Association of clinical BRCA testing with multigene assay result

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Abstract

ations increase breast cancer risk and are most commonly riple-negative tumors but also occur in hormone receptor tive, HER2-negative subtypes in which multigene assays vant therapy. Data on the relationship between BRCA status gene assay results remain limited in Asian populations. This er study evaluated 2,542 Korean patients with HR-positive, ative breast cancer who underwent multigene testing. BRCA was independently associated with high-risk classification 95% CI 1.80–7.80). In BRCA-mutated patients, family history creased high-risk likelihood. Multiple BRCA testing indications trend toward higher genomic risk in mutation carriers.

Introduction

ations significantly increase the lifetime risk of breast cancer. y are strongly associated with triple-negative breast cancer, lso found in hormone receptor-positive, HER2-negative in which multigene assays are commonly used for risk on and treatment decision-making. However, the ip between BRCA status and multigene assay outcomes nclear, particularly in Asian populations. This study es the association between clinical indications for BRCA d multigene assay results in Korean breast cancer patients.

Methods and Materials

icenter study included 2,542 patients with hormone receptor- HER2-negative breast cancer who underwent multigene etween 2013 and 2024. BRCA testing was performed in aged under 40 years, those with bilateral breast cancer, or h a personal or family history of breast or ovarian cancer ird-degree relatives. Out of a total 2,542 patients, 781 nder went BRCA testing according to clinical indications. he assays included Oncotype DX, MammaPrint, EndoPredict, FREE, and each result was classified into high-risk or low- s based on each test-specific criteria. Statistical analyses formed using chi-square tests and logistic regression in SPSS.

		Multigene test Low risk (n=626)	Multigene test High risk (n=155)	P-value
Age	<40	216 (34.5%)	65 (41.9%)	0.084
	≥40	410 (35.5%)	90 (58.1%)	
T stage	pT1	518 (84.2%)	103 (70.1%)	<0.001
	pT2-T3	97 (15.8%)	44 (29.9%)	
Nstage	pN0	511 (83.1%)	112 (76.2%)	0.086
	pN+	90 (14.6%)	33 (22.4%)	
Histologic grade	1	222 (35.5%)	22 (14.2%)	<0.001
	2	380 (60.7%)	96 (61.9%)	
	3	24 (3.8%)	37 (23.9%)	
PR	Negative	48 (7.8%)	29 (19.7%)	<0.001
	positive	567 (92.2%)	118 (80.3%)	
Her-2	0	165 (26.4%)	33 (21.3%)	0.003
	1	321 (51.3%)	67 (43.2%)	
	2	140(22.4%)	55 (35.5%)	
BRCA test	Negative /VUS	604 (96.5%)	133 (82.6%)	<0.001
	Mutation	22 (3.5%)	22 (14.2%)	
Familial history of breast cancer, ovary cancer	No	268 (42.9%)	63 (40.9%)	0.647
	yes	356 (57.1%)	91 (59.1%)	
	Unilateral	497 (79.4%)	134 (86.5%)	0.046
	bilateral	129 (20.6%)	21 (13.5%)	

Table 1. Clinicopathologic characteristics of BRCA tested patients with fulfilling the indications for BRCA testing.

Results

Patients were categorized as BRCA-tested group (n=781) or non-tested group (n = 1,596). In the BRCA-tested group, 19.8% were classified as high risk and 80.2% as low risk by multigene assay. pT stage, pN stage, histologic grade, progesterone receptor status, and Ki-67 level was independently associated with high risk and multigene assay result. BRCA mutation was identified in 44 patients (7 BRCA1 mutation, 37 BRCA2 mutation). BRCA mutation was independently associated with high-risk classification on multigene assay (OR 3.75, 95% CI 1.80-7.80, p < 0.001).

In subgroup analysis of BRCA mutation group, among 30 patients with a family history, 20 (66.7%) were classified as high risk. Multivariate analysis also confirmed that familial history of breast or ovarian cancer was independently associated with high-risk in BRCA-mutation patients. (OR 24.73, p <0.05). An association between BRCA testing indications and high-risk multigene assay results was not statistically significant when only one indication was present.

		Multigene test Low risk (n=22)	Multigene test High risk (n=22)	P-value
Number of BRCA indication	1	18 (81.8%)	11 (50.0%)	0.049
	2	4 (18.2%)	8 (36.4%)	
	3	0 (0%)	3 (13.6%)	
Familial history of cancer	None	6 (28.6%)	1 (4.5%)	0.019
	Others	4 (19.0%)	1 (4.5%)	
	Breast, ovary	11 (52.4%)	20 (90.9%)	
age	<40	9 (40.9%)	10 (45.5%)	0.761
	≥40	13 (59.1%)	12 (54.5%)	
Bilaterality	Unilateral	17 (77.3%)	16 (72.7%)	0.728
	bilateral	5 (22.7%)	6 (27.3%)	

Table 2. Association between BRCA testing indication factors and multigene assay results among BRCA mutation carriers.

		Univariate HR [95%CI] (p-value)	Multivariate HR [95%CI] (p-value)
Age	<40 vs >=40	1.37[0.96-1.96] (0.09)	1.24 [0.72-2.14] (0.43)
T stage	pT2-3 vs T1	2.26 [1.51-3.39] (<0.001)	2.34 [1.47-3.74] (<0.001)
N stage	pN+ vs pN0	1.63 [1.06-2.52] (0.03)	1.84 [1.10-3.07] (0.02)
PR	Negative vs positive	2.90 [1.76-4.80] (<0.001)	3.18 [1.79-5.66] (<0.001)
Ki-67	≥20 vs <20	4.32 [2.44-8.44] (<0.001)	2.84[1.47-3.74] (<0.001)
BRCA test	Mutation vs negative/VUS	4.54[2.44-8.44] (<0.001)	3.75 [1.80-7.80] (<0.001)
	Bilateral vs unilateral	0.60 [0.37-0.99] (0.048)	0.74 [0.39-1.44] (0.394)

Table 3. Hazard ratio of multigene test high risk derived from univariate and multivariate regression model in BRCA tested group.

Discussion

In this study, we explored the application of multigene assays—commonly used to estimate the potential benefit of adjuvant chemotherapy—to patients with hereditary breast cancer predisposition. Consistent with previous reports, the presence of a BRCA mutation was associated with a higher likelihood of being classified as high risk by multigene testing. Among the 44 patients with BRCA mutations, 30 had a family history of breast or ovarian cancer, and approximately 67% of these patients were categorized as high risk. In addition, 34% of BRCA mutation carriers met two or more clinical indications for BRCA testing, and about 70% of them were assigned to the high-risk group.

In patients met BRCA test indication, none of the individual BRCA testing indication factors—such as family history, bilaterality, or young age—demonstrated a significant independent association with high-risk multigene assay classification. Also, the presence of multiple BRCA testing indications did not demonstrate a significant association with high-risk categorization on the multigene test in BRCA tested group. Although the number of BRCA mutation carriers in our study was limited, our findings suggest that clinical factors may be useful in identifying patients more likely to benefit from chemotherapy.

Conclusions

In Korean patients with hormone receptor-positive, HER2-negative breast cancer, BRCA mutation was significantly associated with high-risk classification on multigene assay. In BRCA-mutated patients, the presence of a family history further increased the likelihood of high-risk classification. Further large-scale studies are needed to evaluate the associations and interactions between each clinical factor and multigene assay outcomes.

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