Prospective Evaluation of Universal *BRCA* Testing for Women With Triple-Negative Breast Cancer

Trisha S. Emborgo (iD), BA,[1] Donika Saporito, MS, CGC,[2] Kimberly I. Muse (iD), MS,[1]
Angelica M. Gutierrez Barrera, MS,[3] Jennifer K. Litton, MD,[3] Karen H. Lu, MD,[1,2,4] Banu K. Arun, MD[1–3,*]

[1]Breast and Ovarian Cancers Moon Shots Program, The University of Texas MD Anderson Cancer Center, 1155 Pressler Street, Houston, TX, USA; [2]Clinical Cancer Genetics Program, The University of Texas MD Anderson Cancer Center, 1155 Pressler Street, Houston, TX, USA; [3]Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, 1155 Pressler Street, Houston, TX, USA and [4]Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, 1155 Pressler Street, Houston, TX, USA

*Correspondence to: Banu K. Arun, MD, Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, 1155 Pressler Street, Unit 1354, Houston, TX, USA (e-mail: barun@mdanderson.org).

Abstract

Background: Limited published literature exists on women with triple-negative breast cancer (TNBC) diagnosed over the age of 60 years with breast cancer gene (*BRCA*) pathogenic variants. Our study determined whether the rate of *BRCA* pathogenic variants in a prospective cohort of TNBC patients outside the definition of current clinical genetic testing (GT) guidelines warrants a change in recommendations. **Methods:** A prospective study of 395 women with TNBC underwent genetic counseling and 380 (96.2%) underwent clinical *BRCA* GT regardless of age of diagnosis beginning January 2014 to October 2015 at The University of Texas MD Anderson Cancer Center, Houston. TNBC patients older than 60 years who did not meet clinical GT guidelines had comprehensive sequencing and large rearrangement GT as part of the research protocol. **Results:** Fifty-one of 380 (13.4%) women with TNBC who underwent clinical *BRCA* GT were *BRCA* positive. Of the 86 patients diagnosed at age over 60 years and underwent GT, only two (2.3%) were positive for *BRCA*. These two patients would have met clinical testing criteria due to family or ancestral history. **Conclusions:** Our study does not support universal *BRCA* testing for TNBC patients diagnosed older than 60 years as their only risk factor for a *BRCA* pathogenic variant. Both of the positive *BRCA* patients older than 60 years identified would have met current National Comprehensive Cancer Network criteria for testing. Therefore, our study demonstrates that the National Comprehensive Cancer Network guidelines provide sufficient criteria for identifying *BRCA* pathogenic variants in women with TNBC at 60 years or younger.

Triple-negative breast cancer (TNBC) is a heterogeneous subtype of breast cancer identified as estrogen receptor (ER) negative, progesterone receptor (PR) negative, and human epidermal growth factor receptor 2 (HER2/*neu*) negative. These three receptors are absent in approximately 15–20% of breast cancer case patients in the United States (1,2). TNBC's clinical features include an increased mortality rate during the first 5 years and risk of recurrence occurring between 1 and 3 years (3).

Pathogenic variants (commonly referred to as "germline pathogenic variants") in breast cancer genes (BRCA1) or *BRCA2* statistically significantly increase the overall lifetime risk for breast and ovarian cancers in women (4,5). Women with TNBC have an 11–31% likelihood of possessing a *BRCA* pathogenic variant (6–11). The National Comprehensive Cancer Network (NCCN) published clinical testing guidelines that recommended individuals with TNBC age 60 years or younger undergo *BRCA*

genetic testing (GT) (12). Clinical criteria for testing individuals with TNBC also include those with a family history (FH) per NCCN clinical testing guidelines (12). *BRCA* pathogenic variants in TNBC patients have implications for early cancer detection and cancer prevention in at-risk blood relatives (13–16). Our previous prediction models have shown that testing all TNBC patients younger than 50 years may reduce the risk of new breast cancers by 23% and ovarian cancers by 41% (11). Furthermore, a recent study has shown that *BRCA* pathogenic variants in affected patients can have important treatment implications, hence stressing the importance of identifying patients with *BRCA* pathogenic variants (16).

