The Association Between Body Mass Index and Presenting Symptoms in African American Women with Ovarian Cancer

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Abstract

Background: Ovarian cancer, the most lethal gynecologic malignancy, typically comes to clinical attention due to nonspecific gastrointestinal or pelvic symptoms. African Americans with ovarian cancer have a greater mortality burden than whites and are also much more likely to be obese. The objective of this study is to explore whether the presentation and duration of symptoms differ by body mass index (BMI) in African Americans with ovarian cancer.

Methods: We conducted a case-only analysis using data from a multicenter population-based study of invasive epithelial ovarian cancer in African American women. Information on risk factors and symptoms leading to diagnosis was obtained in a telephone interview. Frequency and duration of symptoms by BMI categories were compared using logistic regression and linear regression analyses.

Results: Of the 326 women, ~60% was obese (BMI ≥ 30), with 30.8% having a BMI ≥ 35 kg/m². Ninety-four percent of women reported ≥ 1 symptom during the year before diagnosis. We observed differences in frequency of symptoms by BMI categories, with most being reported more frequently by the heaviest women. The reported duration of symptoms was longer in women with higher BMI, with statistically significant trend tests for 6 of the 10 symptoms evaluated.

Conclusion: BMI appears to impact ovarian cancer symptomatology. Women with higher BMI report having symptoms for a longer period of time before diagnosis of ovarian cancer. Healthcare providers should be vigilant and consider ovarian cancer in the differential diagnosis for obese women presenting with abdominal and pelvic symptoms.

Introduction

OVARIAN CANCER IS the deadliest gynecologic malignancy and fifth leading cause of cancer death in women in the United States.¹ In 2013, an estimated 22,240 women were diagnosed with ovarian cancer, while an estimated 14,030 women died from the disease.¹

African American women with ovarian cancer have a disproportionately greater mortality burden than white women.^{1,2} From 2002 to 2008 in the United States, the 5-year relative survival for all stages of ovarian cancer was 44% for white women and 36% for African American women.¹ Although reasons for the survival disparities have not been completely elucidated, obesity may be a contributing factor. African

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American women are nearly twice as likely to be obese as non-Hispanic white women (59% vs. 32%),³ and a growing body of evidence suggests that obesity is associated with both ovarian cancer risk and survival.^{4–6} Meta-analyses and pooled analyses conducted among predominantly white populations have concluded that overweight and obese women are at increased risk for ovarian cancer^{4,5} and have poorer survival after an ovarian cancer diagnosis.⁶ For African American women, some^{7,8} but not all⁹ studies suggest obesity is a risk factor for ovarian cancer. No studies have specifically addressed the effect of obesity on ovarian cancer survival among African American women.

One possible effect of obesity on ovarian cancer that has not been explored is how it may impact the diagnosis of this disease through its effect on symptom recognition. Because there is no efficacious screening method for ovarian cancer, women with ovarian cancer usually come to clinical attention because of symptoms, most frequently pelvic or abdominal discomfort, bowel irregularity, bloating, and to a lesser extent, abnormal vaginal bleeding, and urinary symptoms.^{10–12}

Previous studies suggest that >90% of women report having experienced symptoms during the year before diagnosis.¹³ In addition, symptoms of the cancer were the most common reason for the doctor visit that led to the diagnosis.¹⁰

Excess adipose tissue may interfere with the ability to appreciate early symptoms of ovarian cancer. Several studies suggest that gastrointestinal symptoms such as abdominal pain, diarrhea, and bloating are more prevalent in obese or morbidly obese individuals.¹⁴ This may be related to comorbid illness or could reflect the discomfort associated with excess abdominal weight. If these symptoms arise as a consequence of ovarian cancer, heavier individuals may not appreciate such symptoms as being abnormal if they are already present at baseline. Therefore, identifying any new bloating or pain stemming from ovarian cancer may become increasingly difficult with higher body mass index (BMI) values. Furthermore, other symptoms such as an abdominal lump or distension may be less noticeable in obese women.

The effect of obesity on the types and duration of symptoms before a diagnosis of ovarian cancer has not been reported in previous studies and there are no studies reporting on ovarian cancer symptoms specifically among African American women. The objective of this article is to describe the association between BMI and the frequency and duration of presenting symptoms of invasive epithelial ovarian cancer in African American women.

