Original Research

ONCOLOGY

Emotional distress and quality of life in high and moderate penetrance germline mutations carriers diagnosed with breast cancer: a preliminary study

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Abstract

Background/Objectives. Genetic testing plays a critical role in breast cancer management by identifying individuals with high or moderate penetrance gene mutations. While clinical implications are well established, less is known about the psychological and quality-of-life impact of different genetic risk levels. This preliminary study aimed to explore whether breast cancer patients with high penetrance mutations experience different levels of distress compared to those with moderate penetrance mutations.

Methods. A total of 110 breast cancer patients treated at the Regina Maria Private Health Network in Cluj-Napoca, Romania, were included based on specific eligibility criteria. Participants completed a shortened version of the BREAST-Q questionnaire, focused on core dimensions such as emotional distress, self-concept, appearance, relationships, and financial burden. Descriptive statistics were calculated, and independent t-tests were performed to compare responses between the two genetic risk groups.

Results. Patients with high penetrance mutations reported significantly higher distress levels in several domains, including overall emotional distress ($p = 0.039$), concern for daughters or relatives ($p = 0.043$), changes in appearance ($p = 0.038$), and self-concept ($p = 0.043$). Other factors, such as fear of diagnosis, financial burden, and impact on sexuality, did not show statistically significant differences between groups.

Conclusions. This preliminary study suggests that genetic risk classification may influence the psychosocial experience of breast cancer patients, with high penetrance mutation carriers experiencing greater distress in specific areas. These findings highlight the need for personalized psychosocial support based on genetic profiles and warrant further investigation in larger, longitudinal cohorts.

Keywords: quality of life, genetic testing, psychological distress, oncology quality measures, Romania

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Introduction

Breast cancer remains one of the leading causes of morbidity in women [1]. Advancements in genetic testing have significantly improved our understanding of breast cancer susceptibility, particularly by identifying moderate and high penetrance genes [2,3]. While high penetrance genes such as *BRCA1* (Breast Cancer gene 1) and *BRCA2* (Breast Cancer gene 2) are well-known for their strong association with hereditary breast cancer and the substantial risk they confer, moderate penetrance genes like *ATM* (Ataxia Telangiectasia Mutated), *CHEK2* (Checkpoint Kinase 2), and *PALB2* (Partner and Localizer of BRCA2) also contribute meaningfully to breast cancer development, albeit with a comparatively lower risk [4,5]. If, for high-penetrance mutations, there is evidence-based information and recommendations

in the medical guidelines, [6] for moderate-penetrance defects, the screening and prophylaxis recommendations are most often adapted to each case, which have complex implications from a medical and psycho-emotional point of view [7,8]. As precision medicine continues to evolve, it is increasingly important to consider the biological and clinical implications of these genetic mutations and the broader psychosocial and quality of life (QoL) outcomes they may entail [9,10].

This study assesses whether breast cancer patients with moderate penetrance gene mutations experience a different quality of life than those with high penetrance mutations. By exploring domains such as emotional well-being, physical functioning, body image, and perceived risk, this research seeks to provide a nuanced understanding of how genetic risk levels influence the lived experience of breast cancer. The findings may have implications for tailoring supportive care strategies and informing genetic counselling practices.

Methods

Selection of the cohort

We initially identified a cohort of 547 patients who were diagnosed with breast cancer at the Regina Maria Private Healthcare Hospital Cluj-Napoca, Romania. These patients received their diagnoses and treatments between January 2021 and December 2024, the starting point for our analysis. A subset was selected based on specific criteria from this total cohort.

Following the application of the eligibility criteria, 110 patients were ultimately included in the study. These individuals met all inclusion requirements and provided complete responses to the quality-of-life questionnaire. Figure 1 illustrates the selection process, while the eligibility criteria are detailed in the following paragraph.

Patients were included in the study based on four key criteria, as follows:

(1) confirmed diagnosis of breast cancer

(2) presence of a pathogenic variant in a gene classified as either high or moderate penetrance

(3) no evidence of metastatic disease at the time of inclusion, to reduce potential confounding effects on quality of life

(4) minimum of six months since the completion of primary treatment (surgery, chemo-therapy, or radiotherapy), allowing for a more stable assessment of quality-of-life out-comes

(5) consent to participate by completing the quality-of-life questionnaire.

