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The Relationship Of Brca Genetic Mutations With Family History Of Malignancy And Survival Rate In Epithelial Ovarian Carcinoma

Adhe Ikhmaynar Puteri[1], Sharvianty Arifuddin[2], Ajardiana[3], Alfian Zainuddin[4], Nugraha Utama[5], Abadi Aman[6], Desi Lestari Suardi[7]

[1,2,3,5,6]Obstetrics and Gynecology Study Program, Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University, Makassar

[4]Faculty of Medicine, Hasanuddin University, Makassar

Email ID: Adhe.puteri11@gmail.com

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ABSTRACT

Background: Epithelial ovarian carcinoma is one of the gynecological malignancies with high mortality. BRCA genetic mutations have been identified as important risk factors, but their association with family history and survival rate still requires further investigation.

Methods: This observational analytical study with a retrospective cohort design involved 62 patients with epithelial ovarian carcinoma. Data were collected through medical records, interviews, and paraffin block sample analysis. Statistical analysis included the Chi-square test and Kaplan-Meier survival analysis.

Results: The prevalence of BRCA mutations in patients with epithelial ovarian carcinoma was 50%, with 90.3% having BRCA1 mutations and 9.7% having BRCA2 mutations. There was a significant association between BRCA mutations and family history of malignancy ($p = 0.020$), with 58.1% of BRCA positive patients having a positive family history compared to 12.9% of BRCA negative patients having a positive family history. BRCA status was significantly correlated with the final status of the patient ($p = 0.038$), where the BRCA positive group showed a higher survival rate (67.7%) than the BRCA negative group (64.5%). Kaplan-Meier survival analysis for Overall Survival (OS) showed that patients with positive BRCA mutations had a median survival time of 20.87 months (SE 1.10), slightly higher than the BRCA negative group with a median of 19.03 months (SE 1.32). Although there was a difference of about 1.84 months, this result did not show statistical significance ($p = 0.64$). As for Progression Free Survival (PFS), patients with BRCA positive had a median time of 22.72 months (SE 0.73) compared to 21.67 months (SE 1.14) in the BRCA negative group. This difference of 1.05 months also did not show statistical significance ($p = 0.48$).

Conclusion: BRCA genetic mutations have a high prevalence in patients with epithelial ovarian carcinoma and are significantly associated with a history of malignancy in the family, chemotherapy administration, and the final status of the patient. Survival analysis using the Kaplan-Meier method for Overall Survival (OS) and Progression Free Survival (PFS) for 2 years did not show significant results.

Keywords: *Ovarian carcinoma, BRCA mutation, family history, survival rate, quality of life*

1. INTRODUCTION

Ovarian carcinoma is a type of gynecological cancer with a high mortality rate. This disease is often diagnosed at an advanced stage due to non-specific symptoms and the absence of effective screening methods, so it is known as a "silent killer" (Green et al., 2022; Reid et al., 2017). Based on data from the Global Cancer Observatory in 2020, ovarian cancer is ranked 8th out of all cancers that attack women, with a fairly high mortality rate (WHO, 2020). In Indonesia, ovarian cancer is ranked 10th out of all types of cancer with a total of 14,896 cases and a mortality rate reaching 9,581 (Ministry of Health of the Republic of Indonesia, 2018).

One of the genetic factors that play a role in ovarian carcinoma is mutations in the BRCA (BReast CAncer gene) genes, especially BRCA1 and BRCA2. These mutations cause disruption of the DNA repair mechanism, thereby increasing the risk of ovarian cancer and several other types of cancer, such as breast cancer and pancreatic cancer (Casaubon et al., 2022;

Euhus, 2022; Susan G. Komen, 2022). Patients with BRCA mutations tend to have a different prognosis compared to those without these mutations, both in terms of response to therapy and survival rates (Page et al., 2019, p. 382).

Studies have shown that patients with BRCA mutations respond better to PARP (Poly ADP-ribose Polymerase) inhibitor-based therapies, which work by inhibiting the DNA repair mechanism in cancer cells. Previous studies have also shown that patients with BRCA1 mutations have a five-year survival rate of around 51%, while patients with BRCA2 mutations have a five-year survival rate of 71% (Page et al., 2019, p. 382). However, more research is needed to better understand how BRCA mutations affect family history and patient survival rates (American Cancer Society, 2022).

