# BREAST CANCER TREATMENT IN GENETIC MUTATION CARRIERS: SURGICAL TREATMENT, PROPHYLACTIC MASTECTOMY

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# *GENETİK MUTASYON TAŞIYICILARINDA MEME KANSERİ TEDAVİSİ: CERRAHİ TEDAVİ, PROFİLAKTİK MASTEKTOMİ*

## ABSTRACT

Objective: Breast cancer is the most common type of cancer among women, and risk-reducing treatments have gained importance in recent years with the detection of genetic mutations.

Method: Patients who underwent prophylactic mastectomy in our clinic between January 2018 and January 2023 were evaluated retrospectively. Surgical procedures performed on all patients, complications developing secondary to the surgery, the time of sending the patients to adjuvant treatment, the necessity of secondary operation, and disease-free survival were evaluated.

Results: In 4 of the 15 patients with genetic mutations who underwent prophylactic mastectomy, this surgery was performed before tumor formation. Complications such as capsular contracture, skin necrosis and nipple necrosis developed in 6 patients, and reoperation was required in 4 patients. In the follow-up of all patients, oncological principles were adhered to, and no recurrence or metastasis was observed in any of them.

Conclusion: With the expansion of the genetic mutation panel, patients have started to gain time, and as physicians, we need to guide these people in accordance with oncological principles. Prophylactic mastectomy is the method we recommend in this study for tumor-free survival.

**Keywords:** Brca, Prophylactic Mastectomy, risk-reducing surgery.

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# ÖZET

Amaç: Meme kanseri kadınlar arasında en sık görülen kanser tipi olup son yıllarda genetik mutasyonların saptanmasıyla risk azaltıcı tedaviler önem kazanmıştır.

Yöntem: Ocak 2018- Ocak 2023 arası genetik mutasyona sahip olduğu için kliniğimizde proflaktik mastektomi yapılan hastalar retrospektif olarak değerlendirildi. tüm hastalara yapılan cerrahi prosedürler, ameliyata ikincil gelişen komplikasyonlar, hastaların adjuvan tedaviye gönderilme zamanları, ikincil operasyon gerekliliği, hastalıksız sağ kalım süreleri değerlendirildi.

Bulgular: Proflaktik mastektomi yapılmış 15 genetik mutasyonlu hastaların 4'ünde tümor oluşmadan bu ameliyat uygulanıştır. 6 hastada beklenen komplikasyonlardan kapsül kontraktürü, cilt nekrozu ve meme başı nekrozu gibi komplikasyonlar gelişmiş olup 4 hastada re-operasyon gerekliliği olmuştur. Tüm hastaların takiplerinde onkolojik prensiplere bağlı kalınmış olup hiç birinde nüks veya metastaz görülmemiştir.

Sonuç : Genetik mutasyon panelinin genişlemesi ile hastalar zaman kazanmaya başlamış olup, hekim olarak bu kişilere onkolojik prensiplere uygun yol göstermemiz gerekmektedir. proflaktik mastektomi tümörsüz sağ kalım için bizim bu çalışmamızda önerdiğimiz yöntemdir.

**Anahtar Sözcükler:** BRCA, proflaktik mastektomi, risk azaltıcı cerrahi.

# INTRODUCTION

In worldwide, breast cancer is the most common cancer type detected among women. Since 1996, molecular diagnostic tests for breast and ovarian cancers have been introduced and there has been an increase in the use of those tests. (1). Thanks to the new generation multigen panels, the analysis of people who are predisposed to cancer and at risk has become possible. The risk of developing breast cancer is associated with many factors, including genetic predisposition and genetic susceptibility, family history, lifestyle, exogenous hormone intake, and personal medical history (2). Although attempts for early diagnosis and prevention of breast cancer progression are increasing globally, prophylactic mastectomy is one of the recommended methods for surgeons in high-risk patients (3).

Hereditary breast cancers constitute 5-10% of all breast cancers. BRCA 1 and 2 are responsible for 16% of these, and pathogenic variants in PALB2 , TP53 (Li-Fraumeni Syndome), PTEN (Cowden Syndrome), STK 11 and CDH1 the lifetime risk of developing breast cancer in those with this genetic mutation is 60-80% (4,5). Prophylactic mastectomy is recommended as a method to prevent breast cancer in patients with genetic mutations who are determined to be at high risk of breast cancer, especially BRCA mutation (6). This surgical method has become popular in patients diagnosed with breast cancer or at high risk. However, the definition of high risk is difficult and should be given after detailed discussion with the patient and health care team.

Bilateral prophylactic mastectomy is an effective method in definitively preventing cancer in patients with hereditary breast cancer (7). 20-40% of patients undergo mastectomy when they have no signs of malignancy. If these patients develop complications while protecting them from cancer, they face poor cosmetic results and a significant psychological burden (8).

In patients diagnosed with breast cancer, unilateral surgery is the first treatment method, and contralateral prophylactic breast surgery carries a risk in terms of additional complications. At the same time, the patient's comorbidities, socioeconomic status, insurance coverage also play a role in deciding this surgery (9).

In this study, we aimed to compile the surgical methods we applied in patients with known genetic mutations. We retrospectively analyzed patients who did not have breast cancer, had undergone reconstructive breast surgery, or were diagnosed with cancer and had contralateral breast surgery. We aimed to present the complications and secondary surgery requirements in this way.