Genetic testing

Sequencing data generated on the Illumina platform (Illumina Inc., San Diego, CA, USA) and aligned to the human reference genome (GRCh37/hg19) served as the basis for genetic testing. Variants were analyzed with specialized software tools, referencing the gnomAD and ClinVar databases. GATK (version 4.3.0.0, Broad Institute, Cambridge, MA, USA) was employed for variant calling, while VarSeq (version 2.4.0, Golden Helix, Bozeman, MT, USA) and Alamut Visual (version 1.11, SOPHiA GENETICS, Rolle, Switzerland) facilitated annotation and interpretation. ExomeDepth (version 1.1.15, University of Cambridge, Cambridge, UK) was applied to detect copy number variations (CNVs). Pathogenicity was assessed by a clinical team following ACMG guidelines.

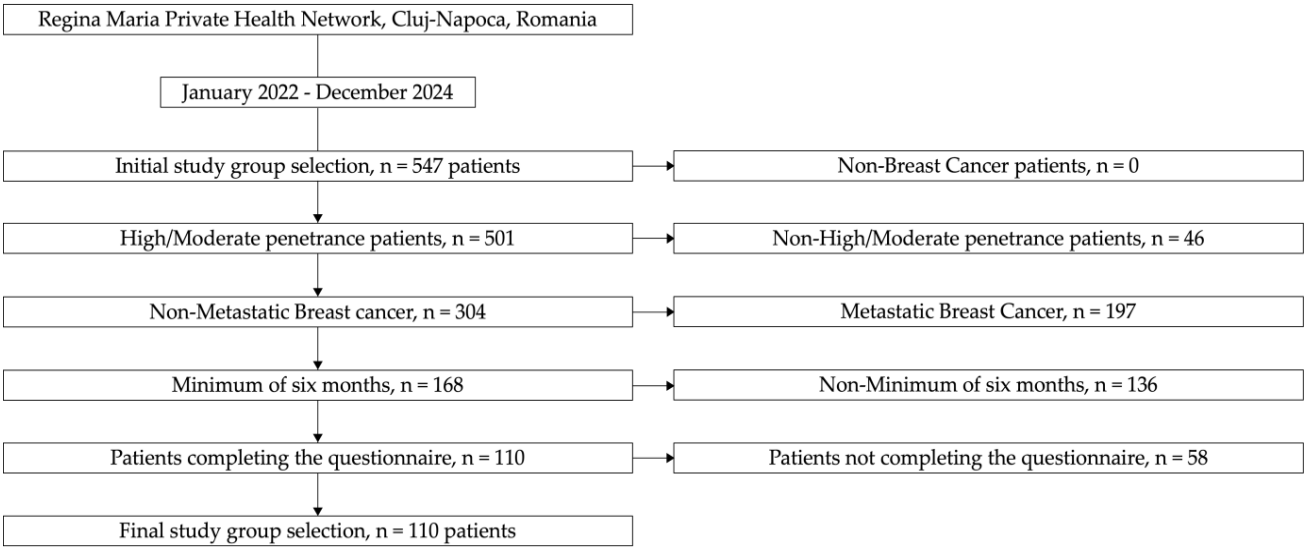

Figure 1. Patient selection flowchart.

Confirmation of significant findings was carried out through Sanger sequencing using the ProDye® Terminator Sequencing System (Promega Corporation, Madison, WI, USA), as well as Eurofins Genomics' Sanger sequencing services (Ebersberg, Germany). All pathogenic, likely pathogenic, and variants of uncertain significance were reported; only clinically relevant variants were considered during genetic counselling in this study.

Distress measurement

To assess key elements of the mastectomy and breast reconstruction experience, we employed a condensed version of the BREAST-Q Version 2.0 (2017), developed at McMaster University under the direction of Dr. Anne F. Klassen [11]. While the full BREAST-Q encompasses diverse domains such as physical and psychological effects, cancer-related anxiety, fatigue, and work-related impact, our adapted version focused on the most relevant dimensions for our analysis. These included medical issues related to the chest, emotional health, body image, and key psychosocial outcomes associated with both mastectomy and reconstruction. To reduce respondent burden while preserving the instrument's clinical value, we selected a core set of items that addressed physical alterations, emotional discomfort, and psychosocial impacts tied to the diagnosis and treatment process.

