HHS Public Access

Author manuscript

Gynecol Oncol. Author manuscript; available in PMC 2019 May 01.

Published in final edited form as:

Gynecol Oncol. 2018 May ; 149(2): 337–340. doi:10.1016/j.ygyno.2018.02.014.

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

David A. Barrington, MD[1], **Macie L. Champion, MD**[1], **Teresa Boitano, MD**[1], **Christen L. Walters-Haygood, MD**[2], **Meagan B. Farmer, MS**[3], **Ronald D. Alvarez, MD, MBA**[2], **Jacob M. Estes, MD**[2], and **Charles A. Leath III, MD, MSPH**[2]

[1]University of Alabama at Birmingham, Department of Obstetrics & Gynecology

[2]University of Alabama at Birmingham, Division of Gynecologic Oncology

[3]University of Alabama at Birmingham, Department of Medical Genetics

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 2003–2015, 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

Corresponding Author: Charles A. Leath, III, MD, MSPH, Room 10250, 619 19th Street South, Birmingham, Alabama 35249, cleath@uabmc.edu.

Conflict of Interest Report: None

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.

Keywords

Genetic testing; Genetic predisposition; Ovarian cancer; African Americans

Introduction

In 2017 it is estimated that greater than 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 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.

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.

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.

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.

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 populations have a higher proportion of *BRCA2* mutations compared to homogenously white samples [17]. A case-control study published in *JAMA* in 2005 showed AA women with a history of breast or ovarian cancer were less likely than white women to undergo genetic testing [12].

Our study demonstrates that in a geographic region of the United States where AA represent nearly 30% of the population, the number of AA patients as a proportion of all patients referred to our Gynecologic Cancer Risk Assessment Clinic was low. Cancer Registry data from our institution suggests that the low representation of AA women in our Gynecologic Cancer Risk Assessment Clinic is unlikely to be explained by disease incidence in this population. During the study period, out of a total of 5706 cases of breast cancer treated at our institution, 1417 (24%) occurred in AA women. Similarly, 312 (20%) of the 1509 cases of ovarian cancer treated occurred in AA women. While AA women comprise 25% of breast and 20% of ovarian cancers managed in our institution, they represent a disproportionately small number of women undergoing genetic evaluation for hereditary cancers in our clinic. This underrepresentation may perhaps be explained by a variety of reasons, including: poor access to health care, under identification of referral indications, or lack of patient or provider education on importance of genetic counseling/testing. Moreover, universal germline testing was not the standard of care throughout the study period. As previously discussed, AA women are less likely than white women to develop ovarian cancer, so another possibility is that a lower percentage of AA women meet criteria for referral; however, the fact that the pathogenic variant rates are similar to white women in those tested suggest that these women may represent an enriched sample. If we are testing only the highest risk women, we are likely not capturing many women, including AA, in whom genetic testing is warranted, thereby preventing adequate genetic counseling and potential risk reducing interventions from occurring.

Though overall pathogenic mutation rates were similar between AA women and white women, the distribution between *BRCA1* and *BRCA* 2 pathogenic mutations were different. When a mutation was present, AA women were more likely to harbor a *BRCA2* mutation. Of 22 identified pathogenic *BRCA* mutations in AA women, 14 were *BRCA2* (63.6%) compared to 84 of 206 pathogenic *BRCA* mutations in white women (40.8%). As mentioned previously, small series of AA women with breast cancer have shown a relatively comparable proportions of *BRCA1* and *BRCA 2* mutations. However, our study is notable

for a higher overall mutation rate as well as a larger proportion of *BRCA2* mutations in AA women.

Of the AA women referred to our clinic, rates of genetic testing were comparable to white women, potentially signifying that barriers to genetic counseling may be overcome when evaluated in a dedicated clinic. However, this counseling is of course limited to those we are able to capture in our clinic, and multifactorial barriers to genetic counseling can be difficult to identify and overcome, though some studies are investigating this further. Data suggest that among AA women, those with greater perceived benefit of genetic testing, higher income, and higher risk of pathogenic *BRCA* variants are more likely to undergo testing [18]. Additionally, older age may be associated with lower receipt of physician recommendation [19].