Although NCCN recommends *BRCA* GT for patients with TNBC younger than 60 years, some studies suggest that increasing the recommended age of testing to older than 60 years may identify more TNBC patients with *BRCA* pathogenic variants (6).

Furthermore, recent promising results of oral polyadenosine diphosphate-ribose polymerase (PARP) inhibitors for metastatic breast cancer with BRCA pathogenic variants may tempt healthcare providers to test all TNBC patients for BRCA (17–19). Therefore, our aim in this study was to determine whether the rate of BRCA pathogenic variants in a prospective cohort of TNBC patients outside the definition of current clinical GT guidelines warrants a change in recommendations.

Methods

Cohort Identification

Consecutive patients with TNBC underwent genetic counseling (GC) regardless of age of diagnosis between January 2014 and October 2015. Written informed consent was obtained, and this prospective study was approved by The University of Texas MD Anderson Cancer Center's (UTMDACC) institutional review board. All patients were referred by UTMDACC physicians or outside physicians and evaluated by the Clinical Cancer Genetics Program. They were offered GC and upon completion of the session, if agreed, were consented to the study and GT for the BRCA1 and BRCA2 genes. TNBC patients age 60 years or younger underwent clinical GT (12). Patients with prior BRCA comprehensive sequencing testing underwent testing for BRCA large rearrangement. TNBC patients with personal and/or FH who met clinical BRCA testing criteria may have undergone clinical GT for additional genes other than BRCA as clinically indicated after pedigree review. TNBC patients over the age of 60 years without an FH according to NCCN guidelines, who did not meet clinical GT criteria, underwent research comprehensive sequencing and large rearrangement GT for BRCA1 and BRCA2 (Integrated BRACAnalysis) through Myriad Genetic Laboratories, Inc. as part of an institutional review board-approved human patients research protocol with written consent among participants. FH was defined by February 2015 NCCN guidelines (12).

TNBC Pathology

TNBC was defined as ER and PR 0–9% hormone receptor low-positive tumor and HER2/*neu* gene 0, 1+, or 2+ with no amplification via FISH of a ratio of less than 2.0 (20). ER and PR 0–9% inclusion criteria were used based on a Sanford et al. (20) publication and has become standard in our practice. Patients with pathology records from an outside institution had their pathology reviewed by breast pathologists at UTMDACC. If discrepancies occurred between the outside pathology report and the institution's pathology review, our institution's pathology was used to determine the patient's eligibility for the study. If both HER2/*neu* immunohistochemistry and fluorescence in situ hybridization were available, fluorescence in situ hybridization was used as the preferred HER2/*neu* evaluation.

Statistical Methods

The objective of the study was to determine if there is an increased identification of high-risk hereditary breast cancer patients through implementation of universal BRCA1 and BRCA2 GT of all women with TNBC. Data were summarized with descriptive statistics (ie, means, SDs, frequencies, and percentages). The Fisher test was used to analyze the age group and BRCA pathogenic variant status considering one table cell had an expected cell count of less than five. P less than .05 indicated

statistically significant difference. IBM SPSS Statistics Version 22 (SPSS, Inc, Armonk, NY) was used to analyze the data. All tests were two-sided.

Results

All TNBC patients were referred for GC and GT at UTMDACC. A total of 395 of 424 TNBC UTMDACC (93.4%) patients were included in this study. All 395 female patients were eligible based on pathology report review confirming TNBC. Our study targeted stage I–III TNBC patients during enrollment, in which 360 (91.1%) of 395 were stage I–III, and 35 of 395 ended up having stage IV TNBC after their complete work-up. All 395 TNBC female patients underwent GC. Of those, 380 underwent GT. From TNBC diagnosis to GT, 278 of 380 (73.2%) had GT within 1 year. A summary of the length of time from TNBC diagnosis to GT is found in Table 1. Patient demographics are summarized in Table 2 and Figure 1. The overall median age of TNBC diagnosis was 52.0 years (range, 25.0–84.0 years), the median age of TNBC diagnosis for patients diagnosed age 60 years or younger was 48.0 years (range, 25.0–60.0 years), and the median age of TNBC diagnosis for patients diagnosed older than 60 years was 65.0 years (range, 61.0–84.0 years). A total 206 (52.2%) of the study population were white, 85 (21.5%) were black, 67 (17.0%) were Hispanic, and 26 (6.6%) were Asian. Thirteen (3.3%) reported Ashkenazi Jewish (AJ) ancestry, and 11 (2.8%) did not have any ancestry information available.