Additionally, we adopted the distress assessment methodology previously validated by Cătană et al. (2025) to measure patient distress during the breast cancer journey. This approach complemented the BREAST-Q items and allowed us to capture a more comprehensive picture of the anguish experienced from diagnosis through recovery [12]. The selected items specifically targeted emotional reactions to genetic findings, anxiety surrounding surgery, concerns about physical appearance, financial pressures, effects on intimate and family relationships, and sexuality-related worries. Distress levels were rated on a scale from 1 to 5, with 1 indicating minimal discomfort and 5 representing extreme anguish. By integrating Cătană et al.'s validated measurement method, we ensured consistency and robustness in quantifying distress, providing a focused yet meaningful evaluation of patient-reported quality of life throughout the breast cancer treatment continuum (see Table I.)

Statistical methods

To assess the levels of distress experienced by breast cancer patients, we first performed a descriptive analysis of all questionnaire items, calculating measures such as means, standard deviations, medians, and 95% confidence intervals. These descriptive statistics provided an overview of the general distress patterns across the sample. To determine whether there were statistically significant differences in distress levels be-tween patients with moderate vs. high penetrance gene mutations, we conducted in-dependent t-tests for each distress-related category. This approach allowed for directly comparing the two genetic risk groups across multiple quality-of-life dimensions. All statistical analyses were performed using Jamovi software (version 2.6.17, The Jamovi Project, Sydney, Australia). At the same time, figures and visual data representations were created using Microsoft® Excel for Mac (version 16.83, Microsoft Corporation, Redmond, WA, USA).

Table I. Questions from Cătană's short version scale used to assess quality of life in the study.

No. Crt.	Question
1.	How much distress has the genetic diagnosis caused you? (Fear related to genetic diagnosis)
2.	How much distress did the time between receiving the diagnosis and achieving full recovery cause in your physical appearance? (Change in appearance)
3.	How much distress did the time between receiving the diagnosis and achieving full recovery impact your self-concept? (Change in self-concept)
4.	How much has the diagnosis interfered with your personal relationships, and how distressing has this been? (Interference with personal relationship)
5.	How much distress did the time between receiving the diagnosis and achieving full recovery cause in your couple's relationship? (Impact on couple relationship)
6.	How much distress did the time between receiving the diagnosis and achieving full recovery have on your employment? (Impact on employment)
7.	How much distress did the time between receiving the diagnosis and achieving full recovery cause in your concerns for your daughters or other relatives? (Concern related to daughters or relatives)
8.	How much distress did the time between receiving the diagnosis and achieving full recovery cause in terms of financial burden? (Financial burden)
9.	How much distress did the time between receiving the diagnosis and achieving full recovery cause about your sexuality? (Impact on sexuality)
10.	How much overall emotional distress have you experienced related to the diagnosis and treatment? (Overall emotional distress)

Results

This section presents the main findings of our study, focusing on the distribution of gene mutations and the quality-of-life and distress indicators reported by breast cancer patients carrying either moderate or high penetrance genetic mutations. The data include descriptive statistics and comparative analyses, aiming to highlight potential differences in patient experiences based on genetic risk. Visual figures and statistical tables are used to support a comprehensive understanding of the questionnaire outcomes and their variation across subgroups.

Figures 2 and 3 illustrate the distribution of gene mutations within the high and moderate penetrance groups, respectively, offering insight into the cohort's genetic composition.

Table II summarizes the descriptive statistics for the entire study sample based on the questionnaire responses, including mean scores, standard deviations, and confidence intervals for each item assessed.

Table III provides a breakdown of the same variables, grouped by gene penetrance category, allowing for subgroup comparison.

Table IV presents further comparative analysis between the two groups, including results from independent t-tests evaluating potential differences in quality-of-life and distress-related variables.

Table II. Descriptive analysis of the statistical data obtained from the questionnaire.

	Mean	SE	95% Confidence Interval		Median	SD	Shapiro-Wilk	
			Lower	Upper			W	P
Age	49.26	0.7492	47.78	50.75	48.00	7.857	0.962	0.003
Fear related to genetic diagnosis	3.43	0.0944	3.24	3.61	4.00	0.990	0.892	<.001
Change in appearance	3.52	0.0920	3.34	3.70	4.00	0.965	0.892	<.001
Financial burden	3.66	0.1003	3.46	3.86	4.00	1.052	0.879	<.001
Overall emotional distress	3.45	0.0963	3.25	3.64	4.00	1.010	0.897	<.001
Concerns related to daughters or relatives	3.49	0.1094	3.27	3.71	4.00	1.147	0.898	<.001
Impact on couple's relationship	3.45	0.1054	3.25	3.66	4.00	1.106	0.898	<.001
Change in self-concept	3.43	0.1084	3.21	3.64	4.00	1.137	0.902	<.001
Impact on employment	3.36	0.1223	3.12	3.61	4.00	1.283	0.891	<.001
Interference with personal relationship	3.64	0.1101	3.42	3.85	4.00	1.155	0.872	<.001
Impact on sexuality	3.33	0.0993	3.13	3.52	3.00	1.041	0.902	<.001

