Clinicopathologic Features among Pathogenic Variants/Likely Pathogenic Variants, Variants of Unknown Significance, and Wild Type of BRCA1/2 in Breast Cancer

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Case Report

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Abstract

Background

Approximately 5–10% of breast cancers are BRCA-positive. Because of higher grades and proliferation indices, these prognoses are poor compared to sporadic breast cancers. This study analyzed the clinicopathologic features of breast cancer based on BRCA gene status.

Methods

A total of 315 women with breast cancer underwent genetic assessments between 2006 and 2019. BRCA gene status was classified as either pathogenic variant/likely pathogenic variants (PV/LPV), variant of unknown significance (VUS), or wild type. The following clinicopathologic variables were assessed: age, body mass index (BMI), clinical and pathologic stages, treatment modalities, and oncologic outcomes.

Results

Upon assessing their BRCA gene status, there were 97 patients (30.8%) with PV/LPV and 53 patients (16.8%) with VUS. Although the most treatment modalities including neoadjuvant chemotherapy, adjuvant chemotherapy and target therapy were more frequently administrated in BRCA-positive breast cancer patients, in multivariate analysis, neoadjuvant chemotherapy did not show statistical significance between three groups. The immunohistochemical staining results, such as estrogen receptor, progesterone receptor, and HER2/neu gene, triple negative breast cancer were all strongly showed significantly different between the three groups. And the Ki67 index had a significantly higher expression in BRCA-positive breast cancer ($p < 0.001$). Oncologic outcomes, such as locoregional recurrence, distant metastasis, and death, were not significantly different between the three groups ($p = 0.587$, 0.071, and 0.742, respectively).

Conclusion

The Ki67 index had a significantly higher expression in BRCA-positive breast cancer. This implies its potential as an efficient prognostic factor in BRCA-positive breast cancer.

Introduction

Hereditary breast cancer, which accounts for approximately 5–10% of breast cancer, primarily occurs in patients with known risk factors (e.g., under 40 years old, bilateral breast cancer, personal history of ovarian cancer, familial history of breast or ovarian cancer, male breast cancer and triple negative breast cancer (TNBC)). It has different molecular properties and prognosis compared to other breast cancers in

general (1–3). Hereditary breast/ovarian cancer is associated with BRCA1/2 gene, while other breast cancer-causing genes include TP53, ATM, PTEN, CDH1, and CHEK2 (4, 5).

Many studies have investigated the clinicopathologic characteristics, molecular characteristics, and prognosis of BRCA1/2-positive hereditary breast cancer, allowing it to be differentiated from general breast cancer. However, because of conflicting results between studies, the prognosis of BRCA1/2-positive breast cancer is not definitive. Because BRCA1/2-positive breast cancer had a higher percentage of cell growth and responded more sensitively to chemotherapy, Levin et al. reported a better prognosis; however, McLaughlin, et al. and Kotsopoulos, et al. reported a decreased overall survival rate associated with the pathogenic variant/likely pathogenic variant (PV/LPV) of BRCA1/2 genes (6–8).

The Korean Hereditary Breast Cancer study (KOHBRA study) research group has also continuously reported studies on the clinical features and prognosis of Korean patients with BRCA1/2-positive breast cancer (9, 10). Studies on variants of unknown significance (VUS) are insufficient because most studies focus on the comparative analysis of PV/LPV and wild type breast cancer. Certain VUS, such as L1780P, have long been defined as unclassified variants, but have recently been recategorized into PV/LPV. Thus, studies on the clinical significance of unclassified mutations have been actively conducted in recent years (11–13).

This study compared and analyzed the clinicopathologic features, molecular characteristics, and oncologic characteristics of PV/LPV, VUS, and wild type breast cancer in BRCA genes. We tried to assess determining factors regarding the direction of treatment and prognosis of breast cancer according to BRCA1/2 gene status based on the results of the study.

Methods

The medical records of breast cancer patients who underwent surgery and neoadjuvant or adjuvant treatment were retrospectively reviewed and analyzed for BRCA gene mutation at the Kyungpook National University Hospital from 2006 to 2019. The study was approved by the university's Institutional Review Board (KNUCH 2020-02-026).

The following clinical variables were assessed: age at breast cancer diagnosis, body mass index (BMI), sex, family and personal history of breast or ovarian cancer, multifocality, type of breast and axillary surgery, neoadjuvant or adjuvant chemotherapy, adjuvant radiotherapy, adjuvant target therapy, and adjuvant hormone therapy. In contrast, the PV/LPV assessed included the following: cancer type, histologic grade, mean clinical and pathologic tumor size, clinical and pathologic stage, estrogen receptor (ER), progesterone receptor (PR), HER2/neu gene, and Ki67 index. A survival curve was used to analyze oncologic results, such as overall survival, locoregional recurrence, distant metastasis, and death during the follow-up period.