Materials and Methods

Study participants

The cases used in the analyses are from the African American Cancer Epidemiology Study (AACES), a population-based, case-control study of ovarian cancer in African American women in 10 geographic regions: North Carolina, South Carolina, Georgia, Alabama, Tennessee, Louisiana, Texas, New Jersey, Ohio, and Detroit. Duke University is the lead institution for the study. Institutional review board approval was obtained from all participating institutions.

Details of recruitment have been described elsewhere.⁸ Briefly, women with ovarian cancer are identified using rapid case ascertainment systems through state cancer registries, Surveillance, Epidemiology, and End Results registries, or individual hospital registries. Inclusion criteria are African American/black race (full or mixed), aged 20–79 years, diagnosis of invasive, epithelial ovarian cancer, no history of ovarian cancer, and ability to complete an interview in English. Among women identified as potential cases, 14% died before they could be contacted and 12% could not be contacted. The participation rate among women contacted was 67%.⁸ The median time between diagnosis and case identification was 134 days and between diagnosis and interview was 163 days.

The study population for these analyses consists of 326 African American women with ovarian cancer recruited between December 2010 and December 2013.

Data collection

Data are collected through an interviewer-administered computer-assisted telephone interview (CATI). During the symptom section of the survey (shown in Table 1), ovarian cancer cases are asked to recall whether they had any of the 10 symptoms during the year before diagnosis, and if so, for how many months. The symptom questionnaire is based on one used in a prior population-based study of ovarian cancer, which demonstrated that each of these symptoms was significantly more common in ovarian cancer cases than controls.¹³ Women also are asked to report their height and weight 1 year before diagnosis. Additional survey information includes demographic characteristics; reproductive, gynecologic, and medical history; hormone use; family history of cancer; lifestyle characteristics such as smoking, alcohol consumption, and physical activity; and psychosocial characteristics such as perceived discrimination, cultural and folk beliefs, access to medical care, trust in physicians, and religiosity. Comorbid conditions are assessed

TABLE 1. SYMPTOM QUESTIONS FROM THE AFRICAN AMERICAN CANCER EPIDEMIOLOGY STUDY SURVEY

“During the year before you were diagnosed with ovarian cancer, did you have any of the following symptoms?”^a

Pelvic or abdominal discomfort, such as heaviness, pressure, or pain
 Change in bowel habits such as diarrhea, constipation, gas, or bloating
 Urinary symptoms (need to urinate more often than usual, difficulty emptying bladder, or painful urination)
 Distended or hard abdomen
 Lump in abdomen
 Fatigue or loss of appetite
 Side or back pain (with or without exertion)
 Abnormal bleeding not associated with periods
 Weight gain, swelling in the extremities, or water retention
 Nausea, vomiting, heartburn, or indigestion
 Any other symptoms

^aFor each symptom for which the woman responded “yes,” she was asked to report the duration of time when she experienced that symptom.

using the self-reported Charlson comorbidity scale.¹⁵ Because all women had ovarian cancer, we did not include a diagnosis of cancer in the calculation of their comorbidity score.

Statistical analysis

Four BMI categories were used in the analyses, based on the World Health Organization International Classification: BMI <25 (normal), BMI 25–<30 (preobese), BMI 30–<35 (obese class I), and BMI ≥35 kg/m² (obese class II or heavier).¹⁶ Comparisons of symptom frequency by BMI categories were performed with logistic regression models, calculating odds ratios (ORs) and 95% confidence intervals (CIs) for each category using BMI <25 as the referent category. Durations of symptoms across BMI categories were compared using linear regression models. Both age-adjusted and multivariable-adjusted analyses were performed. Risk factors included in the multivariable-adjusted model were those that were statistically significantly associated with obesity and any individual symptom in bivariate analyses. The covariates include age (continuous), highest completed educational level, marital status, history of pelvic inflammatory disease, oral contraceptive use (using categories from Table 2), and Charlson comorbidity index (continuous). To test for trends in the associations between BMI and symptom frequency or duration, models were run with BMI as a continuous variable.

