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Short communication

Racial disparities in the treatment of endometrial intraepithelial neoplasia in postmenopausal women

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ABSTRACT

Disparities in endometrial cancer has increased during the past decade with Black women more likely to be diagnosed at a later stage and have higher mortality. The majority of research has been focused on cultural barriers, socioeconomic status, lack of access to care, comorbidities, and tumor histology to explain these disparities. Limited studies have been conducted on the disparity in the treatment of endometrial intraepithelial neoplasia(EIN). We sought to analyze the differences in treatment used in the management of postmenopausal women with EIN to evaluate whether race/ethnicity is a contributing factor. An IRB approved retrospective study was conducted amongst women at a single institution diagnosed with EIN. Ethnicity/race was defined as non-Hispanic White, non-Hispanic Black, Hispanic, and Asian. Demographic and clinical data was extracted. Multivariable logistic regression was used to examine the association between ethnicity/race and treatment, adjusted for age, BMI, and underlying medical conditions such as cardiovascular disease and diabetes. In total, 254 patients were analyzed. A significant association between ethnicity/race and treatment with non-Hispanic Black women less likely to be treated with surgical management compared to non-Hispanic White women (OR = 0.326, 95 %CI 0.129–0.827, p = 0.026). Importantly, after adjusting for clinical risk factors(age, BMI, CVD, diabetes), non-Hispanic Black women remained at an increased risk of not undergoing surgical intervention (OR = 0.333, 95 % CI 0.125–0.882, p = 0.027). Future research is imperative to evaluate the root cause of this disparity in the healthcare system.

1. Introduction

Endometrial cancer is the most common gynecological malignancy in the United States and is marked by one of the worst racial disparities in solid tumor outcomes (Park, 2021; Doll and Winn, 2019; Gamble and Doll, 2021). In 2023, the mortality rate amongst non-Hispanic Black women (17.6 deaths/100,000) was more than twice that of any other racial or ethnic group (4.2–7.8 deaths/100,000) (Somasegar, 2023). Black women are also more likely to be diagnosed with more aggressive histologic subtypes and advanced disease at time of diagnosis (Park, 2021). Disparities in treatment have also been cited throughout the literature. Compared to White women, Black women were found to be less likely to undergo surgery within 6 weeks of diagnosis, undergo a minimally invasive approach, and receive nodal evaluation (Huang, 2020).

The most common histologic subtype of endometrial cancer is endometroid adenocarcinoma which accounts for nearly 80 % of new diagnoses. The precursor lesion of endometrioid adenocarcinoma is EIN. Patients with a diagnosis of EIN carry a 27–40 % risk of developing endometrial cancer (Nees, 2022). A study conducted by GOG found that amongst women diagnosed with atypical hyperplasia, the risk of concurrent endometrial carcinoma in hysterectomy specimen was 42.7 % (Trimble, 2006). However, some patients may be treated with medical management with progestins rather than definitive, guideline concordant hysterectomy due to underlying medical comorbidities or fertility preservation (Trimble, 2006). The efficacy of progestin-based therapy is variable but many studies have found high rates of disease regression with one systemic review showing a complete response to progestins of

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66 % (Gunderson, 2012).

Although racial disparities in treatment and outcome are well recognized in patients with a diagnosis of endometrial cancer, little research has been devoted to studying racial differences in the treatment of EIN. Thus, the aim of our study was to investigate racial/ethnic differences in the treatment of EIN amongst postmenopausal women.

2. Methods

This retrospective cohort study was approved by the Institutional Review Board. All patients diagnosed with EIN between January 2016 to January 2023 were identified. Diagnosis was determined by either endometrial biopsy or dilation and curettage. All patients included in this study were treated by a gynecologic oncologist. Baseline characteristics were collected including race, ethnicity, BMI, age, and history of underlying medical conditions (diabetes and cardiovascular disease). Data on treatment modality was categorized as medical management, observation, or surgical management. Medical management was defined as treatment with either megestrol acetate, medroxyprogesterone acetate, levonorgestrel-releasing intrauterine device(LNG-IUD), or medroxyprogesterone acetate plus LNG-IUD. Study data was managed using REDCap electronic data capture tools. For analysis, we grouped patients into self-reported categories of: non-Hispanic White, non-Hispanic Black, Hispanic, and Asian. Univariant analysis with chi square test was used to examine the association between race and surgical treatment. Multivariable logistic regression was used to examine the association between ethnicity/race and treatment, adjusting for BMI, age, diabetes, and cardiovascular disease (CVD). CVD was defined as a history of hypertension, coronary artery disease, or peripheral vascular disease. BMI was stratified into < 30 kg/m2, 30–34.9 kg/m2, 35–39.9 kg/m2, and > 40 kg/m2. Patients were excluded if race and ethnicity were not available or unclear. Pre-menopausal patients (defined as having a menstrual period within the last 12 months) were excluded given non-surgical treatment is an option for fertility preservation.

