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Mitigating disparity?: Treatment patterns, survival, and recurrence rates by race, ethnicity, and hospital site across a large urban health system

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ABSTRACT

Objective: National data have shown worse endometrial cancer (EC) outcomes among racial and ethnic minorities. We aimed to analyze EC patient outcomes within a large urban academic health system, with a focus on patterns of care and recurrence rates.

Methods: This was a retrospective chart review of EC patients at three system hospitals from 1/1/07–12/31/17. Demographic and clinical factors, including time from EMB to surgery, rate of chemotherapy completion, persistent or recurrent disease, and palliative care referrals were extracted. Descriptive statistics and survival curves were generated. Analysis was done using SAS version 9.4.

Results: Black patients had lower overall survival compared to all others on univariate analysis only ($p < 0.0001$). Hospital site was associated with OS, with the academic anchor and satellite 1 having higher rates of all-cause mortality compared to satellite 2 (HR 4.68 academic anchor, 95 % CI 1.72–12.76, HR 5.36 satellite 1, 95 % CI 1.85–15.52). Time from EMB to surgery and rates of persistent disease following primary treatment were higher in Black patients. After adjusting for stage and grade, chemotherapy completion rate was significantly associated with race. Palliative care was utilized more for Black than White patients after adjusting for stage and grade ($p = 0.005$).

Conclusions: Racial disparities in EC are caused by a complex web of interconnected factors that ultimately lead to worse outcomes in Black women. While precision medicine has helped to close the gap, social determinants of health should be addressed, and models focusing on the complex interactions between biologic, genetic, and social factors should be utilized.

1. Introduction

Demographic groups within the United States are not equally affected by endometrial cancer (EC), making the reduction of racial disparities in treatment and outcomes a major focus of national cancer organizations (American Cancer Society, 2019; American Cancer Society, 2021; Institute of Medicine (US), 1999; Goss et al., 2009; Institute of Medicine (US), 2003). There is a substantial disparity in EC case fatality despite the high rate of surgical treatment among incident cases. Additionally, there is a relative paucity of evidence and controversy about the causes of racial disparities in EC (American Cancer Society, 2021; Randall and Armstrong, 2003).

The incidence of EC is similar between White and Non-Hispanic (NH) Black women after accounting for varying hysterectomy rates affecting the ratio of at-risk patients to total number of women in each population (Temkin et al., 2016). Based on the largest contemporary National Cancer Database (NCDB) registry analysis from 2016, the percentage of Black patients with advanced-stage EC (IIIC/IV) was nearly twice that of

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NH White (17 % vs 9.8 %, $p < 0.001$) (Fader et al., 2016). Furthermore, while uterine cancer incidence overall has been increasing at a rate of approximately 1 % per year, non-endometrioid tumors increase at a rate of 3.1 % annually, with serous carcinomas increasing by almost 5 % per year (Eakin et al., 2022). The largest increases in non-endometrioid subtypes have been observed in NH Black, Hispanic, and Asian women, with Black women being diagnosed with non-endometroid histologies at rates 2–4 times more than White women (Clarke et al., 2022; Abel et al., 2021; Johnson et al., 2020). Fatality is consistently higher in the NH Black population even when accounting for the higher frequency of late-stage disease at diagnosis. Survival is lower for NH Black women for every stage at diagnosis, with the disparity persisting after controlling for demographic, clinicopathologic and facility-related factors (American Cancer Society, 2019; Fader et al., 2016). Multiple studies have continued to demonstrate that even with guideline-concordant care, Black women are more likely to present with advanced disease and are 21 % more likely to die from disease when compared with White women (Ferriss et al., 2021).

Analysis of the NRG Oncology/GOG 210 study patients who underwent hysterectomy for EC showed higher rates of adjuvant chemotherapy only or radiotherapy plus chemotherapy in NH Black women compared to White, and no difference in rates of adjuvant radiotherapy alone when stratified by tumor subtype, stage, or European Society for Medical Oncology risk category (Felix et al., 2018). In a pooled analysis of racial disparities among stage III EC patients, Black patients were found to have higher rates of "sandwich" therapy or concurrent chemoradiation compared with non-Black patients, with worse overall survival rates seen in the Black cohort (Patrich et al., 2023).

A retrospective cohort study of the Surveillance, Epidemiology, and End Results (SEER) program (1991–1999) showed that except for a modest association with hospital surgical volume, provider and hospital characteristics were largely unrelated to survival for Black women with EC. The great majority of the difference in survival was explained by differences in tumor and clinical characteristics at presentation (Armstrong et al., 2011). We would therefore expect that with equal access to gynecologic oncology care and multidisciplinary cancer resources, health care disparities according to race would be mitigated.

