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Characteristics of African American women at high-risk for ovarian cancer in the southeast: Results from a Gynecologic Cancer Risk Assessment Clinic

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HIGHLIGHTS

- Knowledge of cancer related germline mutations in African American women is limited.
- African Americans are underrepresented in genetic cancer risk assessment clinics.
- Compared to white women, African Americans show similar rates of pathogenic variants.

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ABSTRACT

Objectives. Describe patient characteristics in African American (AA) women seen for gynecologic cancer related genetic counseling at a large southeastern comprehensive cancer center.

Methods. We reviewed an IRB approved, prospective observational cohort of patients from a Gynecologic Cancer Risk Assessment Clinic. Data evaluated included personal cancer history, family history, frequency of genetic testing, frequency/type of genetic mutations, and frequency of surgical intervention. Standard statistical statistics were utilized.

Results. 1227 patients were evaluated from 2003 to 2015, of which 95 (7.7%) were AA. Sixteen patients had a personal history of ovarian cancer. 21 women (22%) underwent genetic counseling only; subsequent genetic testing was not recommended based on absence of risk factors. Of the seventy-four AA patients in whom genetic testing was recommended, sixty-six (69.5%) completed testing. Of women tested, 37 (56%) had abnormal results. Eight and 14 patients had pathogenic variants in *BRCA1* and *BRCA2*, respectively. Two were found to have pathogenic *PALB2* variants; one had a pathogenic *ATM* variant and one constitutional *MLH1* epimutation case was identified. Eleven had *BRCA* variants of uncertain significance. Of the patients with abnormal testing, six of 22 women with pathogenic *BRCA* variants underwent risk-reducing salpingo-oophorectomy (RRSO).

Conclusions. Our study demonstrates that in a region where AAs represent 27% of the population, the proportion of AA patients referred to a Gynecologic Cancer Risk Assessment Clinic remains low. Pathogenic variant and variant of uncertain significance rates were high in patients tested, likely representing a selection bias of high-risk patients. Endeavors should continue to identify minorities at risk for ovarian cancer and institute measures to provide thorough genetic counseling and testing.

1. Introduction

In 2017 it is estimated that >22,000 American women will be diagnosed with ovarian cancer, and this highly aggressive disease will result in over 14,000 deaths [1]. While ovarian cancer, like most cancers, is thought to be primarily sporadic in nature, up to 20% of ovarian cancer cases are attributed to pathogenic germline variants [2], including

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pathogenic variants in *BRCA1*, *BRCA 2*, *TP53*, and Lynch syndrome genes (*MLH1*, *MSH2*, *MSH6, PMS2, EPCAM*), among others [3]. Some studies suggest that pathogenic variants in other genes, including *BRIP1*, *RAD51C*, and *RAD51D* may also be associated with predisposition to ovarian cancer [4–6]. Given the risk of germline pathogenic variants in women diagnosed with epithelial ovarian cancer as well as the potential for cancer risk reduction in relatives [7], the National Comprehensive Cancer Network now recommends genetic evaluation and testing for those who have an epithelial ovarian cancer.

Although the rate of ovarian cancer in African American (AA) women is lower than that seen in white, Hispanic, and Asian women, AA women have worse five-year survival across all ages when compared in white women (36% vs. 44%) [8–10]. Furthermore, information regarding ovarian cancer in AA women is limited and underrepresented in available literature [11]. In addition, there are few studies focused on the evaluation of hereditary ovarian cancer syndromes in AA women with ovarian cancer [12,13]. The objective of this study was to examine the results of genetic counseling in a cohort of AA patients seen within a Gynecologic Cancer Risk Assessment Clinic and describe their characteristics as well rates and results of genetic testing.

2. Materials and methods

We performed a cohort study from patients enrolled in an Institutional Review Board approved prospectively gathered observational cohort study of all patients evaluated from 2003 to 2015 in a dedicated Gynecologic Cancer Risk Assessment Clinic in a NCI designated Comprehensive Cancer Center. This multidisciplinary clinic is composed of a faculty gynecologic oncologist and cancer genetic counselors. Detailed genetic evaluation, including counseling and testing, is performed for high-risk individuals. Patients are referred to this clinic for four general indications: (1) women with a personal history of ovarian, breast or other gynecologic cancers, (2) unaffected women with a strong family history of cancer, (3) women with a first, or less commonly, a second degree relative with a positive germline test who have not themselves undergone germline testing and (4) women who have undergone germline testing at an outside institution, were found to have a pathogenic germline variant, and need either surveillance and/or prophylactic surgical recommendations. Data on AA women evaluated in this clinic was abstracted from medical record review and personal and family history intake questionnaires. Data points collected included patient demographics, family and personal history of cancer, frequency of genetic testing, frequency and types of germline genetic variants, and performance of risk-reducing salpingo-oophorectomy (RRSO) or mastectomy. Genetic test results were utilized in combination with ClinVar (www.clinvar.com) to describe the specific pathogenic germline variants.