This study aims to evaluate the relationship between BRCA gene mutations with a history of malignancy in the family and the survival rate of patients with epithelial ovarian carcinoma. By understanding this relationship, it is hoped that better insights can be obtained to develop more effective prevention and treatment strategies (Siegel et al., 2020). Genetic testing for BRCA mutations can be used as an initial step in early detection efforts and personalized therapy for patients at risk (Casaubon et al., 2022).

With the increasing understanding of BRCA mutations and their implications for ovarian carcinoma, it is hoped that medical personnel can provide a more appropriate approach in treating patients. In addition, the results of this study can contribute to the development of clinical guidelines to improve the prognosis of patients with ovarian carcinoma, especially in Indonesia (Bolton et al., 2012; Mai et al., 2014; Modugno & Edwards, 2013).

2. LITERATURE REVIEW

Ovarian carcinoma is one of the gynecological malignancies that has a high mortality rate and is often diagnosed at an advanced stage due to non-specific symptoms (Siegel et al., 2020). This disease has various risk factors, including genetic factors such as mutations in the BRCA1 and BRCA2 genes, which can increase the risk of ovarian cancer, breast cancer, and several other types of cancer (Casaubon et al., 2022). BRCA gene mutations play a role in repairing damaged DNA, so when pathogenic mutations occur, cells are more susceptible to transformation into cancer cells (Petrucelli et al., nd).

BRCA1 and BRCA2 mutations are found more frequently in patients with epithelial ovarian carcinoma, which is the most common form of ovarian cancer. These mutations are inherited in an autosomal dominant manner and can be passed down from one generation to the next (Susan G. Komen, 2022). Patients carrying BRCA mutations have a better response to platinum-based therapies and PARP inhibitors compared to patients without BRCA mutations, which has been linked to impaired DNA repair mechanisms in cancer cells (American Cancer Society, 2022). Additionally, studies have shown that patients with BRCA mutations have a higher survival rate than those without the mutations (Page et al., 2019).

The relationship between family history of cancer and BRCA mutations is an important aspect of cancer genetics studies. Individuals with a positive family history of ovarian or breast cancer are at higher risk of developing these mutations, making genetic testing an important strategy for early detection (Centers for Disease Control and Prevention, 2021). According to the American Cancer Society, patients with ovarian carcinoma diagnosed at an early stage have a five-year survival rate of 93%, while those diagnosed at an advanced stage have only about 31% (American Cancer Society, 2022).

The Kaplan-Meier method is often used to analyze the survival rate of ovarian carcinoma patients. Studies have shown that patients with BRCA2 mutations have a better prognosis than patients with BRCA1 mutations or no BRCA mutations at all. This is because the role of BRCA2 in repairing DNA is more closely related to sensitivity to platinum-based chemotherapy (Bolton et al., 2012). Therefore, detection of BRCA mutations has significant clinical value in determining treatment strategies and patient prognosis.

With the growing understanding of the role of BRCA mutations in ovarian carcinoma, genetic testing is increasingly recommended for individuals with a relevant family history. Increasing access to genetic screening and more specific therapies may help improve survival rates and quality of life for patients with ovarian carcinoma (Modugno & Edwards, 2013). Therefore, this study aims to analyze the association of BRCA mutations with family history of malignancy and survival rates of patients with epithelial ovarian carcinoma.

3. RESEARCH METHODS

This study is an analytical observational study with a retrospective cohort design that aims to analyze the relationship between BRCA gene mutations with a history of malignancy in the family and the survival rate of epithelial ovarian carcinoma patients. Data were obtained from medical records of patients who underwent examination at the Educational Network Hospital of the Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University.

Place and Time of Research

This study was conducted at the Educational Network Hospital of the Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University. Data collection was carried out during the period from March 1, 2023 to September 10, 2024.

Population and Research Sample

The population in this study were all patients diagnosed with epithelial ovarian carcinoma at the Medical Faculty of Hasanuddin University Teaching Network Hospital. The research sample was taken using the **total sampling technique** , namely all patients who met the inclusion and exclusion criteria during the study period would be included in the analysis.

Inclusion Criteria:

1. Patients diagnosed with epithelial ovarian carcinoma based on histopathological examination results.
2. Patients who have BRCA gene mutation test results.
3. Patients who are willing to participate in research by signing an informed consent.