Given the body of evidence, it is clear that factors other than more aggressive histology and worse stage at diagnosis contribute to the disparity seen in Black women (Giaquinto et al., 2022). The aim of the current study was to analyze characteristics and outcomes of EC patients within a large urban academic health system, with a focus on patterns of care delivery, recurrence rates, and use of palliative care services. Analysis included the academic anchor as well as two satellite hospitals within the same health system, with the hypothesis that health care disparities would become evident with delivery of patient care further from the academic anchor. We further aimed to characterize any disparities within the health system by race, ethnicity, insurance status, and primary language.

2. Methods

This was a retrospective chart review performed at a large urban academic health system. The institutional cancer registry was queried for all EC cases treated at three system hospitals between January 1st, 2007 and December 31st, 2017. The three hospitals were part of a single health system with shared resources, with a central academic anchor and two satellite hospitals. The satellite hospitals included in the cancer registry query were selected due to the relatively large proportion of gynecologic oncology patients seen at these sites, as well as the volume of shared resources and physicians between the academic anchor and these sites. Although demographics across the 3 sites are similar, the satellites were smaller urban hospitals with lower volume, fewer academic resources, and a larger proportion of chemotherapy done by medical oncologists when compared with the anchor.

Inclusion criteria for analysis were a diagnosis of EC of any histology diagnosed and treated between 1/1/07 and 12/31/17 within the health system. Patients who did not have their initial treatment within the system, as well as charts without complete clinical data, were excluded. Incomplete clinical data included missing race, missing date of endometrial biopsy (EMB), EMB earlier than 1/1/07, as well as inconsistent dates of EMB, surgery, recurrence, and/or last contact with gynecologic oncology.

Recorded variables included the following demographic factors: age at diagnosis, self-reported race, ethnicity (Hispanic versus Non-Hispanic), primary language (English versus Non-English), and insurance status (managed care, Medicaid, Medicare, uninsured, or private). Clinical factors were additionally extracted as follows: date of first and last contact with a gynecologic oncologist, date of EMB, date of surgery, primary tumor site and histology, hospital site, adjusted TNM stage, tumor grade, receipt of radiation as primary treatment, receipt and completion of chemotherapy, vital status (dead versus alive), recurrence (local versus distant), BMI at time of surgery or first encounter, gravity, parity, and referral to palliative care. Age at EMB served as a proxy for age at diagnosis.

Descriptive statistics were generated and differences in demographic characteristics, TNM stage, tumor grade, and histology were compared across racial and ethnic groups. Distribution of cases by hospital site and race were additionally compared. Chi-square or Fisher's exact test was used for categorical variables, and the ANOVA or Kruskal-Wallis test was used for continuous variables. Kaplan-Meier curves were generated for overall survival by race, ethnicity, and race/ethnicity combinations. Multivariate analyses were performed to control for age at diagnosis, hospital site, TNM stage, histology, and grade.

Secondary outcomes analyzed included time from EMB to surgery, rates of persistent disease after primary treatment, recurrence rates (local versus distant), rates of completion of chemotherapy, receipt of radiation as primary treatment, and palliative care referrals. Chi-square test was used to analyze categorical variables and Kruskal-Wallis test was used for continuous variables. Univariate and multivariate analyses of disease recurrence were performed. Results were confirmed using cause-specific Cox Proportional hazard regression models.

3. Results

3.1. Patient demographics

Initial query of the system tumor registry yielded 3195 cases with 1434 patients included in the final analysis (Fig. 1). Patient characteristics at time of surgery or at initial encounter with a gynecologic oncologist if no surgery was performed are reported in Table 1. Over two-thirds of the final study population were seen at the main academic anchor (n = 958, 68.7 %). Nine-hundred and five patients were White (63 %), 279 were Black (19 %), 130 were Asian (9 %), and 121 were Other race (8 %). Eighty-six percent of patients were Non-Hispanic (n = 1220) and 14 % Hispanic (n = 199). A majority of patients (n = 1220, 90.1 %) reported English as their primary language. Most patients were either insured by Medicare (n = 577, 41.3 %) or a managed-care HMO/PPO (n = 554, 39.6 %). The mean age at time of diagnosis was 63.5 years (range 32–94 years).

3.2. Tumor characteristics

Tumor characteristics are described in Table 2. The vast majority of patients (n = 987, 75.2 %) had stage I disease on final surgical pathology. Although this pattern was seen across all races, Black patients had a lower proportion of early stage disease and a higher burden of stage III and IV disease. Distribution of grades was relatively even, with 488 patients (37.8 %) having grade 1/well-differentiated disease and 440 patients (34.1 %) with poorly differentiated or undifferentiated disease.