Table III. Descriptive analysis of the statistical data obtained from the questionnaire grouped based on the gene penetrance.

	Group	Mean	SE	95% Confidence Interval		Median	SD	Shapiro-Wilk	
				Lower	Upper			W	P
Age	M[1]	49.51	1.192	47.11	51.91	48	8.344	0.934	0.009
	H[2]	49.07	0.961	47.14	50.99	49	7.507	0.979	0.378
Fear related to genetic diagnosis	M	3.27	0.162	2.94	3.59	3	1.132	0.901	<.001
	H	3.56	0.108	3.34	3.77	4	0.847	0.868	<.001
Change in appearance	M	3.31	0.146	3.01	3.60	3	1.025	0.903	<.001
	H	3.69	0.113	3.46	3.92	4	0.886	0.873	<.001
Financial burden	M	3.53	0.157	3.21	3.85	4	1.101	0.887	<.001
	H	3.77	0.129	3.51	4.03	4	1.007	0.865	<.001
Overall emotional distress	M	3.22	0.141	2.94	3.51	3	0.985	0.896	<.001
	H	3.62	0.128	3.37	3.88	4	1.003	0.883	<.001
Concerns related to daughters or relatives	M	3.24	0.174	2.90	3.59	3	1.217	0.903	<.001
	H	3.69	0.135	3.42	3.96	4	1.057	0.885	<.001
Impact on couple's relationship	M	3.47	0.160	3.15	3.79	4	1.120	0.897	<.001
	H	3.44	0.141	3.16	3.73	4	1.103	0.900	<.001
Change in self-concept	M	3.18	0.159	2.86	3.50	3	1.112	0.893	<.001
	H	3.62	0.144	3.33	3.91	4	1.128	0.889	<.001
Impact on employment	M	3.14	0.198	2.75	3.54	3	1.384	0.882	<.001
	H	3.54	0.151	3.24	3.84	4	1.177	0.892	<.001
Interference with personal relationship	M	3.43	0.173	3.08	3.78	3	1.208	0.872	<.001
	H	3.80	0.140	3.52	4.08	4	1.093	0.865	<.001
Impact on sexuality	M	3.12	0.161	2.80	3.45	3	1.130	0.915	0.002
	H	3.49	0.121	3.25	3.73	4	0.942	0.872	<.001

Note 1. M – Moderate penetrance gene group 2. H – High penetrance gene group.

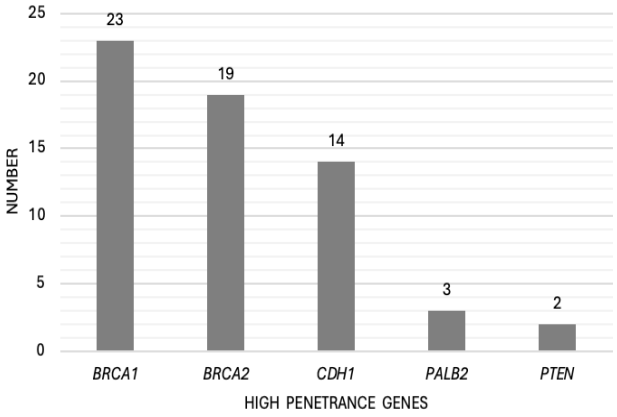

Figure 2. Distribution of Patients by Gene Mutation in the High Penetrance Group. The figure below displays a clustered column chart showing the number of patients with mutations in each high penetrance gene, highlighting the genetic distribution within this group.