3. Results

From January 2016 to January 2023, 277 postmenopausal women presented to a gynecologic oncologist for consultation for the treatment of EIN. Of those women, 23 women were excluded from the analysis due to inadequate race/ethnicity data. Demographic information for all patients meeting study criteria is summarized in Table 1. The median age at diagnosis was 62 (range 42–90). 62.6 % of patients identified as non-Hispanic White (159), 16.54 % non-Hispanic black (42), 13.78 % Asian (35) and 7.09 % Hispanic (18). 131 patients (51.6 %) were diagnosed with CVD and 58 patients (22.8 %) had a diagnosis of diabetes. The average BMI for the cohort was 36.5 with a statistically significant difference in BMI between non-Hispanic Black (39.8), Hispanic (33.1), Asian (30.3), and non-Hispanic White women (37.3) (p < 0.01).

254 patients were included in the analysis. In the univariant analysis,

patients who identified as non-Hispanic Black were 67 % less likely to undergo surgical intervention (95 % CI 0.129–0.827, p = 0.026). 78.57 % of non-Hispanic Black and 91.82 % non-Hispanic White underwent surgical intervention. There was no statistically significant difference for other racial groups with 94.29 % Asian and 94.44 % Hispanic undergoing surgery. After adjusting for clinical risk factors (age, BMI, CVD, diabetes), non-Hispanic Black women remained at an increased risk of not proceeding with surgical intervention (OR = 0.333, 95 % CI 0.125–0.882, p = 0.027). (Table 2).

In an analysis of the 9 patients who did not receive either medical or surgical treatment, 7 were offered surgical intervention and 2 were offered medical management due to a history severe cardiac disease. All 9 patients declined medical treatment for reasons not specified. ECOG performance status ranged from 0 to 3 with the majority of patients scoring a 0 (5 out of 9). Chart review of the 16 patients that underwent medical management showed that 6 women were not offered surgical intervention due to either severe cardiac disease, uncontrolled hypertension, dementia, or limited mobility (ECOG performance status 3). Diabetes was not listed as a reason for not undergoing surgical intervention and the average A1c for those with diabetes was 6.9. In addition, 9 out of the 16 patients that underwent medical management were offered surgical intervention but declined with 3 non-Hispanic Black women citing anxiety about undergoing surgery. Of note, 50 % of non-Hispanic White women and 87 % of non-Hispanic black women were counselled that guideline concordant care was surgical intervention but declined and opted to undergo medical management. The average time between diagnosis of EIN and treatment with progesterone based therapies was 57.2 days compared to 78.1 days of patients undergoing surgical intervention (p < 0.01). Lastly, 35.2 % of patients were upgraded from EIN to endometrial cancer on final pathology.

4. Discussion

To our knowledge, this is the first reported study of racial disparities in the treatment of EIN. The results of this study demonstrated that postmenopausal non-Hispanic Black women were less likely to be treated with surgical intervention compared to non-Hispanic White. This disparity was noted after controlling for age, CVD, BMI, and diabetes with non-Hispanic Black women being 67 % less likely to undergo surgical intervention after being diagnosed with EIN.

There are some limitations to this study. First, we investigated a single health center rather than several across the country. Another limitation is the small sample size in some of the subgroups. Hispanic patients constituted a small subgroup that was under-powered to detect a difference. Lastly, a major limitation is the difficulty in stratifying race and ethnicity as the groups do not capture the diversity that they represent (e.g., non-Hispanic White: Puerto Rican, Mexican, South America, etc). A strength of this study was that race and ethnicity was self-reported as compared to physician reported. Self-reported identification has been found to be more reliable and thus decreases the risk of misclassification (Desmond, 2023).

Table 1
Demographic Parameters.