As expected based on national trends, most patients had endometrioid adenocarcinoma histology (n = 914, 63.7 %). Black patients had a

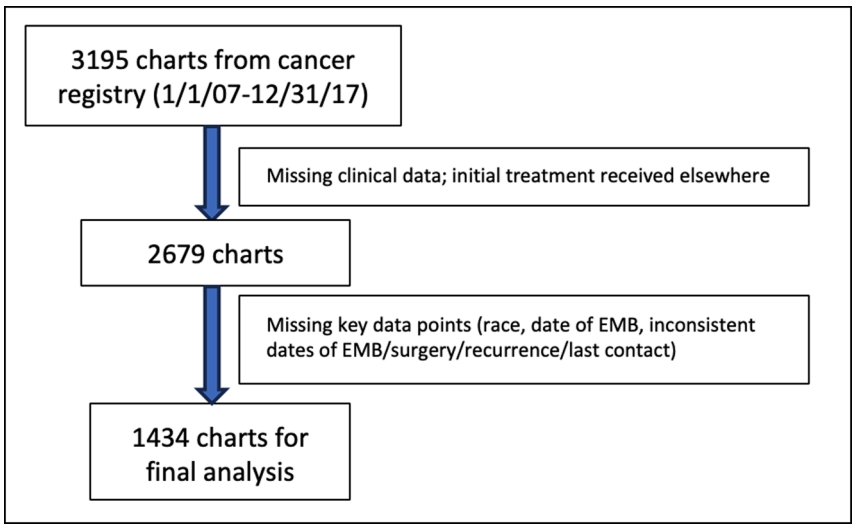

Fig. 1. Patient Record Selection.

Table 1
Patient characteristics.

Characteristic	ALL (n = 1434)	ASIAN (n = 130)	BLACK (n = 278)	OTHER (n = 121)	WHITE (n = 905)	P value§
Age at EMB – mean (SD)	63.5 (11.6)	58.0 (11.5)	65.5 (11.2)	62.4 (13.0)	63.9 (11.2)	<0.0001
BMI at surgery*** – mean (SD)	31.3 (8.7)	25.9 (5.5)	34.7 (8.6)	32.4 (8.4)	30.9 (8.7)	<0.0001
Gravidity*** – median (IQR)	2.0 (1.0, 3.0)	2.0 (0.0, 3.0)	3.0 (1.0, 4.0)	2.0 (1.0, 4.0)	2.0 (0.0, 3.0)	<0.0001
Parity*** – median (IQR)	1.0 (0.0, 3.0)	1.0 (0.0, 2.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	1.0 (0.0, 2.0)	<0.0001
Spanish/Hispanic origin* – no. (%)						<0.0001
Hispanic	199 (14.0)	1 (0.8)	13 (4.7)	55 (45.8)	130 (14.5)	
Non-Hispanic	1220 (86.0)	128 (99.2)	263 (95.3)	65 (54.2)	764 (85.5)	
English as primary language* – no. (%)	1229 (90.1)	86 (69.9)	258 (97.7)	92 (79.3)	793 (92.1)	<0.0001
Insurance* – no. (%)						<0.0001
MANAGED CARE (HMO, PPO)	554 (39.6)	58 (46.8)	81 (30.1)	42 (34.7)	373 (42.2)	
MEDICAID	185 (13.2)	34 (27.4)	50 (18.6)	25 (20.7)	76 (8.6)	
MEDICARE	577 (41.3)	27 (21.8)	125 (46.5)	45 (37.2)	380 (43.0)	
NOT INSURED	7 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)	6 (0.7)	
PRIVATE/SELF-PAY/INSURAN	75 (5.4)	5 (4.0)	12 (4.5)	9 (7.4)	49 (5.5)	
Hospital– no. (%)						<0.0001
	295 (20.6)	60 (46.2)	68 (24.5)	12 (9.9)	155 (17.1)	
	154 (10.7)	10 (7.7)	59 (21.2)	11 (9.1)	74 (8.2)	
SATELLITE 1	985 (68.7)	60 (46.2)	151 (54.3)	98 (81.0)	676 (74.7)	
SATELLITE 2						
ACADEMIC ANCHOR						

significantly lower rate of endometrioid adenocarcinoma (n = 128, 46 %) and higher rates of serous adenocarcinoma (n = 56, 20.1 %) and carcinosarcoma (n = 20, 7.2 %) compared to the overall cohort (p < 0.0001). In contrast, Asian women had relatively higher rates of endometrioid adenocarcinoma (n = 99, 76.2 %), and lower rates of carcinosarcoma, clear cell, and serous adenocarcinomas compared to the overall cohort (n = 4, 3.1 %; n = 0, 0 %; n = 7, 5.4 %, respectively).

