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Extremes in body mass index affect overall survival in women with cervical cancer

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HIGHLIGHTS

- Underweight and overweight/obese women with cervical cancer have worse RFS and OS.
- There is no difference in stage at diagnosis across BMI categories.
- Optimizing weight in cervical cancer patients may improve outcomes.

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ABSTRACT

Objective. To examine the effect of BMI on pathologic findings, cancer recurrence and survival in cervical cancer patients.

Methods. A retrospective cohort study of cervical cancer patients treated from July 2000 to March 2013 was performed. BMI was calculated, and patients were classified by BMI. The primary outcome was overall survival (OS). Secondary outcomes included stage, histopathology, disease-specific survival (DSS) and recurrence free survival (RFS). Kaplan–Meier survival curves were generated and compared using Cox proportional hazard ratios.

Results. Of 632 eligible patients, 24 (4%) were underweight, 191 (30%) were normal weight, 417 (66%) were overweight/obese. There was no difference in age ($p = 0.91$), stage at presentation ($p = 0.91$), grade ($p = 0.46$), or histology ($p = 0.76$) between weight categories. There were fewer White patients in the underweight (54%) and overweight/obese (58%) groups compared to the normal weight (71%) group ($p = 0.04$). After controlling for prognostic factors, underweight and overweight/obese patients had worse median RFS than normal weight patients (7.6 v 25.0 months, $p = 0.01$ and 20.3 v 25.0 months, $p = 0.03$). Underweight patients also had worse OS (10.4 v 28.4 months, $p = 0.031$) and DSS (13.8 v 28.4 months, $p = 0.04$) compared to normal weight patients. Overweight/obese patients had worse OS than normal weight patients (22.2 v 28.4 months, $p = 0.03$) and a trend toward worse DSS (21.9 v 28.4 months, $p = 0.09$).

Conclusion. Both extremes of weight (underweight and overweight/obesity) were associated with worse survival in patients with cervical cancer. Optimizing weight in cervical cancer patients may improve outcomes in these patients.

1. Introduction

Low body mass index (BMI) has been associated with poor prognosis in a variety of cancer types including cervical cancer [1–3]. The concept of cachexia and unintentional weight loss in cancer has been long accepted, but as adult obesity rates reach epidemic proportions in the United States the effect of body weight on cancer outcomes becomes less clear [4]. Recent estimates show that the majority (65%) of Americans are either overweight or obese and a third of adults meet the criteria for obesity (BMI > 30) [5]. Obesity is associated with an increased risk of developing and dying from multiple types of malignancies including endometrial, breast, colon, ovarian, and pancreatic cancers [6]. While increasing BMI has been associated with increased death rates from cancer, there is inconsistent data on the effects of BMI on cervical cancer survival [3,6–10].

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The primary objective of our study was to evaluate the effect of BMI on overall survival from cervical cancer. We also sought to evaluate any variation in histopathology, stage, and risk of recurrence based on BMI.

2. Methods

2.1. Study design, setting, and participants

Following Institutional Review Board approval (#12-1603) at the University of North Carolina at Chapel Hill (UNC), a single-institution retrospective cohort study was performed. All patients diagnosed with cervical cancer and treated at UNC from July 1, 2000 until March 30, 2013 were eligible for inclusion. UNC is a tertiary care academic hospital in a suburban setting with a large catchment area serving the women of North Carolina. The STROBE guidelines were followed in the implementation and reporting of this study [11].

Patients diagnosed with cervical cancer were identified via a database of the weekly Gynecologic Oncology Multidisciplinary Disposition Conference. All gynecologic cancer patients treated at UNC are presented at this conference; therefore, this database is the most accurate way to identify all cervical cancer patients at our institution. Patients were eligible if chart review showed a pathologic diagnosis of International Federation of Gynecology and Obstetrics (FIGO) stages IAI to IVB cervical cancer [12]. A gynecologic pathologist confirmed all pathologic diagnoses. BMI was then calculated using documented height and weight at the time of initial presentation to the gynecologic oncology clinic. Women without available BMI information were excluded from the study.

2.2. Variables and data sources

The primary outcome of interest was overall survival (OS). OS was defined as the time from the biopsy date documenting cancer to death from any cause. The primary exposure of interest was BMI. BMI was evaluated as a categorical variable. Patients were defined as underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), and overweight/obese (BMI ≥ 25) as previously described by Kizer et al [3].