A total 380 (96.2%) of 395 eligible patients underwent BRCA GT. Fifty-one of 380 (13.4%) were identified as having a BRCA pathogenic variant, 45 of 380 (11.8%) had a BRCA1 pathogenic variant, and six patients (1.6%) had a BRCA2 pathogenic variant. Additional study population demographics (ie, race, ER, PR, and HER2/*neu*) are listed in Table 2. Fifteen of 395 (3.8%) were not tested; 10 of 395 (2.5%) patients decided not to pursue BRCA testing, indicating they would like more time to consider GT, and five of 395 (1.3%) did not give a specific reason for declining. Eight of 395 (2.0%) met clinical testing criteria based solely on the age of diagnosis, four of 395 (1.0%) met clinical testing criteria based solely on FH, and one of 395 (0.3%) met clinical testing criteria based on age of diagnosis and FH.

The overall median age of BRCA positive patients was 42.0 years (range, 25.0–64.0 years). The rate of BRCA pathogenic variants comparing groups of patients age 60 years or younger with those older than 60 years is summarized in Table 3. Out of 380 tested patients, 294 (77.4%) were in the group younger than 60 years. Among these, 49 (16.7%) were BRCA positive and 237 (80.6%) were BRCA negative. Of 380 tested patients, 86 (22.6%) were in the group older than 60 years. Among these, two (2.3%) were BRCA positive and 80 (93.0%) were BRCA negative. Using the Fisher test, there was a statistically significant difference between the rate of BRCA pathogenic variants in those 60 years and younger and those older than 60 years ($P = .001$). Two of 86 (2.3%) patients older than 60 years who were BRCA positive would have met current NCCN guidelines for GT based on family or ancestral history. Patient A was diagnosed with TNBC at 64 years; however, there was a known BRCA1 pathogenic variant, 358del3insTT, previously identified in the family. Patient B was diagnosed with TNBC at 62 years and reported bilineal AJ ancestry. Patient B tested positive for an AJ founder pathogenic variant BRCA1, c.68_69delAG (p.Glu23Valfs).

In addition to age of diagnosis, we further analyzed BRCA pathogenic variant status based solely on FH. We identified patients with an FH of breast and/or ovarian (BOV) cancer. Of
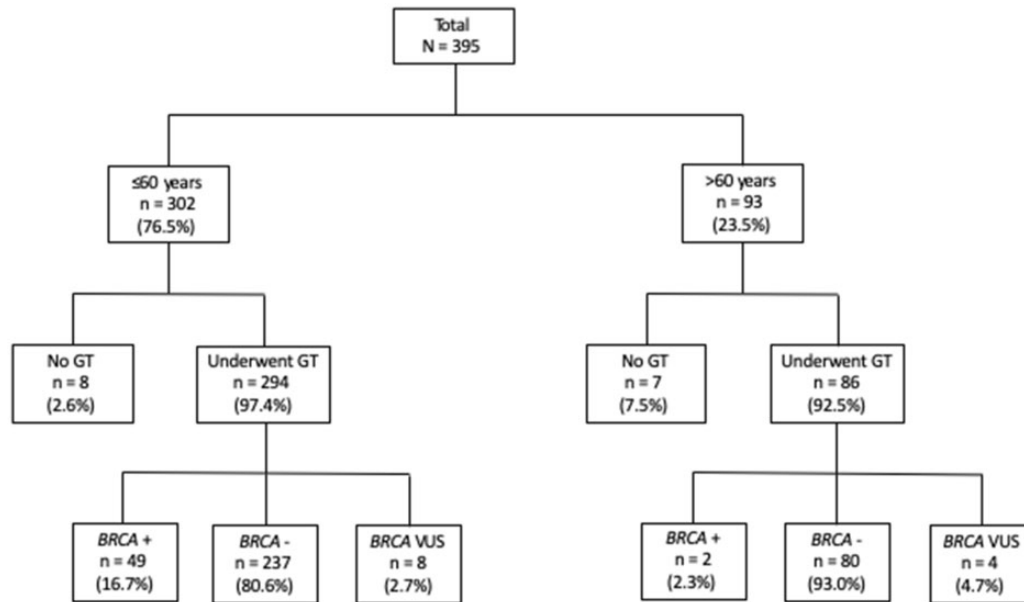
Figure 1. Universal *BRCA* testing for women with TNBC study population flow chart. GT = genetic testing; + = positive; − = negative; TNBC = triple-negative breast cancer; VUS = variant of uncertain significance.