3.3. Survival data

3.3.1. Race and overall survival

Vital status was determined for each patient to date of data extraction or last known follow up. The median duration of follow-up since diagnosis was 3.6 years (range 0 to 14.5 years). A total of 182 deaths occurred, with deaths noted between 0 and 8.9 years after EMB. Supplementary materials 1 and 2 demonstrate the Kaplan-Meier curves for time to death for all patients and for patients stratified by racial group, respectively. Survival rates were significantly different between the four racial groups (p < 0.0001). Specifically, post-hoc pairwise comparisons showed that Black patients had a significantly shorter overall survival compared to Asian patients (p < 0.0001), White patients (p = 0.0001), and patients of other races (p = 0.0002). Kaplan-Meier estimates of overall survival probability at five years are provided in Supplementary material 3. The overall survival probability at 5 years was 0.85 for the whole cohort (95 % CI: 0.83–0.87), 0.92 for Asian patients (95 % CI: 0.85–0.96), 0.76 for Black patients (95 % CI: 0.70–0.82), 0.87 for White patients (95 % CI: 0.84–0.89), and 0.87 for patients of Other race (95 % CI: 0.84–0.89).

On multivariable analysis, race was no longer significantly associated with overall survival after adjusting for age at EMB, hospital site, tumor histology, grade, and initial TNM stage (p = 0.64). Note that initial TNM stage and grade were found to be important confounders in the relationship between race and overall survival. Hospital site was noted to be associated with differences in overall survival, with the academic anchor and satellite 1 having significantly higher rates of all-cause mortality compared to satellite 2 (HR 4.68 academic anchor, 95 % CI 1.72–12.76, HR 5.36 satellite 1, 95 % CI 1.85–15.52) (Table 3).

3.3.2. Ethnicity and overall survival

As shown in Supplementary material 4, overall survival did not differ significantly between Hispanic and Non-Hispanic patients (p = 0.11). Multivariate analysis did not change this result, with no significant difference in overall survival between Hispanic and Non-Hispanic patients after adjusting for age at EMB, hospital site, tumor histology,

Table 2
Tumor characteristics.

Characteristic	ALL (n = 1434)	ASIAN (n = 130)	BLACK (n = 278)	OTHER (n = 121)	WHITE (n = 905)	P value§
TNM stage** – no (%)						<0.0001
1	987 (75.2)	93 (76.9)	150 (58.4)	84 (78.5)	660 (79.7)	
2	72 (5.5)	8 (6.6)	23 (8.9)	3 (2.8)	38 (4.6)	
3	160 (12.2)	16 (13.2)	43 (16.7)	14 (13.1)	87 (10.5)	
4	94 (7.2)	4 (3.3)	41 (16.0)	6 (5.6)	43 (5.2)	
Grade** – no (%)						<0.0001
Undifferentiated	38 (2.9)	5 (4.2)	10 (4.1)	4 (3.5)	19 (2.3)	
Poorly Differentiated	402 (31.2)	26 (21.7)	121 (49.6)	35 (31.0)	220 (27.1)	
Moderately Differentiated	362 (28.1)	29 (24.2)	48 (19.7)	33 (29.2)	252 (31.0)	
Well Differentiated	488 (37.8)	60 (50.0)	65 (26.6)	41 (36.3)	322 (39.6)	
Histology – no. (%)						<0.0001
Adenocarcinoma NOS	93 (6.5)	7 (5.4)	19 (6.8)	12 (9.9)	55 (6.1)	
Carcinosarcoma	59 (4.1)	4 (3.1)	20 (7.2)	6 (5.0)	29 (3.2)	
Clear Cell adenocarcinoma	27 (1.9)	0 (0.0)	9 (3.2)	4 (3.3)	14 (1.5)	
Endometrioid adenocarcinoma	914 (63.7)	99 (76.2)	128 (46.0)	75 (62.0)	612 (67.6)	
Leiomyosarcoma or Sarcoma	23 (1.6)	2 (1.5)	2 (0.7)	3 (2.5)	16 (1.8)	
Mixed Cell adenocarcinoma	183 (12.8)	11 (8.5)	44 (15.8)	10 (8.3)	118 (13.0)	
Serous Adenocarcinoma	135 (9.4)	7 (5.4)	56 (20.1)	11 (9.1)	61 (6.7)	

* 1–5 % of the data were missing.
** 8–10 % of the data were missing.
*** 20–35 % of the data were missing.
§ The Chi-square or Fisher's exact test was used for categorical variables and the ANOVA or Kruskal-Wallis test was used for continuous variables.
† Grade was coded as: 1 = Well Differentiated, 2 = Moderately Differentiated, 3 = Poorly Differentiated, 4 = Undifferentiated.

Table 3
Univariable and multivariable analysis for the effect of race on overall survival.

