Published in final edited form as:

Am J Surg. 2020 January ; 219(1): 145–149. doi:10.1016/j.amjsurg.2019.06.012.

Rate of BRCA mutation in patients tested under NCCN genetic testing criteria

Anna C. Beck^a, Haimiao Yuan^a, Junlin Liao^a, Pamela Imperiale^b, Krysten Shipley^a, Lillian M. Erdahl^a, Sonia L. Sugg^a, Ronald J. Weigel^a, Ingrid M. Lizarraga^{a,*}

^aUniversity of Iowa Hospitals and Clinics, 200 Hawkins Drive, Iowa City, IA, 52242, USA

^bUniversity of Iowa Carver College of Medicine, 375 Newton Road, Iowa City, IA, 52242, USA

Abstract

Background: BRCA genetic testing is recommended by the National Comprehensive Cancer Network (NCCN) in breast cancer patients who meet specific criteria. Limited data are available on the likelihood of detecting a mutation when these guidelines are followed.

Methods: A retrospective chart review examined patients with breast cancer who underwent BRCA testing based on NCCN guidelines.

Results: Twelve (6.0%) of the 199 patients had a deleterious BRCA mutation. Family history of BRCA mutations (50%, $p = 0.019$), age ≥ 45 at diagnosis (9.7%, $p = 0.034$) and meeting ≥ 3 NCCN criteria (13.3%, $p = 0.03$) yielded the highest rates of BRCA mutation. Having a family history of BRCA mutation and age ≥ 45 were associated with increased rate of BRCA mutation on multivariate analysis (OR 14.3, CI 1.2–166.3; OR 11.6, CI 1.2–108.6).

Conclusion: Select NCCN criteria are associated with higher rates of BRCA mutations. Waiting for genetic testing results to guide surgical management may be warranted in this subset of patients.

Summary for table of contents

Following NCCN guidelines for BRCA genetic testing in patients with breast cancer yielded a 6.0% detection rate of BRCA mutation. The criteria which yielded the highest rates of BRCA mutation were: family history of BRCA mutations (50%), age ≥ 45 at diagnosis (9.7%) and meeting ≥ 3 NCCN criteria (13.3%). Meeting only one criterion yielded a mutation rate of 2.3%.

Keywords

Breast cancer; BRCA; NCCN; Genetic testing; Family history

*Corresponding author. University of Iowa Hospitals and Clinics Department of Surgery, Rm 4636 JCP, 200 Hawkins Drive, Iowa City, IA, 52242, USA., Ingrid-lizarraga@uiowa.edu (I.M. Lizarraga).

Conflicts of interest

No authors have conflicts of interest to disclose.

Introduction

BRCA1 and *BRCA2* are cancer susceptibility genes with strong links to hereditary breast cancer with reported rates in the overall population of approximately 0.07–0.6%^{1–3} and 2–6% in breast cancer patients.^{4–6} *BRCA* mutations increase a patient's lifetime risk of breast cancer to 41–74%^{2,7,8} and provide a 11–40% risk of having a second, contralateral breast cancer.^{7,9} Genetic testing for *BRCA* is advised by the National Comprehensive Cancer Network (NCCN) in patients who meet one of 7 criteria based on age, sex, breast cancer type, and family history of cancer. Determining whether to recommend testing in individuals with a cancer history requires personalized risk assessment and genetic counseling. If NCCN criteria are met and the patient has undergone appropriate genetic counseling, either targeted *BRCA* or multi-gene testing can be considered.

NCCN criteria for *BRCA1* and *BRCA2* testing are based on previous retrospective studies and large meta-analyses. Specific clinical scenarios with a high risk for *BRCA* mutations have been identified. Breast cancers that do not express estrogen and progesterone receptors and do not overexpress HER2/neu [triple negative breast cancer (TNBC)] have been associated with rates of *BRCA* mutation between 7 and 28%.^{10–12} Men who develop breast cancer have a 4–16% rate of *BRCA2* mutations.¹³ Women who develop breast cancer at a young age (< 45 years old) also have a greater likelihood of *BRCA* mutation.¹⁴ Additionally, family history of specific cancers including pancreatic, prostate, and ovarian cancers are also associated with increased rates of *BRCA* mutation,^{15–17} as is Ashkenazi Jewish ancestry, with a reported 12.5% rate in those with breast cancer.¹⁸ Risk prediction models exist, such as BRCAPRO and BOA-DICEA, which calculate the likelihood of an individual having a *BRCA* mutation and may guide the decision to undergo testing.^{19,20} Both models target a 10% risk of mutation as the threshold for testing. Current practice utilizes national guidelines to select patients for *BRCA* testing rather than requiring patients to meet predictive thresholds based on these models.²¹