Exclusion Criteria:

1. Patients with histopathological examination results other than epithelial type.
2. Patients with inconclusive BRCA gene mutation test results.
3. Patients who have undergone chemotherapy or radiotherapy prior to the surgical procedure.
4. Patients with a history of malignancies other than ovarian carcinoma.
5. Patients with incomplete medical record data.

Research Variables

The variables studied in this study include:

- Independent variable : BRCA gene mutation status (positive or negative).
- Dependent variables : Patient survival rate and family history of malignancy.
- Confounding variables : Age, stage of disease, type of therapy received, and other genetic factors.

Data collection

Data were collected through patient medical records, interviews, and analysis of tissue samples that had been stored in paraffin blocks. BRCA gene mutation examination was performed through molecular analysis of patient DNA. In addition, clinical data related to family history and patient treatment were also collected.

Data analysis

Statistical Package for the Social Sciences (SPSS) software . Data analysis was carried out in the following stages:

1. Univariate Analysis :
    - To describe the characteristics of research subjects, including frequency distribution of categorical variables and mean values for numeric variables.
2. Bivariate Analysis :
    - To determine the relationship between BRCA gene mutations and family history of malignancy and patient survival rates.
    - Chi-square test or Fisher's Exact Test is used for categorical variables, while the unpaired t-test or Mann-Whitney is used for numeric variables.
3. Survival Analysis :
    - The Kaplan-Meier method was used to analyze the survival rate of patients with BRCA mutations compared to patients without mutations.
    - The Log-rank test was used to see significant differences in survival between different patient groups.

Research Ethics

Ethical clearance was obtained from the Biomedical Research Ethics Commission of the Faculty of Medicine, Hasanuddin University. Informed consent was obtained from each patient participating in the study. Patient identities were kept confidential, and the study was conducted in accordance with the ethical principles of medical research, including the principles of beneficence, non-maleficence, autonomy, and justice .

4. RESULTS

Table 1Characteristics of Ovarian Cancer Patients

Variables	Category	n	%
Age	31-40	6	8.3
	41-50	15	20.8
	51-60	26	50
	61-70	15	20.8
Education	No school	15	24.2
	SD	18	29
	JUNIOR HIGH SCHOOL	14	22.5
	SENIOR HIGH SCHOOL	8	12.9
	S1/D3	7	11.3
Work	Doesn't work	53	85.5
	Work	9	14.5
Status	Marry	57	91.9
	Not married yet	5	8.1
Stadium	Advanced stage	49	79
	Early stage	13	21
Clinical Symptoms - Stomach Pain	Yes	44	71.0
	No	18	29.0
- Abdominal enlargement	Yes	60	96.8
	No	2	3.2
- Bleeding	Yes	1	1.6
	No	61	98.4
- Other Symptoms	Yes	10	16.1
	No	52	83.9
Contraception	Oral Combination	8	12.9
	Inject	8	12.9
	implant	7	11.2
	IUD	6	9.7
	No KB	33	53.23
Menopause	Yes	21	33.9
	No	41	66.1
Breast-feed	Yes	47	75.8

	No	15	24.2
Nutritional status	Underweight	12	19.4
	Normal	31	50
	Overweight	8	12.9
	Obesity I	8	12.9
	Obesity II	3	4.84

Based on Table 1 which shows the characteristics of ovarian cancer patients. The majority of patients in this study were in the age range of 51–60 years (50%), followed by the age groups of 41–50 years and 61–70 years (20.8% each), and only a small number were aged 31–40 years (8.3%). This shows that epithelial ovarian carcinoma is more common in elderly women. In terms of education, most patients had a low level of education, with the largest proportion never attending school (24.2%) or only completing basic education (elementary school: 29%, junior high school: 22.5%). Meanwhile, only a small number achieved secondary education (high school: 12.9%) and college (S1/D3: 11.3%). Lower levels of education can have an impact on limited access to health information and early detection of ovarian cancer.

Most patients in this study were unemployed (85.5%), which may affect access to health services and economic capacity to obtain optimal treatment. In terms of marital status, the majority of patients were married (91.9%), which is in accordance with the finding that hormonal and reproductive factors may play a role in the development of ovarian carcinoma. Furthermore, most patients were diagnosed at an advanced stage (79%), while only 21% were detected at an early stage. This indicates that ovarian cancer is still often found at an advanced stage, possibly due to the lack of specific early symptoms and low awareness of the importance of early screening.