BRCA1/2 genetic testing was performed for breast cancer patients with at least one of the following conditions: under 40 years old, bilateral breast cancer, family history of breast cancer or ovarian, history

of breast or ovarian cancer, male breast cancer or TNBC.

Laboratory testing for BRCA gene screening was performed using a 20 mL blood sample on the exons 22 and 26 for gBRCA1 and gBRCA2, respectively, via polymerase chain reaction (PCR) and a direct sequencing method as previously described[13]. The PCR was conducted using the SimpliAmp thermal cycler (Applied BioSystems, Foster City, CA, USA) with the QIAGEN® Multiplex PCR plus kit (Qiagen, Venlo, Germany) and Accupower® PCR PreMix (Bioneer Corp., Daejeon, Republic of Korea). The direct sequencing method based on Sanger sequencing was conducted using 3500xL Dx Genetic Analyzer (Applied BioSystems). The basic concepts of clinical interpretation of detected mutations were in accordance with the 2015 ACMG/AMP guidelines[14]. The results of gBRCA1/2 were all reviewed again based on the current knowledge and reported as wild type (no PV/LPV), VUS, and PV/LPV by laboratory physicians.

Among all 368 cases, 28 cases with bilateral breast cancer were considered as one case, 24 cases were excluded due to insufficient information, and one case of metastatic breast cancer from lung cancer was excluded. The final analysis included a total of 315 cases (Fig. 1).

Statistical analysis was performed using SPSS version 25 (SPSS Inc., Chicago, Il, USA), ANOVA for continuous variables, Pearson's Chi-square test and Fisher's exact test for categorical variables, and Kaplan–Meier Survival curve for oncologic results. p-values ≤ 0.05 were considered statistically significant.

Results

Among the 315 patients who underwent BRCA1/2 gene testing, 97 cases of BRCA gene PV/LPV, 53 BRCA1/2 VUS, and 165 wild type variants were identified. The most common reason for undergoing genetic testing was family history of breast or ovarian cancer (n = 148, 47.0%), while the second most common reason was being younger than 40 years at diagnosis (n = 143, 45.4%). However, there was little difference in the ratio of reasons for evaluation for BRCA1/2 gene mutation among the three groups (Fig. 2).

The mean age of the all patients was 45.3 years (SD, ± 11.0). Although the mean age at diagnosis was significantly younger in group of wild type in BRCA gene, there were no significant differences in mean BMI, family history of breast or ovarian cancer, multifocality, type of breast and axillary surgery. However, the incidence of personal history of breast cancer was significantly higher in PV/LPV group in BRCA gene ($p < 0.001$). In treatment, the neoadjuvant chemotherapy, adjuvant chemotherapy was more administrated in PV/LPV group of BRCA gene and the targer therapy was highly performed in wild type of BRCA gene (Table 1, Fig. 2).

Table 1
Clinical characteristics of patients with breast cancer who were evaluated the BRCA gene status

	Overall population (n = 315)	Wild type (n = 165)	VUS* (n = 53)	PV/LPV† (n = 97)	p-value
Mean age (years, ±SD)	45.3 ± 11.3	43.8 ± 10.7	44.0 ± 11.2	48.5 ± 11.7	0.003[a)]
Mean body mass index (kg/m^2, ±SD)	23.0 ± 3.6	23.2 ± 4.0	22.6 ± 2.7	23.0 ± 3.2	0.500[a)]
Gender (n, %)					0.221[c)]
Female	307 (97.5)	163 (98.8)	51 (96.2)	93 (95.9)	
Male	8 (2.5)	2 (1.2)	2 (3.8)	4 (4.1)	
Family History of breast or ovarian cancer (n, %)					
Yes	148 (47.0)	78 (47.3)	21 (39.6)	49 (50.5)	0.544[b)]
No	167 (53.0)	87 (52.7)	32 (60.4)	48 (49.5)	
Personal History of breast or ovarian cancer (n, %)					< 0.001[c)]
Yes	13 (4.1)	1 (0.6)	1 (1.9)	11 (11.3)	
No	302 (95.9)	164 (99.4)	53 (98.1)	85 (88.7)	
Multifocality (n, %)	64 (20.3)	29 (17.6)	13 (24.5)	22 (22.7)	0.441[b)]
Type of breast surgery (n, %)					0.100[b)]
Breast conserving surgery	195 (61.9)	111 (67.3)	32 (60.4)	52 (53.6)	
Mastectomy	120 (38.1)	54 (32.7)	21 (39.6)	45 (46.4)	
Type of axillary surgery (n, %)					0.060[b)]

a) ANOVA test; *b)* Pearson's Chi-square test; * Variants of Unknown Significance; †Pathogenic variant/Likely pathogenic variant