We also conducted sensitivity analyses in which we excluded underweight women (BMI <18 kg/m²). There were only four women in this category and results were essentially unchanged when they were excluded from the analysis; therefore, we present the analyses including these women in the BMI <25 category. Stratified analyses were performed to determine if there were any differences in the association by histologic type (serous vs. all others), geographic location (north [New Jersey, Ohio, Michigan] vs. south [all other sites]), and median time between diagnosis and recruitment (<163 days vs. ≥163 days). All analyses were performed using SAS version 9.3.

Results

Distributions of select participant characteristics are presented in Table 2. Most (77%) women included were aged ≥50 years. Approximately 60% of the women were obese, with the largest proportion (31%) of women in the BMI ≥35 category. The majority of women (64%) reported a history of oral contraceptive use and 88% reported being pregnant at least once. Most women were never smokers (56%), while 10% were current smokers. The most common primary reason for the doctor visit was symptoms of the tumor (65%).

Table 3 presents distributions of reported symptoms by prediagnosis BMI categories and ORs associated with reporting each symptom, comparing overweight, obese, and severely obese women to women of normal weight. The overwhelming majority of women (94.2%) reported having at least one symptom during the year before diagnosis. Of these, 9.2% reported one symptom, 24.7% reported 2–3 symptoms, and 60% reported ≥4 symptoms. The most common symptoms, reported by more than half of the cases, were bowel irregularity (62.0%), fatigue or loss of appetite (55.8%), pelvic or abdominal discomfort (54.9%), distended

TABLE 2. SELECTED CHARACTERISTICS OF OVARIAN CANCER CASES, THE AFRICAN AMERICAN CANCER EPIDEMIOLOGY STUDY

Characteristic	Cases, n ^a (%)
Age (years)	
20–39	18 (5.5)
40–49	57 (17.5)
50–59	115 (35.3)
60–69	85 (25.9)
70–79	51 (15.6)
Highest completed educational level	
Less than high school	53 (16.3)
High school/some college	183 (56.1)
College degree or greater	90 (27.6)
BMI (kg/m ²)	
<25	47 (14.3)
25–<30	83 (25.3)
30–<35	95 (29.0)
≥35	101 (30.8)
Smoking history	
Current	34 (10.4)
Former	111 (34.1)
Never	181 (55.5)
Medical history	
Endometriosis	38 (11.8)
Uterine fibroids	155 (47.7)
Pelvic inflammatory disease	29 (9.0)
Polycystic ovary syndrome	4 (1.2)
Ovarian cyst	63 (19.3)
Family history of cancer (first degree relative)	
Yes—ovarian cancer	18 (5.7)
Yes—breast cancer	70 (22.1)
Oral contraceptive use duration (months)	
0–<3	117 (36.0)
3–<36	90 (27.7)
36–<60	26 (8.0)
≥60	92 (28.3)
Number of pregnancies	
0	39 (12.0)
1–3	177 (54.3)
>3	110 (33.7)
Primary reason for doctor visit that led to diagnosis	
Symptoms of the tumor	209 (65.1)
Unrelated gynecological symptoms	2 (0.6)
Routine screening or check-up	23 (7.2)
Pregnancy	1 (0.3)
Infertility	1 (0.3)
Totally unrelated symptoms	85 (26.5)
Histology	
Serous	193 (62.3)
Clear cell	5 (1.6)
Endometrioid	39 (12.6)
Mucinous	19 (6.1)
Other	54 (17.4)
Stage	
I	114 (37.9)
II	33 (11.0)
III	112 (37.2)
IV	42 (14.0)

^aNumber of cases may not total 326 due to missing values for some variables.

BMI, body mass index.

