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The Impact of Mental Illness on Uptake of Genetic Counseling for Hereditary Breast Cancer and Ovarian Cancer in a Multiethnic Cohort of Breast Cancer Patients

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Abstract

We evaluated whether mental illness is a barrier to genetic counseling for hereditary breast and ovarian cancer (HBOC) in multiethnic breast cancer patients. We conducted a retrospective analysis of 308 women with newly diagnosed breast cancer and eligible for HBOC genetic testing seen in the breast clinic of an academic, urban medical center from 2007 to 2015. Uptake of genetic services and history of mental health disorder (MHD), defined as a psychiatric diagnosis or treatment with an antidepressant, mood stabilizer, anxiolytic, or antipsychotic medication, were ascertained by medical chart review. The mean age at breast cancer diagnosis was 56 years, with 44% non-Hispanic whites, 37% Hispanics, and 15% non-Hispanic blacks. Ninety-nine (32%) women met study criteria for MHD, 73% had a genetics referral, 57% had genetic counseling, and 54% completed *BRCA* testing. Uptake of genetic counseling services did not differ by race/ethnicity or presence of MHD. In multivariable analysis, younger age at diagnosis, Ashkenazi Jewish heritage, and family history of breast cancer were associated with HBOC genetic counseling. A relatively high proportion of breast cancer patients eligible for HBOC genetic testing were referred to a genetic counselor and referral status did not vary by MHD or race/ethnicity.

Keywords

anxiety; *BRCA* genetic testing; breast cancer; depression

BACKGROUND

Breast cancer confers significant morbidity and mortality, and germline mutations in the *BRCA1* and *BRCA2* genes confer the greatest impact on breast cancer risk. An estimated 2–7% of breast cancers result from inherited mutations in *BRCA1* and *BRCA2* (1). For women with hereditary breast and ovarian cancer (HBOC) syndrome, risk management options include intensive screening with mammography and breast MRI (2,3), risk-reducing

surgeries (prophylactic mastectomy, bilateral salpingo-oophorectomy) (4,5), and chemoprevention (6), which improve early detection and reduce cancer incidence and mortality (7). Counseling, screening, and preventive measures associated with *BRCA* testing have also been shown to improve the quality of life, reduce psychological distress about cancer, and increase the accuracy of risk perception and knowledge about genetics (8).

Guidelines for genetic screening have been published by the National Comprehensive Cancer Network (NCCN) (9). Although the prevalence of *BRCA* mutations is similar across the U.S. ethnic groups (except for Ashkenazi Jews), genetic counseling is less likely to occur among non-white women and those with lower educational and income levels (10,11). Furthermore, women from racial/ethnic minorities are less likely to seek breast cancer preventive care (12,13), contributing to their higher rates of late stage diagnosis and poorer clinical outcomes (11,14,15). Additionally, while it is well-documented that psychiatric illness negatively affects adherence to a broad range of medical recommendations (16,17,18), including mammography (19,20–23), psychiatric history has not been studied as a predictor of genetic testing uptake. Mentally ill patients are also underrepresented in genetic testing studies (24–27). We aimed to evaluate whether psychiatric illness poses a barrier to genetic counseling for HBOC.

METHODS

From 2007 to 2015, 1313 women with newly diagnosed breast cancer seen by a medical or surgical oncologist at Columbia University Medical Center (CUMC), New York, NY, were approached for enrollment in a prospective research database. Participants completed a self-administered questionnaire in English or Spanish on demographics (age, race/ethnicity, Ashkenazi Jewish heritage, education, annual household income) and breast cancer risk factors (parity, menopausal status, first or second-degree family history of breast or ovarian cancer), and consented to allow investigators to access their electronic health record (EHR) for future research. Breast cancer stage and tumor characteristics were ascertained from the EHR. Subjects were classified as having a history of a mental health disorder (MHD) if their medical record indicated either a specific psychiatric diagnosis or treatment with an antidepressant, mood stabilizer, anxiolytic, or antipsychotic medication. Prescriptions for hypnotics alone or for psychotropic medication for a non-psychiatric indication (such as benzodiazepines for nausea) were excluded. Uptake of genetics referral, genetic counseling, and *BRCA* testing was determined by review of outpatient records of the medical/surgical oncologists and genetic counselors as well as documentation of genetic test results. This study protocol was approved by the CUMC Institutional Review Board.

