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Obesity and endometrial cancer: A lack of knowledge but opportunity for intervention

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Abstract

Objective: The causal link between obesity and endometrial cancer is well-established, however obese women's knowledge of this relationship is unknown. Our objective was to explore patients' understanding of this relationship and assess the acceptability of a technology-based weight loss intervention.

Methods/Materials: Obese women with Type I endometrial cancer/hyperplasia were surveyed about their assessment of their body mass, knowledge of the relationship of obesity and endometrial cancer, and eating and activity habits. Interest in participation in an intervention also was assessed.

Results: Eighty-one women with early stage (71.6% stage I) and grade (41.7% grade 1) disease completed the survey. The median BMI was 35.4 kg/m² (IQR 32.2–43.5 kg/m²) and the average age was 59.3 (SD 11.1) years. 76.25% of women were unable to categorize their BMI correctly and 86.9% of those incorrectly underestimated their BMI category. One-third (35.9%) were unaware of any association between obesity and endometrial cancer and 33.3% responded that obesity decreased or did not significantly increase the risk of endometrial cancer. 59% expressed interest in a weight loss intervention.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to report that is relevant to this research.

Conclusions: Endometrial cancer survivors with obesity underestimated their obesity and lacked knowledge regarding the link between obesity and endometrial cancer. However, the majority expressed interest in electronically delivered weight loss interventions.

Keywords

Epidemiological survey; obesity; endometrial hyperplasia/cancer

INTRODUCTION

Approximately one-third of American women are obese, defined by a body mass index (BMI) of $>30 \text{ kg/m}^2$. In addition, 7% of women suffer with extreme or morbid obesity (BMI $> 40 \text{ kg/m}^2$) (1). Obesity increases the risk for many health problems, including heart disease, diabetes, and cancer. It is one of the strongest risk factors for the development of endometrial cancer, the most common gynecologic malignancy in the United States. Approximately 80% of the estimated 52,630 new cases expected in 2014 will be classified as type 1, or estrogen dependent disease (2). Though the incidence of type 2, non-estrogen dependent, endometrial cancers has remained stable over the years, type I endometrial cancer is on the rise (3). While reproductive factors such as early menarche, late menopause, nulliparity, and anovulation contribute to a woman's overall lifetime exposure to estrogen, the major source of excess estrogen in most post-menopausal patients is the conversion of androstenedione to estrone via aromatase in the peripheral fat. Hence, the development of excess peripheral fat in patients with obesity is the most important modifiable risk factor for the development of endometrial cancer.

Once diagnosed, despite overall good oncologic outcomes for patients with early stage endometrial cancer, quality of survivorship is clearly still affected: BMI is inversely associated with physical, functional, and social/emotional well-being after diagnosis. Fader et al demonstrated that higher BMI is associated with poor physical health scores and lack of energy, as well as lower quality of life scores for fulfillment of work and enjoyment of life (4). Ultimately, among women with endometrial cancer, those who are obese are more likely to die of their cancer or co-morbidities compared to those with normal BMIs (5). A recent study by Ward and colleagues found that women with endometrial cancer were overall more likely to die of cardiovascular disease (35.8%) than cancer (18.9%), and after 5 years the risk of death from cancer is less than that of the combination of hypertension, coronary heart disease, and hyperlipidemia, co-morbidities frequently associated with obesity (6).

Although there is an abundance of medical research demonstrating the physiology underlying the link between obesity and endometrial cancer, several prior studies have shown that the general population of women is uninformed of this well-established link (7, 8). Soliman et al reported that 58% of over 1500 women in an urban population were unaware that obesity increased the risk for endometrial cancer (9). Middle-aged cancer survivors additionally report low physical activity levels (10), and that two-thirds of oncology patients actually gain additional weight after diagnosis (11), demonstrating an opportunity for intervention in this particular patient population.

None of these studies have addressed the level of knowledge of patients in active treatment or surveillance for endometrial hyperplasia or carcinoma, and we hypothesized that women who already experienced this diagnoses would also be unaware of the link between obesity and development of endometrial cancer. Additionally, women who experience an obesity-related co-morbidity such as endometrial cancer may be willing to participate in a weight loss intervention, since obesity is a modifiable risk factor and a cancer diagnosis may be an event that could promote lifestyle change. Such change may decrease the future risk of morbidity and mortality from other obesity-related conditions, such as cardiovascular disease. Our primary objective was to assess patient knowledge on the link between obesity and endometrial cancer and to assess interest in weight loss interventions delivered via electronic means such as telephone and internet—a rapidly growing approach to the delivery of lifestyle modification interventions for weight control that can reduce participant burden and costs (12).