TABLE 3. FREQUENCY OF REPORTED SYMPTOMS IN YEAR BEFORE OVARIAN CANCER DIAGNOSIS AND ODDS RATIOS AND 95% CONFIDENCE INTERVALS BY PREDIAGNOSIS BODY MASS INDEX CATEGORIES, THE AFRICAN AMERICAN CANCER EPIDEMIOLOGY STUDY

Symptom	BMI categories (kg/m ²)					p Trend ^a
	All	<25	25–<30	30–<35	≥35	
Pelvic/abdominal discomfort						
<i>n</i> (%)	179 (54.9)	26 (55.3)	42 (50.6)	52 (54.7)	59 (58.4)	
Age-adjusted OR (95% CI)		1.0 (Ref)	0.88 (0.42–1.83)	0.95 (0.46–1.96)	1.19 (0.58–2.43)	0.38
MV adjusted OR ^b (95% CI)		1.0 (Ref)	0.78 (0.35–1.73)	0.81 (0.37–1.78)	0.97 (0.45–2.10)	0.59
Bowel irregularity						
<i>n</i> (%)	202 (62.0)	33 (70.2)	56 (67.5)	56 (59.0)	57 (56.4)	
Age-adjusted OR (95% CI)		1.0 (Ref)	0.91 (0.41–1.99)	0.59 (0.27–1.26)	0.55 (0.26–1.18)	0.05
MV adjusted OR ^b (95% CI)		1.0 (Ref)	0.80 (0.35–1.86)	0.47 (0.21–1.05)	0.42 (0.19–0.94)	0.02
Urinary symptoms						
<i>n</i> (%)	127 (39.0)	17 (36.2)	32 (38.6)	34 (35.8)	44 (43.6)	
Age-adjusted OR (95% CI)		1.0 (Ref)	1.17 (0.54–2.49)	0.95 (0.45–1.99)	1.36 (0.65–2.84)	0.47
MV adjusted OR ^b (95% CI)		1.0 (Ref)	1.00 (0.44–2.26)	0.75 (0.33–1.68)	1.17 (0.54–2.56)	0.58
Distended or hard abdomen						
<i>n</i> (%)	169 (52.0)	24 (51.1)	45 (54.2)	44 (46.3)	56 (55.5)	
Age-adjusted OR (95% CI)		1.0 (Ref)	1.16 (0.56–2.42)	0.81 (0.39–1.65)	1.15 (0.56–2.33)	0.96
MV adjusted OR ^b (95% CI)		1.0 (Ref)	1.08 (0.50–2.35)	0.76 (0.35–1.62)	1.15 (0.54–2.44)	0.73
Lump in abdomen						
<i>n</i> (%)	70 (21.5)	16 (34.0)	16 (19.3)	21 (22.1)	17 (16.8)	
Age-adjusted OR (95% CI)		1.0 (Ref)	0.49 (0.21–1.13)	0.62 (0.28–1.37)	0.45 (0.20–1.01)	0.37
MV adjusted OR ^b (95% CI)		1.0 (Ref)	0.48 (0.20–1.14)	0.60 (0.26–1.39)	0.45 (0.19–1.05)	0.41
Fatigue or loss of appetite						
<i>n</i> (%)	182 (55.8)	23 (48.9)	48 (57.8)	52 (54.7)	59 (58.4)	
Age-adjusted OR (95% CI)		1.0 (Ref)	1.50 (0.72–3.13)	1.20 (0.59–2.45)	1.45 (0.71–2.95)	0.32
MV adjusted OR ^b (95% CI)		1.0 (Ref)	1.39 (0.63–3.03)	1.03 (0.48–2.21)	1.47 (0.69–3.12)	0.20
Side or back pain						
<i>n</i> (%)	166 (50.9)	20 (42.6)	42 (50.6)	50 (52.6)	54 (53.5)	
Age-adjusted OR (95% CI)		1.0 (Ref)	1.47 (0.70–3.09)	1.55 (0.75–3.20)	1.63 (0.79–3.34)	0.19
MV adjusted OR ^b (95% CI)		1.0 (Ref)	1.33 (0.61–2.86)	1.44 (0.68–3.07)	1.53 (0.73–3.22)	0.20
Abnormal vaginal bleeding						
<i>n</i> (%)	59 (18.1)	5 (10.6)	13 (15.7)	19 (20)	22 (21.8)	
Age-adjusted OR (95% CI)		1.0 (Ref)	1.99 (0.63–6.32)	2.63 (0.87–8.01)	3.22 (1.06–9.75)	0.07
MV adjusted OR ^b (95% CI)		1.0 (Ref)	2.23 (0.67–7.44)	2.36 (0.74–7.48)	3.00 (0.96–9.40)	0.11
Weight gain/swelling						
<i>n</i> (%)	141 (43.4)	18 (38.3)	36 (43.4)	37 (39.0)	50 (49.5)	
Age-adjusted OR (95% CI)		1.0 (Ref)	1.20 (0.57–2.54)	0.93 (0.45–1.94)	1.57 (0.76–3.26)	0.26
MV adjusted OR ^b (95% CI)		1.0 (Ref)	1.05 (0.47–2.31)	0.81 (0.37–1.78)	1.44 (0.67–3.09)	0.32
Nausea/vomiting/indigestion						
<i>n</i> (%)	108 (33.1)	11 (23.4)	24 (28.9)	31 (32.6)	42 (41.6)	
Age-adjusted OR (95% CI)		1.0 (Ref)	1.41 (0.61–3.25)	1.55 (0.69–3.50)	2.31 (1.04–5.13)	0.09
MV adjusted OR ^b (95% CI)		1.0 (Ref)	1.32 (0.55–3.15)	1.48 (0.63–3.47)	2.11 (0.92–4.83)	0.16
Mean number of symptoms reported	4.3	4.1	4.3	4.2	4.6	