Though somewhat limited in scope, this study presents important descriptive characteristics of a very large cohort of AA women evaluated for potential hereditary breast and/or ovarian cancer predisposition. Additional studies are needed to further evaluate referral patterns for AA women at risk for these cancer syndromes. Examining referral indication and referring provider specialty more closely may help to further elucidate the cause of this potential under referral of AA women to genetic counseling.

This study adds to the limited body of literature on AA women and hereditary breast and/or cancer syndromes. We noted that these women appear to be underrepresented in genetic counseling centers even in areas of the country where they represent significant proportions of the population. When referred, these women have high rates of genetic testing uptake, enabling both the identification and exclusion of identifiable pathogenic variants. High pathogenic variant rates in those tested suggest we are currently testing only the highest risk patients and may not be capturing many women in whom testing is indicated. Barriers to genetic referral are complex and poorly understood, but promising opportunities exist for further analysis and study. Endeavors should continue to identify minorities at risk for hereditary cancer syndromes including those with an increased risk of ovarian cancer and institute measures to provide thorough genetic counseling and testing. Further understanding of referral patterns may help to elucidate targets for interventions that can help to overcome genetic testing and counseling disparities. As many primary care and gynecology providers routinely refer patients for breast cancer screening, targeting and educating breast health providers may offer an opportunity to increase appropriate referrals of AA women to genetic counseling. Multidisciplinary clinics may assist in overcoming access to care disparities and time burden for patients requiring multiple visits and evaluations. Endeavors should continue to identify minorities at risk for hereditary cancer syndromes including those with an increased risk of ovarian cancer and institute measures to provide thorough genetic counseling and testing

Acknowledgments

Grant Support: CAL was supported in part by the NIH 5K12HD001258-14, 3P30CA013148-43S3 and U10CA18055.

Funding Support: Funding was also provided by both the Lynne Cohen Foundation as well as the Norma Livingston Ovarian Cancer Foundation

References

1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017; 67(1):7–30. [PubMed: 28055103]
2. Walsh T, et al. Mutations in 12 genes for inherited ovarian, fallopian tube, and peritoneal carcinoma identified by massively parallel sequencing. Proc Natl Acad Sci U S A. 2011; 108(44):18032–7. [PubMed: 22006311]
3. Norquist BM, et al. Inherited Mutations in Women With Ovarian Carcinoma. JAMA Oncol. 2016; 2(4):482–90. [PubMed: 26720728]
4. Minion LE, et al. Hereditary predisposition to ovarian cancer, looking beyond BRCA1/BRCA2. Gynecol Oncol. 2015; 137(1):86–92. [PubMed: 25622547]
5. Tung N, et al. Frequency of mutations in individuals with breast cancer referred for BRCA1 and BRCA2 testing using next-generation sequencing with a 25-gene panel. Cancer. 2015; 121(1):25–33. [PubMed: 25186627]
6. Desmond A, et al. Clinical Actionability of Multigene Panel Testing for Hereditary Breast and Ovarian Cancer Risk Assessment. JAMA Oncol. 2015; 1(7):943–51. [PubMed: 26270727]
7. Marchetti C, et al. Risk-reducing salpingo-oophorectomy: a meta-analysis on impact on ovarian cancer risk and all cause mortality in BRCA 1 and BRCA 2 mutation carriers. BMC Womens Health. 2014; 14:150. [PubMed: 25494812]
8. Collins Y, et al. Gynecologic cancer disparities: a report from the Health Disparities Taskforce of the Society of Gynecologic Oncology. Gynecol Oncol. 2014; 133(2):353–61. [PubMed: 24406291]
9. Albain KS, et al. Racial disparities in cancer survival among randomized clinical trials patients of the Southwest Oncology Group. J Natl Cancer Inst. 2009; 101(14):984–92. [PubMed: 19584328]
10. Srivastava SK, et al. Racial health disparities in ovarian cancer: not just black and white. J Ovarian Res. 2017; 10(1):58. [PubMed: 28931403]
11. Chornokur G, et al. Global ovarian cancer health disparities. Gynecol Oncol. 2013; 129(1):258–64. [PubMed: 23266352]
12. Armstrong K, et al. Racial differences in the use of BRCA1/2 testing among women with a family history of breast or ovarian cancer. Jama. 2005; 293(14):1729–36. [PubMed: 15827311]
13. Forman AD, Hall MJ. Influence of race/ethnicity on genetic counseling and testing for hereditary breast and ovarian cancer. Breast J. 2009; 15(Suppl 1):S56–62. [PubMed: 19775331]
14. Pal T, et al. BRCA sequencing and large rearrangement testing in young Black women with breast cancer. J Community Genet. 2014; 5(2):157–65. [PubMed: 24013928]
15. Pal T, et al. Early onset breast cancer in a registry-based sample of African-american women: BRCA mutation prevalence, and other personal and system-level clinical characteristics. Breast J. 2013; 19(2):189–92. [PubMed: 23320992]
16. Greenup R, et al. Prevalence of BRCA mutations among women with triple-negative breast cancer (TNBC) in a genetic counseling cohort. Ann Surg Oncol. 2013; 20(10):3254–8. [PubMed: 23975317]
17. Lee R, et al. Recruitment, genetic counseling, and BRCA testing for underserved women at a public hospital. Genet Test. 2005; 9(4):306–12. [PubMed: 16379544]
18. Jones T, et al. Predictors of BRCA1/2 genetic testing among Black women with breast cancer: a population-based study. Cancer Med. 2017
19. Thompson HS, et al. Receipt of genetic counseling recommendations among black women at high risk for BRCA mutations. Genet Test Mol Biomarkers. 2012; 16(11):1257–62. [PubMed: 23057569]