	Overall population (n = 315)	Wild type (n = 165)	VUS* (n = 53)	PV/LPV† (n = 97)	p-value
Sentinel lymph node biopsy	211 (67.0)	102 (61.8)	36 (67.9)	73 (75.3)	
Axillary lymph nodes dissection	104 (33.0)	63 (38.2)	17 (32.1)	24 (24.7)	
Neoadjuvant chemotherapy (n, %)	63 (20.0)	24 (14.5)	9 (17.0)	30 (30.9)	0.009[b)]
Adjuvant chemotherapy (n, %)	189 (60.2)	100 (60.6)	24 (45.3)	65 (67.0)	0.012[c)]
Adjuvant radiotherapy (n, %)	218 (69.2)	120 (72.7)	38 (71.7)	60 (61.9)	0.143[b)]
Adjuvant target therapy (n, %)	42 (13.4)	33 (20.1)	5 (9.4)	4 (4.1)	< 0.001[b)]
Adjuvant hormone therapy (n, %)	196 (62.2)	110 (66.7)	35 (66.0)	51 (52.6)	0.086[b)]

a) ANOVA test; *b)* Pearson's Chi-square test; * Variants of Unknown Significance; †Pathogenic variant/Likely pathogenic variant

The most common type of breast cancer was invasive ductal carcinoma (n = 273, 86.7%) and histologic grade was grade 2 (n = 142, 45.5%). However, there were significantly many histologic grade 3 in PV/LPV group of BRCA gene (p = 0.036). Clinical T stage was lower in wild type of BRCA gene, but it was not statistically significant in multivariate analysis. About the immunohistochemical staining results with estrogen receptor (ER), progesterone receptor (PR), HER2/neu gene and Ki67 index, there was strongly statistical differences in ER, PR, HER2/neu gene, Ki67 index and triple negative breast cancer (TNBC). Although the ER, PR, HER2/neu gene showed positive results in wild type of BRCA gene, the Ki67 index and the incidence of TNBC was significantly higher in PV/LPV group of BRCA gene ($p < 0.001$) (Table 2).

Table 2
Pathologic characteristics and tumor stages of patients with breast cancer who were evaluated the BRCA gene status

	Overall population (n = 315)	Wild type (n = 165)	VUS* (n = 53)	PV/LPV† (n = 97)	p-value
Cancer type (n, %)					
Ductal carcinoma *in situ*	22 (7.0)	15 (9.1)	4 (7.5)	3 (3.1)	0.207[c)]
Invasive ductal carcinoma	273 (86.7)	134 (81.2)	49 (92.5)	90 (92.8)	
Others	20 (6.3)	16 (9.7)	-	4 (4.1)	
Histologic grade (n, %)					0.036[b)]
Grade 1	21 (6.7)	13 (7.9)	5 (9.4)	3 (3.1)	
Grade 2	142 (45.5)	83 (50.3)	26 (49.1)	33 (34.0)	
Grade 3	126 (40.4)	56 (33.9)	18 (34.0)	52 (53.6)	
Mean clinical tumor size (cm, ±SD)	3.0 ± 2.2	3.1 ± 2.3	3.3 ± 2.4	2.7 ± 1.9	0.300[a)]
Clinical T stage (n, %)					0.034[c)]
Tis	24 (7.6)	17 (10.3)	4 (7.5)	3 (3.1)	
T1	108 (34.3)	55 (33.3)	17 (32.1)	36 (37.1)	
T2	137 (43.5)	69 (41.8)	18 (34.0)	50 (51.5)	
T3	40 (12.7)	21 (12.7)	13 (24.5)	6 (6.2)	
T4	6 (1.9)	3 (1.8)	1 (1.9)	2 (2.1)	
Clinical N stage (n, %)					0.694[c)]
N0	183 (58.1)	94 (57.0)	32 (60.4)	57 (58.8)	

a) ANOVA test; *b)* Pearson's Chi-square test; *c)* Fisher's exact test; * Variants of Unknown Significance; †Pathogenic variant/Likely pathogenic variant; Histologic grade was only classified in invasive carcinomas.

