Gynecologic Oncology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

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

Clinical characteristics associated with racial disparities in endometrial cancer outcomes: A surveillance, epidemiology and end results analysis

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HIGHLIGHTS

- Black women have poorer endometrial cancer survival than White women.
- Black women were more likely to present with advanced stage, high-grade tumors.
- Black women were less likely to undergo operative management even when prescribed.
- White women were more likely to receive combination VBT and EBRT.
- Combination VBT and EBRT was associated with improved all-cause mortality.

ARTICLE INFO

Article history:
Received 18 September 2017
Received in revised form 14 December 2017
Accepted 16 December 2017
Available online xxxx

Keywords:
Uterine neoplasm
Healthcare disparities
SEER program
Hysterectomy
Radiotherapy

ABSTRACT

Objectives. Racial disparities exist for endometrial cancer. We examined patterns of care and factors associated with poor outcomes for Black women with endometrial cancer.

Methods. We studied 110,826 endometrial cancer patients diagnosed between 1980 and 2008 with minimum 5 years follow-up in the Surveillance, Epidemiology, and End Results database. Trends over time in sociodemographics, disease characteristics and treatment factors were analyzed over four eras: 1980–1989, 1990–1999, 2000–2004, 2005–2008. Using sequential Cox proportional hazards and Fine-Gray competing risk models we determined the association between potential explanatory variables and racial disparities in all-cause mortality (ACM) and cancer-specific mortality (CSM), respectively.

Results. Clinical characteristics of Black and White women were relatively constant over time. The unadjusted hazard ratio (HR) among Black women for ACM and CSM were 1.91 (95% CI 1.86–1.97) and 2.35 (95% CI 2.26–2.43), respectively. Adjustment for sociodemographics, disease presentation and surgery decreased the ACM HR to 1.29 (95% CI 1.24–1.34) and CSM HR to 1.18 (95% CI 1.11–1.26) without further decrease from controlling for radiotherapy. Black women were less likely to undergo operative management even when prescribed. Total and radical hysterectomy, and vaginal brachytherapy (VBT) were associated with improved ACM and CSM. Combination VBT and external beam radiotherapy was associated with improved ACM.

Conclusion. Racial disparities in endometrial cancer survival are predominantly attributable to increased advanced stage, high-grade and aggressive histologic subtype tumors and differential use of surgery in Black women. Intensified surgical and radiation treatment is associated with improved survival, raising questions about treatment adaptations that may potentially reduce survival disparities.

1. Introduction

Endometrial cancer is the most common gynecologic malignancy among women in the United States with over 60,000 new cases and 10,500 deaths in 2016 [1]. The five-year relative survival from uterine neoplasms among all women decreased from 85.2% in 2000 to 81.7% in 2006–2012 [2]. Uterine neoplasm incidence and death rates are predicted to increase in coming decades [1]. Racial disparities in survival are drastic. The mortality rate in Black women is 80% higher than in White women and five-year survival rates are 85% and 66% among White and Black women, respectively despite lower endometrial cancer incidence among Black women [1,3]. Historical analyses of survival disparities show Black women are significantly younger at time of diagnosis and have higher rates of advanced stage and aggressive histologic variant

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https://doi.org/10.1016/j.ygyno.2017.12.021
0090-8258/

primaries [4,5]. Yet, even these epidemiologic differences do not fully account for survival disparities as for nearly every stage, grade and histologic subtype, survival among Black women is significantly lower than their White counterparts [4,5]. Endometrial cancer is subdivided into Type I and Type II. Risk factors for Type I disease include unopposed estrogens from obesity, nulliparity, late menopause, diabetes, hypertension, estrogen-only hormone replacement therapy and Tamoxifen. Racial differences in rates of several of these comorbidities associated with endometrial cancer also fail to account for survival disparities [6–8].

Patterns of care analyses from 1 to 2 decades prior partially attribute this disparity to operative treatment differences [3,5,9–12]. Management of early stage disease is primarily surgical. Late stage disease is typically treated with single or combination chemotherapy and radiation [13]. Historically, Black women received definitive surgical management less often than White women but equitable use of comprehensive surgical staging with lymphadenectomy was noted in the early 2000s [5,9,11]. Recent investigations studied surgery and radiation as binary treatment variables limiting the ability to understand variations in the therapeutic interventions prescribed [14,15].

Advancements in clinical research and evolving patient demographics necessitate a contemporary analysis of racial disparities in endometrial cancer mortality. We aim to analyze potential etiologies underlying this disparity by identifying factors associated with increased overall and disease-specific mortality and trend temporal variations in these factors in order to elucidate potential avenues for intervention.

2. Materials and methods

2.1. Patient population

The SEER database includes information on cancer incidence and survival in 18 population-based registries covering 30% of the US population. SEER collects information on patient demographics, primary tumor site, tumor morphology, stage at diagnosis, first course of treatment, follow-up for vital status and cause of death. All data are reported in aggregate, de-identified, publically available and exempt from institutional board review. This data source was selected to maximize sample size, representativeness and generalizability of our study. We included patients with endometrial cancer as their first and only malignancy diagnosed with primary site codes 54.0–54.9 and 55.9 between 1980 and 2008 with at least five-year survival data through 2013. Cases diagnosed at autopsy were excluded.