Outcome variable	Factor of Interest		Crude*		Adjusted**	
			Hazard Ratio (95 % CI)	P value	Hazard Ratio (95 % CI)	P value
All-cause mortality	Race			<0.0001†		0.64†
		Black	Reference	–	Reference	
		Asian	0.33 (0.17, 0.65)	0.001	1.00 (0.49, 2.06)	
		Other	0.55 (0.30, 1.00)	0.05	0.64 (0.28, 1.45)	
		White	0.47 (0.34, 0.65)	<0.0001	0.83 (0.56, 1.24)	
	TNM stage					<0.0001†
		1			Reference	–
		2			0.98 (0.42, 2.29)	0.96
		3			3.34 (2.17, 5.15)	<0.0001
		4			10.13 (6.42, 15.99)	<0.0001
	Grade					<0.0001†
		Undifferentiated			2.09 (0.82, 5.37)	0.12
		Poorly Differentiated			3.78 (2.15, 6.64)	<0.0001
		Moderately Differentiated			1.68 (0.91, 3.13)	0.10
		Well Differentiated			Reference	–
	Hospital					0.007†
		Satellite 2			Reference	–
		Satellite 1			5.29 (1.83, 15.29)	0.002
		Academic Anchor			4.83 (1.77, 13.15)	0.002
	Age at EMB				1.03 (1.01, 1.05)	0.0009

grade, and initial TNM stage (p = 0.41) (Supplementary material 5).

3.3.3. Combined Race/Ethnicity and overall survival

Race and ethnicity were combined into a single variable with six categories: Black (N = 276, 19 %), Asian (N = 129, 9 %), Other/Hispanic (N = 55, 4 %), Other/non-Hispanic (N = 65, 5 %), White/Hispanic (N = 130, 9 %), and White/non-Hispanic (N = 764, 54 %). Note that the Black and Asian groups were not divided into Hispanic and non-Hispanic groups as they each had less than 5 % Hispanic patients overall. Overall survival by race/ethnicity combinations is displayed in Fig. 2. Survival rates were significantly different between the six racial-ethnic groups (p < 0.0001, log-rank test). Specifically, post-hoc pairwise comparisons showed that Black patients had a significantly shorter overall survival compared to all groups (Supplementary material 6). However, in the multivariable analysis, the race/ethnicity combination was no longer significantly associated with overall survival after adjusting for age at EMB, hospital site, tumor histology, grade, and initial TNM stage (p = 0.63). Note that initial TNM stage and tumor grade, were again found to be important counfounders in the relationship beetween race/ethnicity and overall survival.

3.4. Secondary outcomes by Race: Time from EMB to surgery, use of radiation as primary Treatment, completion of Chemotherapy, and palliative care referrals

Time from EMB to surgery was significantly longer for Black vs. White patients (median number of days 31.5 vs. 23, p < 0.0001), White vs. Asian patients (23 vs. 13 days, p < 0.0001), Black vs. Asian patients (31.5 vs. 13 days, p < 0.0001), and Black vs. Other patients (31.5 vs. 28 days, p < 0.0001). The rate of radiation as part of primary treatment was significantly higher for Asian vs. White patients (29 % vs. 18.5 %, p = 0.004). The rate of chemotherapy completion was significantly higher in Black vs. White patients (36 % vs. 17 %, p < 0.0001). On multivariate adjusted analysis, after controlling for stage and histology, the rate of

