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High Incidence of Germline BRCA Mutation in Patients with ER low positive/PR low positive/HER-2 neu negative Tumors

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Abstract

Purpose—2015 NCCN guidelines recommend genetic counseling and germline BRCA mutation testing be offered to women under age 60 with triple negative breast cancer (TNBC). As a result of the 2010 ASCO/CAP guidelines in breast cancer, patients with breast cancers that are ER or PR low-positive (1–9% on immunohistochemistry) are no longer strictly considered to have TNBC and may not be referred for genetic counseling. However, the incidence of BRCA mutation in patients with hormone receptor (HR) low-positive breast cancers remains unknown, and current ASCO/CAP guidelines may result in under-testing for BRCA mutation.

Methods—We reviewed a prospectively maintained research database of breast cancer patients evaluated at UT MD Anderson Cancer Center between 2004 and 2014, identifying 314 patients with ER<10%, PR<10%, HER-2 neu negative breast cancers with known BRCA mutation status.

Results—314 patients had breast cancers expressing ER and PR <10%; 238 (75.8%) had HR negative (ER and PR <1%) cancers and 76 (24.2%) had HR low-positive (ER and/or PR 1–9%) cancers. Among patients with HR negative tumors, 86 of 238 (36.1%) had a BRCA 1/2 mutation, while among the HR low-positive group, 30 of 76 (39.5%) had a BRCA 1/2 mutation. In multivariate analysis, HR status (HR<1% vs. HR 1–9%) was not significantly associated with BRCA 1/2 mutation.

Conclusion—The incidence of BRCA 1/2 mutation is similar in patients with HR low-positive and HR negative breast cancers. We recommend offering genetic counseling and BRCA testing to patients under age 60 with ER low-positive breast cancers.

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Keywords

Triple negative breast neoplasms; Genes; BRCA1; Genes; BRCA2; Immunohistochemistry; Genetic Counseling

Introduction

Germline BRCA1 and BRCA2 mutations, which confer an increased lifetime risk of breast and ovarian cancers, are frequently associated with triple negative breast cancers (TNBC).[1] Among patients with TNBC, the incidence of BRCA1/2 mutation is estimated to range from 11–37%[2–5] with higher rates reported in younger patients, compared with BRCA1 and BRCA2 mutation rates of <1–7% and 1–3% respectively, for breast and ovarian cancer patients unselected for age, cancer subtype and family history.[6] Accordingly, current National Comprehensive Cancer Network (NCCN) guidelines recommend all patient under age 60 with TNBC be referred for genetic counseling and consideration of BRCA testing.[7]

In 2010 the American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP) issued an updated guideline on immunohistochemical (IHC) testing of ER and PR in breast cancer which included a recommendation that adjuvant endocrine therapy be considered for all patients with tumors expressing ER ≥ 1%.[8] This was informed by the evolving understanding of breast cancer subtypes provided by tissue microarray analysis,[9] and in part by the robust body of evidence demonstrating improved outcomes in patients with strongly hormone receptor positive breast cancer who received adjuvant endocrine therapy.[10] In making this recommendation, the 2010 ASCO/CAP guideline effectively redefined triple negative breast cancer to include only those tumors expressing ER <1% and PR <1%. However in practice, considerable debate continues regarding what ER and PR percentage defines a hormone receptor (HR) positive tumor.

Early studies demonstrating the benefit of endocrine therapy in HR positive breast cancers used ligand binding assays (LBA) to assess ER status, with ER values expressed in fmol/mg. Historically, a value ≥ 10 fmol/mg was used to define ER positivity.[11] While IHC has now replaced LBA, no nomogram exists that allows the conversion of LBA values to IHC values. This makes extrapolation of the results of early studies at the lower limits of estrogen positivity particularly difficult.