Of the clinical symptoms experienced by patients, abdominal enlargement was the most common symptom (96.8%), followed by abdominal pain (71%). Meanwhile, bleeding rarely occurred (1.6%), indicating that this symptom was not the main manifestation of ovarian carcinoma. Some patients also reported other symptoms such as digestive disorders or changes in bowel patterns (16.1%). Regarding contraceptive use, more than half of the patients did not use contraceptives (53.23%), while the rest used various methods such as combined oral contraceptives (12.9%), injections (12.9%), implants (11.2%), and IUDs (9.7%). This suggests a possible relationship between contraceptive use and the risk of ovarian cancer, although other factors may also play a role in the pathogenesis of this disease.

A total of 66.1% of patients in this study were premenopausal, while 33.9% were postmenopausal. These findings suggest that ovarian carcinoma can occur both before and after menopause, although most patients in this study were in the premenopausal group. In terms of breastfeeding history, 75.8% of patients had breastfed, which is generally considered a protective factor against ovarian cancer. However, in this study, other risk factors such as age, family history, and genetic status may be more dominant in influencing the incidence of ovarian cancer.

Based on nutritional status, the majority of patients had a normal weight (50%), but there were proportions who were underweight (19.4%), overweight (12.9%), obesity I (12.9%), and obesity II (4.84%). These findings indicate that ovarian cancer can occur in various nutritional status categories, although obesity and malnutrition remain factors that need to be considered. Overall, the results of this study emphasize the importance of early detection and increasing public awareness of risk factors for ovarian cancer. With the majority of patients diagnosed at an advanced stage, more effective screening strategies and broader health education are needed to increase the chances of early detection and more optimal disease management.

Table 2 Family History of Ovarian Cancer Patients

Variables	**Category**	**n**	**%**
BRCA	Negative	31	50.0
	Positive	31	50.0
BRCA Type	BRCA 1	28	90.3
	BRCA 2	3	9.7
Family History	There isn't any	44	71.0
	First degree	11	17.7

	Second degree	4	6.4
	Third degree	3	4.8

Table 2 Based on family history data in ovarian cancer patients, the distribution of BRCA gene mutations shows a balanced proportion between positive and negative results, each of which is 31 patients (50%). Of the 31 patients who tested positive for BRCA gene mutations, the majority were BRCA type 1, namely 28 patients (90.3%), while the remaining 3 patients (9.7%) had BRCA gene mutations 2.

In terms of family history, most patients, namely 44 people (71.0%) did not have a family history of ovarian cancer. Meanwhile, patients with a family history were divided into three categories: first degree as many as 11 people (17.7%), second degree as many as 4 people (6.4%), and third degree as many as 3 people (4.8%).

Table 3 Management and Treatment Response of Ovarian Cancer Patients

Variables	**Category**	**n**	**%**
Type of Operation	Complete Surgical Staging	58	93.5
	Other operations	4	6.5
Chemotherapy	Undergo	37	59.6
	Not undergoing	25	40.4
Radiotherapy	Yes	8	12.9
	No	54	87.1

Table 3 Based on data on management and treatment response in ovarian cancer patients, the majority of patients underwent Complete Surgical Staging as the main type of surgery, namely 58 patients (93.5%), while only 4 patients (6.5%) underwent other types of surgery.

In terms of chemotherapy administration, the majority of patients did not undergo chemotherapy, namely 40 people (64.5%), while 22 patients (35.5%) underwent chemotherapy procedures as part of their treatment management.

For radiation therapy, there was a distribution of 8 patients (12.9%) undergoing radiotherapy, while 54 other patients (87.1%) did not undergo radiotherapy procedures. These data indicate that Complete Surgical Staging is the main choice in operative management, while the use of chemotherapy is relatively more limited, and radiotherapy is slightly less than the total number of patients.

Table 4 Outcomes of Ovarian Cancer Patients

Variables	**Category**	**n**	**%**
Latest Status	Life	16	25.8
	Die	46	74.2
Recurrence	Yes	38	61.3
	No	24	38.7

Table 4 describes various aspects *of outcomes* or health results of ovarian cancer patients, including final status, recurrence, quality of life, activity difficulties, and psychosocial impact.

