PS3-03-07: Breast and Ovarian Cancer Genomic Risk Assessment: 10-Year Experience from a High-Risk Program

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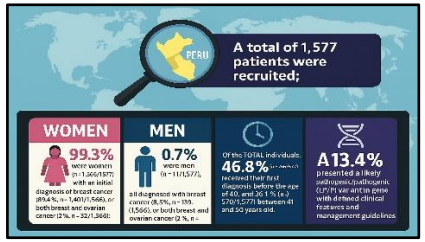
Background

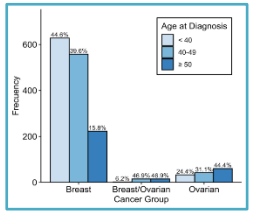
Breast cancer (BC) is one of the most common cancers among women in both Peru and worldwide. Ovarian cancer (OC), due to the difficulty of early detection, also represents a significant public health concern in the country. In recent years, genetic testing has become essential for identifying individuals at high risk for hereditary cancer predisposition syndromes, guiding decisions related to prevention, early detection, and treatment. In Peru, the use of genetic testing is still developing. This work presents an inter-institutional collaborative experience that has facilitated access to genetic testing and contributed to the implementation of a multidisciplinary care system for managing high-risk patients.

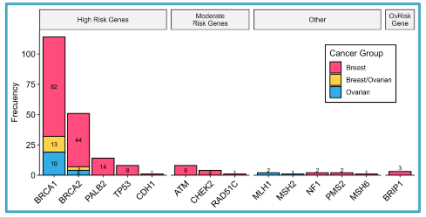
Methods and Materials

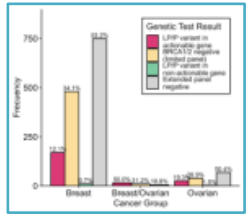
This study includes individuals diagnosed with breast and/or ovarian cancer who were referred for Medical Genetics evaluation at the National Institute of Neoplastic Diseases (INEN) between August 2013 and March 2020. The participants met the inclusion criteria of the interinstitutional protocol INEN13-48 on hereditary cancer and underwent genetic testing at the City of Hope (IRB No. 96144). The main objective is to identify the genomic profile of patients with breast and/or ovarian cancer and to evaluate the clinical impact of genetic testing on cancer management.

Results









Female with LP/P variant in actionable gene (N = 211)

		High Risk Genes				Moderate Risk Genes			Ovarian Risk Gene	Other			
	Overall	BRCA1	BRCA2	PALB2	CDH1	TP53	ATM	CHEK2	RAD51C	MLH1	MSH2	MSH6	PMS2	NF1
	N = 211	N = 104	N = 50	N = 19	N = 13	N = 10	N = 10	N = 9	N = 5	N = 23	N = 11	N = 11	N = 11	N = 10
Control Risk Breast Cancer														
Imaging-based surveillance	53 (100.0%)	16 (30.2%)	16 (30.2%)	5 (9.4%)	0 (0.0%)	6 (11.3%)	7 (13.2%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)
Rejected recommendations	38 (100.0%)	16 (42.1%)	10 (26.3%)	5 (13.2%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	2 (5.3%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Unilateral/Bilateral risk-reducing mastectomy (RRM)	31 (100.0%)	19 (61.3%)	9 (29.0%)	3 (9.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
New BC diagnosis after RRM	6 (100.0%)	3 (50.0%)	2 (33.3%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	83	60	13	0	1	2	0	1	0	2	1	0	1	1
Control Risk Ovarian Cancer														
Underwent risk-reducing salpingo-oophorectomy (RRSO)	58 (100.0%)	33 (56.9%)	20 (34.5%)	5 (8.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rejected recommendations	25 (100.0%)	10 (40.0%)	6 (24.0%)	5 (20.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)
Previous ovarian surgery	19 (100.0%)	8 (42.1%)	7 (36.8%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
New OC diagnosis after RRSO	2 (100.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	107	61	17	1	1	8	7	4	0	2	1	1	1	2

Discussion

A total of 1,577 patients were recruited; 99.3% were women (n=1,566) with an initial diagnosis of breast cancer (89.4%), ovarian cancer (8.5%), or both (2%). Only 0.7% were men (n=11), all diagnosed with breast cancer. Regarding age at diagnosis, 46.8% received their first diagnosis before age 40, and 36.1% between 41 and 50 years. Overall, 13.4% (n=212) carried a likely pathogenic/pathogenic (LP/P) variant in genes with established clinical relevance; 0.8% (n=12) carried LP/P variants in genes without defined clinical features. Among those with negative results, 34.5% had negative *BRCA1/BRCA2* testing, and 51.2% had a negative extended gene panel. The most frequent LP/P variants were found in *BRCA1* (53.8%) and *BRCA2* (24%). One percent carried more than one LP/P variant. LP/P detection rates were 12% for breast cancer, 19.5% for ovarian cancer, and 50% for combined breast/ovarian cancer. The most recurrent variants were *BRCA1* c.68_69del (6%) and *BRCA2* c.1219C>T (4%). Among male patients, 9% carried a BRCA2 variant. In clinical genetics follow-up (n=212), 72% received high-risk breast cancer management recommendations and 54% for ovarian cancer. Among high-risk breast cancer patients: 34% initiated imaging-based surveillance, 26% underwent prophylactic mastectomy (10% were diagnosed with a new breast cancer), and 34% declined recommendations. In the high-risk ovarian cancer group: 18% had a prior ovarian surgery, 49% underwent prophylactic salpingo-oophorectomy (with 2 new ovarian cancers detected), and 23% declined intervention. To date, 36.7% of patients have died, and 17% were lost to follow-up.

Conclusions

Ensuring access to genetic testing and recognition of hereditary cancer syndromes is essential. In this cohort, 13% of individuals carried an actionable LP/P variant, similar to findings in other populations. This underscores the need for sustained funding not only to expand access to genetic testing but also to strengthen multidisciplinary high-risk care in our institution, taking into account the geographic and economic barriers present in our country.

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References:

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide. CA Cancer J Clin. 2018;68(6):394–424.
2. Kuchenbaecker KB, Hopper JL, Barnes DR, Phillips KA, Mooij TM, Roos-Blom MJ, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. JAMA. 2017;317(23):2402–16.
3. Yurgelun MB, et al. NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic. JNCCN. 2024;22(1):1–30.
4. Villarreal-Garza C, Alvarez-Gómez RM, Pérez-Plasencia C, Herzog J, Castillo D, Mohar A, et al. The genetic landscape of hereditary breast cancer in Latin America: results from the LACAM consortium. JCO Precis Oncol. 2020;4:185–98.
5. Weitzel JN, Blazer KR, Macdonald DJ, Culver JO, Offit K. Prevalence of BRCA mutations in Latin America and implications for clinical management. J Glob Oncol. 2019;5:1–12.
6. Li J, Meisel JL. Genetic testing and clinical management of hereditary breast and ovarian cancer syndromes in low- and middle-income countries. The Oncologist. 2021;26(8):e1365–74
7. Torres D, Rashid MU, Gil F, Umaña A, Ramírez-Clavijo S, Forero-Castro M, et al. BRCA1/2 mutations in Latin America: a systematic review. Lancet Oncol. 2019;20(3):e142–52.