We used multivariable logistic regression to assess whether MHD, age at breast cancer diagnosis, menopausal status, race/ethnicity, Ashkenazi Jewish heritage, education, parity, annual household income, family history of breast or ovarian cancer, or stage of breast cancer were associated with uptake of genetic counseling. Sociodemographic and clinical characteristics were compared according to genetic counseling uptake and analyzed using Chi-square or Fisher's exact test. Univariate and multivariable analyses were conducted using logistic regression to identify covariates significantly associated with the genetic counseling uptake. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for

each covariate using the regression model, and p-trend was reported using Wald chi-square test. The multivariable logistic regression model was adjusted using the following covariates: age, Ashkenazi Jewish heritage, education, family history, and stage of breast cancer. The majority of variables were selected for inclusion based on their significance in bivariate analysis. All variables with a p-value of less than 0.05 were included in the final model. Remaining variables were removed if they were non-significant and did not change any remaining parameter estimates by more than 10%. Referral for testing was not included in the final model, as this variable was highly correlated with genetic counseling and therefore biased all other variable parameter estimates towards the null. All statistical analysis was conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

From 2007 to 2015 (Fig. 1), 1313 women with newly diagnosed breast cancer were enrolled and 348 (26.5%) met NCCN guidelines for *BRCA* genetic testing (8). We excluded 37 patients with missing data and 3 who had family members who had negative HBOC genetic testing. The remaining 308 women were included in our analysis. Our sample was racially and ethnically diverse with 44% non-Hispanic white, 37% Hispanic, and 15% non-Hispanic black women, and included 8% Ashkenazi Jews (Table 1). Nearly a third met the study criteria for a history of MHD. The majority of patients with MHD had a history of a mood ($n = 74$) or anxiety disorder ($n = 25$) and several had an adjustment disorder ($n = 4$), substance use disorder ($n = 4$), or psychotic disorder ($n = 5$). Antidepressants ($n = 74$), benzodiazepines ($n = 53$), and hypnotics ($n = 30$) were the most commonly prescribed medications though several patients were taking antipsychotics ($n = 14$), mood stabilizers ($n = 3$), or stimulants ($n = 3$).

Of the 308 women with newly diagnosed breast cancer and eligible for HBOC genetic testing, 225 (73%) had a documented genetics referral, 175 (57%) completed a genetics consultation, and 167 (54%) had *BRCA* testing. Of the 8 patients who sought counseling but did not complete testing, 6 were declined insurance coverage. All of the women who underwent genetic testing were seen by a genetic counselor. In multivariable analysis (Table 2), younger age at diagnosis, Ashkenazi Jewish heritage, first or second-degree family history of breast or ovarian cancer, and early breast cancer stage were significantly associated with genetic counseling. Compared with women 65 years or older, those who were less than 45 were 9.5 times as likely to receive genetic counseling ($p < 0.001$). Those of Ashkenazi Jewish heritage were five times as likely to get genetic counseling (OR = 5.20, 95% CI: 1.40–19.26, $p = 0.014$). Women with a family history of breast or ovarian cancer were more likely to receive genetic counseling compared with those without a family history (OR = 2.24, 95% CI: 1.19–4.23, $p = 0.013$). Of the demographic variables, only race was significantly associated with MHD ($p = 0.0073$). The prevalence of MHD was 38.7% for non-Hispanic white women, 31.0% for Hispanics, 20.0% for non-Hispanic blacks, and 15.4% for others. However, in multivariable analyses, race/ethnicity and MHD were not associated with HBOC genetic counseling.