HR low-positive breast cancer is relatively rare, and its response to endocrine therapy has been assessed mostly in subset analyses of larger trials. A 2011 paper reporting the influence of tamoxifen on breast cancer outcomes stratified by ER positivity assessed by both LBA and IHC showed no benefit to adjuvant endocrine therapy in patients with 1–9% ER positive tumors. Of note, despite the inclusion of 683 patients in this trial, only 7 had breast cancers that were 1–9% ER positive, reflecting the difficulty of systematic analysis of this relatively rare breast cancer subtype.[12]

The debate surrounding the definition of ER positivity has been further fueled by recent data suggesting that ER low-positive tumors often express the basal-like molecular phenotype associated with TNBC, rather than the luminal phenotype associated with hormone-receptor

positive breast cancer.[13–15] Emerging data also suggests worse overall survival in patients with ER low-positive tumors compared to those with ≥ 10% ER-positive tumors.[16,17]

Women with HR low-positive tumors, who as a result of the 2010 ASCO/CAP guideline are now considered to have HR positive breast cancer, may not be referred for genetic counseling and BRCA testing. This may be causing inappropriate "under-testing" for BRCA mutations in this population. We sought to identify the incidence of deleterious germline BRCA mutation in patients with HR low-positive tumors, hypothesizing that it would be comparable to the incidence in patients with HR negative tumors.

Methods

We reviewed a prospectively maintained research database of all patients with a diagnosis of breast cancer referred for genetic counseling and testing at The University of Texas MD Anderson Cancer Center between February 2004 and May 2014. We identified patients with ER<10% PR <10% HER-2 neu negative breast cancers with known BRCA test results. All external pathology was reviewed at our institution; where external pathology and internal pathology reports differed, internal pathology was used. Only pathology reports that included a numerical value for percent ER staining were used. Where HER-2 neu IHC and fluorescent in situ hybridization (FISH) were both available, FISH was used to make a final determination of HER-2 neu status. In patients who received neoadjuvant chemotherapy and had both pre- and post-chemotherapy tissue with ER and PR status, the pre-chemotherapy specimen was used. The study was approved by our center's Institutional Review Board.

Statistical Methods

All variables of interest were summarized using descriptive statistics, including mean (standard deviation (SD)) for continuous variables and frequency (percent) for categorical variables. Patient characteristics were summarized according to ER status and BRCA mutation status. Two groups with ER and PR <1% and with ER and/or PR 1–9% were compared in each variable. Two sample t-test or Wilcoxon rank-sum test were used for continuous variables and Chi-square test or Fisher's exact test were used for categorical variables. Univariate and multivariate logistic regression models were fitted considering BRCA mutation status (BRCA mutation versus no BRCA mutation) as a response variable and other patient characteristics as predictor variables. A p-value of less than 0.05 indicated statistical significance. SAS 9.4 (SAS Institute INC, Cary, NC) was used for data analysis.

Cohort Determination

We identified 526 patients with ER<10% PR <10% HER-2 neu negative breast cancers who underwent genetic testing for deleterious BRCA mutation. We excluded 160 patients whose ER or PR status was not quantified (i.e., reported only as "negative" or "low-positive), 22 patients with p53 mutations or BRCA mutations of unknown significance, 19 patients with ductal carcinoma in site (DCIS) without invasive breast cancer, and 11 patients with a second breast cancer that was ER/PR positive or HER-2 neu positive, leaving 314 patients with ER<10% PR <10% HER-2 neu negative breast cancers with informative BRCA test results.

Results

Patient and tumor characteristics are summarized in Table 1. Median age at diagnosis was 44 years (range 22–76 years); only 25 patients (8.0%) were ≥ 60 years old at the time of diagnosis. Nine patients (2.9%) had a personal history of ovarian cancer, 99 (31.6%) had a first degree relative with breast cancer, and 31 (9.9%) had a first degree relative with ovarian cancer. Two hundred and ninety-six patients (94.3%) presented with stage I-III breast cancer, 16 patients (5.1%) with stage IV breast cancer, and two patients had unknown stage. Ninety four patients with BRCA1 mutations were identified, and 22 patients with BRCA2 mutations were identified. There was a trend toward younger age at diagnosis in the HR low-positive group compared with the HR negative group. Family history of breast or ovarian cancer, personal history of ovarian cancer, race, and stage did not vary significantly between the HR negative and HR low-positive groups. Two hundred and thirty-eight patients (75.8%) had tumors that were HR negative (ER and PR <1%), while 76 patients (24.2%) had tumors that were HR low-positive. The HR low-positive group included 59 patients with ER 1–9% and PR<1% tumors, 15 patients with ER 1% and PR 1–9% tumors, and 11 patients with ER 1–9% and PR 1–9% tumors. Among the HR negative group, 86 of 238 (36.1%) had a BRCA mutation, while among the HR low-positive group, 30 of 76 (39.5%) had a BRCA mutation. There was no significant difference in the rate of BRCA mutation between the two groups (p = 0.60). Univariate analysis is summarized in Table 2. In univariate analysis, younger age at diagnosis of breast cancer (OR (95% CI), 0.98 (0.95–1.00)), personal history of ovarian cancer (14.58 (1.80–118.03)), first degree relatives with breast cancer (3.21 (1.95–5.27)), any relatives with breast cancer (1.89 (1.07–3.35)), first degree relatives with ovarian cancer (4.97 (2.20–11.21)), and any relatives with ovarian cancer (4.53 (2.67–7.70)) were associated with increased odds of BRCA mutation.

