Gynecologic Oncology 133 (2014) 38–42

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Endometrial cancer in morbidly obese women: Do racial disparities affect surgical or survival outcomes?

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HIGHLIGHTS

- The excess of type II endometrial cancers among black women is present in a morbidly obese population.
- Race is not a significant predictor of survival after adjustment for clinical and treatment variables.
- Despite similar comorbidities, rates of open vs. minimally invasive procedures and lymph node dissection, black women have longer hospital stays following surgery for endometrial cancer compared to white women.

ARTICLE INFO

Article history:
Received 20 September 2013
Accepted 11 January 2014

Keywords:
Endometrial carcinoma
Morbid obesity
Race/ethnicity

ABSTRACT

Objective. Endometrial cancer mortality disproportionately affects black women and whether greater prevalence of obesity plays a role in this disparity is unknown. We examine the effect of race on post-surgical complications, length of stay, and mortality specifically in a morbidly obese population.

Methods. Black and white women with endometrial cancer diagnosed from 1996 to 2012 were identified from the University Pathology Group database in Detroit, Michigan, and records were retrospectively reviewed to obtain clinicopathological, demographic, and surgical information. Analysis was limited to those with a body mass index of 40 kg/m^2 or greater. Differences in the distribution of variables by race were assessed by chi-squared tests and *t*-tests. Kaplan–Meier and Cox regression analyses were performed to examine factors associated with mortality.

Results. 97 white and 89 black morbidly obese women were included in this analysis. Black women were more likely to have type II tumors (33.7% versus 15.5% of white women, p-value = 0.003). Hypertension was more prevalent in black women (76.4% versus 58.8%, p-value = 0.009), and they had longer hospital stays after surgery despite similar rates of open vs minimally invasive procedures and lymph node dissection (mean days = 5.4) compared to whites (mean days = 3.5, p-value = 0.036). Wound infection was the most common complication (16.5% in whites and 14.4% in blacks, p-value = 0.888). Blacks were more likely to suffer other complications, but overall the proportions did not differ by race. In univariate analyses, black women had higher risk of endometrial cancer-related death (p-value = 0.090). No racial differences were noted in adjusted survival analyses.

Conclusion. A more complete investigation, incorporating socio-demographic factors, is warranted to understand the effects of morbid obesity and race on endometrial cancer.

Introduction

More than 8100 women will die from endometrial cancer in 2013, making it the 8th leading cause of cancer-related death among women in the United States [1]. Endometrial cancer mortality disproportionately affects black women, as they are 2.5 times more likely to die than their white counterparts [2]. Various institution and population-based studies have consistently shown that African–American women are more likely to be diagnosed with more aggressive histological subtypes and later-stage disease, yet the survival disparity exists across every stage and subtype [3]. There are likely many elements contributing to this disparity (reviewed in [4]), and identification of potentially modifiable factors is critical to reduce this survival disparity.

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0090-8258/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ygyno.2014.01.013

Obesity, a strong risk factor for development of endometrial cancer, may also play a role in survival. Obesity (defined as having a body mass index >30 kg m^{-2}) is more prevalent in African–American populations than in non-Hispanic white populations, and until recently, the rates have been increasing in the United States [5]. Morbid obesity, defined as having a body mass index ≥40 kg m^{-2}, has increased by 70% between 2000 and 2010 and is more common among African–Americans, particularly women [6]. This is reflected in a hospital-based study, with 47% of African–American patients reported to be morbidly obese versus 33% of the white patients [7]. The risk of dying from endometrial cancer is 6 times greater in this population compared to those with healthy BMI (RR = 6.25, 95% CI: 3.75, 10.42), twice as high as the risk seen for those who are obese (defined as BMI = 30–39.9 kg/m^2) [8].

Recent work that has focused on the morbidly obese population with respect to endometrial cancer has shown that total laparoscopic hysterectomy and robotic surgery are feasible and result in fewer perioperative complications [9–11], although these results may not be valid for extremely or "super" obese (BMI ≥50 kg m^{-2}) women [12]. Length of hospital stay has not been reported to vary by BMI for some hospitals [7] but has for others [12], with longer stays associated with increasing BMI. Similarly, the association between BMI and survival is also unclear, depending on various endpoints and BMI classifications. The confounding effect of BMI on the association between race and endometrial cancer survival is well-described [13]. In this study we examine the effect of race on comorbidities, post-surgical complications, length of stay, and endometrial cancer survival in a smaller but specific morbidly obese population.

Methods

Black and white women who received surgical treatment for endometrial cancer between 1996 and 2012 were identified from a database from the Wayne State University/Karmanos Cancer Institute, maintained by the University Pathology Group (UPG) in Detroit, Michigan. After local Institutional Review Board approval, a retrospective record review was conducted to obtain clinical, demographic, treatment, and surgical outcome information for each case, including height and weight measurements at the time of surgery. Body mass index (BMI) was calculated from these values, and the analysis was limited to morbidly obese patients, defined by a BMI of 40 kg/m^2 or greater. Treatment and survival information from the medical records was supplemented by linking case information to the Metropolitan Detroit Cancer Surveillance System (MDCSS), a member of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program.