Management of breast cancer may significantly change if a *BRCA* mutation is present. Detection of a mutation is ideally completed prior to undergoing definitive cancer management. When a patient with breast cancer undergoes *BRCA* testing, results may take several weeks and delay surgical planning. Delay to therapy in breast cancer has been shown to adversely affect survival outcomes.^{22,23} Anxiety related to a delay in treatment may also in part explain the well-documented association between genetic testing and choice of contralateral prophylactic mastectomy even when the results are negative.^{24,25}

Recent data suggest that expansion of testing may be appropriate^{26,27} but currently NCCN guidelines are the most widely used criteria for testing and inform insurance coverage decisions. Limited data is available regarding the likelihood of detecting a *BRCA* mutation when the NCCN criteria are followed. We hypothesize that certain groups of patients who meet testing guidelines are more likely to have a mutation detected. The present study examines a population of patients with breast cancer at a single institution to determine which indications for *BRCA* testing correlate with higher rates of *BRCA* mutations.

Methods

Study population

After obtaining IRB approval, a retrospective, single institution review identified 363 sequential patients who underwent *BRCA* testing between January 2008 and July 2015. Patients eligible for genetic counseling were identified at a clinic visit or at a multi-disciplinary tumor board. Patients were seen by a genetic counselor and underwent testing based on NCCN guidelines.²¹ Of these 363 patients with *BRCA* testing, 199 patients presented with breast cancer prior to testing and comprised our cohort of interest. Results of mutations other than *BRCA* from panel testing were not examined, as the data were not available for all patients and there is currently a paucity of guidelines regarding surgical management of patients with breast cancer and a non-*BRCA* mutation. Demographic information, reasons for testing, family history, clinical stage, histological stage, hormone receptor status, and decisions in surgical and medical management were collected.

Definition of testing criteria

Of the 13 indications for *BRCA* genetic testing outlined in the NCCN guidelines, 7 criteria were identified that pertained to patients with a diagnosis of cancer (Table 1).²¹ A close relative was defined as any first, second, or third degree relative. Gleason scores for family members with prostate cancer were not available and all reports of close family members with prostate cancer were included. Criteria were first examined individually. Criteria were then separated into three categories of testing: young age (<45 years), family history, and high-risk breast cancer in order to identify whether specific combinations of risk factors were more predictive. Rates for *BRCA* mutations were gathered by individual testing criteria and type of reason for testing.

Genetic testing and variant classification

Patients underwent genetic testing for hereditary breast and ovarian cancer syndrome through analysis of *BRCA1* & *BRCA2* alone or panel-based testing that included analysis *BRCA1* & *BRCA2*. Germline DNA was isolated from peripheral blood or buccal swab and analyzed by a commercial laboratory (Myriad Genetic Laboratories or Invitae). Within this study, positive results were defined as having a pathogenic or likely pathogenic variant in *BRCA1* or *BRCA2*. Negative results were defined as having no variant, a likely benign variant, or a variant of uncertain significance (VUS) in *BRCA1* & *BRCA2*.

Statistical analysis

Variables were examined using Stata 15.1 (StataCorp, College Station, Texas). Chi-square and Fisher's exact test were used to analyze categorical variables. Student t-test and ANOVA were used for continuous variables. Multivariate logistic regression was used to assess confounding variables. Significance was defined using α of 0.05. Variables with *p*-value 0.2 on univariate analysis were included in the backward stepwise multivariate logistic regression.

Results

Demographics

Of the 199 breast cancer patients who underwent testing, 12 had a deleterious *BRCA* mutation detected (6%) and 187 did not (94%). Seven (3.5%) had a *BRCA* VUS detected. Patient demographics are detailed in Table 2. There was no significant difference in age, race, or histologic type. Compared to patients without a *BRCA* mutation, fewer patients with *BRCA* mutations had tumors that were ER positive (25% versus 66%, $p = 0.003$) or PR positive (25% versus 60%, $p = 0.01$). There was no significant difference in Her2 status between patients with *BRCA* mutation compared to those without (17% versus 11%, $p = 0.144$). Patients with TNBC comprised 18% of the entire cohort (36/199), and all but 5 of these were under the age of 60 at diagnosis. Three patients with TNBC had a *BRCA* mutation (8.3%) and 3 (8.3%) had a *BRCA* VUS.