^a*p*-Value for trend calculated from multivariable model that includes term for BMI as continuous variable.

^bMultivariable (MV) model adjusted for age, education, length of oral contraceptive use, number of pregnancies, history of pelvic inflammatory disease, marital status, and Charlson comorbidity index.

Bold type indicates statistically significant associations.

CI, confidence interval; OR, odds ratio.

or hard abdomen (52.0%), and side or back pain (50.9%). The least frequently reported symptoms were abnormal vaginal bleeding (18.1%) and lump in the abdomen (21.5%).

The majority of symptoms were reported more frequently by overweight and obese women than women with BMI ≤25; however, most comparisons between BMI categories were not statistically significant. Age-adjusted analyses showed statistically significantly higher ORs for women with BMI ≥35 for abnormal vaginal bleeding (OR 3.22, 95% CI 1.06–

9.75) and nausea/vomiting/indigestion (OR 2.31, 95% CI 1.04–5.13), but the multivariable adjusted ORs were not statistically significant. Two symptoms, a lump in the abdomen and bowel irregularity, were reported less frequently among the most obese women. The association between BMI and lump in the abdomen was not statistically significant, whereas the association with bowel irregularity showed a statistically significant linear trend between higher BMI and lower reported prevalence of this symptom.

TABLE 4. MEAN DURATION OF SYMPTOMS (IN MONTHS) IN THE YEAR BEFORE DIAGNOSIS OF OVARIAN CANCER BY PREDIAGNOSIS BODY MASS INDEX CATEGORIES, THE AFRICAN AMERICAN CANCER EPIDEMIOLOGY STUDY

Symptom	All	BMI categories (kg/m ²)				p Trend ^a
		<25	25–<30	30–<35	≥35	
Pelvic/abdominal discomfort						
Mean duration (months)	5.6	4.1	5.9	5.8	6.0	
p-Value ^b		Ref	0.11	0.11	0.068	0.26
Bowel irregularity						
Mean duration (months)	5.6	3.7	5.4	5.0	6.1	
p-Value		Ref	0.057	0.13	0.006	0.005
Urinary symptoms						
Mean duration (months)	5.1	3.0	6.1	5.0	5.2	
p-Value		Ref	0.011	0.10	0.089	0.38
Distended or hard abdomen						
Mean duration (months)	4.3	3.1	4.5	4.5	4.7	
p-Value		Ref	0.14	0.11	0.070	0.04
Lump in abdomen						
Mean duration (months)	4.2	3.5	2.8	4.7	5.7	
p-Value		Ref	0.57	0.30	0.078	0.01
Fatigue or loss of appetite						
Mean duration (months)	4.9	3.4	4.4	4.8	5.8	
p-Value		Ref	0.29	0.12	0.007	0.03
Side or back pain						
Mean duration (months)	5.7	3.7	5.7	6.3	5.7	
p-Value		Ref	0.089	0.028	0.010	0.40
Abnormal vaginal bleeding						
Mean duration (months)	5.8	4.8	6.1	5.4	6.5	
p-Value		Ref	0.66	0.86	0.49	0.95
Weight gain/swelling						
Mean duration (months)	5.5	4.3	5.8	4.6	6.4	
p-Value		Ref	0.19	0.73	0.045	0.05
Nausea/vomiting/indigestion						
Mean duration (months)	5.3	2.8	5.3	4.8	6.4	
p-Value		Ref	0.44	0.24	0.022	0.02
Any symptom ^c						
Mean duration (months)	7.0	5.3	7.1	6.6	7.9	
p-Value		Ref	0.001	0.23	0.058	0.01