Multivariable logistic regression analysis is summarized in Table 3. In multivariate analysis age, personal history of ovarian cancer, having a first degree relative with breast cancer, and having any relative with ovarian cancer showed significant associations with BRCA mutation stats. After adjusting for age, personal history of ovarian cancer, first degree relatives and all relatives with breast cancer, first degree relatives and all relatives with ovarian cancer, race and stage, HR status (ER and PR <1% vs. ER and/or PR 1–9%) was not significantly associated with BRCA mutation.

Discussion

Our study demonstrates a comparable incidence of deleterious germline BRCA mutation in patients with HR low-positive and HR negative breast cancers. These results confirm our hypothesis that only performing genetic counseling and BRCA testing in patients under age 60 with ER <1% PR <1% HER-2 neu negative tumors is likely to result in under-testing for BRCA mutation in patients whose sole indication for BRCA testing is TNBC.

Current NCCN guidelines recommend genetic counseling and germline BRCA testing for patients ≤ 60 years old with TNBC and for patients ≤ 50 years old with a diagnosis of breast cancer, regardless of subtype. Therefore, patients between the ages of fifty-one and sixty with HR low-positive tumors comprise the population most at risk for under-testing due to

HR low-positive status. Our study population included thirteen patients aged 51–60 with HR low-positive tumors; of these thirteen patients, two were identified as BRCA mutation carriers. One patient with an ER low-positive/PR negative tumor was identified as a BRCA1 mutation carrier, and one patient with an ER negative/PR low-positive tumor was identified as a BRCA2 mutation carrier. Therefore in our population, the number needed to test in order to identify one BRCA mutation carrier in women aged 51–60 with HR low-positive tumors was 6.5.

To our knowledge, this is the first study reporting the incidence of BRCA mutation in patients with HR low-positive breast cancers. These results add to the growing body of literature suggesting a biologic difference in ER/PR low-positive (1–9%) vs ER/PR strongly positive (≥10%) breast cancers. Previous studies have documented that the molecular phenotypes of HR 1–9% breast cancers are more in line with HR negative breast cancers than with HR strongly positive breast cancers, as are clinical outcomes.[13,16] The present study should encourage further caution in grouping HR low-positive and HR positive breast cancers in the design of clinical trials and in the treatment of individual patients.

The 2010 ASCO/CAP guidelines recommend that endocrine therapy be considered for breast cancers expressing ER ≥ 1% based on robust data supporting the use of adjuvant endocrine therapy in patients with strongly ER-positive breast cancers including the EBCTCG 2011 meta-analysis, which demonstrated a 39% decrease in recurrence rate after 10 years of adjuvant endocrine for patients with ER-positive breast cancer. Of note, the EBCTCG 2011 meta-analysis analyzed ER by LBA, and demonstrated a benefit for endocrine therapy at ER levels ≥ 10 fmol/mg. No benefit was seen for patients with tumors with ER levels 1–9 fmol/mg. Extrapolating evidence of benefit from this data to patients with tumors that are 1–9% ER positive by IHC is problematic, as strict correlation between LBA and IHC assays is not possible at the lower limits of ER positivity. It has been suggested that an IHC-based Allred score of ≥ 2, corresponding to 1–10% ER staining on IHC, should correspond to LBA values of 10 fmol/g. However, even when this relatively broad range is used, a significant number of samples remain discordant at the lower limit of ER positivity.[18] Other studies have suggested correlating 0.5 fmol/mg ER levels to 10% staining; [19] regardless of the exact value used, a significant number of discordant results remain at the lower threshold of ER positivity, and caution is required when extrapolating data for this patient population.[20–22]

Some patients with ER/PR low-positive breast cancers will have luminal subtype tumors likely to benefit from endocrine therapy, and it remains reasonable to consider adjuvant endocrine therapy in these patients, particularly as these therapies are often well-tolerated. However, the potential benefit of endocrine therapy to a small number of patients with HR low-positive tumors should not come at the expense of under-testing for BRCA, which has been an unintended consequence of the 2010 ASCO/CAP guideline.