METHODS/MATERIALS

We assessed a convenience sample of 81 women between who had a biopsy-proven diagnosis of either endometrial hyperplasia or endometrial carcinoma and presented for outpatient care at the Gynecologic Oncology practices at the University of Pennsylvania. Women with obesity (BMI > 30 kg/m²), 18 years of age or older, and English-speaking were asked to complete a self-administered survey. This study was reviewed and approved by the University of Pennsylvania Institutional Review Board (#815858) and all participants provided written informed consent prior to any study activities.

In advance of scheduled appointments, we prescreened electronic medical records for both a history of endometrial hyperplasia/carcinoma and most current BMI. Women who met these criteria (n = 172), were eligible to be provided with an overview of the study and potentially given a survey to complete based on the availability of study staff. Eighty one women (47%) agreed to complete the survey.

The survey queried patient characteristics, such as age, weight, height and income. Additional questions asked about subjects' self-perception of height, weight and BMI category, knowledge of the effect of obesity on cancer risk, diet and exercise patterns and interest in participation in a weight loss intervention. Questions were selected from a bank of previously validated questions provided by the Center for Disease Control and Prevention (CDC), World Health Organization (WHO), Behavioral Risk Factor Surveillance System and the Harvard Forums of Health Survey (9).

Participants' self-reported height and weight were compared to the actual office measurements from the day of survey completion. The patient's self-assessment of their BMI classification was evaluated on a categorical scale utilizing the World Health Organization (WHO) classifications without the corresponding numerical BMI values (i.e. "underweight, average, overweight, slightly obese, moderately obese or very obese" which corresponds to BMI ranges of <18.5, 18.5–24.9, 25–29.9, 30–34.9, 35–39.9 and 40 kg/m² respectively). Dietary habits were assessed by average daily servings of dairy, protein, vegetables, fruits and grains. Routine exercise activities were evaluated by the average

minutes per week spent at the following activities: walking, jogging, running, swimming, racket sports, other aerobic activities (i.e. exercise classes or videos) or lower intensity exercise (i.e. stretching or yoga). Subjects' knowledge regarding the relation between obesity and endometrial cancer was measured by asking "How does obesity affect the risk of endometrial cancer", with responses based on a five-level Likert scale. A similar question was asked of the association between obesity and lung cancer.

Women also were asked about their interest in participation in a formal weight loss support program and asked to quantify their weight loss goal in pounds. The questionnaire also assessed availability of access to different technologies, including text messaging and private wireless (WiFi) internet as well as patient preference on different platforms of delivery of a weight loss intervention, including in-person meetings, telephone, text messages, or internet.

All demographic and categorical data were reported as means ($\pm$ SD) or medians (IQR) and compared using χ^2 tests, Fisher's exact tests or Wilcoxon-Mann-Whitney tests as appropriate. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Spearman rank correlation analyzed the association between knowledge of increased cancer risk and demographic factors. Logistic regression was utilized to evaluate the association between dependent and independent variables. Two-sided p-values of <0.05 were considered statistically significant. Statistical analyses were performed using Stata 12.1 (StataCorp., College Station, Texas).

RESULTS

Detailed demographic data is summarized in Table 1, but the participants were predominantly early stage and grade disease (71.6% stage I and 41.7% grade 1); yet 20.8% were grade 3 histology. The median BMI was $35.4 \text{ kg}/\text{m}^2$ (Interquartile Range 32.2–43.5 kg/m^2) and the average age was 59.3 (Standard Deviation 11.1) years. Although there was a high correlation between self-reported and actual height ($r=0.95$, $p<0.001$) and weight ($r=0.94$, $p<0.001$), the majority of patients (76.25%) did not categorize their BMI correctly, with lower correlation between reported BMI and actual BMI category ($r=0.42$, $p<0.001$). 86.9% of those incorrectly underestimated their true BMI category (FIGURE 1A). There was a statistically significant association between knowledge of cancer risk and higher BMI ($p=0.009$), non-white race ($p=0.005$) and income (0.007), a marginally significant association with age ($p=0.06$) but no association for interest in participation in a weight loss intervention ($p=0.6$).

Over one-third (35.9%) were unaware of any association between obesity and endometrial cancer and another 33.3% responded that obesity decreased or did not significantly increase the risk of endometrial cancer (FIGURE 1B). There was no statistically significant association between the knowledge of increased cancer risk and any of the demographic factors or interest in participation in a weight loss intervention. The answers to the distracter question of the link between obesity and lung cancer ranged from 56.3% of women reporting "I don't know" and 12.5% reporting "No change", to 2.5% reporting a decreased risk, 16.3% reporting "Increase a little" and 11.3% reporting "Increase a lot".