Table 1. Length of time from TNBC diagnosis to *BRCA* GT (N = 380)*

Length of time, y	No. (%)
0–1	278 (73.2)
<2	20 (5.3)
3–5	29 (7.6)
6–10	21 (5.5)
>11	32 (8.4)

*GT = genetic testing; TNBC = triple-negative breast cancer.

390 patients included in the FH analyses, 159 (40.8%) had an FH of BOV. A total of 155 of 390 (39.7%) patients with an FH of BOV underwent GT. Of those 155 with an FH of BOV who underwent GT, 35 (22.6%) patients were *BRCA* positive. The details of *BRCA* pathogenic variant prevalence based on FH for additional cancer relationships (breast, ovarian, pancreatic, and prostate) are listed in Table 4. Patients who were adopted or did not have any FH available were not included in this portion of the analyses.

Discussion

Our study does not support universal *BRCA* testing for TNBC patients diagnosed older than 60 years as their sole risk factor for a *BRCA* pathogenic variant. Both of the positive *BRCA* patients older than 60 years old identified would have met current NCCN criteria for testing based on their FH or ancestry. Of note, the GC referral guidelines at our institution include a holistic view of the patient's personal and FH of cancer. The guidelines serve to refer appropriate patients for GC, in which they would receive a detailed risk assessment to determine if GT for *BRCA* is warranted. This policy increases the likelihood that patients who are appropriate for GC and/or GT are captured during their care at our institution. Individuals who order GT are expected to utilize clinical judgement and professional guidelines to determine who may benefit from GT and what specific testing is beneficial for that individual. Our study demonstrates

that NCCN guidelines provide sufficient criteria for identifying *BRCA* pathogenic variants in women with TNBC at age 60 years or younger.

With the implementation of universal *BRCA* testing of TNBC patients, our study found 51 of 380 (13.4%) total *BRCA* deleterious pathogenic variants regardless of age of diagnosis. Hartman et al. (6) performed a retrospective study identifying a 10.6% prevalence rate of *BRCA* pathogenic variants, regardless of age of diagnosis, in an unselected community oncology network patient population of TNBC. Their testing cohort categorized individuals with TNBC based on their age of diagnosis of younger than 50 years and 50 years or older (6). They did not report specifically on individuals diagnosed with TNBC at age 60 years or older (6). Sharma et al. (8) prospectively studied Kansas City academic and community practices, which exhibited a 15.5% prevalence rate of *BRCA* pathogenic variants among patients, including all ages of TNBC diagnosis. Three of 32 positive *BRCA1/2* individuals in their cohort were over the age of 60 years at time of diagnosis (8). All three individuals would have met NCCN testing guidelines based on their additional personal and/or FH (8). Greenup et al. (9) performed a retrospective study identifying a 30.9% *BRCA* positive prevalence for a TNBC GC cohort. In their *BRCA* positive patient population, five of 139 positive *BRCA1/2* patients were 60 years or older when they were diagnosed with cancer (9). It is unknown whether these five patients would have met clinical testing criteria based on their FH or ancestry (9). As noted in their report, their high *BRCA* positive prevalence of 30.9% may be an overestimate in an unselected TNBC group due to the selection of their own cohort of patients referred to GC based on FH and early onset of diagnosis (9). Couch et al. (10) compiled 12 different TNBC studies and identified 11.2% of TNBC patients with *BRCA1* (8.5%) and *BRCA2* (2.7%) pathogenic variants. Twelve of 204 *BRCA1* or *BRCA2* positive TNBC patients were older than 60 years (10). From those older than 60 years and without an FH of cancer, only 1.4% had a *BRCA* pathogenic variant (10). Their study supported the NCCN guidelines that testing for *BRCA* in TNBC women should only be implemented before 60 years of age in the absence of FH