^ap-Value for trend calculated from multivariable model that included terms for BMI, age, and Charlson comorbidity index as continuous variables, and education, duration of oral contraceptive use, number of pregnancies, history of pelvic inflammatory disease, and marital status as categorical variables.

^bp-Values derived from linear regression models adjusted for age.

^cMean duration for the symptom reported for longest period of time for each woman.

Bold type indicates statistically significant associations.

Table 4 presents the average duration of symptoms among those women who reported each symptom stratified by BMI categories, with p-values for the comparison of women in the higher BMI categories to normal weight women. The average duration of individual symptoms ranged from 4.2 months for lump in abdomen to 5.8 months for abnormal vaginal bleeding. Overall, women with a BMI <25 reported the shortest average duration for having any symptom, with a difference of 2.6 months when compared to women with BMI ≥35 (5.3 months vs. 7.9 months). For each of the symptoms, women with a BMI <25 had the shortest duration of symptoms with the exception of lump in abdomen. Analyses of trends in symptom duration by BMI categories showed statistically significant associations of longer symptom duration with increasing BMI for bowel irregularity, distended or hard abdomen, lump in abdomen, fatigue or loss of appetite, weight gain/swelling in the extremities, and nausea/vomiting/indigestion.

Trend tests using BMI categories were comparable to those using BMI as a continuous variable. We also repeated the analyses excluding women who reported symptoms for the entire 12 months on the supposition that symptoms related to ovarian cancer would likely have more recent onset. We observed similar trends of longer duration of symptoms among the overweight and obese women compared to normal weight women (data not shown).

Additional analyses were performed to assess if symptom prevalence or duration differed by time between diagnosis and interview (<163 days [median] vs. ≥163 days), by region (north vs. south), or by histology (serous vs. nonserous). The prevalence of the symptoms did not differ significantly across these strata except for two instances. Fatigue/loss of appetite was reported significantly more often by women from the south compared to the north (61% vs. 43%, $p=0.001$) and abnormal vaginal bleeding was significantly more common

TABLE 5. STAGE DISTRIBUTION OF OVARIAN CANCER CASES BY BODY MASS INDEX CATEGORIES, THE AFRICAN AMERICAN CANCER EPIDEMIOLOGY STUDY

Stage	All, n (%)	BMI categories (kg/m ²)			
		<25, n (%)	25–<30, n (%)	30–<35, n (%)	≥35, n (%)
Stage I	114 (37.9)	15 (33.3)	28 (36.8)	35 (39.8)	36 (39.1)
Stage II	33 (11.0)	8 (17.8)	8 (10.5)	6 (6.8)	11 (12.0)
Stage III	112 (37.2)	15 (33.3)	31 (40.8)	34 (38.6)	32 (34.8)
Stage IV	42 (14.0)	7 (15.6)	9 (11.8)	13 (14.8)	13 (14.1)
Missing	25	2	7	7	9

among women with nonserous histology compared to serous histology (29% vs. 10%, $p < 0.001$). Given the multiple comparisons made across strata, the differences in the prevalence of these two symptoms may be a chance finding and should be interpreted cautiously. The average reported duration of symptoms was ~0.6 months longer among northern compared to southern women, ~0.2 months longer for nonserous than serous cases, and ~0.7 months longer for women whose time since diagnosis was greater than the median. The general trend that women with BMI <25 had a shorter duration of symptoms before diagnosis was quite consistent across strata defined by region, time since diagnosis, or histology.

Finally, there were no significant associations between stage at diagnosis and BMI (Table 5) or between stage at diagnosis and symptom frequency or duration (data not shown).