CONCLUSIONS

In this retrospective study, 57% of patients meeting NCCN guidelines for *BRCA* testing completed genetic counseling for HBOC. The rate of uptake of genetic counseling in our population was higher than in many other described populations (e.g., 7.325.1% in the Geneva Cancer registry) (28). The relatively high rate of uptake of genetic services likely relates to the fact that our subjects all had a prior cancer diagnosis and were receiving treatment at a tertiary care cancer center, reflecting a tendency towards follow-through on indicated health care recommendations. Mental illness did not negatively affect the uptake of genetic counseling. The relatively high overall uptake of genetic counseling may have limited our ability to detect a relationship between mental illness and genetic testing behavior. While other studies have indicated disparities in genetic counseling uptake among racial/ethnic minority groups and patients with lower household income (10,11), these factors did not significantly impact uptake of genetic counseling in our study. Consistent with prior studies, younger patients and those with less advanced cancers were more likely to seek genetic counseling services (10,28).

While we did not find an association between mental illness history and uptake of genetic counseling, we were not able to account for severity of mental illness or to assess for potential differences in uptake based on specific psychiatric diagnoses due to small numbers. In a recent meta-analysis of mammography uptake, Mitchell et al. found that patients with more severe mental illness were less likely to comply with recommended breast cancer screening; however, this disparity was not apparent among patients with distress alone (23). Additionally, prior work has shown an association between medical non-adherence and depression, but not anxiety (29). Individuals with anxiety or adjustment disorder may not differ from the general population in terms of genetic counseling behaviors, or might even be more likely to seek these services.

Strengths of our study include the racial and socioeconomic diversity of the sample and the detailed clinical information from the EHR complemented with self-report data. Our 57% genetic counseling uptake rate is high compared with rates in previous studies, perhaps reflecting relatively easy access to genetic counseling services at our academic medical center.

Since this study was conducted at a single urban academic institution, our results may not be generalizable to other settings. Other limitations of our study include the retrospective design for ascertaining the history of mental disorder and referral to genetics via the EHR, and limiting the sample to women with an established breast cancer diagnosis.

Documentation of mental illness and discussion of genetic counseling might be incomplete. Chart review did not provide adequate information to determine the date of MHD diagnosis and breast cancer diagnosis or receipt of genetic counseling/testing. Therefore, we cannot assess the temporality of events, and whether MHD diagnosis predated opportunity to discuss genetic counseling.

In conclusion, mental health disorder history was not associated with reduced uptake of HBOC genetic counseling in this cohort of women with breast cancer. Future work should

aim to further clarify barriers to uptake of genetic counseling services among both women with breast cancer and high-risk women.

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Figure 1.
Study population.

Table 1.
Sociodemographic and Clinical Characteristics Related to Receiving Genetic Counseling Among Eligible Women Who Have Been Diagnosed With Stage 0–4 Breast Cancer (N = 308)

Characteristic	Missing data n (%)	No genetic counseling (N = 133, 43%) n (%)	Yes genetic counseling (N = 175, 57%) n (%)	Total (N = 308) n (%)	p-value
Age, years					
<45		8 (6.0)	32 (18.3)	40 (13.0)	0.018
45–54		64 (48.1)	73 (41.7)	137 (44.5)	
55–64		29 (21.8)	32 (18.3)	61 (19.8)	
65+		32 (24.1)	38 (21.7)	70 (22.7)	
Mean (SD)		57.7 (11.1)	55.2 (12.4)	56.3 (11.9)	0.061
Menopausal status					
Premenopausal	35 (11)	53 (44.9)	80 (51.6)	133 (48.7)	0.273
Postmenopausal		65 (55.1)	75 (48.4)	140 (51.3)	
Race/ethnicity					
Non-Hispanic white		55 (41.3)	82 (47.7)	137 (44.5)	0.215
Non-Hispanic black		24 (18.05)	21 (12.00)	45 (14.6)	
Hispanic		46 (34.6)	67 (38.3)	113 (36.7)	
Other		8 (6.0)	5 (2.86)	13 (4.2)	
Ashkenazi Jewish					
No		130 (97.7)	154 (88.0)	284 (92.2)	0.002
Yes		3 (2.3)	21 (12.0)	24 (7.8)	
Education					
High school or less	27 (9)	50 (42.0)	45 (27.8)	95 (33.8)	0.013
College or more		69 (58.0)	117 (72.2)	186 (66.2)	
Nulliparous					
No		106 (79.9)	147 (84.0)	253 (82.1)	0.329
Yes		27 (20.3)	28 (16.0)	55 (17.9)	
Annual family income					
\$0–\$30,000	60 (19)	38 (36.9)	60 (41.4)	98 (39.5)	0.690
\$30,001–\$100,000		40 (38.8)	49 (33.8)	89 (35.9)	
\$100,000+		25 (24.3)	36 (24.8)	61 (24.6)	