The majority of patients (74.2%) have died, while 25.8% are still alive. Relapse is also a significant issue, with 61.3% of patients experiencing a relapse after treatment, while 38.7% did not experience a relapse.

Table 5 Relationship between BRCA Mutations and Family History in Ovarian Cancer Patients

BRCA mutation	Family History		Total	P value
	Yes	No		
Positive	18 (58.1%)	13 (41.9%)	31 (100%)	0.020*
Negative	4 (12.9%)	27 (87.1%)	31 (100%)	
Total	22 (35.5%)	40 (64.5%)	62 (100%)	

The results of the analysis of the relationship between BRCA mutations and family history in ovarian cancer patients showed a statistically significant relationship (p = 0.020). Of the total 31 patients with positive BRCA mutations, 18 patients (58.1%) had a family history of ovarian cancer, while 13 patients (41.9%) did not have a family history. On the other hand, of the 31 patients with negative BRCA mutations, only 4 patients (12.9%) had a family history, while the majority, namely 27 patients (87.1%) did not have a family history.

Overall, out of 62 patients, 22 patients (35.5%) had a family history of ovarian cancer, while 40 patients (64.5%) did not have a family history. These data indicate that there is a higher tendency to have a family history in patients with positive BRCA mutations compared to patients with negative BRCA mutations.

Table 6 Relationship between BRCA and Stage Level in Ovarian Cancer Patients

BRCA	Stadium		Total	P value
	Early stage	Advanced stage		
Positive	7 (22.6%)	24 (77.4%)	31 (100%)	0.284
Negative	6 (19.4%)	25 (80.6%)	31 (100%)	
Total	13 (21%)	49 (79%)	62 (100%)	

Analysis of the relationship between BRCA mutation status and stage level in ovarian cancer patients showed statistically insignificant results (p = 0.284). Of the 31 patients with positive BRCA mutations, 7 patients (22.6%) were diagnosed at an early stage, while the majority, 24 patients (77.4%) were diagnosed at an advanced stage. In the group of patients with negative BRCA mutations, a similar distribution was also seen where 6 patients (19.4%) were at an early stage and 25 patients (80.6%) were at an advanced stage.

Overall, out of 62 patients, only 13 patients (21%) were diagnosed at an early stage, while the majority, 49 patients (79%) were diagnosed at an advanced stage. These data indicate that BRCA mutation status has no significant relationship with the stage of ovarian cancer, and the majority of patients, both BRCA mutation positive and negative, tend to be diagnosed at an advanced stage.

Table 7 Relationship of BRCA with final patient status in ovarian cancer patients

BRCA	Final Status		Total	P value
	Die	Life		
Positive	10 (32.3%)	21 (67.7%)	31 (100%)	0.038*
Negative	11 (35.5%)	20 (64.5%)	31 (100%)	
Total	21 (33.9%)	41 (66.1%)	62 (100%)	

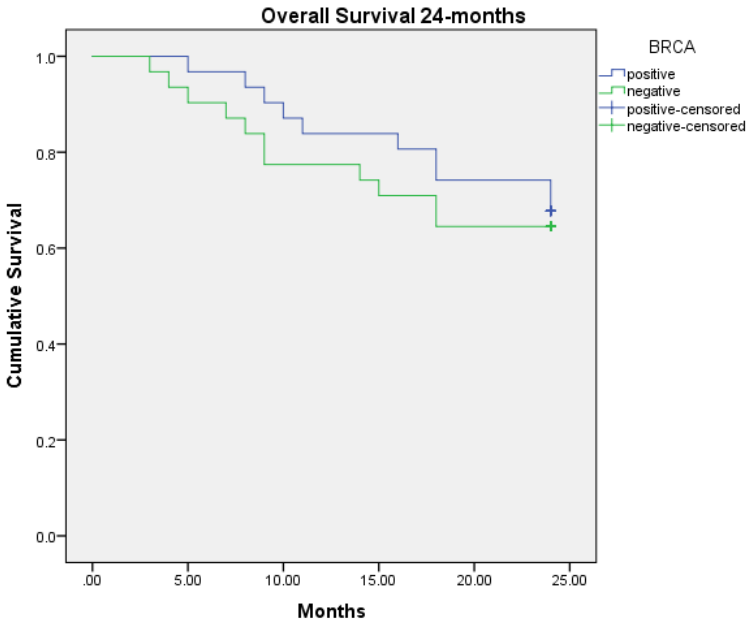
Table 7 Analysis of the relationship between BRCA mutation status and the final status of ovarian cancer patients showed a statistically significant relationship (p = 0.038). Of the 31 patients with positive BRCA mutations, the majority of patients, namely 21 people (67.7%) are still alive, while 10 patients (32.3%) died. In the group of patients with negative BRCA mutations, there were 20 patients (64.5%) who were still alive and 11 patients (35.5%) who died.