BRCA mutation rates by NCCN testing criterion

Adherence to NCCN guidelines was confirmed in 98.5% of subjects. The most common NCCN guideline criteria for which patients were tested were being diagnosed with breast cancer at any age and having a strong family history (criterion 6, $n = 118$), being diagnosed with breast cancer at 50 years old and having a limited family history (criterion 4, $n = 100$), and being diagnosed with breast cancer at 45 years of age (criterion 2, $n = 87$). The number of patients meeting each criterion by mutation status is demonstrated in Fig. 1. These criteria were not mutually exclusive. Only one criterion for testing was identified in 84 patients (42%), while 62 (31%) had two criteria, and 45 (22%) had 3 or more.

Having a known family history of a *BRCA* mutation (criterion 1) yielded the highest rate of mutation (50%) and was significantly higher than the rate of mutation in the overall population ($p = 0.019$).

Criterion 5 (age 60 at time of diagnosis and TNBC) and criterion 2 (age 45 at time of diagnosis) had *BRCA* mutation rates of 9.7% and 9.3%, respectively, which were higher than the rate of *BRCA* mutation in the overall cohort (6%). Most of the patients tested under criteria 2 or 5 also met at least 1 other requirement for testing (78.1% for criterion 2 and 71.0% for criterion 5).

On multivariate analysis, having a known family history of a *BRCA* mutation (criterion 1) and being diagnosed with breast cancer at age 45 (criterion 2) remained statistically significant for the likelihood of detecting a *BRCA* mutation when compared to other NCCN criteria for undergoing genetic testing (Table 3).

Rates of mutation by category of NCCN criteria

Types of reasons for genetic testing were analyzed in the three categories as identified in Table 1 - young age, high risk cancer, and family history. The rate of *BRCA* mutation was not significantly different among these 3 groups (7.8%, 7.8%, and 6.4% $p = 0.877$). High risk family history was the reason for testing in 140 patients (70.4%); young age (< 45y) at diagnosis in 128 (64.3%); and high-risk cancer [triple negative breast cancer (TNBC), male

breast cancer or 2 primaries] in 50 (25.1%). Those who underwent *BRCA* testing for young age at diagnosis accounted for 75% of patients in whom a *BRCA* mutation was detected but only 41.7% of patients who did not have a *BRCA* mutation ($p = 0.034$). A similar proportion of patients had family history as a criterion for testing when comparing those who had a *BRCA* mutation and those who did not (83.3% versus 78.1%). Likewise, high risk cancer was present in a similar percentage of patients with a *BRCA* mutation versus those without (25% versus 20.9%). Meeting criteria in more than one category did not significantly increase rate of *BRCA* mutation. Thirteen patients (6.5%) had young age, high risk cancer, and family history all as reasons for testing, but only 1 patient in this subset had a *BRCA* mutation detected (7.2%) which was not significantly elevated compared to the overall population ($p = 0.566$).

Regardless of criteria type, meeting three or more individual NCCN criteria for testing was associated with a significantly increased rate of *BRCA* mutation, as shown in Table 4. 13.3% of patients with 3 criteria for testing had a *BRCA* mutation detected compared to 2.4% of patients with 1 criterion for testing. For patients meeting only 1 requirement for testing, the only criteria that identified a deleterious *BRCA* mutation were age <45 at diagnosis [criterion 2, *BRCA* mutation rate 1/19 (5.2%)] and family history of breast cancer at any age of diagnosis [criterion 6, *BRCA* mutation rate 1/49 (2.0%)].

