Disparities in treatment and survival for women with endometrial cancer: A contemporary national cancer database registry analysis ☆

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HIGHLIGHTS

- Race, payer status, and region of treatment correlate with advanced stage endometrial cancer at diagnosis
- Insurance status and region of treatment predict failure to receive appropriate cancer care
- Race, payer status, and treatment at low-volume centers predict shorter survival for patients with advanced endometrial cancer

ARTICLE INFO

ABSTRACT

Purpose. The study aim was to identify contemporary socioeconomic, racial, ethnic, and facility-related factors associated with stage at diagnosis, receipt of cancer treatment, and survival in women with endometrial cancer (EC).

Patients and methods. Women diagnosed with EC between 1998 and 2010 were identified from the National Cancer Database. Variables associated with the outcomes of interest were assessed using multivariable Cox proportional hazards and logistic regression.

Results. Among 228,511 women identified, the percentage of blacks with stage IIIC/IV disease at diagnosis was nearly twice that of non-Hispanic whites (17.8% vs 9.8%; $P < 0.001$). Patients with advanced disease who were insured with Medicare were less likely to receive standard-of-care postoperative radiotherapy and/or chemotherapy than those with private insurance (odds ratio: OR 0.80, $P < 0.001$), as were those residing in the South (reference) in comparison to the Northeast, Atlantic, Great Lakes, and Midwest regions (OR 1.3–1.7, all $P < 0.001$). Those residing in the Mountain region were even less likely to receive appropriate treatment (OR 0.7, $P < 0.001$). Five-year stage IIIC/IV survival was 42.8% for non-Hispanic whites vs 24.6% for blacks (hazard ratio 1.3, $P < 0.001$). Other factors associated with inferior 5-year survival included payer status (not insured, Medicaid, Medicare, vs private, ORs 1.2–1.3, all $P < 0.01$), and treatment at low-volume centers (<5 vs ≥30 cases/year, HR 1.3, $P < 0.001$).

Conclusions and relevance. Socioeconomic, geographic and facility-related factors predict advanced endometrial cancer stage, failure to receive cancer care, and shorter survival. Black women had especially poor survival. Nationwide standardization and concentration of treatment at high-volume centers may improve outcomes.

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1. Introduction

Alarming survival disparities persist for patients with cancer despite national efforts to address inequalities in health care [1,2]. Root causes are multifactorial and include provider, health care facility, and patient-related factors, according to a landmark Institute of Medicine report, with the comparative impact of each component varying by

cancer site [1]. Women with gynecologic malignancies are particularly vulnerable to health care inequalities. Almost two decades since a report from the U.S. National Cancer Database (NCDB) demonstrated disturbing racial differences in histology, receipt of cancer care and survival rates among black compared with white women with endometrial cancer (EC) [3], significant disparities in cancer outcome persist based on race/ethnicity, socioeconomic status and other factors. In 2015, 5-year all-stage survival for white women with EC was 84%, compared with 61% for black women [4], and a population-based study found that 9% of black patients did not receive any cancer-directed treatment, compared with 4% of white patients [5]. Further, the incidence of EC in blacks is increasing at a faster rate than in whites. SEER (Surveillance, Epidemiology, and End Results Program) data show that between 2000 and 2011, the age-adjusted annual percentage change in the incidence of EC was 0.6 for non-Hispanic whites and 2.5 for blacks [6]. These are worrisome findings when recognizing that EC is the most common gynecologic malignancy, with more than 50,000 new cases diagnosed annually in the United States [4].

Potential causes of these disparities are multifactorial and include race, ethnicity, socioeconomic status, education level, payer status, comorbid conditions, distance to provider or health care facility, environmental factors, and variations in genetic susceptibility and tumor histology [7]. Other considerations include provider expertise, surgical volume and hospital size, type of treatment center (community vs comprehensive cancer center), and geographic location. Because such data are often not readily available, and large cohorts are necessary to perform multivariable analysis, these relationships are poorly understood. We aimed to identify socioeconomic, demographic, and health care facility–related factors responsible for disparities in diagnosis, treatment, and survival in women with EC in a contemporary NCDB dataset.

2. Methods

We used the NCDB registry to identify women with a diagnosis of EC from January 1, 1998, through December 31, 2010. The NCDB is an oncologic outcomes database sourced from hospital registry data that are collected in more than 1,500 Commission on Cancer–accredited facilities and represent roughly 70% of all patients with newly diagnosed cancer in the United States. This study received exempt status from the Mayo Clinic Institutional Review Board, Rochester, Minnesota; individual study patients and hospitals were deidentified before delivery of the public use file.

