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Black race independently predicts worse survival in uterine carcinosarcoma☆

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HIGHLIGHTS

- Both progression free and overall survival are significantly decreased in Black women with uterine carcinosarcoma compared to White women.
- Racial differences in survival are most notable in early stage disease.
- On multivariate analysis, Black race is independently associated with risk of death.

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ABSTRACT

Objective. GOG 150 suggested that Black women had worse survival compared to White women with uterine carcinosarcoma. Our objective was to compare treatment and survival outcomes between Black and White women at a National Comprehensive Cancer Network (NCCN) cancer center serving a diverse racial population.

Methods. An IRB approved retrospective cohort study of uterine carcinosarcoma patients diagnosed between 2000 and 2012 was performed. Survival was compared by race and stratified by stage. Median progression free and overall survival (PFS and OS) were calculated using Kaplan–Meier estimates and compared with the log-rank test. Multivariate survival analysis was performed with Cox proportional hazards model.

Results. 158 women were included: 93 (59%) were Black and 65 (41%) were White. 95 (60%) had early stage disease and 63 (40%) had advanced stage disease. Black women had a shorter PFS (7.9 vs. 14.2 months, $p < 0.001$) and OS (13.4 vs. 30.8 months, $p < 0.001$). There was no difference in survival between Black and White women with advanced stage disease (OS 8.5 vs. 11.8, $p = 0.18$). However, PFS and OS were worse in Black women compared to White women with early stage disease (PFS 13.6 vs. 77.4, $p = 0.001$), (OS 25.4 vs. 94.7, $p = 0.003$). On multivariate analysis accounting for age, stage, BMI, and adjuvant treatment, Black race remained independently associated with risk of death (HR 2.0; 95% CI 1.25–3.23).

Conclusions. Black women with uterine carcinosarcoma have worse survival compared to White women despite similar patient and treatment characteristics. This difference is largely due to differences in survival in early stage disease.

Background

Uterine carcinosarcomas, also known as malignant mixed Müllerian tumors, are rare and aggressive malignancies. They represent approximately 4% of uterine cancers and are associated with a poor prognosis [1,2]. As more is understood about their histologic and molecular profile, carcinosarcomas are now thought to be more similar to poorly differentiated endometrial carcinomas than other uterine sarcomas [3]. Accordingly, recent FIGO staging has delineated that carcinosarcomas will be staged similar to endometrial adenocarcinomas with most considering Stage I or II tumors being early stage disease [4]. Moreover, although carcinosarcomas were traditionally included in uterine sarcoma clinical trials, they are now evaluated separately in clinical trials [5,6].

Advanced stage disease is almost always fatal, and roughly 50% of patients with disease confined to the uterus will have recurrent disease, even those who underwent complete surgical staging [7,8]. Stage (including adnexal involvement, positive cytology, lymph node involvement), grade, tumor size and location, cell type, lymphovascular space invasion and depth of invasion have all been associated with a poor

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prognosis in various studies [7,9]. Unfortunately, adjuvant therapy trials have been uniformly disappointing in their ability to improve outcomes in patients with this disease [5,10,11].

Black women appear to have almost twice the incidence of carcinosarcomas compared to White women; however, little is known about the effects or associations of race on outcome of this disease [12]. Recent attention has focused on racial disparity in the treatment and outcomes of other gynecologic malignancies, especially ovarian carcinoma. Potential causes of disparity in outcomes include: differences in socioeconomic status, geographic limitations, insurance status, differential treatment, differences in stage at presentation, and tumor biology [12–14]. Population based studies of epithelial ovarian cancer have suggested that Black women are less likely to receive standard therapy and have worse progression free (PFS) and overall survival (OS) compared to non-Black patients [15–17]. The Gynecologic Oncology Group (GOG) protocol 150, the largest prospective trial to date, with 206 eligible patients, evaluated adjuvant treatment in uterine carcinosarcomas [10]. In a subgroup analysis, this trial suggested that Black race, compared to White, was associated with greater risk of recurrence and death [10]. However, the number of Black patients in this trial was small ($n = 58$). The objective of our study was to compare treatment and survival outcomes between Black and White women with uterine carcinosarcoma at a National Comprehensive Cancer Network (NCCN) cancer center serving a large volume of Black women with gynecologic malignancies.

Methods

This retrospective cohort 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). Subjects were identified through the institutional tumor registry, which captures all new cancer diagnoses. Eligible subjects included women diagnosed with uterine carcinosarcoma between 2000 and 2012. A gynecologic pathologist confirmed all cases at the time of diagnosis.

Demographics, tumor characteristics, treatment methods, and survival were abstracted from the medical record. Race was self-reported at the time of initial evaluation. During the study interval, two patients who self identified as other races were not included in this analysis. Progression free survival (PFS) was calculated as the time between date of diagnosis and date of recurrence, identified by either physical exam or imaging. Overall survival (OS) was defined as the time between date of diagnosis and date of death. Surviving patients were censored at their last known follow-up at our institution.