Discussion

We identified a 6% deleterious *BRCA* mutation rate in breast cancer patients who underwent genetic testing based on NCCN guidelines at our Midwestern academic institution. This rate is equivalent to the previously published rate of 2–6% *BRCA* mutation in all patients with breast cancer^{4–6} and less than the 10% targeted by *BRCA* testing risk models.^{19,20} Detecting *BRCA* mutations in patients who have breast cancer is important for pre-operative planning and may affect decisions for chemotherapy in TNBC.^{28–30} Because of the higher risk of ipsilateral recurrence and contralateral breast cancer in *BRCA* positive patients, counseling about bilateral mastectomy is appropriate.⁷ Surgical planning is commonly delayed until the results of *BRCA* genetic testing is available to avoid the need to return to the operating room for additional procedures. Delaying surgical planning for only the highest yield *BRCA* mutation testing may prevent delaying treatment for the majority of patients who have undergone genetic testing, thereby reducing the risk of adverse outcomes associated with the delay to breast cancer management. In our cohort, patients with 3 NCCN criteria for testing, a known family history of a *BRCA* mutation or age 45 at time of diagnosis had the highest yield for identifying a mutation with testing.

A recent large single institution study by Cropper et al.³¹ examined the positive predictive value (PPV) of the NCCN criteria for *BRCA* testing. They performed a retrospective chart review of patients with breast cancer who were referred for genetic counseling and found 9.2% of patients had a *BRCA* mutation in their population. Like us, they showed that 2 NCCN criteria for testing improved the PPV from 3.2% to 12% but no specific combination of criteria improved PPV. Unlike our study however, they found age 45 as a sole reason for testing to have a low rate of *BRCA* mutation at 1.7%. We identified a significantly higher

rate of *BRCA* mutation of 5.2% in those with age ≥ 45 as the sole NCCN criteria and 9.3% in all patients with age ≥ 45 as a reason for testing.

Both Cropper et al. and our study found a very low yield of deleterious *BRCA* mutation for patients meeting only one criterion for testing. The rate in this subgroup is equal to or less than that reported from testing all patients with breast cancer.^{4–6} Studies comparing *BRCA* mutation rates in women with breast cancer who do and do not meet NCCN guidelines consistently find that the yield of deleterious mutations is similar.^{26,27} Current concordance with NCCN guidelines for *BRCA* testing varies between 27 and 70%.^{32,33} Simplifying testing criteria may reduce disparities noted in genetic testing of patients with breast cancer as well as shorten the delay associated with waiting for genetic results by making it a standard part of breast cancer work up.^{34,35} This stance is supported by the recent American Society of Breast Surgeons consensus guideline on genetic testing.³⁶ If testing were a standard part of the breast cancer work up, it must occur in the setting of appropriate genetic counseling and informed decision making on the part of the patient. Although not all institutions treating breast cancer have access to genetic counselors, a recent study suggests that most patients feel well informed with physician led counseling and testing.³⁴

Limitations of this study include its retrospective nature and completion at a single institution with its own specific population. The retrospective nature of the study prevents us from identifying any patients who met NCCN criteria but were not tested. Additionally, the small number of *BRCA* mutations detected limits the power of the study, and the ability of certain NCCN criteria to detect mutations may have been missed. Generalizing findings from single institutions should be applied with caution. A large, prospective, multi-institutional study would be required to confirm the generalizability of our findings.

Conclusion

The rate of detection of deleterious *BRCA* mutations in patients with breast cancer tested based on NCCN guidelines varied widely depending on the type and number of criteria met. This study improves understanding of the relative probability of a patient having a *BRCA* mutation when using NCCN guidelines for testing. *BRCA* detection rates were significantly increased when the reasons for testing were age ≥ 45 at time of diagnosis, having a known family history of a *BRCA* mutation, and meeting ≥ 3 of NCCN criteria for testing. Waiting for genetic testing results to guide surgical management may be warranted in this subset of patients. Conversely, for the majority of patients who undergo genetic testing as a result of NCCN guidelines, results are unlikely to contribute to surgical management and should not delay surgical planning.

Financial disclosures

A.C.B. was supported by the NIH grant T32CA148062.