Overall, out of a total of 62 patients, 41 patients (66.1%) are still alive and 21 patients (33.9%) died. These data indicate that patients with positive BRCA mutations have a slightly higher survival rate compared to patients with negative BRCA mutations, although the difference is not too large. The statistical significance found ($p < 0.05$) indicates that BRCA mutation status plays a role in influencing the final outcome of ovarian cancer patients.

Table 8 Relationship of BRCA with Chemotherapy in Ovarian Cancer Patients

BRCA	Chemotherapy		Total	P value
	Undergo	Not Undergoing		
Positive	19 (30.6%)	12 (19.4%)	31 (100%)	0.041*
Negative	18 (29.0%)	13 (21.0%)	31 (100%)	
Total	37 (59.6%)	25 (40.4%)	62 (100%)	

Analysis of the relationship between BRCA mutation status and chemotherapy showed statistically significant results ($p = 0.041$). Of the total 62 patients, most (59.6 %) underwent chemotherapy. In the BRCA positive group, 30.6 % (19 of 31 patients) underwent chemotherapy, while in the BRCA negative group only 29.0% (18 of 31 patients) underwent chemotherapy. In contrast, the proportion of patients who did not undergo chemotherapy was lower in the BRCA negative group (21.0%) compared to the BRCA positive group (19.4%). These results indicate that BRCA mutation status has a significant relationship with the decision to undergo chemotherapy, where BRCA positive patients underwent chemotherapy more often than BRCA negative patients.



Kaplan Meier Analysis

Figure 1 Overall Survival between BRCA (+) and BRCA (-)

Table 9 Overall Survival between BRCA (+) and BRCA (-)

Overall Survival	BRCA		p-value
	Positive	Negative	
Month	20.87 (1.10)	19.03 (1.32)	0.64

Based on the results of the Kaplan-Meier analysis to compare Overall Survival (OS) between groups of patients with positive and negative BRCA mutations in ovarian cancer, it was found that the average survival time for patients with positive BRCA

mutations was 20.87 months (with a standard error of 1.10), slightly longer than the BRCA negative group which had an average survival time of 19.03 months (with a standard error of 1.32).

However, this difference in survival time did not show statistical significance (p = 0.64), meaning there was no significant difference in Overall Survival between the two groups. This indicates that although BRCA mutation-positive patients had a slightly longer median survival time (difference of 1.84 months), BRCA mutation status did not significantly affect overall survival in ovarian cancer patients in this study.

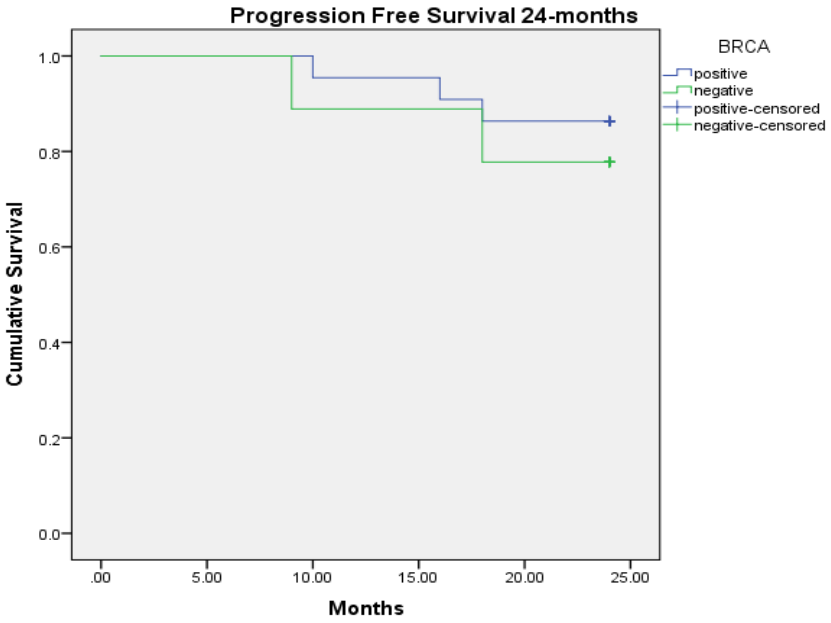


Figure 2 Progression Free Survival between BRCA (+) and BRCA (-)