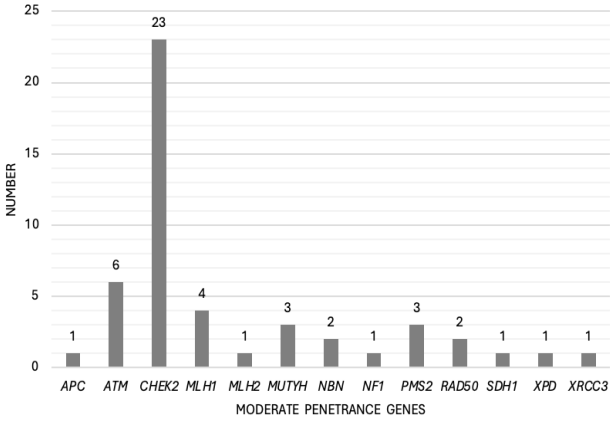

Figure 3. Distribution of Patients by Gene Mutation in the Moderate Penetrance Group. The figure below displays a clustered column chart showing the number of patients with mutations in each high penetrance gene, highlighting the genetic distribution within this group.

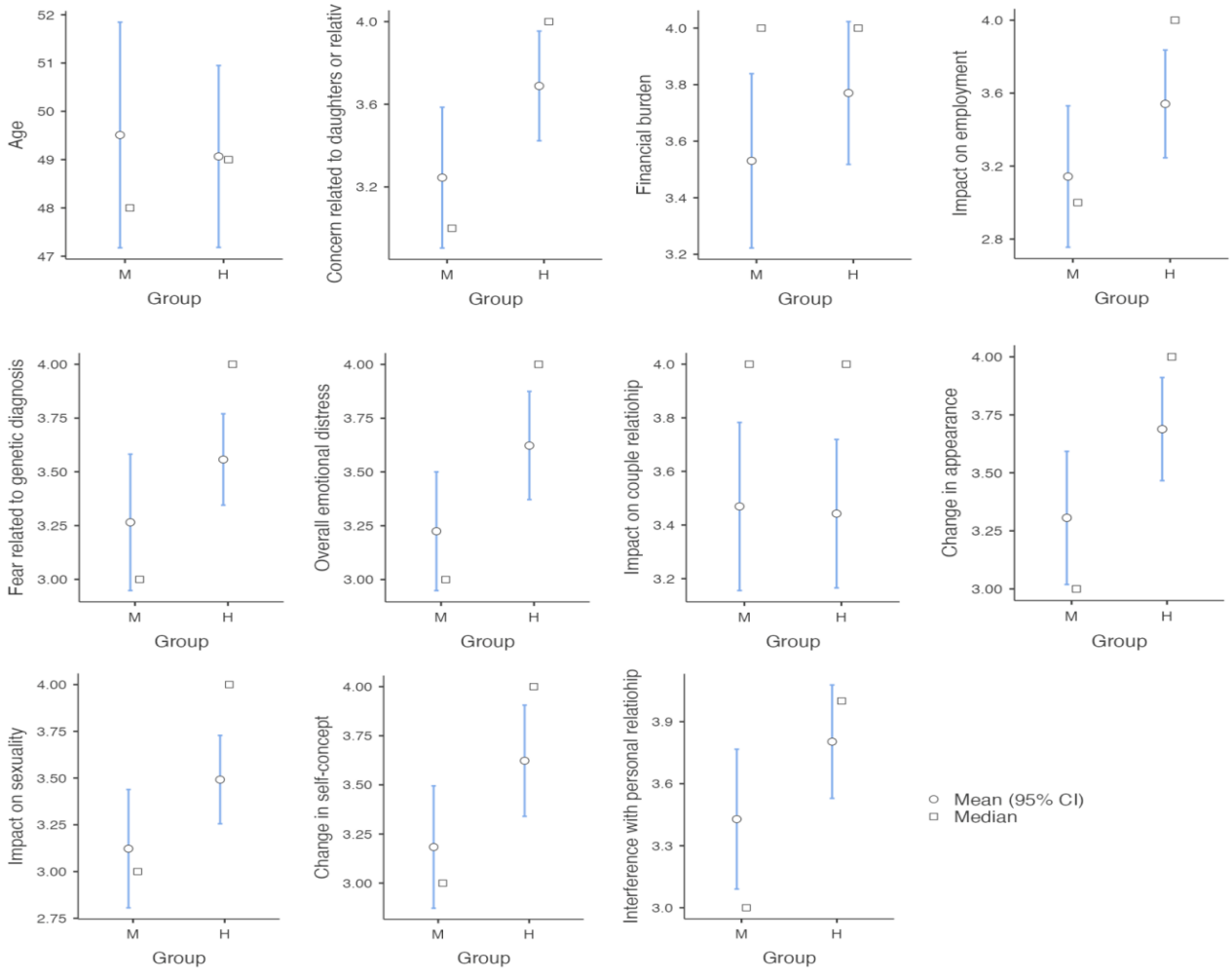

Figure 4. Comparison of Distress and Quality of Life Indicators Between Moderate and High Penetrance Groups. This figure presents the mean, 95% confidence intervals, and medians for various distress and quality-of-life factors among breast cancer patients with moderate (M) and high (H) penetrance gene mutations.