Characteristic	Missing data n (%)	No genetic counseling (N = 133, 43%) n (%)	Yes genetic counseling (N = 175, 57%) n (%)	Total (N = 308) n (%)	p-value
Family history of breast or ovarian cancer					
No		62 (46.6)	62 (35.4)	124 (40.3)	0.047
Yes		71 (53.4)	113 (64.6)	184 (59.7)	
Stage of breast cancer					
0		17 (12.8)	26 (14.9)	43 (14.0)	0.020
1		36 (27.1)	61 (34.9)	97 (31.5)	
2		46 (34.6)	68 (38.9)	114 (37.0)	
3		25 (18.8)	12 (6.9)	37 (12.0)	
4		9 (6.8)	8 (4.6)	17 (5.5)	
Mental health disorder					
No		88 (66.2)	121 (69.1)	209 (67.9)	0.579
Yes		45 (33.8)	54 (30.9)	99 (32.1)	
Genetic testing					
No		133 (100.0)	8 (4.6)	141 (45.8)	<0.0001
Yes		0 (0.00)	167 (95.4)	167 (54.2)	
Referral for testing					
No		79 (59.4)	4 (2.3)	83 (26.9)	<0.0001
Yes		54 (40.6)	171 (97.7)	225 (73.1)	

Bold values are statistically significant.

Logistic Regression Univariate and Multivariable Analysis of Variables Related to Receiving Genetic Counseling Among Eligible Women Diagnosed with Breast Cancer Stage 0–4 ($N=308$)

Characteristic	n (%)	Univariate analysis		Multivariable analysis	
		Odds ratio (95% confidence interval)	p-value	Adjusted odds ratio (95% confidence interval)	p-value
Age					
<45		3.37 (1.36–8.34)	0.027	9.59 (3.01–30.50)	0.001
45–54		0.96 (0.54–1.71)		2.07 (0.96–4.45)	
55–64		0.94 (0.47–1.85)		0.99 (0.45–2.17)	
65+		Reference		Reference	
Menopausal status					
Premenopausal	35 (11)	1.31 (0.81–2.12)	0.273		
Postmenopausal		Reference			
Race and ethnicity					
Non-Hispanic white		Reference	0.225		
Non-Hispanic black		0.59 (0.30–1.16)			
Hispanic		0.98 (0.59–1.62)			
Other		0.42 (0.13–1.35)			
Ashkenazi Jewish					
No		Reference	0.005	Reference	0.014
Yes		5.91 (1.73–20.26)		5.20 (1.40–19.26)	
Education					
High school or less	27 (9)	0.53 (0.32–0.88)	0.013	0.68 (0.39–1.18)	0.168
College or more		Reference		Reference	
Nulliparous					
No		Reference	0.330		
Yes		0.75 (0.42–1.34)			
Annual family income					
\$0–\$30,000	60 (19)	Reference	0.691		
\$30,001–\$100,000		0.78 (0.43–1.39)			
\$100,000+		0.91 (0.48–1.75)			

Characteristic	n (%)	Univariate analysis		Multivariable analysis	
		Odds ratio (95% confidence interval)	p-value	Adjusted odds ratio (95% confidence interval)	p-value
Family history of breast cancer					
No		Reference	0.048	Reference	0.013
Yes		1.59 (1.00–2.52)		2.24 (1.19–4.23)	
Stage of breast cancer					
0		0.90 (0.43–1.89)	0.027	0.85 (0.38–1.91)	0.052
1		Reference		Reference	
2		0.87 (0.50–1.52)		0.61 (0.32–1.18)	
3		0.28 (0.13–0.63)		0.24 (0.09–0.63)	
4		0.53 (0.19–1.48)		0.57 (0.17–1.90)	
Mental health disorder					
No		Reference	0.580		
Yes		0.87 (0.54–1.41)			

Bold values are statistically significant.