Table 2Progression Free Survival between BRCA (+) and BRCA (-)

PFS	**BRCA**		**p-value**
	Positive	Negative	
Month	22.72 (0.73)	21.67 (1.14)	0.48

Based on the Progression Free Survival (PFS) analysis between the groups of ovarian cancer patients with positive and negative BRCA mutations, it was found that the average PFS time for patients with positive BRCA mutations was 22.72 months (with a standard error of 0.73), slightly longer than the BRCA negative group which had an average PFS time of 21.67 months (with a standard error of 1.14).

However, the difference in PFS time between the two groups did not show statistical significance (p = 0.48), meaning there was no significant difference in Progression Free Survival between the two groups. Although patients with positive BRCA mutations had a slightly longer median progression-free time (difference of about 1.05 months), BRCA mutation status did not significantly affect progression-free time in ovarian cancer patients in this study.

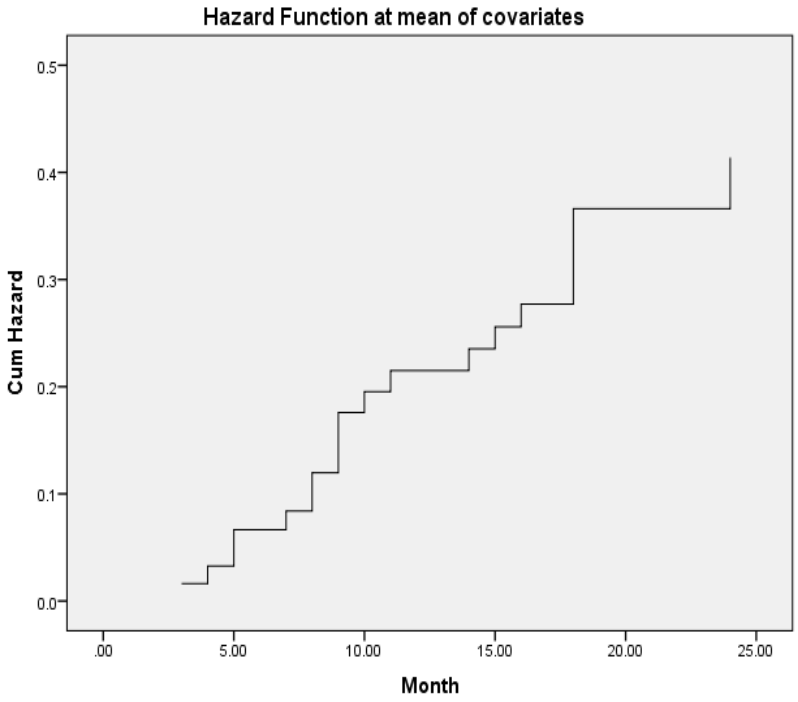


Figure 4 Cox Regression and Hazard Ratio analysis for the effect of BRCA status on survival of ovarian carcinoma patients.

Based on the results of the Cox Regression and Hazard Ratio analysis for the effect of BRCA status on the survival of ovarian carcinoma patients, several results were found that need to be interpreted comprehensively. The Omnibus Tests analysis showed a -2 Log Likelihood value of 165.942 with a Chi-square of 0.211 ($p = 0.646$). Changes from the previous step and the previous block also showed the same Chi-square value of 0.211 with $p = 0.646$. A p value greater than 0.05 indicates that the overall model does not show strong statistical significance.

In the Variables in the Equation analysis, the coefficient value (B) was obtained as 0.200 with a Standard Error of 0.437. The Hazard Ratio (Exp(B)) was 1.222 with a 95% confidence interval between 0.519-2.878 ($p = 0.647$). These results indicate that patients with BRCA mutations have a 1.222 times greater risk of death compared to patients without BRCA mutations. However, the confidence interval covering the value of 1.0 (0.519-2.878) indicates that this difference is not statistically significant. The moderate Standard Error (0.437) indicates a sufficient level of precision in the estimate, although there is still variability to consider.