Table IV. Independent T-Test analysis of the groups.

	Statistic	P
Age	0.294	0.770
Concerns related to daughters or relatives	-2.045	0.043
Financial burden	-1.191	0.236
Fear related to genetic diagnosis	-1.547	0.125
Overall emotional distress	-2.088	0.039
Impact on employment	-1.630	0.106
Impact on couple's relationship	0.126	0.900
Change in appearance	-2.098	0.038
Impact on sexuality	-1.870	0.064
Change in self-concept	-2.043	0.043
Interference with personal relationship	-1.706	0.091

Finally, figure 4 visually contrasts the distress levels and quality-of-life factors between patients in the moderate and high penetrance groups, displaying mean values with corresponding confidence intervals and medians for each item.

Discussion

This section explores the implications of the findings presented in the results, focusing on the psychological and quality-of-life differences observed between breast cancer patients with high vs. moderate penetrance gene mutations. By analyzing key areas of distress—such as emotional burden, appearance-related concerns, and the impact on relationships—this discussion aims to contextualize the results within the broader clinical and psychosocial landscape. We interpret the two groups' statistically significant and non-significant differences and consider possible underlying factors. The findings are compared with existing literature to highlight similarities, discrepancies, and potential avenues for future research and clinical practice.

Interpretation of distress and quality-of-life differences between genetic risk groups

This study aimed to investigate differences in distress and quality-of-life indicators among breast cancer patients carrying mutations in moderate vs. high penetrance genes. The results provide important insights into how genetic risk levels may influence patients' emotional and psychosocial experiences following diagnosis and treatment.

Figures 2 and 3 presented the distribution of mutations within the high and moderate penetrance gene groups, confirming the genetic heterogeneity in our cohort. Figure 4 visually compared the distress levels across the two groups, supporting the findings detailed in tables II–IV.

A key finding is that several distress-related factors showed statistically significant differences between the two groups, as evidenced by the independent t-test results (Table IV). Specifically, patients in the high penetrance group reported significantly higher distress regarding overall emotional impact ($p = 0.039$), change in appearance ($p = 0.038$), concern related to daughters or relatives ($p = 0.043$), and change in self-concept ($p = 0.043$).

These differences can be interpreted considering the psychological burden of high-risk gene mutations. For example, BRCA1 and BRCA2 mutations not only suggest a high probability of cancer recurrence but also carry substantial hereditary implications, often affecting family planning, reproductive decisions, and fears about passing the mutation to children. This could explain the significantly greater concern about relatives and daughters reported by this group. Patients with moderate penetrance mutations may perceive their diagnosis as less genetically deterministic, which could mitigate this source of distress.

Similarly, the high penetrance group's increased distress related to changes in appearance and self-concept may stem from more aggressive treatments (e.g., bilateral mastectomy) often recommended for these patients as preventative measures. Such interventions can lead to more visible physical changes and identity disruption, particularly in body image and femininity perception. This supports this subgroup's statistically significant difference in distress related to appearance and self-concept.

On the other hand, some categories—such as fear related to genetic diagnosis ($p = 0.125$), financial burden ($p = 0.236$), impact on employment ($p = 0.106$), and impact on sexuality ($p = 0.064$)—did not show statistically significant differences between the two groups. One plausible explanation is that these factors reflect more universal concerns tied to a cancer diagnosis rather than genetic penetrance specifically. For instance, fear at the time of diagnosis or the economic implications of cancer treatment is likely to affect all patients regardless of genetic risk classification. Similarly, changes in sexual well-being may result from surgery or hormone therapy and are not necessarily dependent on the patient's genetic mutation type.