Discussion

Consistent with previous studies,^{10–13} our data demonstrate that symptomatology is a crucial aspect of the diagnosis of ovarian cancer: 94.2% of women reported experiencing at least one symptom during the year before diagnosis, while 65.1% cited “symptoms of the tumor” as the primary reason for the doctor visit that led to the diagnosis.

In the absence of efficacious screening modalities, early diagnosis for ovarian cancer is largely based on symptomatology and is therefore affected by patient and physician awareness of these often nonspecific symptoms.¹⁷ The importance of symptom recognition is emphasized by the Centers for Disease Control and Prevention’s “Inside Knowledge: Get the Facts about Gynecologic Cancer” initiative.¹⁸ This program, which supports the Gynecologic Cancer Education and Awareness Act of 2005 (or Johanna’s Law), encourages women to be aware of what is normal for them so that they can recognize the warning signs of gynecologic cancers and seek medical care.

Given the increasing prevalence of obesity,³ it is important to understand how BMI affects recognition of ovarian cancer symptoms. To our knowledge, this is the first study to explore how body weight impacts symptom presentation in ovarian cancer. In this study of African American women with ovarian cancer, ~85% of the women had a BMI >25 and nearly one-third was severely obese (BMI ≥35). Understanding symptom presentation in this population is particularly important because obesity is more prevalent in African Americans, and African American women are more likely to be diagnosed with ovarian cancer at a later stage.^{19,20}

We hypothesized that obese women would be less likely to present with abdominal symptoms, such as distended or hard abdomen, lump in the abdomen, pelvic or abdominal dis-

comfort, and weight gain. This was based on the notion that excess centripetal adipose tissue and increased comorbidities may interfere with an ability to appreciate such subtle and nonspecific complaints as stemming from a cause other than a benign or previously diagnosed health condition. While our findings for lump in abdomen are in the direction we hypothesized, the data did not exhibit a significant dose-response relationship.

For the majority of other symptoms, women with BMI ≥35 were more likely to report these symptoms compared to normal weight women, although most associations were not statistically significant. In addition, overweight and obese women reported having a longer average duration for most symptoms. The average reported duration for having any symptom was >2 months for the most obese women compared to women with normal BMI.

Lump in abdomen and distended or hard abdomen had the shortest average duration, before diagnosis (~4 months). The longest average duration was ~6 months for abnormal vaginal bleeding, side or back pain, pelvic/abdominal discomfort, and weight gain/swelling in extremities. This is somewhat consistent with a prior study that queried women about how soon they would contact their doctor for a given symptom. The shortest anticipated waiting time was for persistent abdominal pain and the longest anticipated waiting times were for extreme fatigue, persistent bloating, back pain, persistently feeling full, and changes in bowel habits.¹⁷

Data were not available to evaluate the reasons for the longer duration of symptoms in women with higher BMI. Such delays in diagnosis from the time of symptom onset may be due to patient-related or physician-related factors. Our study focused on the patient perspective, using data from a questionnaire administered to study participants. Although our findings are based on patient-reported data, rather than medical records, it is important to recognize that most of the symptoms associated with ovarian cancer are subjective in nature; it would be quite difficult, if not impossible, to assess them through direct measurement. In addition, it is not uncommon for women ultimately diagnosed with ovarian cancer to experience symptoms for several months before seeking medical attention. Frequently cited reasons causing patients to delay seeking medical attention include fear, perception that symptoms are not serious, and repeat appearance of a previous benign condition.²¹

The presence of other medical conditions may interfere with one’s ability to appreciate new symptoms as stemming from ovarian cancer; distinguishing such nonspecific symptoms from benign physiological changes can be very difficult. In a prior study of women with ovarian cancer, those with certain comorbidities reported significantly more symptoms

than other women in the clinic population.²² Another study evaluating the perceived cause of symptoms related to ovarian cancer demonstrated that <10% of patients suspected cancer as the cause.²³ Women in this study with a BMI ≥ 35 had more comorbid conditions on average, with a mean Charlson comorbidity index of 1.63 compared to 1.15 for women with BMI <25. This may partially explain the trend toward increased prevalence and increased average duration for the majority of symptom categories in this weight group.