Variables abstracted from the medical record include age at surgery, FIGO grade, FIGO stage, histologic type (defined as either type I or type II) [14], cervical involvement, depth of myometrial invasion, lymphovascular space invasion, open versus minimally invasive surgery, lymph node involvement, and the number of lymph nodes dissected. The type I endometrial cancers commonly referred to as the endometrioid type, included histologically, those tumors which can be adenocarcinoma with or without squamous differentiation and often are well differentiated. Type II endometrial cancer, or nonendometrioid tumors, encompassed the remaining of cases. The common histology of this subtype was uterine serous carcinoma (USC). All Hematoxylin and Eosin slides were reviewed by gynecologic pathologists at the Wayne State University to confirm the histology and grade of tumor. A clinical history of other comorbid conditions, hypertension and diabetes, post-surgical complications, and days admitted to the hospital (calculated as date of surgery to date of discharge) were also recorded. The post-surgical complications were defined as any complication occurring in the immediate post-operative period from the date of surgery to the date of discharge from the hospital. Post-surgical complications evaluated included wound infection, vaginal or pelvic infection, sepsis or other wide-spread infection, anemia or hemorrhage, thromboembolism, congestive heart failure or myocardial infarction, acute renal failure or insufficiency, and other pulmonary or gastrointestinal complications. These complications were assessed individually and as a summary count (none, 1, or 2 or more).

Differences in the distribution of clinical and demographic variables by race were assessed by chi-squared tests for categorical variables and *t*-tests for continuous variables. For categorical variables with less than 5 women in a category, Fisher's exact test was reported. Racial differences in overall survival, endometrial cancer-related survival, and other causes of death (death due to all causes minus the endometrial cancer-related deaths) were evaluated using Kaplan–Meier curves and log rank tests. Cox proportional hazard models evaluated the effect of race on survival, using 3 models. The first model adjusted for clinical variables: age, histology type, FIGO stage, and FIGO grade. The second model included the previous variables and included surgery type, chemotherapy, and radiation. The full model included the clinical and treatment variables listed above along with comorbidities (BMI, hypertension, diabetes) and the occurrence of any surgical complication. Adjusted hazard ratios and 95% confidence intervals were estimated using proportional hazard models to evaluate risk of death. All analyses were completed using SAS statistical software, version 9.2 (SAS Institute Inc., Cary, NC).

Results

A total of 186 morbidly obese women (97 white women and 89 black women) with endometrial cancer were identified for this analysis. Eighty-two white women were identified with endometrioid carcinoma, 2 with mucinous carcinoma, 5 with mixed carcinoma (serous and endometrioid), 8 with serous carcinoma and 1 with undifferentiated carcinoma. However in the African–American population, 57 women had endometrioid carcinoma, 6 had mixed carcinoma (serous and endometrioid), 1 had mucinous carcinoma, 16 had serous carcinoma, 2 had clear cell carcinoma and 2 were identified with endometrial intraepithelial carcinoma (Table 1). Black women were more likely to be diagnosed with type II tumors (33.7% of black women versus 15.5% of white women, p-value = 0.003) and had higher grade tumors (FIGO grade 3; 46.1% of black women versus 20.6% of white women, p-value < .001). Other clinical variables, including age at surgery, FIGO stage, cervical involvement, depth of myometrial invasion, lymphovascular space invasion (LVI), and lymph node involvement, were similar between the groups. Similarly, the percent of open vs minimally invasive procedures, percent undergoing lymph node dissection, mean number of pelvic and aortic lymph nodes collected when done, and post surgical treatment with radiation and chemotherapy were similar by race.

The mean BMI in this morbidly obese population was slightly higher for black women (49.2 kg/m^2) than for white women (47.0 kg/m^2, p-value = 0.09). Black women were more likely to be hypertensive than white women (76.4% versus 58.8%, respectively, p-value = 0.009), but rates of diabetes were similar (p-value = 0.636). On average, black women had longer hospital stays after surgery (mean days = 5.4) compared to white women (mean days = 3.5, p-value = 0.036). Wound infection was the most common complication in both white and black women (16.5% and 14.4%, respectively, p-value = 0.888). Black women were more likely to suffer other complications, but overall the number and type of post-surgical complications did not differ between the groups (Table 2).

In univariate analyses, black women had a non-significant higher risk of death, both from any cause (log rank p-value = 0.092) and from endometrial cancer-related (log rank p-value = 0.090) (Figs. 1a and b). There was no association between race and other causes of death (log rank p-value = 0.53) (Fig. 1c). In multivariable adjusted models, race was not associated with death from any cause after adjusting for clinical variables (HR = 1.19, 95% CI: 0.55, 2.54), clinical and treatment variables (HR = 1.35, 95% CI: 0.62, 2.95) or all potential