It is also important to consider the psychological resilience and coping mechanisms that may vary individually rather than genetically. Some patients with moderate-risk genes may experience equally severe distress due to personal history, prior trauma, or lack of support systems. Moreover, cultural attitudes toward hereditary risk and limited access to genetic counselling may influence how patients interpret and internalize their diagnoses.

While the p-values in some categories approached significance (e.g., impact on sexuality, $p = 0.064$; interference with personal relationships, $p = 0.091$), these may warrant further exploration in larger or longitudinal cohorts to determine whether subtle but meaningful differences emerge over time.

In summary, the findings suggest that patients with high penetrance gene mutations face higher levels of distress in some psychosocial regions, likely due to the implications of their genetic risk. However, the overall emotional burden of breast cancer appears substantial across both groups, reinforcing the need for personalized

psychological support irrespective of mutation type. These results underline the importance of integrating tailored counselling and supportive care strategies into breast cancer management, with special attention to those with high genetic risk.

Comparison with existing literature

Individuals identified as having high genetic risk (*BRCA1/2* mutation carriers) often experience significant emotional distress [13]. This includes increased anxiety about cancer development, guilt related to the potential transmission of the gene to offspring, decisional conflict around surveillance vs. risk-reducing surgery (mastectomy or oophorectomy), body image concerns and sexual dysfunction after preventive measures. In moderate-risk individuals (*CHEK2*, *ATM* mutations), the burden tends to be lower but still present, mainly due to uncertainty and less clarity in management guidelines [14,15]. In the WISDOM study, a participant with a *CHEK2* mutation reported significant anxiety due to the uncertainty of her cancer risk and the appropriate screening measures [16].

Quality of life is often compromised due to ongoing health surveillance and medical appointments, social isolation stemming from anxiety or lifestyle changes and concerns around insurance discrimination and family dynamics [17,18].

In a previously published, recent study conducted at Regina Maria Private Health Network in Bucharest, 61 patients with moderate-to-low-penetrance mutations who underwent bilateral mastectomy with reconstruction were assessed using a modified BREAST-Q questionnaire.

The results showed that the "Emotional Distress" item was significantly correlated with concerns for family and financial burdens. The self-concept item showed a significant negative correlation with couple relationship strain (Spearman's rho = −0.261, p = 0.042), indicating that participants experiencing greater difficulties in their intimate relationships tended to report fewer positive changes in their self-perception post-diagnosis. This suggests that relational challenges may undermine the development of a more positive self-concept in this patient group. Still, the most distressing factors reported were interference with personal relationships and financial burden, surpassing concerns about employment impact and sexuality [12].

Studies have shown that genetic counselling can reduce cancer-related worry and improve knowledge, leading to more informed and less distressing decision-making processes. Still, genetic counselling in Romania faces several challenges that limit its effectiveness and accessibility for individuals at risk for hereditary breast cancer: limited availability of trained professionals, lack of public awareness and education, inadequate healthcare infrastructure, cost and reimbursement issues as out-of-pocket costs can be a significant barrier, especially for low-income families, delayed integration into clinical practice and not least ethical and legal concerns, as Romania lacks robust legal frameworks for genetic data privacy and anti-discrimination protections [19,20].

After the "Angelina Jolie effect" [21], the concept of de-escalation of surgery, particularly mastectomy, in individuals who carry mutations in moderate-penetrance genes became an emerging interest in precision medicine and surgical oncology [22]. Evidence-based guidelines now recommend against routine prophylactic mastectomy in moderate-penetrance mutation carriers, unless other risk factors exist (improper imaging evaluation of the breast, increased familial aggregation, poor quality of life due to somatization cosmetic surgery). MRI-based surveillance achieves excellent outcomes in moderate-risk carriers [23].

Implementing tumor boards is important, especially for "outside the guidelines" cases, as they can help reduce unnecessary prophylactic mastectomies. Psychosocial support and shared decision-making to address anxiety and over-treatment tendencies are crucial—particularly in high-penetrance carriers and increasingly relevant for moderate-penetrance carriers as genetic testing expands [24].

Future implications and directions

The findings of this preliminary study underscore the need to integrate psychosocial dimensions more thoroughly into the genetic risk assessment and post-diagnostic care of breast cancer patients. The observed heightened distress in individuals with high penetrance mutations—especially regarding emotional burden, self-concept, and family-related concerns—suggests that genetic information might significantly influence the subjective cancer experience.