Table 2. Universal *BRCA* testing for women with TNBC study population demographics*

	Age group		
	≤60 y	>60 y	Total
Category	No. (%)	No. (%)	No. (%)
Total			
	302 (76.5)	93 (23.5)	395
Age of Dx, y			
Mean (SD)	46.7 (8.62)	66.4 (4.74)	51.4 (11.49)
Median	48.0	65.0	52.0
Range	25.0–60.0	61.0–84.0	25.0–84.0
Race			
White	143 (47.4)	63 (67.7)	206 (52.2)
Black	65 (21.5)	20 (21.5)	85 (21.5)
Hispanic	59 (19.5)	8 (8.6)	67 (17.0)
Asian	24 (7.9)	2 (2.2)	26 (6.6)
Other	5 (1.7)	0 (0.0)	5 (1.3)
Unknown	6 (2.0)	0 (0.0)	6 (1.5)
AJ ancestry			
Yes	10 (3.3)	3 (3.2)	13 (3.3)
No	282 (93.4)	89 (95.7)	371 (93.9)
Unknown	10 (3.3)	1 (1.1)	11 (2.8)
Underwent GT			
Yes	294 (97.4)	86 (92.5)	380 (96.2)
No	8 (2.6)	7 (7.5)	15 (3.8)
BRCA status			
Positive	49 (16.7)	2 (2.3)	51 (13.4)
Negative	237 (80.6)	80 (93.0)	317 (83.4)
VUS	8 (2.7)	4 (4.7)	12 (3.2)
ER			
0%	267 (88.4)	85 (91.4)	352 (89.1)
1–5%	33 (10.9)	8 (8.6)	41 (10.4)
6–9%	2 (0.7)	0 (0.0)	2 (0.5)
PR			
0%	282 (93.4)	88 (94.6)	370 (93.7)
1–5%	18 (6.0)	5 (5.4)	23 (5.8)
6–9%	2 (0.7)	0 (0.0)	2 (0.5)
HER2/*neu*			
0	159 (52.6)	42 (45.2)	201 (50.9)
1+	72 (23.8)	24 (25.8)	96 (24.3)
2+ w/ no amp	71 (23.5)	27 (29.0)	98 (24.8)

*AJ = Ashkenazi Jewish; Dx = diagnosis; ER = estrogen receptor; GT = genetic testing; HER2/*neu* = human epidermal growth factor receptor 2; PR = progesterone receptor; TNBC = triple-negative breast cancer; w/ no amp = with no amplification; VUS = variants of uncertain significance.

Table 3. Rate of *BRCA* pathogenic variants in TNBC patients between age groups (N = 395)

	Age group		
Category	≤60 y, No.	>60 y, No.	P*
No. in age group	302	93	
Underwent GT	294	86	
BRCA status			
Positive	49	2	.001
Negative	237	80	
VUS	8	4	

*Fisher test, two-sided. GT = genetic testing; TNBC = triple-negative breast cancer; VUS = variants of uncertain significance.

(10). As shown in Table 5, our study supports previous studies in which the frequency of pathogenic variant *BRCA* pathogenic variants regardless of age of diagnosis in TNBC is approximately 11–31% (6,8–10).