References

1. Narod SA, Foulkes WD. *BRCA1* and *BRCA2*: 1994 and beyond. *Nat Rev Canc*. 2004;4:665–676.

2. Prevalence and penetrance of BRCA1 and BRCA2 mutations in a population-based series of breast cancer cases. Anglian Breast Cancer Study Group. *Br J Canc.* 2000;83:1301–1308.
3. Maxwell KN, Domchek SM, Nathanson KL, Robson ME. Population frequency of germline BRCA1/2 mutations. *J Clin Oncol.* 2016;34:4183–4185.
4. Tung N, Lin NU, Kidd J, et al. Frequency of germline mutations in 25 cancer susceptibility genes in a sequential series of patients with breast cancer. *J Clin Oncol.* 2016;34:1460–1468. [PubMed: 26976419]
5. Malone KE, Daling JR, Doody DR, et al. Prevalence and predictors of BRCA1 and BRCA2 mutations in a population-based study of breast cancer in white and black American women ages 35 to 64 years. *Cancer Res.* 2006;66:8297–8308. [PubMed: 16912212]
6. Cancer Facts & Figures. American Cancer Society; 2018 <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf>. Accessed February 20, 2019.
7. Kuchenbaecker KB, Hopper JL, Barnes DR, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. *J Am Med Assoc.* 2017;317:2402–2416.
8. Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. *J Clin Oncol.* 2007;25:1329–1333. [PubMed: 17416853]
9. van den Broek AJ, van 't Veer LJ, Hooning MJ, et al. Impact of age at primary breast cancer on contralateral breast cancer risk in BRCA1/2 mutation carriers. *J Clin Oncol.* 2016;34:409–418. [PubMed: 26700119]
10. Rummel S, Varner E, Shriver CD, Ellsworth RE. Evaluation of BRCA1 mutations in an unselected patient population with triple-negative breast cancer. *Breast Canc Res Treat.* 2013;137:119–125.
11. Fostira F, Tsilaidou M, Papadimitriou C, et al. Prevalence of BRCA1 mutations among 403 women with triple-negative breast cancer: implications for genetic screening selection criteria: a Hellenic Cooperative Oncology Group Study. *Breast Canc Res Treat.* 2012;134:353–362.
12. Gonzalez-Angulo AM, Timms KM, Liu S, et al. Incidence and outcome of BRCA mutations in unselected patients with triple receptor-negative breast cancer. *Clin Cancer Res.* 2011;17:1082–1089. [PubMed: 21233401]
13. Couch FJ, Farid LM, DeShano ML, et al. BRCA2 germline mutations in male breast cancer cases and breast cancer families. *Nat Genet.* 1996;13:123–125. [PubMed: 8673091]
14. Young SR, Pilarski RT, Donenberg T, et al. The prevalence of BRCA1 mutations among young women with triple-negative breast cancer. *BMC Canc.* 2009;9:86.
15. Norquist BM, Harrell MI, Brady MF, et al. Inherited mutations in women with ovarian carcinoma. *JAMA Oncol.* 2016;2:482–490. [PubMed: 26720728]
16. Mersch J, Jackson MA, Park M, et al. Cancers associated with BRCA1 and BRCA2 mutations other than breast and ovarian. *Cancer.* 2015;121:269–275. [PubMed: 25224030]
17. Moran A, O'Hara C, Khan S, et al. Risk of cancer other than breast or ovarian in individuals with BRCA1 and BRCA2 mutations. *Fam Cancer.* 2012;11:235–242. [PubMed: 22187320]
18. Warner E, Foulkes W, Goodwin P, et al. Prevalence and penetrance of BRCA1 and BRCA2 gene mutations in unselected Ashkenazi Jewish women with breast cancer. *J Natl Cancer Inst.* 1999;91:1241–1247. [PubMed: 10413426]
19. Euhus DM, Smith KC, Robinson L, et al. Pretest prediction of BRCA1 or BRCA2 mutation by risk counselors and the computer model BRCAPRO. *J Natl Cancer Inst.* 2002;94:844–851. [PubMed: 12048272]
20. Antoniou AC, Pharoah PP, Smith P, Easton DF. The BOADICEA model of genetic susceptibility to breast and ovarian cancer. *Br J Canc.* 2004;91:1580–1590.
21. Genetic/familial high-risk assessment: breast and ovarian. National comprehensive cancer Network clinical practice guidelines in oncology. https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf; 2019 Accessed February 20, 2019.
22. Chavez-MacGregor M, Clarke CA, Lichtensztajn DY, Giordano SH. Delayed initiation of adjuvant chemotherapy among patients with breast cancer. *JAMA Oncol.* 2016;2:322–329. [PubMed: 26659132]
23. Bleicher RJ, Ruth K, Sigurdson ER, et al. Time to surgery and breast cancer survival in the United States. *JAMA Oncol.* 2016;2:330–339. [PubMed: 26659430]