Future research should pursue the following directions:

1. Longitudinal studies: longitudinal designs are essential to capture the dynamic nature of distress over time. These would help determine how emotional and psychosocial responses evolve from diagnosis through treatment, recovery, and survivorship and how these trajectories differ by genetic risk level.

2. Larger and more diverse cohorts: replicating this study in broader and more demographically diverse populations would improve generalizability and allow for subgroup analysis based on age, socioeconomic status, cultural background, and healthcare access.

3. Inclusion of treatment variables: future studies should control for treatment modalities (e.g., mastectomy vs. lumpectomy, reconstruction, chemotherapy) to isolate the psychosocial impact attributable to genetic risk rather than to the nature of treatment received.

4. Comprehensive psychosocial tools: employing the full BREAST-Q or other validated, multidimensional quality-of-life instruments may provide a deeper understanding of patient experiences, including resilience, coping strategies, and support system effectiveness.

5. Intervention development: the data highlight the potential benefit of tailored psychosocial interventions. Future efforts should focus on developing and testing

risk-informed counselling strategies, psycho-educational materials, and support programs specific to mutation type and penetrance level.

6. Health system integration: these insights advocate for closer collaboration between oncologists, genetic counsellors, and mental health professionals to ensure that high-risk patients receive timely, personalized psychosocial support as part of standard care.

7. Impact on family dynamics and planning: given the elevated concern for relatives observed in high-penetrance carriers, future research could examine how genetic information affects family planning, intergenerational communication, and the psychological well-being of family members, especially daughters.

In conclusion, expanding the psychosocial dimension of precision oncology to include genetic risk-based emotional support promises to improve both clinical outcomes and patient quality of life.

Limitations

Although this study offers meaningful insights into the distress and quality-of-life differences between breast cancer patients with high and moderate penetrance gene mutations, several limitations must be acknowledged to contextualize the findings appropriately and guide future research efforts:

1. Sample size constraints: with 110 participants, the sample was relatively small, which may have limited the statistical power of the analysis, especially for variables with borderline significance. Larger, more diverse cohorts are needed to validate these results.

2. Use of a shortened questionnaire: to enhance clinical feasibility, a condensed version of the BREAST-Q was used. While efficient, this adaptation may have omitted relevant domains and nuances in the whole instrument, potentially underestimating the complexity of patient experiences.

3. Cross-sectional study design: as the data were collected at a single time point, the study cannot assess how distress and quality-of-life factors evolve throughout the cancer journey. A longitudinal design would better capture these temporal dynamics.

4. Lack of adjustment for treatment-related variables: the analysis did not stratify results based on surgical type, chemotherapy, hormone therapy, or reconstruction technique—factors that may independently influence distress levels regardless of genetic risk.

5. Cultural and geographical limitations: conducted in a single private healthcare network in Romania, the study's findings may not be generalizable to populations in other countries with different healthcare systems, cultural attitudes, or access to genetic counselling.

Despite these limitations, the study represents a valuable step toward understanding how genetic risk impacts the emotional and psychosocial dimensions of breast cancer survivorship. Future research with broader, more diverse samples and longitudinal follow-up will be crucial for developing personalized, risk-informed support strategies for these patients.

Conclusions

This preliminary study highlights the importance of considering genetic penetrance when evaluating the psychological and quality-of-life outcomes of breast cancer patients. Our findings show that individuals with high penetrance gene mutations—such as *BRCA1*, *BRCA2*, and *TP53*—tend to experience significantly higher levels of distress in several key areas, including emotional burden, concerns about family members, changes in self-concept, and physical appearance. These elevated distress levels may be linked to the increased hereditary implications and more aggressive treatment strategies commonly associated with high-risk gene mutations.

In contrast, certain distress factors, such as financial burden, fear related to diagnosis, and sexual well-being, did not differ significantly between high and moderate penetrance groups. This suggests that some challenges are shared universally among breast cancer patients, regardless of genetic background.

Overall, these results emphasize the need for individualized, risk-informed psychosocial support for the clinical and emotional aspects of care. Genetic counselling and psychological interventions should be tailored to the specific concerns associated with different levels of genetic risk. Further research with larger and more diverse samples, as well as longitudinal follow-up, are essential to validate and expand on these initial findings and better support the long-term well-being of breast cancer survivors.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Regina Maria Rețeaua Privată de Sănătate (Regina Maria Health Network) (code: NO 324/18.04.2025; approval date: 18 April 2025)

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