Research Highlights

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

Table 1

Characteristics of African American Women Evaluated from 2003–2015 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)

Table 2

Gene	Pathogenic Variant*	Type of Genetic Test
BRCA1 (N=8)		
Mutation 1	c.5251C>T (p.Arg1751Ter)	BRCA 1/2 Only
Mutation 2	c.824_825ins10 (p.?)	BRCA 1/2 Only
Mutation 3	c.5096G>A (p.Arg1699Gln)	BRCA 1/2 Only
Mutation 4	5236delG	BRCA 1/2 Only
Mutation 5	3785del4	BRCA 1/2 Only
Mutation 6	c.5324T>G (p.Met1775Arg)	Site Specific
Mutation 7	c.4603G>T (p.Glu1535Ter) Heterozygous duplication of exons 17/18	BRCA 1/2 Only
Mutation 8	BRCA1	BRCA 1/2 Only
BRCA2 (N=14)		
Mutation 1	c.7485dupT (p.Lys2496Terfs)	Site Specific
Mutation 2	8403delG	BRCA 1/2 Only
Mutation 3	c.2830A>T (p.Lys944Ter)	BRCA 1/2 Only
Mutation 4	U43746.1:n.886_887delGC	BRCA 1/2 Only
Mutation 5	c.2830A>T (p.Lys944Ter)	Panel
Mutation 6	3635ins>100bp	Site Specific
Mutation 7	3678insT	BRCA 1/2 Only
Mutation 8	c.2830A>T (p.Lys944Ter)	
Mutation 9	c.7485dupT (p.Lys2496Terfs)	BRCA 1/2 Only
Mutation 10	c.7485dupT (p.Lys2496Terfs)	Site Specific
Mutation 11	Exact pathogenic variant unknown	Unknown¶
Mutation 12	Exact pathogenic variant unknown	Unknown¶
Mutation 13	c.7485dupT (p.Lys2496Terfs)	Site Specific
Mutation 14	8403delG	BRCA 1/2 Only
PALB2 (N=2)		
Mutation 1	c.3048 delT (p.Phe1016Leufs)	Panel
Mutation 2	c.3048 delT (p.Phe1016Leufs)	Panel
MLH1 (N=1)		
Mutation 1	Hypemethylation of MLH1	Panel
ATM (N=1)		
Mutation 1	c.2921+1G>A	Panel

*Variant nomenclature may vary due to inter-lab reporting differences

¶Predicted to be BRCA1/2 testing only based on timing of test performance