		Total (n = 254)	Non-Hispanic White (n = 159)	Non-Hispanic Black (n = 42)	Hispanic (n = 18)	Asian (n = 35)	p value
Age							
	Mean (SD)	63.7 (8.5)	64.9 (8.7)	62.8 (8.1)	60.9 (8.6)	60.8 (6.6)	0.02
BMI							
	Mean (SD)	36.5 (9.5)	37.3 % (9.8)	39.8 % (8.6)	33.1 (5.5)	30.3 (7.4)	<0.01
	<30	62.5 % (158)	21.5 % (34)	9.5 % (4)	38.9 % (7)	46.6 % (17)	
	30–34.9	16.6 % (42)	21.5 % (34)	23.8 % (10)	22.2 % (4)	31.4 % (11)	
	35–39.9	13.8 % (35)	19 % (30)	19.1 % (8)	33.3 % (6)	11.4 % (4)	
	>40	7.1 % (18)	38 % (60)	47.6 % (20)	5.6 % (1)	8.6 % (3)	
Medical Conditions							
	CVD	44.8 % (131)	50.9 % (81)	57.1 % (24)	44.4 % (8)	51.4 (18)	0.82
	Diabetes	22.8 % (58)	17.6 % (28)	33.3 % (14)	27.78 % (5)	31.4 % (11)	0.08

Table 2

Association between Treatment and Race/Ethnicity.

	Treatment % (n)			Univariant		Multivariant	
	Observation	Medical	Surgical	Odds Ratio(95 % CI)	p value	Odds Ratio (95 % CI)	p value
Non-Hispanic Black	4.76 % (2)	16.67 % (7)	78.57 % (33)	0.326 (0.129–0.827)	0.026	0.333 (0.125–0.882)	0.027
Hispanic	5.56 % (1)	0 % (0)	5.56 % (1)	1.514 (0.186–12.865)	0.738	1.478 (0.173–12.642)	0.721
Asian	2.89 % (1)	2.89 % (1)	94.29 % (33)	1.469 (0.316–6.825)	0.606	1.537 (0.302–7.831)	0.605
Non-Hispanic White	3.14 % (5)	5.03 % (8)	91.82 % (146)	Reference		Reference	

Racial disparities in the treatment, outcome, and incidence of endometrial cancer are well known with Black women having nearly double the mortality rate compared to other racial groups (Doll and Winn, 2019; Gamble and Doll, 2021; Whetstone, 2022). Recent statistics from the American Cancer Society reported an absolute difference of 21 % in 5-year survival rates (Society, 2008). A study of 24,152 women diagnosed with Stage I to III endometrial cancer undergoing primary hysterectomy showed that overall survival was lower for Black women across all stages and all histologic subtypes. Of note, overall survival was particularly impacted amongst women diagnosed with Stage I endometrial endometrioid adenocarcinoma (Saris, 2022).

In an analysis using the SEER database, Black women enrolled in Medicare were less likely to undergo guideline concordant treatment compared with White women (Rodriguez, 2021). These results were consistent with those of a previous study that demonstrated non-Hispanic Black and Hispanic women with endometroid endometrial cancer had lower odds of receiving guideline concordant treatment (Kaspers, 2020). Overall, the results of the studies show racial disparities in the treatment and overall survival of early stage endometroid adenocarcinoma among Black women. Despite our knowledge of these disparities, little is known regarding the underlying etiology. One hypothesis is that molecular and genetic factors may be driving disparities (Javadian and Histopathologic, 2021). However, no clear differences have been found which is expected as race is a social, not biological, construct (Whetstone, 2022). Future research should focus on ancestry, not race, as a potential driver for genetic differences. For example, with the FIGO 2023 molecular classification of endometrial cancer, we may see a difference in POLE by stage and ancestry. Another potential cause could be implicit bias which would negatively influence health care delivery and patient outcomes. Lastly, racial disparities in the treatment of the premalignant condition, subsequently leading to differences in treatment and outcomes of women with endometrial cancer. Our study highlights the need for further research into pre-cancerous conditions and disparities as we demonstrate stark differences in treatment strategies. Future research is imperative to evaluate the root cause of this disparity in the healthcare system. Currently, our institution is investigating cultural and socio-economic factors affecting patients' understanding of their diagnoses and how this impacts the care that they receive through community focus groups. We hope to better define the factors that may affect treatment recommendations and treatment-related decisions through further work within our communities.

CRediT authorship contribution statement

K. Seay: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **A. Katcher:** Writing – review & editing, Investigation, Formal analysis, Conceptualization. **M. Hare:** Writing – review & editing, Investigation. **H. Rahman:** Formal analysis. **C. Sison:** Formal analysis. **G.L. Goldberg:** Supervision. **M. Frimer:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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