The results of our study did not indicate an increase in the identification of *BRCA* positive TNBC women outside of the current NCCN guidelines. Of 86 patients older than 60 years who underwent GT, only two (2.3%) were *BRCA* positive. Both individuals would have met NCCN clinical testing criteria due to FH or ancestral history. Studies have found 3–13% positive *BRCA* pathogenic variants in those 60 years or older (6,8–10). As seen in Table 5, our smaller percentage of 2.3% in contrast to previous studies could be due to our institution's earlier identification of TNBC in patients; thus, referral for GC and diagnosis of *BRCA* positivity occurs earlier. Implementing universal testing of all women with TNBC, regardless of age, would require greater resources, specifically an additional consultation for GC for each patient. In the case of a low-risk patient, they may incur additional costs for GC and/or GT when there are no substantive recommendations. Based on these study results and the NCCN criteria, GC and GT for patients with TNBC are likely to be recommended when deemed appropriate for the patient (based on age of onset and/or FH). Our findings are comparable with previous studies in the literature showing that *BRCA* testing for TNBC older than 60 years is not indicated unless the patients meet other clinical testing criteria. The outlined NCCN criteria provide the ability to capture individuals with *BRCA* pathogenic variants based on several personal and FH characteristics. This study emphasizes that utilizing FH and ancestry are important indicators for *BRCA* positivity in individuals, specifically TNBC women older than 60 years. Although detecting *BRCA* pathogenic variants affects an individual's management recommendations and possible targeted therapy options, the means by which individuals are identified as appropriate candidates for *BRCA* GT should follow the current NCCN guidelines.

Patients without an FH for BOV cancer and PANPRO cancer had a *BRCA* pathogenic variant prevalence of 6.1% regardless of age of diagnosis. Patients with an FH of BOV cancer had a prevalence rate of a *BRCA* pathogenic variant at 22.6%. Our study further supports the higher prevalence rate of a *BRCA* pathogenic variant in families with an FH of BOV (6,8). Additionally, our study evaluates the likelihood of identifying a *BRCA* pathogenic variant in individuals based on the NCCN testing criteria for the *BRCA1/2* genes only. As the knowledge and interest in GT increases in both providers and patients alike, many individuals who elect to undergo GT are more likely to receive testing of many genes (ie, panel test) without considering the implications of other genes. *BRCA* pathogenic variants have been well established to be associated with TNBC; however, many genes on large panel tests do not have an association with TNBC. This type of testing is particularly unnecessary if TNBC is the only basis for testing. GT for multiple genes may benefit some patients when coupled with clinical judgement. When GT is not clinically warranted, uncertainty may increase, as is the case with variants of uncertain significance (VUS). The VUS rate increases as more genes are added to the analysis. If a patient is recommended to undergo GT based on a history of TNBC older than 60 years with no additional personal or FH, they are susceptible to large hereditary cancer panels with genes not associated with their diagnosis. In turn, they have a higher likelihood of identifying a VUS and may be mismanaged based on

Table 4. BRCA pathogenic variant prevalence on TNBC women based on FH (n = 390)

| | | | Family history* | | |
| | | | BOV | | |
Category	None No. (%)	With and without PANPRO No. (%)	With PANPRO No. (%)	Without PANPRO No. (%)	PANPRO without BOV No. (%)
Total					
	208 (53.3)	159 (40.8)	18 (4.6)	141 (36.2)	23 (5.9)
Age of Dx, y					
Mean (SD)	51.1 (11.52)	51.7 (11.2)	52.8 (9.17)	51.6 (11.50)	52.3 (13.13)
Median	51.0	52.0	54.5	52.0	55.0
Range	25.0–81.0	29.0–84.0	32.0–71.0	29.0–84.0	26.0–80.0
Underwent GT					
Yes	197 (50.5)	155 (39.7)	18 (4.6)	137 (35.1)	23 (5.9)
≤60	151 (38.7)	124 (31.8)	15 (3.8)	109 (27.9)	15 (3.8)
>60	46 (11.8)	31 (7.9)	3 (0.8)	28 (7.2)	8 (2.1)
BRCA status					
Positive	12 (6.1)	35 (22.6)	1 (5.6)	34 (24.8)	3 (13.0)
BRCA1	10 (5.1)	32 (20.6)	0 (0.0)	32 (23.4)	2 (8.7)
BRCA2	2 (1.0)	3 (1.9)	1 (5.6)	2 (1.5)	1 (4.3)
≤60	12 (6.1)	33 (21.3)	1 (5.6)	32 (23.4)	3 (13.0)
>60	0 (0.0)	2 (1.3)	0 (0.0)	2 (1.5)	0 (0.0)
Negative	176 (89.3)	117 (75.5)	17 (94.4)	100 (73.0)	20 (87.0)
≤60	133 (67.5)	89 (57.4)	14 (77.8)	75 (54.7)	12 (52.2)
>60	43 (21.8)	28 (18.1)	3 (16.7)	25 (18.2)	8 (34.8)