	Overall population (n = 315)	Wild type (n = 165)	VUS* (n = 53)	PV/LPV† (n = 97)	p-value
N1	98 (31.1)	56 (33.9)	13 (24.5)	29 (29.9)	
N2	21 (6.7)	9 (5.5)	6 (11.3)	6 (6.2)	
N3	13 (4.1)	6 (3.6)	2 (3.8)	5 (5.1)	
Mean pathologic tumor size (cm, ±SD)	1.8 ± 1.4	1.8 ± 1.0	1.8 ± 1.5	1.8 ± 1.1	0.412[a)]
Pathologic T stage (n, %)					0.09[c)]
Tis	28 (8.9)	17 (10.3)	4 (7.5)	7 (7.2)	
T1	169 (53.7)	96 (58.2)	27 (50.9)	46 (47.4)	
T2	98 (31.1)	40 (24.2)	18 (34.0)	40 (41.3)	
T3	17 (5.4)	11 (6.7)	2 (3.8)	4 (4.1)	
T4	3 (1.0)	1 (0.6)	2 (3.8)	-	
Pathologic N stage (n, %)					0.182[c)]
N0	221 (70.6)	119 (72.1)	34 (64.2)	70 (72.2)	
N1	76 (24.3)	37 (22.4)	13 (24.5)	26 (26.8)	
N2	13 (4.2)	7 (4.2)	5 (9.4)	1 (1.0)	
N3	3 (1.0)	2 (1.2)	1 (1.9)	-	
Estrogen receptor, positive (n, %)	211 (67.0)	124 (75.2)	38 (72.3)	49 (50.5)	< 0.001[b)]
Progesterone receptor, positive (n, %)	194 (61.6)	118 (71.5)	33 (61.1)	43 (44.3)	< 0.001[b)]
HER2 gene, positive (n, %)	56 (17.8)	40 (24.2)	10 (18.9)	6 (6.2)	0.001[b)]

a) ANOVA test; *b)* Pearson's Chi-square test; *c)* Fisher's exact test; * Variants of Unknown Significance; †Pathogenic variant/Likely pathogenic variant; Histologic grade was only classified in invasive carcinomas.

	Overall population (n = 315)	Wild type (n = 165)	VUS* (n = 53)	PV/LPV† (n = 97)	p-value
Ki67 index, high (> 15%) (n, %)	173 (54.9)	77 (46.7)	27 (50.9)	69 (71.1)	< 0.001[b)]
Triple negative breast cancer (n, %)	78 (24.8)	25 (15.2)	12 (22.6)	41 (42.3)	< 0.000[b)]

a) ANOVA test; *b)* Pearson's Chi-square test; *c)* Fisher's exact test; * Variants of Unknown Significance; †Pathogenic variant/Likely pathogenic variant; Histologic grade was only classified in invasive carcinomas.

In multivariate analysis, the mean age at diagnosis, personal history of breast or ovarian cancer, performance of adjuvant chemotherapy and target therapy, histologic grade and immunohistochemical staining results showed statistical significance between three groups of BRCA gene status (Table 3).

Table 3
Multivariate analysis of patients with breast cancer who were evaluated the BRCA gene status

	Odds ratio	95% CI	p-value
Mean age at diagnosis	6.196	44.0407–46.5498	0.002
Personal History of breast or ovarian cancer	10.268	0.0192–0.0634	< 0.001
Neoadjuvant chemotherapy	2.915	0.1556–0.2444	0.056
Adjuvant chemotherapy	3.558	0.5465–0.7465	0.030
Target therapy	7.047	0.0959–0.1716	0.001
Histologic grade	3.973	2.0938–2.2844	0.020
Clinical T stage	1.122	1.5742–1.7655	0.327
Estrogen receptor	9.543	0.6176–0.7221	< 0.001
Progesterone receptor	10.644	0.5619–0.6699	< 0.001
HER2/neu gene	6.681	0.1353–0.2202	0.001
Triple negative breast cancer	13.274	0.2436 – 0.1997	< 0.001
High Ki67 index	9.275	0.2808–0.4940	< 0.001

The mean follow-up period was 63.8 months (SD, ± 33.7), while overall survival was 99.0% with no differences among the three groups (p = 0.742). The follow-up period for VUS group of BRCA gene was

approximately 12 months longer than that of the other groups (p = 0.037). During the follow-up period, thirteen cases of locoregional recurrence (4.1%), fifteen cases of distant metastasis (4.8%), and three of death (1.0%) were observed. There were no differences among the three groups for each event (p = 0.587, 0.071, and 0.742, respectively) (Table 4, Fig. 3).