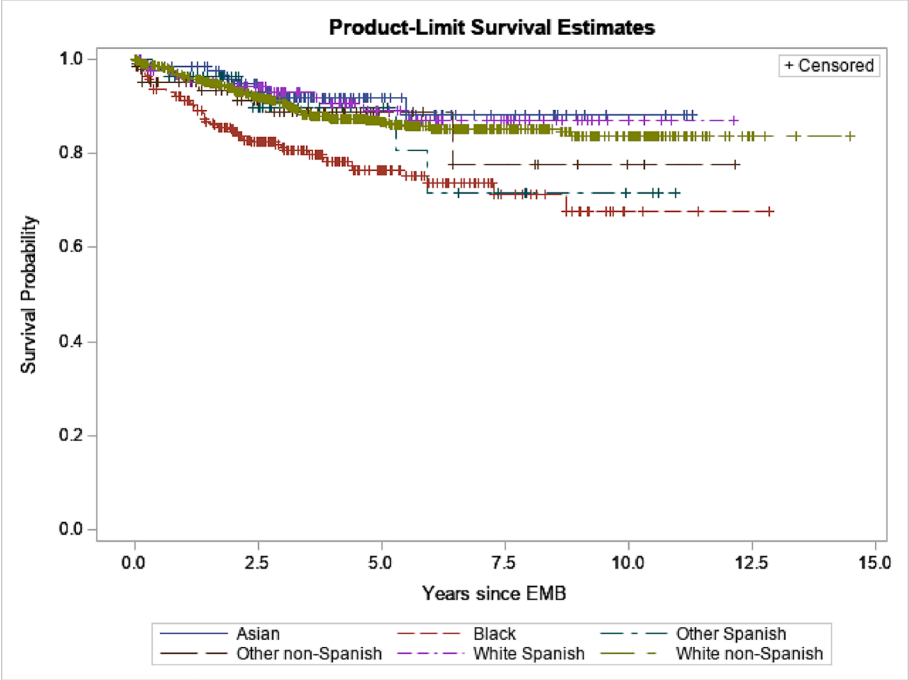

Fig. 2. Overall survival by race/ethnicity combination variables.

chemotherapy completion was noted to be significantly associated with race (p = 0.02). However, given small numbers of recurrent disease, differences between individual races could not be determined. Rate of palliative care referral was significantly higher in Black vs. White patients (22 % vs. 8 %, p < 0.0001), Black vs. Asian patients (22 % vs. 11 %, p = 0.008), and Black vs. Other patients (22 % vs. 10 %, p < 0.005). This persisted on multivariate adjusted analysis, with significantly lower palliative care referral rates for White versus Black patients after controlling for stage and histology (adjusted OR White patients 0.51 95 % CI 0.32–0.82, p = 0.005). Secondary outcome analyses are shown in Table 4.

3.5. Tumor recurrence

Patients with recurrence status classified as 'never disease free' were deemed to have persistent disease after primary treatment; patients with recurrence status of 'local recurrence,' 'distant recurrence,' or 'disease free' were deemed to have no persistent disease after primary treatment. The rate of persistent disease after primary treatment was significantly higher in Black versus White patients (25 % vs. 12 %, p < 0.0001) and in Black versus Asian patients (25 % vs. 9 %, p < 0.0001). In the multivariable analysis of recurrence of any type, hospital site was not significantly associated with recurrence (p = 0.45). Furthermore, hospital site was not found to be a confounder of the relationship between race and recurrence, indicating that rates of recurrence by race changed

Table 4
Secondary outcomes by race & adjusted analyses of secondary outcomes by race.

Outcome	ALL (n = 1434)	ASIAN (n = 130)	BLACK (n = 278)	OTHER (n = 121)	WHITE (n = 905)	P value§
Time from EMB to surgery*, days – median (IQR)	24.0 (11.0, 44.0)	13.0 (0.0, 34.5)	31.5 (15.0, 53.0)	28.0 (18.0, 48.5)	23.0 (11.0, 41.0)	<0.0001
Persistent disease** – no. (%)	175 (15.5)	10 (8.8)	61 (25.3)	21 (20.4)	83 (12.3)	<0.0001
Chemotherapy completed – no. (%)	316 (22.0)	33 (25.4)	101 (36.3)	29 (24.0)	153 (16.9)	<0.0001
Radiation as primary treatment – no. (%)	287 (20.0)	38 (29.2)	63 (22.7)	19 (15.7)	167 (18.5)	0.01
Palliative care referral – no. (%)	155 (10.8)	14 (10.8)	60 (21.6)	12 (9.9)	69 (7.6)	<0.0001

* 12 % of the data were missing.
** 21 % of the data were missing.
§ The Chi-square test was used for categorical variables and the Kruskal-Wallis test was used for continuous variables.

Adjusted Analyses	Factor of Interest		Adjusted Odds Ratio§ (95 % CI)	P value§
Chemotherapy completed	Race			0.02†
		Black	Reference	–
		Asian	1.67 (0.89, 3.15)	0.11
		Other	1.30 (0.67, 2.49)	0.44
		White	0.76 (0.50, 1.16)	0.21
Palliative care referral	Race			0.01†
		Black	Reference	–
		Asian	1.08 (0.53, 2.21)	0.82
		Other	0.78 (0.36, 1.71)	0.54
		White	0.51 (0.32, 0.82)	0.005

§ Adjusted for grade, TNM stage and histology using a multivariable logistic regression model.
† Test of overall significance for Race.

minimally when hospital was added to the analysis.

3.5.1. Local versus distant disease recurrence

Among the 957 patients who had non-persistent disease following primary treatment, 841 or 88 % were deemed disease free. A total of 41 patients (4 %) had local recurrences occurring between 28 days and 9.7 years following primary treatment, and 75 patients (8 %) had distant recurrences occuring between 52 days and 6.7 years following primary treatment. The cumulative incidence curve for recurrence of any type (i.e. local or distant) for all patients and by race is displayed in Supplementary materials 7 and 8, respectively. Supplementary materials 9 and 10 demonstrate cumulative incidence of local recurrence for all patients and by race; Supplementary materials 11 and 12 demonstrate cumulative incidence of distant recurrence for all patients and by race.