3. Results

From 2003 to 2015, a total of 1227 patients presented for genetic counseling and potential testing for one of the four previously listed reasons, of which 95 (7.7%) were AA women. Characteristics of evaluated AA women are presented in Table 1. The mean age of the 95 AA women assessed was 46 years (SD 11.7 years; range 20–76 years). Indications for genetic counseling in AA women included a personal history of breast cancer (n = 25, 26.3%), ovarian cancer (n = 16, 16.8%), or colorectal cancer (n = 1, 1.1%). Fifty-three (55.8%) AA women had no personal history of cancer.

Family histories in evaluated AA women were variable. Thirty-two women (33.7%) had a family history of breast cancer, 14 (14.7%) had a family history of ovarian cancer, and 36 women (37.9%) had a family history of both breast and ovarian cancers. Four women had familial histories of other malignancies (4.2%) including two with uterine and one with colon. Nine patients (9.5%) had no family history of cancer.

Genetic testing was recommended for 74 (77.9%) of the 95 AA women evaluated. Sixty-six of the 95 evaluated AA women (69.5%) underwent genetic testing. Eight (10.8%) women who met criteria declined testing. The remaining 21 (22.1%) women did not meet criteria for genetic testing. Testing modalities included *BRCA1/2* testing in 39 women and multigene panel testing in 18 women, while 9 women were tested for specific *BRCA1/2* mutations identified in a first degree relative. Of these 66 women, pathogenic mutations were identified in 26 patients (39.4%). Pathogenic *BRCA1* and *BRCA2* variants were identified in 8 (12.1%) and 14 (21.2%) women respectively. Four women were found to have other pathogenic variants: One constitutional *MLH1* epimutation, one pathogenic *ATM* variant, and two pathogenic *PALB2* variants. Variants of uncertain significance were identified in 11 women (16.7%). *BRCA2* pathogenic variants were more common than *BRCA1* pathogenic variants in AA women with 75% more (14 versus 8) *BRCA2* mutations. For comparison, during the study period 811 white women underwent testing, and 220 had a pathogenic variants (27.1%), including 122 with *BRCA1* and 84 with *BRCA2*. Specific pathogenic variants and their location are outlined in Table 2.

Table 1
Characteristics of African American women evaluated from 2003 to 2015 at gynecologic cancer risk assessment clinic.

Mean age (years ± st. dev)	46.2 ± 11.7
Personal history of cancer (N = 95)	N, (%)
Breast cancer	25 (26.3)
Ovarian cancer	16 (16.8)
Colorectal cancer	1 (1.1)
No prior cancer	53 (55.8)
Family history of cancer (N = 95)	
Breast cancer	32 (33.7)
Ovarian cancer	14 (14.7)
Breast and ovarian cancer	36 (37.9)
Other	4 (4.2)
No cancers	9 (9.5)
Genetic testing results (N = 66)	
No pathogenic variant	29 (43.9)
BRCA1 mutation	8 (12.1)
BRCA2 mutation	14 (21.2)
Other harmful variants	4 (6.1)
Variant of Uncertain Significance	11 (16.7)
Surgical intervention (N = 42)	
Therapeutic BSO	18 (18.9)
Risk reducing salpingo-oophorectomies	11 (11.6)
Therapeutic mastectomy	11 (11.6)
Prophylactic mastectomy	1 (1.1)
RRSO + PPX mastectomy	1 (1.1)

Eleven AA women (11.6%) underwent risk-reducing salpingo-oophorectomies, six of whom had pathogenic *BRCA* variants. Pathology from these surgeries showed no occult malignancies. Eleven women (11.6%) had therapeutic mastectomies for breast cancer, one woman (1.1%), underwent prophylactic mastectomy, one woman (1.1%) underwent both a risk reducing bilateral salpingo-oophorectomy and prophylactic mastectomy, and 18 women underwent bilateral salpingectomies as part of their ovarian cancer debulking (18.9%), which occurred prior to their genetic counseling visit and subsequent testing.

4. Discussion

Most data regarding AA women and *BRCA* testing exists in the context of breast cancer risk evaluation [14–16]. Pal et al. reported on a series of 144 young AA women with breast cancer who underwent *BRCA* testing which found mutations in 9% of patients with a similar distribution between *BRCA1* (n = 7) and *BRCA2* (n = 6) mutations [14]. Another study of women with triple negative breast cancer demonstrated that 21% of AA women had *BRCA1/2* mutations with *BRCA1* mutations more common than *BRCA2* mutations. In this series, white women had higher rates of mutations (27%) and more *BRCA1* mutations [16]. Previous studies have shown that some ethnically diverse

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