24. Yi M, Hunt KK, Arun BK, et al. Factors affecting the decision of breast cancer patients to undergo contralateral prophylactic mastectomy. *Cancer Prev Res (Phila)*. 2010;3:1026–1034. [PubMed: 20647335]
25. Wang F, Amara D, Peled AW, et al. Negative genetic testing does not deter contralateral prophylactic mastectomy in younger patients with greater family histories of breast cancer. *Ann Surg Oncol*. 2015;22:3338–3345. [PubMed: 26215194]
26. Beitsch PD, Whitworth PW, Hughes K, et al. Underdiagnosis of hereditary breast cancer: are genetic testing guidelines a tool or an obstacle? *J Clin Oncol*. 2019;37:453–460. [PubMed: 30526229]
27. Yang S, Axilbund JE, O’Leary E, et al. Underdiagnosis of hereditary breast and ovarian cancer in medicare patients: genetic testing criteria miss the mark. *Ann Surg Oncol*. 2018;25:2925–2931. [PubMed: 29998407]
28. Robson M, Im SA, Senkus E, et al. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. *N Engl J Med*. 2017;377:523–533. [PubMed: 28578601]
29. Litton JK, Rugo HS, Ettl J, et al. Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. *N Engl J Med*. 2018;379:753–763. [PubMed: 30110579]
30. Clifton K, Gutierrez-Barrera A, Ma J, et al. Adjuvant versus neoadjuvant chemotherapy in triple-negative breast cancer patients with BRCA mutations. *Breast Canc Res Treat*. 2018;170:101–109.
31. Cropper C, Woodson A, Arun B, et al. Evaluating the NCCN clinical criteria for recommending BRCA1 and BRCA2 genetic testing in patients with breast cancer. *J Natl Compr Cancer Netw*. 2017;15:797–803.
32. Chun DS, Berse B, Venne VL, et al. BRCA testing within the Department of Veterans Affairs: concordance with clinical practice guidelines. *Fam Cancer*. 2017;16:41–49. [PubMed: 27589855]
33. Silver MI, Klein W, Samimi G, Minasian L, Loud J, Roberts MC. Concordance with BRCA1/2 testing guidelines among women in the Health of Women (HOW) Study((R)). *Breast Cancer Res Treat*; 2018.
34. Katz SJ, Ward KC, Hamilton AS, et al. Gaps in receipt of clinically indicated genetic counseling after diagnosis of breast cancer. *J Clin Oncol*. 2018;36: 1218–1224. [PubMed: 29528794]
35. White VB, Walsh KK, Foss KS, et al. Genetic testing for hereditary breast cancer: the decision to decline. *Am Surg*. 2018;84:154–160. [PubMed: 29428045]
36. Consensus Guideline on Genetic Testing for Hereditary Breast Cancer. The American Society of Breast Surgeons; 2019 https://www.breastsurgeons.org/about/statements/PDF_Statements/Hereditary_Genetic_Testing_Patients_With_Without_Breast_Cancer.pdf. Accessed February 20, 2019.

Fig. 1.

BRCA results by NCCN testing criteria. Rates of *BRCA* mutation represented by individual NCCN testing criterion. The percentage of patients within each criterion who had a *BRCA* mutation is represented on the graph; 115 patients met more than one criterion and are included more than once. Number of patients per criterion by mutation status are as follows: 1 - *BRCA* mutation n = 2, no mutation n = 2; 2 - *BRCA* mutation n = 8, no mutation n = 78; 3 - *BRCA* mutation n = 0, no mutation n = 11; 4 - *BRCA* mutation n = 8, no mutation = 92; 5 - *BRCA* mutation n = 3, no mutation n = 28; 6 - *BRCA* mutation n = 7, no mutation n = 111; 7 - *BRCA* mutation n = 0, no mutation n = 1.

Table 1

BRCA1/2 testing criteria in patients with breast cancer.