When queried about exercise habits, 23.5% of women reported no regular exercise. For those who did exercise, the majority of women walked, however only 32% of subjects walked more than sixty minutes per week. Fewer women performed higher intensity exercise, with 2 subjects jogging, one subject running, 3 subjects swimming and only 8% participating in greater than 60 minutes per week of “aerobic exercise”. When asked about dietary habits, the median daily servings (1/2 cup) were 2 servings for all dietary factors: dairy (IQR 1–2.75), protein (IQR 1–2.25), vegetables (IQR 1–3), fruits (IQR 1–2) and grains (IQR 1–2.5).

In the assessment of the feasibility of a technology-based weight loss intervention, 74.3% of respondents had text message capability and 65.7% had private wireless internet access. Ultimately, 46.8% of participants were eligible for participation in our pilot intervention with both text and internet access, and over half (59.3%) of subjects expressed interest in enrollment in an intervention). Patient interest in a variety of platforms for interventions (meetings, telephone, internet and cell phone application) were wide ranging (FIGURE 2), but subjects most commonly indicated interest in telephone, with 47% ranking this option first, and internet, with 31% ranking it first.

CONCLUSIONS

The primary aim of this study was to assess obese patients’ understanding of the link between obesity and endometrial cancer and determine the interest in and feasibility of a novel technology-based weight loss intervention. Our study brings a unique perspective in that it examines the awareness between obesity and the increased risk of endometrial cancer in women with both conditions. While most women were correctly able to identify their specific height and weight, they did not subsequently classify themselves into the appropriate WHO BMI category, largely underestimating how obese they actually were. Although the high correlation between the self-reported and actual height and weight may have been significantly influenced by the temporal relationship between participation in our survey at the time of an outpatient visit in which their most recent height and weight was recorded, subjects were then unable to translate those numbers into the correct written description of their WHO BMI category.

Previous authors have determined that there is extremely limited public knowledge regarding the causal link between obesity and endometrial cancer. A 2010 Australian telephone study of the general public reported that many respondents, 44% of whom were obese, did not rate being overweight as a very important risk factor in the development of cancer (10).

Ackermann et al similarly evaluated the knowledge regarding the risks of endometrial cancer and obesity in a healthy patient population, and similarly only 36% of subjects were aware of this causal relationship (13). Studies that have focused on only women’s knowledge have determined a similar lack of knowledge. In the study by Soliman and colleagues, a similar questionnaire to the one used in this study was distributed to 1545 women (24% overweight and 45% obese) in the general Houston community and a substantial proportion of women, particularly black women (58%), were not aware that obesity increased the risk of endometrial cancer (9). In a 2012 survey of urban women, only 18.1% were aware that obesity increases the rate of endometrial cancer, while most women were aware of the

cardiovascular effects of obesity (diabetes: 79.1%, hypertension: 74.2% and heart disease: 73.3%) (14), with similar findings when knowledge was evaluated in the infertility population (endometrial cancer risk: 20.7%) (8). Knowledge of the association between cancer and obesity has also been evaluated in a general population of patients recently diagnosed with cancer, and correspondingly determined a widespread lack of knowledge of obesity as a contributing factor in the development of cancer (15, 16). Our study narrows the focus in the inquiry of the knowledge of the association between obesity and the development of endometrial cancer, well-known to the medical community, to obese women with endometrial cancer. This study provides continued support to the significant gap in knowledge of this association, and demonstrates importantly that this awareness is lacking in the cohort who is most affected by it.

The American Cancer Society Guidelines on Nutrition and Physical Activity recommend getting at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity activity weekly for cancer prevention in the general population, with similar recommendations by the National Comprehensive Cancer Network (NCCN) for cancer survivors and the Center for Disease Control (CDC). Dietary recommendations include eating 2 and ½ cups (5 servings) of fruits and vegetables daily, as well as limiting refined carbohydrates and processed/red meats (17, 18). A recent study of women with stage I endometrial cancer determined that only 41% of respondents were exercising regularly, and those who were exercising had a significantly lower BMI (31.6 vs. 37.3kg/m²). In our study population, the majority of women were not meeting these recommended exercise guidelines, with only 22% attaining these exercise goals, and one-fourth of women not exercising at all. Additionally, only 40% were compliant with dietary recommendations for fruit and vegetable intake. These findings indicate that in this obese patient population, there is room for improvement in diet and exercise and participation in an intervention may assist in attaining these recommendations and provide subsequent weight loss.

