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Do differences in medical comorbidities and treatment impact racial disparities in epithelial ovarian cancer?

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HIGHLIGHTS

- Black women with ovarian cancer have shortened PFS and OS compared to white women.
- Black women have more comorbidities as measured by the Charlson Comorbidity Index.
- Rates of optimal surgical cytoreduction are higher in white women.
- These differences do not account for all differences in survival between races.

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ABSTRACT

Background. Population-based studies of women with epithelial ovarian cancer suggest that black women have worse survival compared to white women. The primary objective of this study was to determine if, at a National Cancer Institute (NCI)-Designated Comprehensive Cancer Center (CCC) serving a diverse racial and socioeconomic population, race is independently associated with differences in survival.

Methods. A retrospective review of women with EOC diagnosed between 2004–2009 undergoing treatment with follow-up at our institution was performed.
Records were reviewed for demographics, comorbidities (as defined by the Charlson Comorbidity Index (CCI)), tumor characteristics, treatment, progression-free (PFS), and overall survival (OS). Survival was calculated using the Kaplan-Meier method and compared with the log-rank test. Multivariate survival analysis was performed with Cox (proportional hazards) model.

Results. 367 patients met inclusion criteria. 54 (15%) were black and 308 (84%) were white. Compared to white women, black women had higher BMI, lower rates of optimal surgical cytoreduction, lower rates of intraperitoneal chemotherapy, and higher CCI scores. The median PFS for black and white women were 9.7 and 14.6 months, respectively ($p = 0.033$). The median overall survival was 21.7 months for black women and 42.6 months for white women ($p < 0.001$). On multivariate analysis, black race independently correlated with a worse overall survival (HR 1.61, 95% CI 1.06–2.43).

Conclusion. In this cohort, racial disparities may be due to higher medical comorbidities and lower rates of optimal surgical cytoreduction. After accounting for these differences, race remained an independent predictor of worse overall survival.

1. Background

Epithelial ovarian cancer (EOC) is the most deadly gynecologic malignancy due to its frequent presentation at an advanced stage and high risk of recurrence following front-line therapy [1]. While white women have a higher incidence of ovarian cancer compared to black women (12.9 per 100,000 versus 9.5 per 100,000) [2], black women

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have worse survival outcomes. This survival difference appears to be independent of tumor stage, grade, and histology [3–5]. Data is lacking on patient-specific factors that may strongly affect survival outcomes.

We sought to further understand the nature of these racial disparities in women with EOC by closely examining patient, tumor, and treatment characteristics not typically captured in population-based studies. The primary objective of this study is to determine if, at a National Cancer Institute (NCI)-Designated Comprehensive Cancer Center (CCC) that serves as a state-wide referral center for a diverse racial and socioeconomic population, race is independently associated with differences in survival.

2. Methods

This was a retrospective cohort study designed to determine if there was a difference in progression-free survival (PFS) and overall survival (OS) between black and white women at our institution. Eligible subjects included women diagnosed with any stage of EOC between 2004 and 2009. Subjects were identified through the UAB hospital tumor registry, which captures all new cancer diagnoses seen within the UAB health system. To be included in this analysis, patients had to receive primary treatment with follow-up at our institution. All records were reviewed for demographics, medical comorbidities, tumor characteristics, treatment, cancer progression and death. Race was determined by self-identification from the patient's intake medical forms. Comorbidities were quantified using the Charlson Comorbidity Index (CCI), which is a validated predictor of hospital mortality [6]. The CCI includes 19 medical conditions that are weighted based on their association with hospital mortality. Because all patients had an invasive malignancy, we did not include "metastatic solid tumor" as part of each patient's score. For our analysis, we separated patients into 3 categories based on CCI: 0, 1, or 2+. To avoid bias, an independent investigator who was not aware of the study's endpoints extracted each patient's CCI from their medical record. PFS was calculated from the time of initiation of chemotherapy until disease recurrence or progression according to clinical assessment, rising CA-125, or radiographic evidence of recurrence. Overall survival was calculated from initiation of chemotherapy until last known follow-up or death from any cause. The study was carried out in accordance with the standards of the Institutional Human Subjects Protection Review Board at the University of Alabama at Birmingham (UAB).

Chi-square (χ^2) test or Fisher's exact test for categorical variables and the *t*-test or Wilcoxon rank sum test for continuous variables were used to compare the difference between white and black patients. Continuous variables were expressed as median ± standard deviation unless stated otherwise. Kaplan-Meier (KM) estimates were performed to detect the difference of the survival curves for white and black patients; the results reported are based on log-rank test. Multivariate survival analysis was performed with the Cox (proportional hazards) model adjusting for age, race, stage, histology, grade, cytoreduction, CCI and BMI. A value of $p < 0.05$ was considered statistically significant. All analyses were performed using SAS statistical software, version 9.3.55.