Chi-square and Student's *t*-test were used to compare variables between groups. Kaplan–Meier survival curves were generated and survival differences were compared using the log-rank test. Statistical tests were considered significant at $p < 0.05$. Multivariate survival analysis was performed with Cox proportional hazards model. All analyses were performed using SPSS statistical software version 21(IBM, Armonk, NY).

Results

158 subjects were included for analysis of which 93 (59%) patients were Black and 65 (41%) were White. The majority of patients had early stage disease ($n = 95$, 60%). Of the 63 patients with advanced stage disease, thirty (47.6%) had gross residual disease following surgery. 80 patients (51%) received adjuvant treatment and 2 patients (1.2%) did not have any surgical treatment due to advanced disease and comorbidities. Median follow-up for the subjects still alive was 24.8 months. Age, BMI, residual disease, adjuvant treatment, histologic subtype, and rates of lymphadenectomy were similar between races (Table 1). Regarding adjuvant therapy, the majority of patients in both arms received either platinum and taxane-based chemotherapy or whole pelvic radiotherapy (31 of 42 Black patients (74%) and 28 of 38 White patients (74%)).

Table 1
Comparison of clinical and demographic factors between Black and White women with uterine carcinosarcoma.

	Black ($n = 93$)	White ($n = 65$)	*p*-value
Age (StDev)	67.6 (10.5)	66.5 (10.9)	0.53
BMI (StDev)	33.7 (10.8)	32.6 (9.7)	0.54
Stage (*n*, %)			
I	39 (42%)	37 (57%)	0.1
II	15 (16%)	4 (6%)	
III	21 (23%)	16 (25%)	
IV	18 (19%)	8 (12%)	
Histology			
Heterologous	42(45%)	22 (34%)	0.29
Homologous	34 (37%)	26 (40%)	
Not specified/indeterminant	17 (18%)	17 (26%)	
Lymphadenectomy	43 (46%)	39 (60%)	0.09
Residual disease	19 (20%)	11 (17%)	0.68
Adjuvant treatment	42 (45%)	38 (58%)	0.21

Survival varied significantly by race. Disease in Black women recurred sooner with a PFS of 7.9 versus 14.2 months ($p < 0.001$) (Fig. 1). OS was also inferior in Black women with a median OS of 13.4 versus 30.8 months ($p < 0.001$) (Fig. 2). In advanced stage disease (stage III and IV), both Black and White races had poor overall survival, with no statistical difference in survival between the groups noted (8.5 versus 11.8 months, $p = 0.18$). Despite similar rates of adjuvant treatment and lymphadenectomy in patients with early stage (stage I and II) disease (Table 2), PFS and OS varied significantly by race. Median PFS was 13.6 months for Black women with early stage disease compared to 77.4 months for White women with early stage disease ($p = 0.001$) (Fig. 3a). Median OS was 25.4 months for Black women with early stage disease compared to 94.7 months for White women with early stage disease ($p = 0.003$) (Fig. 3b).

Multivariate analysis was performed to account for age, stage, BMI, lymphadenectomy and adjuvant treatment. Black race remained independently associated with risk of death for all stages (HR 2.0, 95% CI 1.3–3.2) as well as for early stage disease (HR 3.0, 95% CI 1.5–5.8).

Discussion

In this retrospective cohort study, we analyzed the survival outcomes of 158 women with uterine carcinosarcoma treated at an NCCN cancer center over a 12-year period. We found that there was a strong association with race and survival both by Kaplan–Meier and multivariate analysis. Not surprisingly, we found that regardless of race, patients

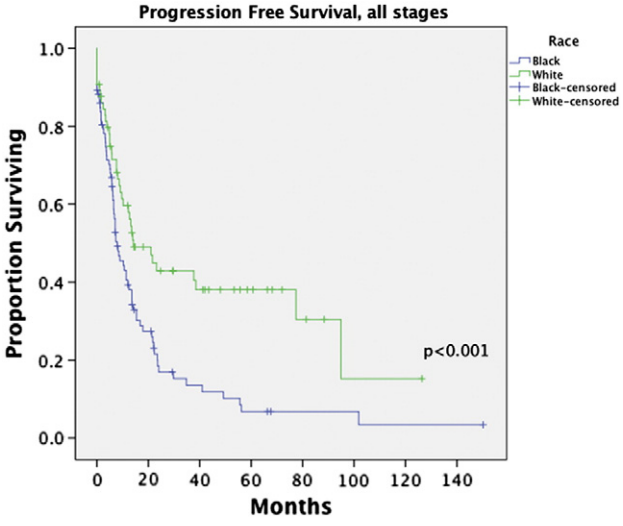

Fig. 1. Progression free survival in women with uterine carcinosarcoma by race.