PS3-03-22: *BRCA1/BRCA2*-tested breast and ovarian cancer patients in Peru: clinical and genomic features

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Background

Likely pathogenic (LP) and pathogenic (P) variants in *BRCA1/BRCA2* are key markers of hereditary cancer syndromes and have major implications for prevention and clinical management. In Peru, breast and ovarian cancers remain significant public health problems due to late diagnoses and limited access to genetic testing. Among breast cancer patients, tumor characteristics are closely linked to BRCA status: carriers of *BRCA1* LP/P variants are more frequently diagnosed with triple-negative breast cancer (TNBC), while *BRCA2* carriers more often present with ER/PR-positive tumors. Understanding the clinical and genomic profiles of *BRCA-tested* patients in Peru is essential to improve risk assessment and guide care for high-risk groups. This study aimed to describe the clinical, demographic, and genomic characteristics of Peruvian patients with breast and/or ovarian cancer who underwent *BRCA1/BRCA2* testing between 2013 and 2020. It represents the first nationwide, large-scale analysis of BRCA-tested cancer patients in Peru. Identifying pathogenic variants and associated clinical patterns is crucial for recognizing individuals at elevated hereditary cancer risk and for supporting the development of effective prevention strategies and precision oncology programs.

Methods and Materials

Individuals diagnosed with breast and/or ovarian cancer were evaluated at the National Institute of Neoplastic Diseases (INEN) between August 2013 and March 2020. Patients meeting the clinical inclusion criteria of the inter-institutional protocol INEN13-48 ("Hereditary and Familial Cancer Study in the Peruvian Population") and the City of Hope IRB #96144 underwent genetic testing performed at City of Hope (COH). For participants diagnosed with both breast and ovarian cancer, only the first cancer diagnosis was used for classification. Geographic origin was categorized into North Coast, Central–South Coast, North Highland, Central–South Highland, and Jungle.

Results

Table 1. Female (N = 1,565)

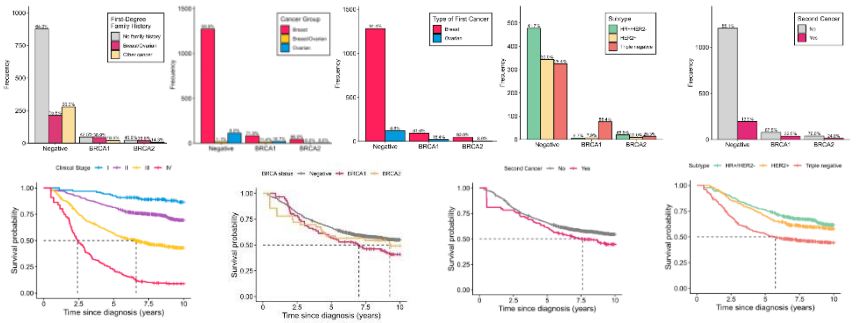
In patients diagnosed with both breast and ovarian cancer, only the first diagnosed cancer was considered for classification
One patient carried actionable variants in both BRCA1 and BRCA2 and was included under BRCA1 for table stratification.

Characteristic	Overall N = 1,565	Negative N = 1,408	BRCA1 N = 114	BRCA2 N = 50	p-value
Age at Diagnosis	41 (12–79)	41 (12–79)	40 (22–66)	42 (24–73)	0.5
Sex					
Female	1,565 (100.0%)	1,408 (100.0%)	114 (100.0%)	50 (100.0%)	
Birthplace Region					
Coast	1,096 (70.0%)	985 (70.0%)	75 (65.8%)	36 (72.0%)	
Highland	362 (23.1%)	323 (23.1%)	30 (26.3%)	9 (18.0%)	
Jungle	84 (5.4%)	76 (5.3%)	5 (4.4%)	3 (6.0%)	
Other country	23 (1.5%)	19 (1.4%)	4 (3.5%)	0 (0.0%)	
First - Degree Family History					<0.001
No family history	947 (60.9%)	876 (64.0%)	48 (42.5%)	23 (46.9%)	
Other cancer	306 (20.0%)	278 (20.3%)	21 (18.6%)	7 (14.3%)	
Breast/Ovarian	277 (18.1%)	214 (15.6%)	44 (38.9%)	19 (38.8%)	
Unknown	35	33	1	1	
Cancer Group					<0.001
Breast	1,398 (89.3%)	1,273 (90.4%)	82 (71.9%)	43 (86.0%)	
Ovarian	135 (8.6%)	112 (8.0%)	19 (16.7%)	4 (8.0%)	
Breast/Ovarian	32 (2.0%)	18 (1.1%)	13 (11.4%)	3 (6.0%)	

Table 2. Female (N = 1,565)

In patients diagnosed with both breast and ovarian cancer, only the first diagnosed cancer was considered for classification
One patient carried actionable variants in both BRCA1 and BRCA2 and was included under BRCA1 for table stratification.