Limitations of our study include a relatively small sample size, although our numbers are in keeping with other studies of HR low-positive tumors. Further investigation with larger numbers of patients is warranted. As every patient in our study was seen in a breast cancer genetics clinic, our study is de facto susceptible to ascertainment bias. The pitfalls of

ascertainment bias in studies of BRCA mutation status have been well-documented.[23] Although many patients in our study would have been tested for BRCA regardless of the HR status of their breast cancer due to strong family history or young age, our results nevertheless did not show a significant difference in BRCA rates between the HR negative and HR low-positive groups. Therefore, we may conclude that in patients whose sole indication for BRCA testing is TNBC, a strategy of testing only patients with ER and PR <1% tumors may results in under-testing.

Our study identified 160 patients whose ER/PR status was reported only as “negative” or “low positive” on pathology. Our study extended from 2004 to 2014, with the 2010 ASCO/CAP guidelines being issued in the middle of this period, therefore we felt the clearest results would be obtained by excluding all 160 of these patients, since a patient with ER 5% staining could variably be classified as negative or low-positive depending on when their pathology was reviewed and the rate at which individual pathologists incorporated the guideline into their practice.

Based on these results, we recommend the following modification to NCCN guidelines: genetic counseling and BRCA testing should be considered for all patients under age 60 with ER<10% PR <10% HER-2 neu negative breast cancers. A strategy of testing only patients with ER <1% PR <1% HER-2 neu negative breast cancers will result in under-testing of patients whose primary indication for BRCA testing is TNBC, and failure to make the potentially life-saving diagnosis of deleterious BRCA mutation carrier status, which may have major health implications for both the tested patient and her family members.

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References

1. Atchley DP, Albarracin CT, Lopez A, et al. Clinical and pathologic characteristics of patients with BRCA-positive and BRCA-negative breast cancer. J Clin Oncol. 2008; 26:4282–8. [PubMed: 18779615]
2. Evans DG, Howell A, Ward D, et al. Prevalence of BRCA1 and BRCA2 mutations in triple negative breast cancer. J Med Genet. 2011 Aug; 48(8):520–2. [PubMed: 21653198]
3. Kwon JS, Gutierrez-Barrera AM, Young D, et al. Expanding the criteria for BRCA mutation testing in breast cancer survivors. J Clin Oncol. 2010 Sep 20; 28(27):4214–20. [PubMed: 20733129]
4. Young SR, Pilarski RT, Donenberg T, et al. The prevalence of BRCA1 mutations among young women with triple-negative breast cancer. BMC Cancer. 2009 Mar 19.9:86. [PubMed: 19298662]
5. Chang J, Hilsenbeck SG, Sng JH, Wong J, Ragu GC. Pathological features and BRCA1 mutation screening in premenopausal breast cancer patients. Clin Cancer Res. 2001; 7:1739–42. [PubMed: 11410514]
6. Balmaña J, Díez O, Rubio IT, Cardoso F. ESMO Guidelines Working Group. BRCA in breast cancer: ESMO Clinical Practice Guidelines. Ann Oncol. 2011 Sep; 22(Suppl 6):vi31–4. [PubMed: 21908500]
7. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian. http://www.nccn.org
8. Hammond ME, Hayes DF, Dowsett M, et al. American Society of Clinical Oncology/College Of American Pathologists guideline recommendations for immunohistochemical testing of estrogen

and progesterone receptors in breast cancer. J Clin Oncol. 2010 Jun 1; 28(16):2784–95. [PubMed: 20404251]