2.2. Defining patient characteristics

Patient demographics included race, education level, household income, marital status, geographic region and population density. We defined race using the SEER coding of White, Black or Other and compared Black and White women for the primary analysis. We created quartiles for average percent of non-high school graduates and median household income in the patient's census tract calibrated according to Census 2000 data. Geographic region is defined according to residential area at time of diagnosis as follows: Northeast (Connecticut, New Jersey), South (Atlanta, Georgia; Rural and Greater Georgia, Kentucky, Louisiana), Central (Detroit, Michigan; Iowa, New Mexico, Utah), West (San Francisco, Hawaii, Seattle, San Jose, Monterey, Los Angeles, California, Alaska). Urban counties are those with population >250,000.

Disease stage was categorized using SEER summary staging as local, regional and distant to maintain comparability over the study time period. Tumor histologic subtypes are categorized according to International Classification of diseases for Oncology ICD-O-3 code numbers as follows: Type I including Endometrioid, Adenocarcinoma, Mucinous subtypes (8010, 8140–8141, 8143, 8210 8211, 8221, 8255, 8261–8263, 8323, 8380, 8381, 8382, 8383, 8480, 8481–8482, 8560, 8570), Type II including Clear Cell, Papillary Serous, Anaplastic subtypes (8310, 8441, 8460–8461, 8260, 8050, 8020–8022) and sarcomas including fibromatous, myxomatous, myomatous and complex mixed and stromal neoplasms (8800–8809, 8810–8839, 8840–8849, 8890–8929, 8930–8999). Grade is categorized as 1, 2, 3, 4 corresponding to well, moderately, poorly differentiated and undifferentiated/anaplastic, respectively.

Treatment characteristics include type of surgery, reason for no cancer directed surgery, lymph node dissection, number of regional lymph nodes positive and receipt of radiotherapy. Reason for no cancer directed surgery was categorized as surgery performed, not recommended, unknown and recommended but not performed due to either patient refusal or unknown reason. Radiation was further categorized as external beam radiation therapy (EBRT), vaginal brachytherapy (VBT) or combination (EBRT and VBT) therapy. We derived data on VBT from the SEER data on implants, a database term inclusive of brachytherapy and infrequent application radium for intracavitary therapy.

2.3. Statistical analysis

Frequency distributions for patient demographics, tumor biology, treatment characteristics, vital status and cause of death were tabulated for All, Black and White women and subsequently stratified by year of diagnosis. We classified year of diagnosis into four eras I-IV: 1980–1989 (I), 1990–1999 (II), 2000–2004 (III), 2005–2008 (IV). Years 2000–2008 were segmented into two eras to enable an analysis of clinical trends in response to publication of potentially practice changing studies during this time period. Associations between categorical covariates and continuous variables were assessed with chi-squared test and independent sample *t*-tests, respectively. All tests were 2-tailed and p-value of <0.05 was statistically significant.

Sequential multivariate analyses were used to assess associations between patient characteristics and survival. We sequentially adjusted for demographics, tumor biology and treatment characteristics to distinguish their respective contributions to all-cause mortality (ACM) and cancer-specific mortality (CSM). Cox proportional hazards models were used to estimate hazard ratios for ACM. To control for competing risks of death we used Fine-Gray semiproportional hazards regression model to estimate adjusted subhazard ratios endometrial CSM [16]. Statistical analyses were conducted using STATA/IC 13 (STATA Corp, College Station, TX).

3. Results

A total of 110,826 eligible patients were identified including 101,372 (91.5%) White and 9454 (8.5%) Black women. Tables 1a, 1b and 1c show the demographic, disease presentation and treatment characteristics of the study population including differences between Black and White women. Most patients were diagnosed between 2000 and 2008. Black women were more likely to be diagnosed younger than age 50 (15.7% vs. 14.0%), less likely to be married (31.4% vs. 52.7%). Black women were more likely to live in neighborhoods with low-income (39.4% vs. 25.9%) and low educational attainment. Fewer Black women presented with disease that was localized (50.9% vs. 70.3%), low-grade (19.9% vs. 37.0%) or Type I histology (61.7% vs. 84.2%). Black women were less likely to undergo surgery (79.8% vs. 90.3%), to have a total hysterectomy (59.7% vs. 69.0%) but more likely to receive radiation (29.4% vs. 26.4%) and forgo operative management even when recommended (7.7% vs. 3.9%). Black women were most likely to receive EBRT (18.2% vs. 15.2%). Table 1c shows treatment characteristics within the cohort receiving radiation. Notably, Black women were less likely to receive combination radiation therapy (11.6% vs. 15.7%). At time of last follow up Black women were less likely to be alive (38.2% vs. 53.4%) and more likely to have died from endometrial cancer (41.2% vs. 21.2%).

Changes in demographics, disease presentation and patterns of care for Black and White women were analyzed during four eras, 1980–1989 (I), 1990–1999 (II), 2000–2004 (III) and 2005–2008 (IV) as shown in Table 2. Among all women, diagnoses at advanced stages increased

Please cite this article as: S. Sud, et al., Clinical characteristics associated with racial disparities in endometrial cancer outcomes: A surveillance, epidemiology and end r..., Gynecol Oncol (2017), https://doi.org/10.1016/j.ygyno.2017.12.021