Criterion	Reason for Testing	Category
1	Family history of known deleterious <i>BRCA1/2</i> gene mutation	Family History
2	Diagnosed with breast cancer 45 years old	Young Age
3	Diagnosed with breast cancer 50 years old and an additional breast cancer primary	High Risk Cancer
4	Diagnosed with breast cancer 50 years old and...	Family History
		Family History of one of the following: 1 close relative with pancreatic cancer 1 close relative with prostate cancer An unknown or limited family history
5	Diagnosed with breast cancer 60 years old with TNBC	High Risk Cancer
6	Diagnosed with breast cancer at any age and...	Family History
		Family History of one of the following: 1 close relative with breast cancer diagnosed at age 50 1 close relative with ovarian carcinoma 1 close relative with male breast cancer Ethnicity with higher mutation frequency (e.g., Ashkenazi Jewish)
7	Personal history of male breast cancer	High Risk Cancer

Table 2

Patient demographics.

Variable	BRCA mutation (n = 12)	No BRCA mutation (n=187)	P value
Age at testing (years)			0.222
<30	1 (8.3%)	3 (1.6%)	
31–40	3 (25%)	29 (15.5%)	
41–50	2 (16.7%)	57 (30.5%)	
51–60	2 (16.7%)	54 (28.8%)	
>60	4 (33.3%)	44 (23.5%)	
Gender (female)	12 (100%)	186 (99.5%)	1
Race			0.357
White	11 (91.2%)	173 (92.5%)	
Hispanic	0 (0%)	4 (2.1%)	
Asian	0 (0%)	3 (1.6%)	
Black	1 (8.3%)	1 (0.5%)	
Ashkenazi Jewish	0 (0%)	3 (1.6%)	
Native American	0 (0%)	2 (1.0%)	
Unknown	0 (0%)	1 (0.5%)	
Histology			0.206
DCIS	2 (16.7%)	28 (14.9%)	
Invasive Ductal Carcinoma	8 (66.7%)	135 (72.2%)	
Invasive Lobular carcinoma	0 (0%)	13 (3.9%)	
Other	0 (0%)	6 (3.2%)	
Unknown	2 (16.7%)	5 (2.7%)	
ER positive	3 (25.0%)	124 (66.3%)	0.003
PR positive	3 (25.0%)	114 (60.1%)	0.01
Triple Negative	3 (25.0%)	33 (17.6%)	0.521
Her2 positive	2 (16.7%)	20 (10.7%)	0.144
Clinical TNM Stage			0.155
Stage 0	1 (8.3%)	26 (13.9%)	
Stage I (A-B)	2 (16.7%)	79 (42.2%)	
Stage II (A-B)	4 (33.3%)	59 (31.5%)	
Stage III (A-C)	0 (0%)	10 (5.3%)	
Stage IV	2 (16.7%)	2 (10.7%)	
Unknown	2 (16.7%)	13 (7.0%)	
Bilateral breast cancer	0 (0%)	15 (8.0%)	1
Recurrent breast cancer	0 (0%)	10 (5.4%)	1
Completed panel testing	3 (25%)	67 (35.8%)	

Table 3

Multivariate analysis by NCCN testing criteria.

Criterion	BRCA1/2 Testing Criteria Met:	BRCA mutation (n = 12)	No BRCA mutation (n = 187)	Odds Ratio	95% CI ^a	p value
1	Known family history of BRCA1/2 mutation	2 (16.7%)	2 (1.1%)	14.31	1.2–166.3	0.034
2	Age 45 at diagnosis	9 (75%)	78 (41.7%)	11.61	1.2–108.6	0.032
3	Age 50 and two breast cancer primaries	0 (0%)	11 (5.9%)	–	–	–
4	Age 50 with high risk family history	8 (66.7%)	92 (49.2%)	1.12	0.22–5.7	0.89
5	Age 60 and TNBC	3 (25%)	28 (14.9%)	1.84	0.37–9.2	0.458
6	Any age with high risk family history	7 (58.3%)	111 (59.4%)	1.25	0.28–5.5	0.769
7	Male breast cancer	0 (0%)	1 (0.5%)	–	–	–

^aCI - Confidence Interval.

Table 4

Risk of mutation with multiple NCCN testing criteria.

<i>BRCA1/2</i> Testing Criteria met:	<i>BRCA</i> mutation (n = 12)	No <i>BRCA</i> mutation (n = 187)	p value
Meeting 1 testing criterion	2 (16.7%)	82 (43.9%)	0.076
Meeting 2 testing criteria	4 (33.3%)	58 (31.0%)	1
Meeting 3 testing criteria	6 (50%)	39 (20.9%)	0.03
Meeting 0 testing criteria	0(0%)	8 (4.2%)	–