level of PA reported by our study population particularly in those who were obese compared to similar study populations. From a patient perspective, there is also an expectation regarding the benefits of exercise. In a survey study of Stage I endometrial cancer survivors regarding their level of exercise in the prior 6 months, both self-reported exercisers and non-exercisers indicated that improved physical and emotional well-being is a likely consequence of exercise [17]. Courneya et al also observed positive associations between patients meeting guidelines for exercise and QoL [3]. Similarly, in a study of 200 endometrial cancer survivors, Basen-Engquist found that patients with higher levels of PA and lower BMI reported better physical function and less fatigue [12]. They found significant differences between normal-weight and obese women ($p=0.005$) and between sedentary women and those who met physical activity guidelines ($p=0.000$). The interaction between BMI and PA was not significant, however.

Approximately 74% of our population was overweight or obese with 22% overweight and 52% obese. Although these proportions are higher than rates of obesity in the general public [18], these percentages are in line what has been reported in other series involving endometrial cancer patients [6, 19]. In our study, 48% of women indicated a level of PA that met guidelines which is in line with the PA level of the general population [20]. Approximately 55% of obese endometrial cancer survivors in our study were meeting guidelines for PA which is slightly higher than rates of physical activity meeting guidelines in the general population (43%). The level of PA in our analyses is higher than what has been previously reported in endometrial cancer survivors and may be due to the time period of the analyses as our study was conducted more recently [6]. Differences may also be secondary to geographic region of the studies, as our study was conducted in a large metropolitan area in the north eastern United States, as compared to the prior study, which was conducted in a less populous, colder Canadian location. Conversely, level of activity was based on self-reports which are prone to reporting bias. Additionally, we found no association between BMI and SFWB and EWB. This is consistent with prior reports that have found no association between BMI and mental health function.

Obesity and lack of physical activity (PA) are known risk factors for development of endometrial cancer and thus a high proportion of survivors are also likely to be overweight and obese with a sedentary lifestyle [21]. One could hypothesize that apart from improvements in QOL, physical activity may also reduce rates of recurrence through the insulin pathway by decreasing levels of insulin and insulin like growth factor [22]. Elevated levels of IGF-I activity has been associated with enhanced proliferation in endometrial tissue [23]. Hyperinsulinemia has been positively associated with endometrial adenocarcinoma incidence in the Women's Health Initiative Observational Study though conclusive evidence of an association between physical activity and endometrial cancer specific mortality has not been demonstrated [24]. A recent prospective analysis of BMI and PA in women who participated in the NIH-AARP Diet and Health Study also demonstrated that higher BMI pre-diagnosis increased overall and disease specific mortality in endometrial cancer patients while higher levels of moderate to vigorous PA were associated with lower 5 year all-cause

mortality though no association was observed between physical activity and disease specific mortality [25].

Our study was a cross-sectional study conducted in a large urban medical center which draws patients from both the urban and suburban region which improves the generalizability of our findings and is a strength of our study. There are several potential important limitations. Our study had a response rate of 43% which is lower than what has been previously reported in similar series [19], but the response rate is similar to a 16 page survey sent to colon cancer survivors in the region [9]. We relied on patients self-report of both body weight and height which may be underestimated. Similarly, we relied on patient self report regarding their level of PA which may also be subject to recall bias and are high for this population. Misclassification regarding activity level on self-administered questionnaires is well-known. In a recent prospective study of physical activity in cancer survivors by Loprinzi et al, only 13% engaged in physical activity that met physical activity guidelines, and obese cancer survivors engaged in 47% less PA than normal weight cancer survivors [26]. Additionally, this study cannot establish a causal relationship between BMI, PA, and QoL given it is cross-sectional analysis. We should emphasize as well that our findings represent the experience at one large academic urban medical institution during the time period studied and should be taken as hypothesis generating. Further studies are needed to verify our findings and support the need for prospective clinical studies evaluating exercise interventions in this population to improve quality of life particularly in obese endometrial cancer survivors.

Overall, the results of our study support prior studies demonstrating an association between QoL, BMI, and physical activity. They also demonstrate that among endometrial survivors with elevated BMI, physical activity programs may offer protection from the lower quality of life sometimes observed in this population. We have known for decades that exercise and body weight are associated with reduced incidence, morbidity, and mortality for cardiovascular diseases [27, 28], however no substantial concomitant changes in population level of regular physical activity has been observed [29] and levels of obesity have concurrently increased in the U.S. [18]. Clearly, attempts to increase physical activity level by focusing on long term outcomes relating to incidence, morbidity, and mortality from major chronic diseases does not result in behavior changes. Perhaps a focus on shorter term outcomes such as improved quality of life would be more motivating to patients.