9. Sørlie T, Perou CM, Tibshirani R, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci U S A. 2001 Sep 11; 98(19):10869–74. [PubMed: 11553815]
10. Davies C, Godwin J, Gray R, et al. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet. 2011 Aug 27; 378(9793):771–84. [PubMed: 21802721]
11. Fisher ER, Anderson S, Dean S, et al. Solving the dilemma of the immunohistochemical and other methods used for scoring estrogen receptor and progesterone receptor in patients with invasive breast carcinoma. Cancer. 2005 Jan 1; 103(1):164–73. [PubMed: 15565575]
12. Khoshnoud MR, Löfdahl B, Fohlin H, et al. Immunohistochemistry compared to cytosol assays for determination of estrogen receptor and prediction of the long-term effect of adjuvant tamoxifen. Breast Cancer Res Treat. 2011 Apr; 126(2):421–30. [PubMed: 20957430]
13. Iwamoto T, Booser D, Valero V, et al. Estrogen receptor (ER) mRNA and ER-related gene expression in breast cancers that are 1% to 10% ER-positive by immunohistochemistry. J Clin Oncol. 2012 Mar 1; 30(7):729–34. [PubMed: 22291085]
14. Deyarmin B, Kane JL, Valente AL, et al. Effect of ASCO/CAP guidelines for determining ER status on molecular subtype. Ann Surg Oncol. 2013 Jan; 20(1):87–93. [PubMed: 22875649]
15. Foulkes WD, Stefansson IM, Chappuis PO, et al. Germline BRCA1 mutations and a basal epithelial phenotype in breast cancer. J Natl Cancer Inst. 2003; 95:1482–5. [PubMed: 14519755]
16. Yi M, Huo L, Koenig KB, Mittendorf EA, et al. Which threshold for ER positivity? a retrospective study based on 9639 patients. Ann Oncol. 2014 May; 25(5):1004–11. [PubMed: 24562447]
17. Prabhu JS, Korlimarla A, Desai K, et al. A Majority of Low (1–10%) ER Positive Breast Cancers Behave Like Hormone Receptor Negative Tumors. J Cancer. 2014 Jan 23; 5(2):156–65. [PubMed: 24563670]
18. Harvey JM, Clark GM, Osborne CK, Allred DC. Estrogen receptor status by immunohistochemistry is superior to the ligand-binding assay for predicting response to adjuvant endocrine therapy in breast cancer. J Clin Oncol. 1999 May; 17(5):1474–81. [PubMed: 10334533]
19. Pertschuk LP, Kim DS, Nayer K, et al. Immunocytochemical estrogen and progestin receptor assays in breast cancer with monoclonal antibodies. Histopathologic, demographic, and biochemical correlations and relationship to endocrine response and survival. Cancer. 1990 Oct 15; 66(8):1663–70. [PubMed: 2208020]
20. Stierer M, Rosen H, Weber R, et al. Comparison of immunohistochemical and biochemical measurement of steroid receptors in primary breast cancer: evaluation of discordant findings. Breast Cancer Res Treat. 1998 Jul; 50(2):125–34. [PubMed: 9822217]
21. Zafrani B, Aubriot MH, Mouret E, et al. High sensitivity and specificity of immunohistochemistry for the detection of hormone receptors in breast carcinoma: comparison with biochemical determination in a prospective study of 793 cases. Histopathology. 2000 Dec; 37(6):536–45. [PubMed: 11122436]
22. Chebil G, Bendahl PO, Idvall I, Fernö M. Comparison of immunohistochemical and biochemical assay of steroid receptors in primary breast cancer--clinical associations and reasons for discrepancies. Acta Oncol. 2003; 42(7):719–25. [PubMed: 14690157]
23. Goldgar D, Venne V, Conner T, Buys S. BRCA phenocopies or ascertainment bias? J Med Genet. 2007 Aug.44(8):e86. [PubMed: 17673440]