Table 4
Oncologic outcomes of patients with breast cancer who were evaluated the BRCA gene status

	Overall population (n = 315)	Wild type (n = 165)	VUS* (n = 53)	PV/LPV† (n = 97)	p-value
Mean follow-up period (months, ±SD)	63.8 ± 33.7	61.2 ± 29.6	74.2 ± 27.3	62.6 ± 41.4	0.037[a)]
Overall survival (%)	99.0	99.4	100.0	97.9	0.742
Locoregional recurrence (n, %)	13 (4.1)	6 (3.6)	1 (1.9)	6 (6.2)	0.587
Ipsilateral breast	9 (2.8)	4 (2.4)	-	5 (5.2)	
Ipsilateral supraclavicular lymph node	2 (0.6)	-	1 (1.9)	1 (1.0)	
Ipsilateral internal mammary lymph node	1 (0.3)	1 (0.6)	-	-	
Ipsilateral axillary lymph node	1 (0.3)	1 (0.6)		-	
Distant metastasis (n, %)	15 (4.8)	6 (3.6)	-	9 (9.3)	0.071
Bone	5 (1.6)	4 (2.4)	-	1 (1.0)	
Endometrium	1 (0.3)	-	-	1 (1.0)	
Lung	2 (0.6)	-	-	2 (2.1)	
Liver	2 (0.6)	1 (0.6)	-	1 (1.0)	
Pectoral muscle	1 (0.3)	-	-	1 (1.0)	
Stomach	1 (0.3)	-	-	1 (1.0)	
Contralateral axillary lymph node	3 (1.0)	1 (0.6)	-	2 (2.1)	
Contralateral supraclavicular lymph node	1 (0.3)	1 (0.6)	-	-	
Mediastinal lymph nodes	1 (0.3)	1 (0.6)	-	-	
Death (n, %)	3 (1.0)	1 (0.6)	-	2 (2.1)	0.742

a) ANOVA test; * Variants of Unknown Significance; †Pathogenic variant/Likely pathogenic variant;

Discussion

Breast cancer is a very heterogeneous disease compared to other malignant tumors which is commonly shows heterogeneity even within the same lesion. Since disease progression and treatment response both depend on molecular characteristics, classifying breast cancers and determining their features are crucial for predicting disease prognosis (14). Although the molecular subtypes of breast cancers should be based on gene expression profiling, they can be clinically classified simply based on the ER, PR, HER2/neu gene, and Ki67 index. Among these, the Ki67 index—which is a known marker of cell proliferation—is actively studied for its clinical value as a prognostic factor for treatment (15). High Ki67 expression is a well-known negative prognostic factor since it is strongly associated with a high recurrence rate, high metastatic rate, and low survival rate (16, 17).

The BRCA1/2 gene has the strongest relationship with hereditary breast cancer, accounting for approximately 5–10% of breast cancers. The actual BRCA gene is a tumor suppressor gene which acts to prevent the development of cancer by repairing damaged DNA. However, due to the PV/LPV of BRCA gene cannot suppress the occurrence of cancer, these variants commonly appear in patients with characteristics such as age under 40 years old, bilateral breast cancer, familial history of breast or ovarian cancer, and male breast cancer. Among all 44 autosomes, the PV/LPV of BRCA gene appear on the long arm of chromosome 17 for BRCA1 and the long arm of chromosome 13 for BRCA2 (18, 19).

Hereditary breast cancer has recently been reported to have different clinical features and prognosis compared to sporadic breast cancers; thus, management for these cases could be quite different. For BRCA-positive breast cancer, anti-cancer drugs using a platinum agent reportedly show good responses (20). Although the mechanism of the BRCA gene is not well-known, it reportedly affects the repair of DNA double strands by controlling the cell cycle checkpoint and being involved in chromosome division. Moreover, the BRCA gene can cause differences in sensitivity to anti-cancer agents (21, 22). Poly adenosine diphosphate-ribose polymerase (PARP) inhibitors have recently gathered attention as therapeutic agents for BRCA-positive breast cancer, because homologous recombination cannot be done adequately in these patients (23, 24). Similarly, studying the features of hereditary breast cancer can help to identify factors which can be used as future therapeutic targets, eventually improving patient prognosis.