Univariable and multivariable analyses of disease recurrence are reported in Supplementary material 13. In the univariable analysis, Black patients had a significantly higher cumulative incidence of all types of disease recurrence compared to White patients (Any Type: $p < 0.0001$, Local: $p = 0.003$, Distant: $p = 0.001$). In the multivariable analysis, race was no longer significantly associated with cumulative incidence of disease recurrence after adjusting for initial TNM stage and tumor grade (Any Type: $p = 0.11$, Local: $p = 0.17$, Distant: $p = 0.67$). Cause-specific hazard regression models were run to confirm findings, with similar results.

4. Discussion

In our cohort of 1434 patients treated within an urban academic health system, the occurrence of higher stage and more aggressive histologies for Black women at time of presentation mostly followed known national trends. In comparison to national data, Black patients in our system had equivalent rates of early stage disease (58.4 % vs 54 %), slightly higher rates of regionally advanced disease (stage II and III 25.6 % vs. 22 %), and higher rates of stage IV disease (16.0 % vs. 10 %) (Long et al., 2013).

Black patients had significantly shorter overall survival compared to patients of all other races. Ethnicity did not appear to have an impact on survival. Importantly, however, differences in overall survival were mitigated on multivariable analysis after controlling for age at diagnosis, histology, TNM stage, grade, and hospital site. Hospital site was associated with overall survival on multivariate analysis with no significant interaction between race and hospital. Interestingly, patients at the academic anchor had a higher hazard ratio for death compared to one of the satellite hospitals. Extrapolating from these two observations, we can posit that survival is perhaps worse at the academic anchor due to higher morbidity procedures being performed in an overall sicker patient population compared to the satellites. Additionally, this could be due to higher rates of advanced stage diseases treated at the academic anchor; the specific reasons for this difference were not investigated in this study and warrant further investigation.

Importantly, hospital site was the only factor included in the multivariate survival analysis that was not "fixed" – i.e. a patient's age and tumor characteristics cannot be changed, but the determination of which hospital to be treated at can. The alleviation of survival differences after controlling for hospital site suggests that survival outcomes are, in fact, influenced by the site of treatment, which is in turn determined by a variety of factors including proximity to the hospital, insurance status, socioeconomic status, and access to transportation. Thus, the results of our study suggest that an individual's social and community environments do indeed influence survival outcomes after an EC diagnosis.

The five social determinants of health - economic stability, education access and quality, health care access and quality, neighborhood and built environment, and social community and context – play a large role in a patient's health outcomes, starting with their initial access point to the health care system (Healthy People 2030, 2023). Within these five social domains, there exist multiple factors that influence a patient's ability to access care. In this context, the question then becomes – can the worse outcomes we see among Black patients at all be explained by the interaction of social determinants of health with molecular and genetic aberrations? And if so, to what degree do these interactions occur?

In a 2023 SEER database study on racial and ethnic disparities in type II EC, Karia et al. performed mediation analysis to identify the contribution of various factors influenced by race and ethnicity that ultimately impact EC outcomes. The results showed that mediators accounted for 50.8 % of the excess EC mortality in Black versus White patients. Specifically, variation in sociodemographic and treatment-related factors accounted for 8.1 % and 7.3 % respectively of the excess mortality seen in Black patients (Karia et al., 2023).

In a 2020 editorial on eliminating disparities in EC, Paskett et al. discussed the concepts of access and adherence to high-quality cancer care. The authors highlight that while some studies suggest that equal access to high quality treatment leads to equivalent oncologic outcomes, these studies are performed in settings in which patients self-select for hospitals with high standards of care, and where adherence to protocol is high. The *quality of care* is often left out of these studies (Huang et al., 2020). In an NCDB study, Huang et al. established the following evidence-based quality metrics in EC care: (1) Surgery within 6 weeks of diagnosis; (2) Minimally-invasive surgical approach; (3) Pelvic lymph node assessment; (4) Use of adjuvant radiotherapy; and (5) Chemotherapy for stage III or IV disease. In this study, over 300,000 patients were assessed for adherence to these five metrics with the hypothesis that "perfect adherence" would lead to improved or mitigated outcomes between Black and White patients. The authors found that although "perfect adherence" as well as individual adherence to each of the five quality metrics led to improved survival for both Black and White patients, White patients were more likely than Black to have perfect adherence (50 % versus 38.3 %) and subsequently had a greater survival advantage at 30 days, 90 days, and 5 years (5-year OS 80.3 % White versus 62.5 % Black) (Huang et al., 2020). Interestingly, the demographic analysis showed that while the groups differed in almost all social determinants of health, the disparities remained even after controlling for these factors (Huang et al., 2020). The findings of this study highlight the fact that Black patients are less likely to receive guideline-adherent treatment, and this is not necessarily due to differences in clinical or demographic factors. Furthermore, regardless of receipt of guideline-adherent treatment, Black patients still have worse outcomes overall than white patients (Paskett and Bernardo, 2020).