*TNBC patients who were adopted or did not have any FH available were not included in this analysis. BOV = breast and/or ovarian cancer; Dx = diagnosis; FH = family history; GT = genetic testing; PANPRO = pancreatic and/or prostate cancer; TNBC = triple-negative breast cancer.

Table 5. Summary of BRCA pathogenic variant prevalence in women with TNBC*

Study	Total BRCA pathogenic variant No. (%)	Age group, y (No.)	≥60 y BRCA pathogenic variant No. (%)
Our study (n = 380)	51 (13.4)	>60 (86)	2 (2.3)
Hartman et al. 2012 (6) (N = 199)	21 (10.6)	≥60 (45)	2 (4.4)
Greenup et al. 2013 (9) (n = 450)	139 (30.9)	>60 (38)	5 (13.2)
Sharma et al. 2014 (8) (N = 207)	32 (15.5)	>60 (61)	3 (4.9)
Couch et al. 2015 (10) (N = 1824)	204 (11.2)	>60 (388)	12 (3.1)

*TNBC = triple-negative breast cancer.

incorrect interpretation of a VUS or limited information about other genes that may be present on the panel test. It is important to emphasize that BRCA testing criteria are not created to determine the likelihood of testing positive for a non-BRCA gene.

Without the presence of cellular receptors for targeted breast cancer treatment, TNBC therapy is more limited to chemotherapy, surgery, and radiation therapy. First-line treatment for TNBC has been a combination of anthracyclines and taxanes (21). Tumors resistant to anthracyclines or taxanes have created limited chemotherapeutic options for TNBC patients. Recently, targeted therapies such as PARP inhibitors have been found useful specifically for pathogenic BRCA variants (22,23). TNBC patients who previously failed chemotherapy or who have a rapidly metastatic disease were found to have a longer progression-free survival compared with non-BRCA mutated patients when treated with PARP inhibitors (24–26). Ongoing trials are studying the effects of iniparib, olaparib, and veliparib (24–26). Due to the aggressiveness of TNBC tumors, health-care providers might be tempted to recommend BRCA testing to all TNBC patients for possible treatment with PARPs; however, our study demonstrates standard NCCN guidelines are sufficient to diagnose BRCA pathogenic variants.

A limitation of our study is the small sample size due to the fact the study population was obtained from a GC cohort. Only those patients referred for GC underwent GT. There is a possibility that other TNBC patients were missed because they were not referred; however, based on the historical data of our institution, only fewer than 10% were not referred.

In conclusion, BRCA testing of patients with TNBC older than 60 years, based on age alone, does not yield clinically significant results. To our knowledge, our study provides an addition to the important data found in TNBC women older than 60 years of age. With recent promising data using targeted therapies (PARP inhibitors) in BRCA positive breast cancer, health-care providers might be tempted to recommend testing to all TNBC patients (17–19); however, the results of this study should be taken into consideration and standard NCCN testing guidelines should be followed.