The BRCA gene status can be mainly classified into three types as wild type, VUS and PV/LPV. Among them, some PV/LPV can actually influence the development of breast or ovarian cancer, with their respective risks for development being 7–10 times and 30 times higher than in the general population (25–27). In contrast, wild type BRCA variants do not influence breast and/or ovarian cancer and they have similar occurrence rates within the general population. The VUS can be benign or PV/LPV eventually, even if it has not been confirmed. Therefore, this group is ambiguous in its clinical and pathologic characteristics and this could be a limitation in research of BRCA genes. However, the possibility that these VUS turn out to be PV/LPV in the future cannot be ruled out; thus, it is crucial to study these variants.

Among the several clinical and pathologic factors assessed in this study, we found that the Ki67 index showed significantly higher rates of expression for BRCA-positive breast cancer. And the incidence of TNBC was significantly higher in PV/LPV group of BRCA gene, as well-known (28). For these reasons, the neoadjuvant chemotherapy and adjuvant chemotherapy was also significantly more commonly performed to the patients with BRCA-positive breast cancer compared to the other groups. The Ki67 index —a important prognostic factor of breast cancer—is expressed by the MKI16 gene and is usually involved with cell proliferation. Since it is expressed in all proliferating cells (except in quiescence), it is known to be highly associated with tumor cell proliferation (29). And, also, a high Ki67 index expression in breast cancer is reportedly associated with a worse prognosis regardless of lymph node metastasis (30, 31). We could predict a higher Ki67 index expression in BRCA-positive breast cancer because this is known to have a worse prognosis than general breast cancer. In fact, in our study, a significantly high Ki67 index expression was seen in the PV/LPV group. In contrast, although the VUS group had no differences with the PV/LPV group regarding prognosis, it is still important to be cautious of breast cancers with VUS, because these could potentially be reclassified into PV/LPV.

There are some limitations in our study. There was a relatively small number of subjects because this was a single-center study limited to Korean patients with breast cancer. Additionally, the wild type group was also larger than the other groups, and had a different follow-up period between three groups. This can decrease the reliability of our study. Nevertheless, regardless of oncological outcomes, comparative analysis of the clinicopathological factors of breast cancer based on BRCA gene status is still clinically relevant.

Conclusion

The expression rate of Ki67 factor was significantly higher in breast cancer with PV/LPV of BRCA gene. This suggests the potential availability and clinical value of Ki67 factor expression as a prognostic factor for BRCA-related breast cancer. By presenting data on the clinical features, tumor stage, histological characteristics, and oncological prognosis according to BRCA genotype, this study offers clinical evidence with useful information for predicting prognosis and treatment response of breast cancer patients. This study suggests the importance of continuous interest in VUS of BRCA gene, which is common among Korean breast cancer patients; however, it is yet to be sufficiently studied.

Declarations

Ethics approval and consent to participate

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The ethical approval for the study was obtained from Institutional Review Board of the KNUCH (KNUCH KNUCH 2020-02-026).

Informed consent: Informed consent was written obtained from all individual participants included in the study.

Consent for publication

Not Applicable

Availability of data and material

The data sets generated and/or analyzed in this study are not publicly available. However, they are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no conflict of interest.

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Authors' contributions

JL contributed to the study design and manuscript writing. JK, YSL, SP, JP, CN conducted the literature research and data acquisition, analysis. JK, YSL, SP reviewed the manuscript and JL reviewed, edited the manuscript. GC and BK collected further data and analysed for revision of manuscript. All authors read and approved the final manuscript.