3. Results

367 patients met inclusion criteria. 54 (15%) were black, 308 (84%) were white, and 5 (1%) were other races and were excluded from further analysis. The majority of women were treated with primary surgical resection and post-operative chemotherapy, while only 16 patients (4%) received neoadjuvant chemotherapy. Compared to white women, black women had higher BMI (29.8 vs. 27.8, $p = 0.02$), lower rates of optimal surgical cytoreduction (54% vs. 76%, $p = 0.002$), and lower rates of intraperitoneal (IP) chemotherapy (0% vs. 9%, $p = 0.013$). Tumor histology also varied between the two groups with greater percentages of clear cell, endometrioid and mucinous tumors being present in black women. Age, stage, and grade did not vary significantly between races. Although the most common CCI in both groups was 0, black women were more likely to have a CCI of 1 or 2+ ($p = 0.002$). Full clinical and demographic factors are displayed in Table 1.

PFS and OS varied significantly between races. The median PFS for black and white women were 9.7 and 14.6 months, respectively ($p = 0.036$) (Fig. 1A), while the median overall survival was 21.7 months for black women and 42.6 months for white women ($p < 0.005$) (Fig. 1B). On multivariate analysis, race did not independently influence the PFS, although it did significantly increase the hazard ratio for OS (HR 1.61, 95% CI 1.06–2.43). Factors that independently affected PFS and OS in this model included age, stage, CCI and cytoreduction status (Tables 2, 3). A CCI of 2 or greater showed a 30% increased risk of suboptimal surgical cytoreduction, although this did not reach statistical significance (RR 1.3, 95% CI 0.82–2.1). When stratified by cytoreduction status, white women again had higher overall survival compared to black women after both optimal (54.6 vs. 32.7 months, $p = 0.004$) and suboptimal (20.7 vs. 12.4 months, $p = 0.004$) cytoreduction.

4. Discussion

Racial disparities in ovarian cancer outcomes are complex and multifactorial, and are likely influenced by differences in medical comorbidities, tumor biology, access to and receipt of guideline-adherent care, and sociocultural factors. In this retrospective cohort study, we found that black women with EOC had worse PFS and OS compared to white women. This difference was not subtle: median PFS was almost 5 months shorter for black women and median OS was almost twice as long for white women compared to black women (42.6 vs. 21.7 months). The reasons for these survival differences are multifactorial. Compared to white women, black women were more likely to have more comorbidities and a higher BMI. They were less likely to undergo

Table 1
Comparison of clinical and demographic factors between black and white women with epithelial ovarian cancer.

	Black ($N = 54$)	White ($N = 308$)	*p*-Value
Age (Std dev)	62.7 (11.8)	63.7 (11.9)	NS[a]
BMI (Std dev)	29.8 (5.8)	27.7 (6.3)	0.02
Grade (N, %)			NS
1	2 (4%)	8 (3%)	
2	14 (26%)	54 (18%)	
3	34 (63%)	226 (73%)	
Unknown	4 (7%)	20 (6%)	
Stage (N, %)			NS
1	4 (7%)	19 (6%)	
2	8 (15%)	53 (17%)	
3	35 (65%)	209 (68%)	
4	7 (13%)	27 (9%)	
Histology (N, %)			0.001
Papillary serous	33 (61%)	206 (67%)	
Clear cell	2 (4%)	10 (3%)	
Endometrioid	7 (13%)	33 (11%)	
Mucinous adenocarcinoma	7 (13%)	5 (2%)	
NOS	0 (0%)	10 (3%)	
Other (mixed, signet ring)	5 (9%)	44 (14%)	
Charlson Comorbidity Index			0.002
0	22 (41%)	199 (65%)	
1	20 (37%)	79 (26%)	
2+	12 (22%)	30 (10%)	
Cytoreduction status			0.002
<1 cm (optimal)	29 (54%)	233 (76%)	
>1 cm (suboptimal)	25 (46%)	73 (23%)	
Unknown	0 (0%)	2 (1%)	
IP chemotherapy			0.002
Yes	0 (0%)	28 (9%)	
No	54 (100%)	280 (91%)	
Neoadjuvant chemotherapy			NS
Yes	1 (2%)	15 (5%)	
No	53 (98%)	293 (95%)	

[a] NS = not significant.