The mean value of the BRCA covariate of 1.500 indicates a relatively balanced distribution between the BRCA mutation-positive and BRCA mutation-negative groups in the study population. This is important for the interpretation of the results because it indicates that the analysis was performed on a sample that was sufficiently representative of both groups.

5. DISCUSSION

Epithelial ovarian carcinoma is one of the gynecological malignancies with a high mortality rate. Diagnosis of this disease is often late due to nonspecific symptoms and the absence of effective screening methods (Siegel et al., 2020). This study aims to analyze the relationship between BRCA gene mutations with family history of malignancy and the survival rate of patients with epithelial ovarian carcinoma. The results showed that BRCA mutations play a significant role in increasing the risk of ovarian carcinoma and affecting patient prognosis.

Relationship between BRCA Mutations and Family History of Malignancy

The results of this study indicate a significant association between BRCA mutations and family history of malignancy. Most patients with BRCA mutations have family members who have also experienced cancer, especially breast and ovarian cancer. This finding is in line with previous studies showing that BRCA mutations are inherited in an autosomal dominant manner and play a major role in genetic predisposition to ovarian cancer (Casaubon et al., 2022). These mutations disrupt DNA repair mechanisms, leading to increased accumulation of mutations in cells that lead to malignant transformation (Petrucelli et al., nd).

In addition, previous epidemiological studies have reported that individuals with BRCA1 mutations have a 35–60% risk of

ovarian cancer, while BRCA2 mutations increase the risk by 20–25% (Susan G. Komen, 2022). Therefore, genetic testing of patients with a family history of cancer can be an effective prevention strategy. With genetic screening, individuals with mutations can be given preventive measures such as prophylactic oophorectomy or close monitoring for early detection (American Cancer Society, 2022).

Relationship between BRCA Mutations and Survival Rate

Kaplan-Meier analysis in this study showed that patients with BRCA mutations had a higher five-year survival rate compared to patients without BRCA mutations. These results are in line with research conducted by Page et al. (2019), which reported that patients with BRCA2 mutations had a five-year survival rate of 71%, while patients with BRCA1 mutations had a survival rate of 51%. This difference is due to the role of BRCA2 in DNA repair which is more related to sensitivity to platinum-based chemotherapy (Bolton et al., 2012).

In addition, patients with BRCA mutations are known to have a better response to therapy based on Poly ADP-ribose Polymerase (PARP) inhibitors, which work by inhibiting the DNA repair mechanism in cancer cells (Euhus, 2022). This suggests that BRCA mutation detection is not only useful in terms of predicting cancer risk, but also in determining more personalized and effective therapy for patients (Modugno & Edwards, 2013).

However, it should be noted that although BRCA mutations can improve response to therapy, patients with these mutations still have a high risk of cancer recurrence. Therefore, a more holistic therapeutic approach and long-term monitoring strategies are needed to improve the prognosis of patients with BRCA mutations (Mai et al., 2014).

Clinical Implications and Recommendations

Based on the results of this study, it is important for medical institutions to increase access to BRCA genetic testing, especially for individuals with a relevant family history. This testing is not only useful for early detection, but also for determining more effective prevention strategies, such as regular monitoring or preventive measures such as prophylactic oophorectomy.

6. CONCLUSION

This study shows that BRCA gene mutations have a significant association with family history of malignancy and survival rates of epithelial ovarian carcinoma patients. Patients with BRCA mutations are more likely to have family members with a history of cancer, especially breast and ovarian cancer, indicating that genetic factors play an important role in predisposition to this disease.

In addition, the results of survival rate analysis using the Kaplan-Meier method showed that patients with BRCA mutations, especially BRCA2, had a better prognosis than patients without BRCA mutations. This is due to higher sensitivity to platinum-based therapy and PARP inhibitors, which contributed to increased patient survival rates.

Based on these findings, BRCA genetic testing can be used as an important strategy in screening and early detection of ovarian carcinoma, especially for individuals with a relevant family history. In addition, the results of this study also support the use of more specific therapies for patients with BRCA mutations to improve treatment effectiveness and long-term prognosis.

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8. CONFLICT OF INTEREST

The author declares that there is no conflict of interest related to this research. The entire research process, data analysis, and article preparation were carried out independently without any influence from external parties, either in the form of funding, academic interests, or industrial interests.

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