Table 1

Patient and Tumor Characteristics

Variable	ER and/or PR 1–9% (N=76)	ER and PR <1% (N=238)	P-value
Age at Diagnosis of Breast Cancer (BC), mean ± SD	41.5 ± 10.8	44.2 ± 10.6	0.05
Personal History of Ovarian Cancer (OC)			1.00
No	74(97.4%)	231(97.1%)	
Yes	2(2.6%)	7(2.9%)	
First Degree Relatives with BC *			0.18
No	56(74.7%)	158(66.4%)	
Yes	19(25.3%)	80(33.6%)	
Any Relative with BC			0.85
No	19(25%)	57(23.9%)	
Yes	57(75%)	181(76.1%)	
First Degree Relatives with OC			0.85
No	68(90.7%)	214(89.9%)	
Yes	7(9.3%)	24(10.1%)	
Any Relative with OC			0.92
No	56(73.7%)	174(73.1%)	
Yes	20(26.3%)	64(26.9%)	
Race			0.13
Asian	3(3.9%)	9(3.8%)	
Black	14(18.4%)	29(12.2%)	
Hispanic	17(22.4%)	36(15.1%)	
White	41(53.9%)	163(68.5%)	
Other/Unknown	1(1.3%)	1(0.4%)	
Stage **			0.78
1	18(23.7%)	56(23.7%)	
2	39(51.3%)	114(48.3%)	
3	17(22.4%)	52(22%)	
4	2(2.6%)	14(5.9%)	
BRCA Mutation			0.60
Negative	46(60.5%)	152(63.9%)	
Positive	30(39.5%)	86(36.1%)	
BRCA 1, BRCA 2 Mutation			
Negative	46(60.5%)	152(63.9%)	0.79
BRCA 1	25(32.9%)	69(29%)	
BRCA 2	5(6.6%)	17(7.1%)	

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*Complete family history not available for n = 1 patient

**Staging information not available for n = 2 patients

Table 2

Univariate Logistic Regression Analysis for BRCA Mutation

Variable	Odds Ratio (95% CI)	P-value
Age at Diagnosis of Breast Cancer (BC) (years), mean ± SD	0.98 (0.95–1.00)	0.03
Personal History of Ovarian Cancer (OC)		
No	1.00	
Yes	14.58 (1.80–118.03)	0.01
First Degree Relative(s) with BC		
No	1.00	
Yes	3.21 (1.95–5.27)	<0.0001
Any Relative(s) with BC		
No	1.00	
Yes	1.89 (1.07–3.35)	0.03
First Degree Relative(s) with OC		
No	1.00	
Yes	4.97 (2.20–11.21)	<0.001
Any Relative(s) with OC		
No	1.00	
Yes	4.53 (2.67–7.70)	<0.0001
Race		0.14 *
Hispanic	1.00	
White	0.54 (0.29–0.99)	0.05
Black	0.34 (0.14–0.81)	0.02
Asian	0.71 (0.20–2.51)	0.59
Other/Unknown	0.19 (0.004–8.26)	0.39
Stage		0.42 **
I	1.00	
II	0.64 (0.36–1.13)	0.12
III	0.66 (0.34–1.30)	0.23
IV	0.97 (0.33–2.87)	0.95
HR Status		
ER and PR <1%	1.00	
ER and/or PR 1–9%	1.15 (0.68–1.96)	0.60

* Overall significance of race using Logistic Regression

** Overall significance of stage using Logistic Regression

Table 3

Multivariable Logistic Regression for BRCA Mutation

Variable	Adjusted Odds Ratio (95% CI)	P-value
Age at Diagnosis of Breast Cancer (BC) (years), mean ± SD	0.92 (0.90–0.95)	<0.0001
Personal History of Ovarian Cancer (OC)		
No	1.00	
Yes	24.79 (2.66–231.09)	<0.01
First Degree Relative(s) with BC		
No	1.00	
Yes	4.35 (2.22–8.52)	<0.0001
Any Relative(s) with BC		
No	1.00	
Yes	1.51 (0.72–3.15)	0.28
First Degree Relative(s) with OC		
No	1.00	
Yes	2.80 (0.90–8.64)	0.07
Any Relative(s) with OC		
No	1.00	
Yes	4.93 (2.37–10.25)	<0.0001
Race		0.19*
Hispanic	1.00	
White	0.58 (0.27–1.26)	0.17
Black	0.45 (0.16–1.29)	0.14
Asian	1.07 (0.24–4.74)	0.93
Other/Unknown	<0.001 (<0.001->999.99)	0.99
Stage		0.35**
I	1.00	
II	0.529 (0.26–1.06)	0.07
III	0.69 (0.31–1.55)	0.37
IV	0.74 (0.18–3.02)	0.68
HR Status		
ER and PR <1%	1.00	
ER and/or PR 1–9%	1.09 (0.57–2.08)	0.81

* Overall significance of race using Logistic Regression

** Overall significance of stage using Logistic Regression