Characteristic	Overall N = 1,565	Negative N = 1,408	BRCA1 N = 114	BRCA2 N = 50	p-value
Second Cancer (Presence)					<0.001
No	1,321 (84.4%)	1,206 (86.1%)	77 (67.5%)	38 (76.0%)	
Yes	244 (15.6%)	195 (13.9%)	37 (32.5%)	12 (24.0%)	
Type of Second Cancer					
new Breast	129 (52.9%)	96 (49.2%)	25 (67.6%)	8 (66.7%)	
Thyroid	30 (12.3%)	27 (13.8%)	3 (8.1%)	0 (0.0%)	
Ovarian	20 (8.2%)	8 (4.1%)	9 (24.3%)	3 (25.0%)	
CCR	15 (6.1%)	15 (7.7%)	0 (0.0%)	0 (0.0%)	
End	11 (4.5%)	10 (5.1%)	0 (0.0%)	1 (8.3%)	
Kidney	7 (2.9%)	7 (3.6%)	0 (0.0%)	0 (0.0%)	
Gastric	6 (2.5%)	6 (3.1%)	0 (0.0%)	0 (0.0%)	
Heme	5 (2.0%)	5 (2.6%)	0 (0.0%)	0 (0.0%)	
Sarcoma	5 (2.0%)	5 (2.6%)	0 (0.0%)	0 (0.0%)	
Cervical	4 (1.6%)	4 (2.1%)	0 (0.0%)	0 (0.0%)	
H&N	2 (0.8%)	2 (1.0%)	0 (0.0%)	0 (0.0%)	
Other GI	2 (0.8%)	2 (1.0%)	0 (0.0%)	0 (0.0%)	
Pancreas	2 (0.8%)	2 (1.0%)	0 (0.0%)	0 (0.0%)	
skin	2 (0.8%)	2 (1.0%)	0 (0.0%)	0 (0.0%)	
Bile duct	1 (0.4%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	
Bladder	1 (0.4%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	
Cervix	1 (0.4%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	
Lung	1 (0.4%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	
Unknown	1,321	1,206	77	38	



Discussion

A total of 1,576 patients were included in the study, with a median age at diagnosis of 41 years. The vast majority were female (99.3%), and only 0.7% (n = 11) were male. Family history of cancer was absent in 61% of cases; 18% reported first-degree relatives with breast and/or ovarian cancer, while 20% reported other types of cancer. Breast cancer was diagnosed in 89.5% of patients (n = 1,410), ovarian cancer in 8.5% (n = 134), and both in 2% (n = 32). In breast cancer cases, the most frequent tumor subtype was HR+/HER2– (39.6%), followed by triple-negative (31.3%) and HER2+ (28.1%). Overall, we identified pathogenic variants in *BRCA1* were identified in 7.2% (n = 114) of the whole population, and in *BRCA2* in 3.2% (n = 51). Specifically, 6% of breast cancer patients carried a *BRCA1* pathogenic variant, and 3% had a *BRCA2* variant. *BRCA1*-positive breast tumors were predominantly of the triple-negative subtype (85.4%), whereas HR+/HER2- (47.6%) tumors were the most frequent among *BRCA2*-positive cases. In patients with ovarian cancer, 82% were *BRCA*-negative, while 14% carried *BRCA1* and 2.8% *BRCA2* pathogenic variants. Clinical stage II was the most common at presentation (39.3%), followed by stage III (38.8%), stage I (11%), and stage IV (10%). Additionally, 15% of patients developed a second primary malignancy, most commonly a new breast cancer (52%), followed by other cancers (15%), thyroid (12%), ovarian (8%), and colorectal cancer (6%). Notably, ovarian cancer diagnosis, advanced clinical stage, and triple-negative breast cancer subtype were significantly associated with poorer overall survival ($p < 0.001$ for all).

Conclusions

Patients with P/LP *BRCA1/BRCA2* variants showed an increased risk of developing a second primary cancer, mainly a new breast cancer, highlighting the need for long-term surveillance. Among breast cancer cases, *BRCA1* carriers more frequently presented with triple-negative tumors, while *BRCA2* carriers commonly had luminal subtypes. These findings emphasize the importance of expanding genetic counseling, implementing risk-reduction strategies, and strengthening precision oncology programs. The higher mortality observed in *BRCA1*-mutated patients underscores the need to better characterize their clinical and genomic profiles to optimize care for high-risk populations in Peru.

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