Based on the survey results, we identified a cohort who self-selected as interested in participating in a weight loss support program. Almost 60% of the women surveyed expressed interest in participating in an intervention, and almost half of the overall cohort would be eligible for enrollment based on their technology capabilities, despite the overall older patient population who is affected by endometrial cancer. Additionally, patients reported a variety of interests in different platforms for delivery of a weight loss intervention, most commonly identifying interest programs that did not require face-to-face visits (i.e. via telephone or internet) and are more reasonably integrated into daily lives. However, the variety of preferences speaks to the indication that a single intervention platform will not likely be broadly successful for all women, and instead individualized programs that offer a format that is appealing and usable for an individual patient is the one most likely to elicit success.

Our study is not without limitations. We obtained a lower response rate compared to prior studies reported in the literature. However, this lower response rate does not capture those patients who qualified but were not offered a survey by the clinic administrative staff due to office workflow, and instead is calculated from a denominator of all obese women with endometrial hyperplasia or Type I endometrial cancer who were identified as being able to

be offered a survey. Another limitation is that these data were collected at a single urban tertiary care academic institution during office visits for ongoing care of endometrial cancer, and may not be generalizable to the general knowledge base of all women with endometrial cancer. Additionally, this was a patient population of predominantly early stage and grade cancer, and may also not be representative. However, it is this patient population who experience a 96% 5-year survival SEER (19), and in whom cardiovascular adverse events related to obesity may significantly affect future morbidity and mortality, as they are surviving their cancer diagnosis. Thus it could be argued that this is the optimal patient population in which to enact weight loss interventions for maximal health benefit. Finally, if the survey answer to the question of how obesity affects the risk of endometrial cancer of “increased a little” is less strictly considered a correct answer, the frequency of correct knowledge regarding this association would be increased to 56.4%. However, this still results in almost half of the survey population being unaware of the critical link between obesity and the development of endometrial cancer.

The effect of decreasing BMI on oncologic outcomes for obese women with endometrial cancer is uncertain and warrants further study. Several retrospective studies have not demonstrated a difference in recurrence rates based on obesity, however obesity does impact the risk of death in endometrial cancer patients, with the majority of patients surviving their obesity-related cancer but dying from cardiovascular disease, which is another obesity-related co-morbidity. In addition, there is a paucity of data evaluating either weight loss interventions in patients with endometrial hyperplasia/cancer or the relationship of physical activity, diet and weight with quality of life and survivorship. Given this increasing rate of obesity in our country, it is essential to develop appropriate interventions to reduce cancer incidence, morbidity and death among obese women at risk for endometrial cancer as well as for endometrial cancer survivors.

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19. SEER Stat Fact Sheet: Endometrial Cancer. <http://seer.cancer.gov/statfacts/html/corp.html>

Figure 1A.

Patient self-assessment of BMI category: Percentage of subjects' response to self-assessment of BMI category according to WHO BMI Category compared to actual calculated BMI.

Figure 1B.

How does obesity affect the risk of endometrial cancer: A pie chart demonstrating subjects' knowledge of how obesity affects endometrial cancer.

Figure 2:
Subject Ranking of Interest in Type of Weight Loss Intervention: Ranking in order of preference for favored platform for participation in a weight loss intervention.

TABLE 1:**Participant Demographics**

Demographic	Value[*]
Age (years), mean(sd)	59.38 (11.12)
BMI (kg/m ²), median (IQR)	35.4 (32.2–43.5)
	Range 30–82.4
<u>Race</u>	
White	54 (68.4)
Black	20 (25.3)
Asian	3 (3.8)
Other	2 (2.5)
<u>Ethnicity</u>	
Hispanic	5 (8.5)
Non-Hispanic	54 (91.5)
<u>Income</u>	
<\$25,000	17 (23.0)
\$25,000–50,000	13 (17.6)
\$50,000–75,000	15 (20.3)
>\$75,0000	24 (32.4)
Unknown	5 (6.8)
<u>Stage</u>	
IA	40 (54.1)
IB	14 (18.9)
II	4 (5.4)
IIIA	7 (9.5)
IIIB	0 (0)
IIIC	4 (5.4)
IV	3 (4.1)
Unstaged	2 (2.7)
<u>Grade</u>	
1	30 (41.7)
2	27 (37.5)
3	15 (20.8)
<u>Histology</u>	
Hyperplasia	6 (7.4)
Type I endometrioid	64 (79.0)
Mixed Type I (predominant) +Type II (i.e. serous, clear cell, mucinous, squamous)	11 (13.6)

^{*} Values reported as n (%) unless otherwise noted