Although heavier women tended to have symptoms for a longer duration before diagnosis, it did not appear to impact stage at diagnosis, as there were no statistically significant differences in stage distribution across BMI categories. This finding is consistent with other studies which reported that a more advanced cancer stage was not associated with longer symptom duration, a phenomenon referred to as the “waiting time paradox.”^{10,12,23–25} Patients with aggressive cancers may show symptoms faster and have more rapid physical decline, leading them to seek medical treatment sooner.

Although longer duration of symptoms among heavier women in this study did not correlate with later-stage disease at the time of diagnosis, such delays may still have important clinical consequences. As reported in other research, longer time between first symptom recognition by patients and initiation of treatment was statistically significantly associated with lower quality of life scores and lower patient satisfaction.²³ This may have important ramifications as a higher quality of life score has been reported to be an independent prognostic factor in women with ovarian cancer; improved baseline quality of life scores are associated with increased progression-free survival as well as overall survival.²⁵ Therefore, earlier diagnosis and shorter duration of undiagnosed symptoms may have unrecognized implications and benefits for these patients.

A potential limitation of this study is that women were interviewed a median of 6 months after diagnosis and there was possibly inaccurate recall of the types or durations of some symptoms because we relied on self-reported data. It is unlikely that, however, there was differential misclassification of symptoms by BMI category. We do not believe that the heavier women were more susceptible to reporting errors than normal weight women; therefore, any such errors should be distributed equally among study participants, and the study conclusion would remain valid. Through the rapid ascertainment systems, we attempted to identify and interview study participants soon after their diagnosis, using standardized interview procedures in which we emphasized that only those symptoms that occurred within 1 year of diagnosis should be reported. Furthermore, although patient-reported data are subject to some limitations, determination of the precise onset and duration of symptoms would not be possible by assessing medical records.

We also relied on self-reported data to calculate BMI 1 year before diagnosis. We based our analyses on this time point rather than the time of diagnosis because weight changes related to the diagnosis—either unintentional weight loss or weight gain due to fluid accumulation—could have distorted BMI values at that point. Although using self-reported weight is a limitation, it would have been logistically impossible to obtain comparable data from medical records given the large geographic region covered by the study. While it has been documented that most women tend to underreport their

weight and heavier women tend to underreport their weight to a greater degree than women of lower BMI,^{26–29} self-reported weight has been shown to correlate well with measured weight.^{26,29} Associations between self-reported weight and morbidity outcomes are thought to be valid in most situations, although it is recognized that the magnitude of the associations may be somewhat overestimated for individuals in the highest BMI category.^{26,29,30} While we recognize the limitations of using self-reported anthropometric data, we do not think that it alters the overall conclusions about the association between symptoms and BMI.

Another potential limitation is that the survey questions did not ask about how frequently the women experienced the symptoms, which precluded us from calculating a symptom index based on the presence, duration, and frequency of certain symptoms, similar to what has been reported in recent articles.^{31,32} It is important to note that, however, the symptoms that make up the index (*e.g.*, pelvic/abdominal discomfort, urinary/bowel changes, bloating/weight gain) were reported for a longer duration by obese women than women with lower BMI. Thus, it is likely that if we had been able to evaluate a symptom index, rather than individual symptoms, the conclusion that heavier women are likely to experience symptoms for a longer duration before diagnosis would have held.

The main strengths of this study are that it is, to our knowledge, the first study to evaluate the relationship between BMI and ovarian cancer symptomatology and the first to examine presenting symptoms for ovarian cancer in African American women.

Conclusion

Ovarian cancer is often characterized as a “silent killer,” yet our study showed that most women experience symptoms months before diagnosis. Although they are nonspecific by nature, these symptoms are what cause the majority of patients to seek medical attention. While it is still unclear how obesity impacts the prognosis and risk of ovarian cancer among African American women, this study suggests that higher BMI is associated with increased prevalence and longer duration of most symptoms related to ovarian cancer. Potential mechanisms include having excess adipose tissue or having comorbidities with symptoms that interfere with the identification of those stemming from ovarian cancer. Therefore, healthcare providers should be vigilant and consider ovarian cancer in the differential diagnosis, especially in obese women with a history of several comorbidities.

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