Funding

Notes

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(26):4282–4288.
2. Carey LA, Perou CM, Livasy CA, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. *JAMA*. 2006;295(21):2492–2502.
3. Dent R, Trudeau M, Pritchard KI, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. *Clin Cancer Res*. 2007;13(15):4429–4434.
4. Miki Y, Swensen J, Shattuck-Eidens D, et al. A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. *Science*. 1994;266(5182):66–71.
5. Wooster R, Bignell G, Lancaster J, et al. Identification of the breast cancer susceptibility gene BRCA2. *Nature*. 1995;378(6559):789–792.
6. Hartman AR, Kaldate RR, Sailer LM, et al. Prevalence of BRCA mutations in an unselected population of triple-negative breast cancer. *Cancer*. 2012;118(11):2787–2795.
7. Meyer P, Landgraf K, Hogel B, Eiermann W, Ataseven B. BRCA2 mutations and triple-negative breast cancer. *PLoS One*. 2012;7(5):e38361.
8. Sharma P, Klemp JR, Kimler BF, et al. Germline BRCA mutation evaluation in a prospective triple-negative breast cancer registry: implications for hereditary breast and/or ovarian cancer syndrome testing. *Breast Cancer Res Treat*. 2014;145(3):707–714.
9. Greenup R, Buchanan A, Lorizio W, 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):3254–3258.
10. Couch FJ, Hart SN, Sharma P, et al. Inherited mutations in 17 breast cancer susceptibility genes among a large triple-negative breast cancer cohort unselected for family history of breast cancer. *J Clin Oncol*. 2015;33(4):304–311.
11. Kwon JS, Gutierrez-Barrera AM, Young D, et al. Expanding the criteria for BRCA mutation testing in breast cancer survivors. *J Clin Oncol*. 2010;28(27):4214–4220.
12. Daly MB, Pilarski R, Axilbund JE, et al. Genetic/familial high-risk assessment: breast and ovarian, version 2.2015. *J Natl Compr Canc Netw*. 2016;14(2):153–162.
13. Hartmann LC, Sellers TA, Schaid DJ, et al. Efficacy of bilateral prophylactic mastectomy in BRCA1 and BRCA2 gene mutation carriers. *J Natl Cancer Inst*. 2001;93(21):1633–1637.
14. Saslow D, Boetes C, Burke W, et al.; for the American Cancer Society Breast Cancer Advisory Group. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin*. 2007;57(2):75–89.
15. Scheuer L, Kauff N, Robson M, et al. Outcome of preventive surgery and screening for breast and ovarian cancer in BRCA mutation carriers. *J Clin Oncol*. 2002;20(5):1260–1268.
16. Stebbing J, Ellis P, Tutt A. PARP inhibitors in BRCA1-/BRCA2-associated and triple-negative breast cancers. *Future Oncol*. 2010;6(4):485–486.
17. Somlo G, Frankel PH, Arun BK, et al. Efficacy of the PARP inhibitor veliparib with carboplatin or as a single agent in patients with germline BRCA1- or BRCA2-associated metastatic breast cancer: California Cancer Consortium Trial NCT01149083. *Clin Cancer Res*. 2017;23(15):4066–4076.
18. Tutt A, Robson M, Garber JE, et al. Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and advanced breast cancer: a proof-of-concept trial. *Lancet*. 2010;376(9737):235–244.
19. 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(6):523–533.
20. Sanford RA, Song J, Gutierrez-Barrera AM, et al. High incidence of germline BRCA mutation in patients with ER low-positive/PR low-positive/HER-2 neu negative tumors. *Cancer*. 2015;121(19):3422–3427.
21. von Minckwitz G, Untch M, Blohmer JU, et al. Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes. *J Clin Oncol*. 2012;30(15):1796–1804.
22. Farmer H, McCabe N, Lord CJ, et al. Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy. *Nature*. 2005;434(7035):917–921.
23. Bryant HE, Schultz N, Thomas HD, et al. Specific killing of BRCA2-deficient tumours with inhibitors of poly(ADP-ribose) polymerase. *Nature*. 2005;434(7035):913–917.
24. O'Shaughnessy J, Osborne C, Pippen JE, et al. Iniparib plus chemotherapy in metastatic triple-negative breast cancer. *N Engl J Med*. 2011;364(3):205–214.
25. Fong PC, Boss DS, Yap TA, et al. Inhibition of poly(ADP-ribose) polymerase in tumors from BRCA mutation carriers. *N Engl J Med*. 2009;361(2):123–134.
26. Isakoff SJ, Puhalla S, Domchek SM, et al. A randomized phase ii study of veliparib with temozolomide or carboplatin/paclitaxel versus placebo with carboplatin/paclitaxel in BRCA1/2 metastatic breast cancer: design and rationale. *Future Oncol*. 2017;13(4):307–320.