In our study, three of these five quality metrics were analyzed: surgery within 6 weeks of diagnosis, use of adjuvant radiation, and use of chemotherapy. Notably, all racial groups in our cohort received surgery within the recommended 6 weeks. However, the time from EMB to surgery was significantly longer for Black women compared to all other racial groups (31.5 days vs 24.0). Paradoxically, the rate of chemotherapy completion was significantly higher in Black women versus White women (36 % vs 17 %, $p < 0.0001$). However, this could possibly be explained by higher stage at diagnosis necessitating the use of chemotherapy. Our model did not investigate rates of chemotherapy prescription or completion by stage, but doing so could shed further light on this finding. Despite the timely nature of surgery and the widespread completion of chemotherapy in our system, Black patients had higher rates of persistent disease after primary treatment compared to both White and Asian patients. While our analysis did not analyze treatment patterns between the three hospital sites, we can reasonaby assume that diagnostic and treatment procedures remained equivalent within a health system driven by an academic cancer center following National Comprehensive Cancer Network guidelines and with the same group of physicians providing care across the three sites. Despite this assumption, however, our study demonstrates that care delivery at a high-volume, urban health system anchored by a large academic cancer center does not necessarily mitigate disparities among women with EC.

Overall, it is clear that racial and ethnic disparities in EC occur due to

an amalgam of factors, including socioeconomic factors, treatment-associated factors, molecular and/or genetic alterations, as well as the conceptualization of race in cancer research itself (Doll et al., 2018). Addressing structural racism and how it affects not just care delivery systems but also clinical research is critical. Multiple studies have addressed low representation rates of Black and non-White patients in clinical trials (Clair and Bristow, 2021; Niranjan et al., 2021). A recent study analyzing the use of precision medicine and next generation sequencing in patients with advanced or recurrent EC aimed to reduce disparities in treatment based on molecular targetting. The authors still found racial disparities not only in the number of Black versus non-Black patients prescribed targeted therapies (28.2 % vs. 38.2 %), but also in those enrolled in the trial itself (15 % Black vs. 22.6 % non-Black) (Arend et al., 2021). Thus, as cancer care continues to move towards targeted therapeutics, ensuring equal representation in clinical trials and precision medicine through initiative-based strategies is critical.

Based on our findings, we have been able to implement positive changes including a system-wide tumor board and increasing shared academic resources and clinical trial presence at all sites. Our study's strength lies in the diversity of our urban patient population, yet it is limited by the nature of its retrospective analysis and poor control over historic data and confounding factors. For example, our dataset was unable to distinguish between cancer-specific mortality and those due to other causes and did not account for transfers of care. Additionally, the current study does not analyze differences in surgical benchmarks such as use of minimally-invasive techniques and lymph node assessment. Future studies should focus on identifying factors that led to the increased mortality rate at the academic anchor, as well as identifying differences in the 5 evidence-based quality metrics such as use of MIS by race and hospital site. Further research should also aim to create a model for the complex interactions between the biologic and/or genetic factors and the social factors that lead to disparities in outcomes.

5. Conclusion

Racial disparities in EC are not caused by one single issue, but rather by a complex web of interconnected factors that ultimately lead to worse outcomes in Black women. It is clear that health care disparities are determined by factors as broad as structural racism and social determinants of health to those as precise as tumor molecular alterations. The key to equity for all patients with EC lies in addressing each of these layers – ensuring molecular profiling is done for all patients, identifying aspects of a patient's social setting that could potentially affect adherence to treatment, devoting resources to improving patient navigation of the health system, introducing standardized measures for care and outcomes analysis across the health system, engaging in community-based work to help close gaps in education and access, and finally, continuing to lobby at the administrative and governmental levels for increased financial support. To combat disparities in EC, we as a society need to commit to investing in these interventions; if we do not, the gap in outcomes will continue to grow.

CRediT authorship contribution statement

Katyayani Papatla: Writing – original draft, Investigation, Data curation, Conceptualization. **Theofano Orfanelli:** Writing – original draft, Conceptualization. **Guillaume Stoffels:** Formal analysis. **Tracy Layne:** Supervision, Methodology, Conceptualization. **Elena Baldwin:** Investigation, Data curation. **Aurora Leibold:** Investigation, Data curation. **Stephanie V. Blank:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Samantha Cohen:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2024.101372.

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