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Figures

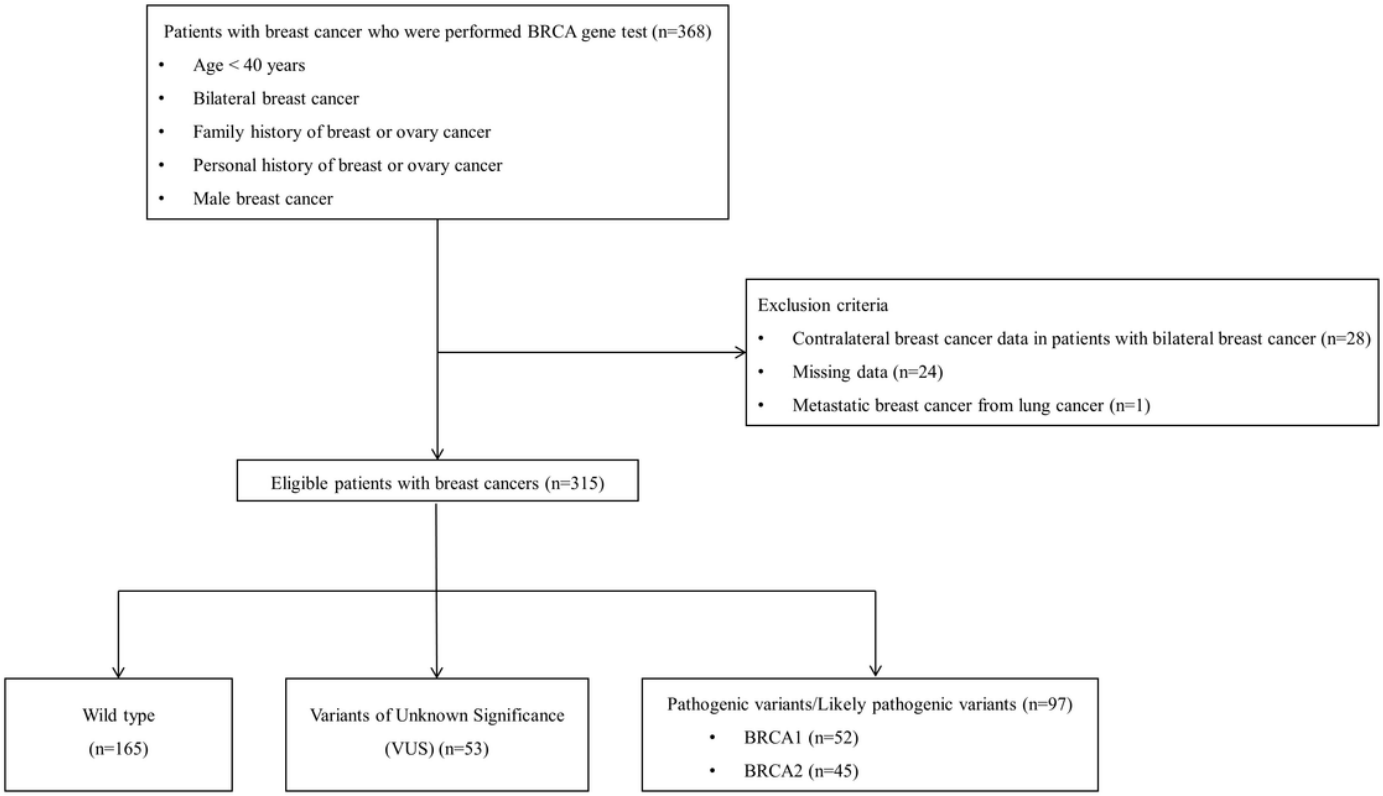

Figure 1

Patient selection diagram.