Secondary outcomes included stage at diagnosis, histopathology, recurrence free survival (RFS), and disease-specific survival (DSS). RFS was defined as the time from the biopsy date documenting cancer to the date of disease recurrence (by imaging or exam) or death from any cause. DSS was defined as the time from biopsy date to death from cervical cancer. Patients with unknown or non-cancer related causes of deaths were excluded from this analysis.

Demographic, pathologic and clinical data were obtained via electronic medical record review. Pathologic variables of interest included stage, grade, and tumor histology. Clinical variables of interest included treatment modality, recurrence, and death. The date of last followup was designated to be any documented hospital or clinic visit and recurrence data was obtained from physician notes, laboratory data and imaging reports. Death data was captured from electronic medical records and from the Social Security Death Index (http://www.genealogybank.com/gbnk/ssdi/).

2.3. Study size and bias

This cohort was a convenience sample of patients with available electronic medical records for review and thus no de novo power analysis was performed for study size. The selected study timeframe for the cohort was intended to allow adequate followup time for death and recurrence data. In order to evaluate for potential selection bias and confounders, demographic and pathologic variables are obtained to evaluate for any significant differences between weight categories.

2.4. Statistical methods

Cox regression modeling was used to explore associations between BMI and time-to event outcomes including RFS, DSS and OS. The Kaplan–Meier method was used to estimate RFS, DSS, and OS curves. The log-rank test was used to test for differences between curve estimates. Parametric modeling was used to obtain BMI hazard ratios with 95% confidence intervals while controlling for age, race, smoking status, grade, stage, and histology. Chi-squared test, with Fisher's exact test as appropriate, was used to test two-group and/or nominal categorical variable comparisons. The nonparametric Jonckheere–Terpstra method was used to test for significant differences across ordered categories for contingency tables where at least one of the variables was ordinal including BMI categories. The Wilcoxon rank-sum test (using normal scores) was used for continuous variables undergoing two-group comparisons and Kruskal–Wallis test was used for continuous variables undergoing three or more comparisons. SAS (v 9.2, Cary, NC) statistical software was used.

3. Results

A total of 671 patients with cervical cancer were identified during the study timeframe. Thirty-nine (5.5%) patients did not have data available for BMI calculation at the time of initial presentation (diagnosis) and thus were excluded from the analysis. Of the remaining 632 patients, the median BMI was 28 (range 11.9–63.1). The distribution of weight is as follows: 4% were underweight (n = 24), 30% (n = 191) were of normal weight, and 66% (n = 417) were overweight or obese. There was no difference in age, stage, grade, histology, or smoking status between weight classes. Underweight and overweight/obese patients were less likely to be White than normal weight patients (54% v 58% v 71%, p = 0.04). Early stage disease (Stages IA and IB) was seen in 63% of underweight, 71% of normal weight, and 70% of overweight/obese (p = 0.91). There was no difference in the proportion of high-grade cancers (grade 3) seen in each weight group with 33% of underweight, 32% of normal weight, and 35% of overweight/obese (p = 0.46). There was no difference in tumor histology between weight groups with

Table 1
Clinical variables by weight category.

	Underweight (n = 24)	Normal (n = 191)	Overweight and obese (n = 417)	p-Value
Age	45.4 (±14.8)	46.7 (±14.8)	46.7 (±13.3)	0.91
Race				0.04
White	13 (54)	135 (71)	242 (58)	
Black	6 (25)	38 (20)	114 (27)	
Other	5 (21)	18 (9)	61 (15)	
Stage				0.91
IA	4 (17)	31 (16)	59 (14)	
IB	11 (46)	104 (54)	234 (56)	
II	3 (13)	26 (14)	57 (14)	
III	4 (17)	25 (13)	52 (12)	
IV	2 (8)	5 (3)	15 (4)	
Grade				0.46
1	1 (4)	25 (13)	50 (12)	
2	6 (25)	66 (35)	129 (31)	
3	8 (33)	61 (32)	147 (35)	
Unknown	9 (38)	39 (20)	89 (21)	
Histology				0.76
Squamous	16 (67)	129 (67)	286 (69)	
Adenocarcinoma	6 (25)	44 (23)	85 (20)	
Smoking status[a]				0.49
Never	10 (42)	83 (43)	176 (42)	
Former	2 (8)	11 (6)	23 (6)	
Current	4 (17)	47 (25)	77 (18)	
Unknown	8 (33)	50 (26)	141 (34)	

Continuous variables are reported as mean (± standard deviation); categorical variables are reported as n (%).

[a] Smoking status as documented in medical record at the time of cancer diagnosis.