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Table 1

Socio-demographic and clinical characteristics (n=213)

Variable	Mean±SD or N (%)
Age — yr	63.6±10.6
Race — no. (%)	
White	178 (84%)
Other	32 (16%)
Pathology type — no. (%)	
Endometroid Adenocarcinoma	158 (75%)
Papillary serous or Clear Cell	35 (17%)
Sarcoma	8 (4%)
Carcinosarcoma	8 (4%)
Other (Undifferentiated)	3 (1%)
Stage — no. (%)	
1	157 (74%)
2	13 (6%)
3	26 (12%)
4	5 (2%)
Unknown	12 (6%)
Treatment Modalities — no. (%)	
Surgery	100 (47%)
Surgery, Chemotherapy	37 (17%)
Surgery, Radiation	47 (22%)
Surgery, Chemotherapy, Radiation	22 (10%)
None or Unknown	7 (3%)
No. of nodes removed	8.9±10.2
Time since diagnosis — no. (%)	
0–2 yr.	69 (32%)
3–4 yr.	94 (44%)
5–6 yr.	50 (23%)
Charlson Comorbidity Score	

Variable	Mean±SD or N (%)
0-1	161 (76%)
2	52 (24%)

Table 2

BMI and Physical Activity Characteristics

Variable	Body Mass Index (kg/m ²)					
	<25.0	25.0–29.9	30.0–34.9	35.0–39.9	40.0	
Overall Sample (n=213)	56 (26%)	47 (22%)	49 (23%)	30 (14%)	31 (15%)	
Stratified by Level of Physical Activity						
<150 min·wk ⁻¹ (n=111; 52%)	31 (28%)	26 (23%)	25 (23%)	13 (12%)	16 (14%)	
150 min·wk ⁻¹ (n=102; 48%)	25 (24%)	21 (21%)	24 (23%)	17 (17%)	15 (15%)	

Table 3
Mean quality of life outcome scores in our study sample and the FACT-G questionnaire validation sample

Quality of Life Outcome ^a	Our Sample (n=213)		Validation Sample (n=23) ^b	
	Mean	SD	Mean	P-value
Composite Outcome				
FACT-G	80.82	19.25	83.92	±13.00 .452
Subscale Outcomes				
PWB	22.98	±5.46	21.86	±6.36 .359
SFWB	21.00	±6.36	23.32	±3.97 .088
EWB	17.46	±6.29	17.96	±4.07 .710
FWB	19.39	±7.11	20.79	±4.25 .356

^a FACT-G, Functional Assessment of Cancer Therapy-Gynecologic; PWB, Physical Well Beings; SFWB, Social/Family Well Being; EWB, Emotional Well Being; FWB, Functional Well Being.

^b From Calhoun et al. [18].

Table 4

Effects of body mass index (BMI) and volume of physical activity on quality of life

Quality of Life Outcome ^d	Overall Effect of BMI (kg/m ²)		Overall Effect of Physical Activity (min·wk ⁻¹)		Effect of BMI Stratified by Level of Physical Activity			
	B	P-value	β	P-value	<150 min·wk ⁻¹ (n=111)		150 min·wk ⁻¹ (n=102)	
					β	P-value	β	P-value
Composite Outcome								
FACT-G	-7.14	.050	-0.68	.364	-8.75	.025	-4.89	.558
Subscale Outcomes								
PWB	-2.32	.002	-0.23	.112	-3.07	<.001	-0.94	.765
SFWB	-1.06	.603	-0.21	.299	0.90	.777	-1.82	.331
EWB	0.44	.899	-0.19	.244	-0.28	.973	-0.68	.845
FWB	-2.44	.008	-0.05	.950	-2.80	.010	-1.94	.284

^aFACT-G, Functional Assessment of Cancer Therapy-Gynecologic; PWB, Physical Well Beings; SFWB, Social/Family Well Being; EWB, Emotional Well Being; FWB, Functional Well Being.

^bDue to non-normality of variables, quality of life outcomes were squared (i.e., quality of life²) to reduce skew in regression models, then back transformed for data presentation.

^cVariables in the regression models included age, race, pathology, stage, treatment type, no. of lymph nodes removed, years since diagnosis, and Charlson comorbidity score.