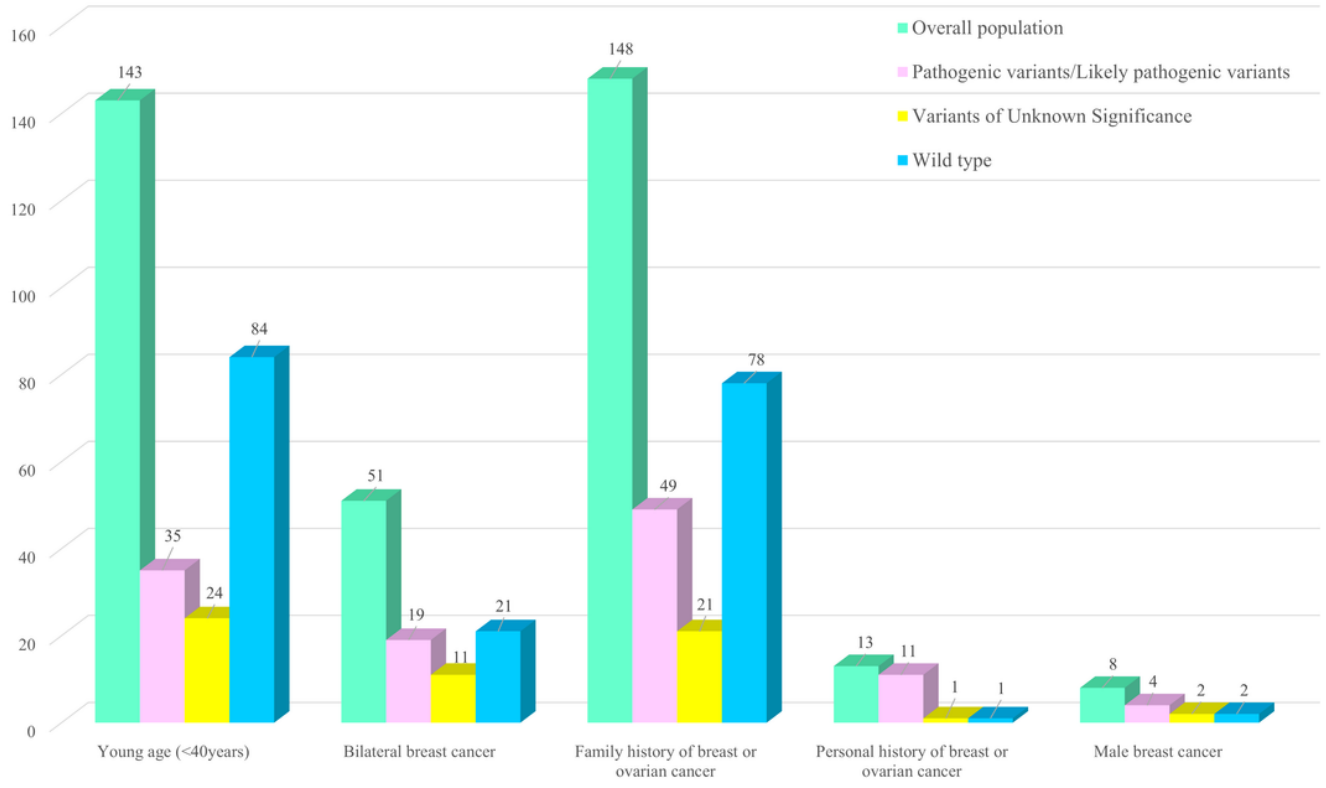

Figure 2

Reasons for evaluating BRCA 1/2 gene status in patients with breast cancer.

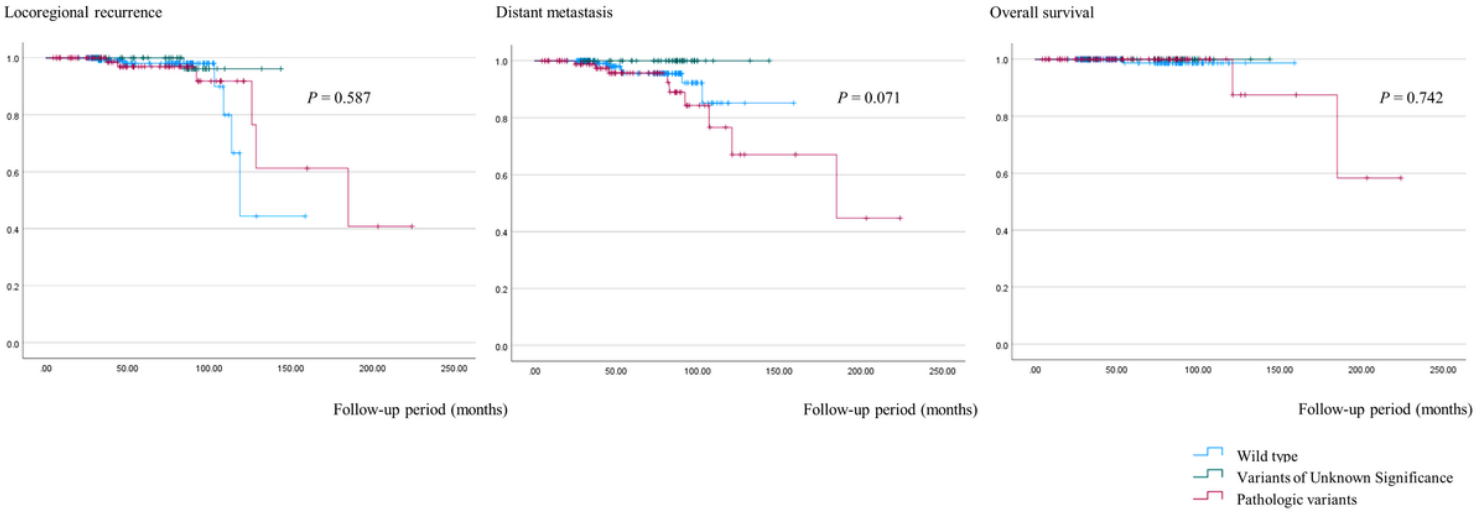

Figure 3

Oncologic outcomes of patients with breast cancer who were evaluated for BRCA 1/2 gene status. Locoregional recurrence (A), distant metastasis (B), and overall survival (C) were not significantly different between the wild type, variants of unknown significance (VUS), and pathogenic variant groups.

Supplementary Files

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- SupplementaryTable.docx