All adult cases of invasive EC of endometrioid, serous, or clear cell histology were included in the analysis. Staging terminology was based on TNM pathologic criteria. For patients without lymph node assessment, T1a tumors were classified as stage IA; T1b and T1 (substage unknown) tumors were excluded unless stage IV (M1). Patients diagnosed at death or autopsy were excluded. The average annual hospital EC volume was ranked by quartiles (1–4, 5–14, 15–29, and ≥30 cases). ZIP code of residence was matched against 2000 US Census data to estimate median household income and the percentage of residents who did not graduate from high school. Payer status was consolidated into the following categories: private insurance (including fee-for-service, health maintenance organizations, and independent physician associations); managed care; VA/TRICARE/Military/Public Health Service; Medicare; Medicare with supplemental coverage; Medicaid (including Medicaid, public health service insurance, and other federal insurance programs); or not insured/self-pay. The remaining patients were classified as "insurance status unknown."

The primary end point was overall survival after hysterectomy for EC; thus, only patients undergoing primary surgery for EC were included in the main cohort. Survival analysis was limited to black and non-Hispanic white patients with stage I or stage IIIC/IV disease and was stratified by stage. Secondary analyses included assessing factors associated with advanced-stage disease among patients with hysterectomy and factors associated with postoperative treatment among patients

with advanced-stage disease. Another secondary analysis was of factors associated with primary surgical management among all patients with EC; for this, the primary cohort was compared with a group of patients identified with EC but who did not undergo surgery. Because stage II-IIIB EC is rare and heterogeneous, multivariable analysis of factors independently associated with advanced-stage disease was limited to a comparison of stage I vs IIIC/IV. Additionally, given current controversies in the definition of optimal management of early-stage EC, we limited the study of adjuvant therapies to patients with stage IIIC or IV disease, because the benefits of postoperative treatment in this cohort are widely accepted.

Demographic variables analyzed included age, Charlson-Deyo comorbidity score [8], race and ethnicity (as classified by NCDB: http://ncdbpuf.facs.org/content/race), socioeconomic status, education status of the ZIP code, and payer status. Race was consolidated into the following categories: non-Hispanic white; Hispanic white; black; American Indian, Aleutian, or Eskimo; Asian/Pacific Islander; other; and unknown. Clinical variables included disease stage, tumor histology, tumor grade, chemotherapy, and radiotherapy. Health system and provider factors were evaluated for their association with survival and secondary outcomes and included geographic location, health care facility–related EC volume defined by quartiles (<5, 5–14, 15–29, and ≥30 cases/year), and urban vs rural location. Factors associated with advanced stage at diagnosis, receipt of surgery, or receipt of adjuvant therapies (chemotherapy and/or radiotherapy), and associations of patient characteristics with race/ethnicity, were examined using χ^2 tests for discrete data and t tests and Kruskal-Wallis tests for continuous data. Wilcoxon rank sum tests were used when the assumption of normality was not valid and there were 2 comparison groups. The independent effects of age, race, ethnicity, socioeconomic status variables, tumor characteristics, treatment-related factors, and health care system factors on advanced stage, receipt of surgery, and receipt of adjuvant therapy were examined using multivariable binomial logistic regression. Survival analysis was performed using the Kaplan-Meier method and log-rank test. Cox proportional hazards models were used to evaluate the independent effect of all variables on survival. $P < 0.05$ was considered significant, and all statistical analyses were performed using SAS version 9.3 (SAS Institute Inc.).

3. Results

A total of 228,511 patients undergoing primary surgery for EC were identified. Patient characteristics stratified by race are shown in Table 1. Patients of race and ethnicity other than non-Hispanic white more commonly were uninsured or insured by Medicaid, lived in ZIP codes with lower incomes and less education, and lived in metro areas. Blacks were more likely to have aggressive disease than non-Hispanic whites, including higher grade and later stage at diagnosis. In particular, the percentages of black patients with serous or clear cell carcinoma were 3.4 and 2.6 times higher, respectively, than for non-Hispanic white patients. This discrepancy was not observed in other categories.

3.1. Factors associated with advanced-stage disease

The percentage of black patients with stage IIIC/IV disease was nearly twice that of non-Hispanic whites (17.8% vs 9.8%, $P < 0.001$); the percentages of high-grade disease (32.8% vs 17.7%, $P < 0.001$) and serous histology (15.2% vs 4.5%, $P < 0.001$) were also significantly higher in the former group (Table 1). This racial disparity in late stage at diagnosis continued, although attenuated, on multivariable analysis (odds ratio [OR] 1.17, $P < 0.001$) (Table 2). Asian/Pacific Islanders also more frequently had advanced disease than non-Hispanic whites on multivariable analysis (OR 1.19, $P < 0.001$). Other factors associated with advanced-stage disease on multivariable analysis included payer status (vs private insurance: not insured, OR 1.41, $P < 0.001$; Medicare, OR 1.14, $P < 0.001$; and Medicaid, OR 1.76, $P < 0.001$) and region of facility