# MATERIAL AND METHODS

We retrospectively screened the patients who were operated in our general surgery clinic and diagnosed with genetic mutation for breast cancer. Prophylactic mastectomy was performed in 14 patients between January 2018- 2023. All patients were informed about the study and informed consent was obtained from all patients regarding the use of their data in this scientific study. For this, ethics committee approval was obtained from SBU Bagcilar Training and Research Hospital and the study was started with the decision numbered 2023/05/10/029.

## Statistical Analysis

The categorical variables were reported as percentages and also continuous variables as mean with standard deviation for descriptive statistics.

# RESULTS

The mean age for all 15 patients described was 49,5 years (range; 31 to 64) and all of them were female. 93,3% of the patients have BRCA 1 and BRCA 2 mutation (14 patients), 6,6% of them have TP53 mutation (Li-Fraumeni syndrom) (1 patient) (Figure 1).

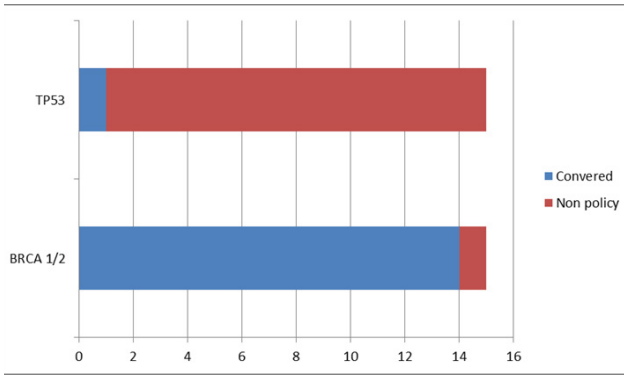


*Figure 1 : Presence of genetic mutation as a potential medical necessity criteria for genetic susceptibility.*

73,3% of the patients have breast cancer at diagnosis(11 patients), 26,6% of them have genetic mutation without breast cancer (4 patients). 26,6 % of the patients were Luminal A breast cancer (4 patients) , 20% of the patients were Luminal B breast cancer (3 patients), 13,3% of them were Her 2 + breast cancer (2 patients), 13,3% of them were Tripple – breast cancer (2 patients) (Figure 2). The avarage of the Ki-67 was 23,7 (range : 1 to 65). Neoadjuvant chemotherapy was increasingly used in 3 patients, and exapt 1 patient all ofthe primary tumors in the breast downstaged.

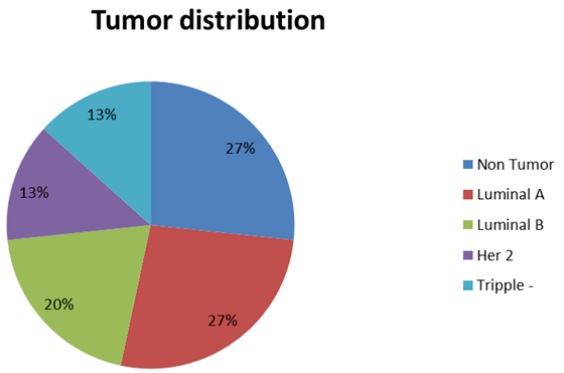


*Figure 2 : Tumor distribution of patients*

Bilateral prophylactic nipple sparing mastectomy were performed with implant for the patients who have genetic mutation but have not encountered with breast cancer. Nipple sparing mastectomy with sentinel lymph node biopsy and contralateral nipple sparing mastectomy were performed with implant for 20% patients (3 patients). Nipple sparing mastectomy with axiller lymph node dissection and contralateral nipple sparing mastectomy were performed with implant for 33,3 % patients (5 patients). Modified radical mastectomy and contralateral mastectomy were performed for 13,3% patients (2 patients). Modified radical mastectomy with expander implant placement and contralateral nipple sparing mastectomy were performed with implant for 6,6 % patients (1 patient). Margins were negative in 100% (n = 11) of cases performed for cancer.

Skin flep necrosis was performed in 2 patients, for 1 of them latissimus dorsi myocutaneous flap used in reconstructive surgery. Capsular contracture was performed in 4 patients, 2 of them haven't been treated with radiotherapy. 3 of this patients were reoperated . 1 of the patient has grade 2 nipple necrosis (Photo 1).

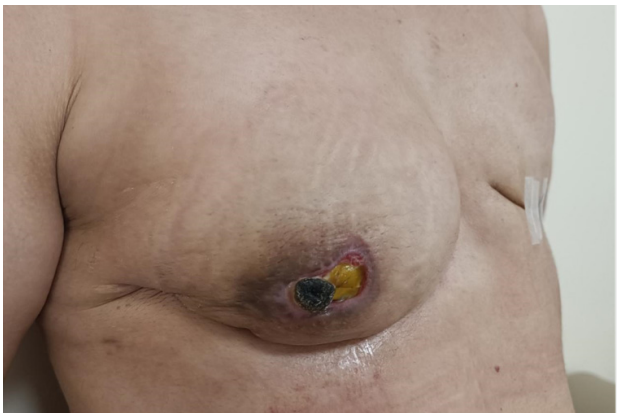

*Photo 1 : Grade 2 nipple necrosis at 12th week*

Adjuvant chemotherapy has been treated with surgery for 73,3% of the patients who have breast cancer. Adjuvant radiotherapy has been treated for 66,6% of the patients who have breast cancer but TP53 mutation.

All patients have controled at 1st, 3rd ,6th and 12th months, and no complications other than previous complications were observed. All of them were followed for an average of 36 months (range 2, 65 months) and 100% of them had overall survival, breast cancer specific survival, recurrence free survival, and metastasis free survival (Photo 2).

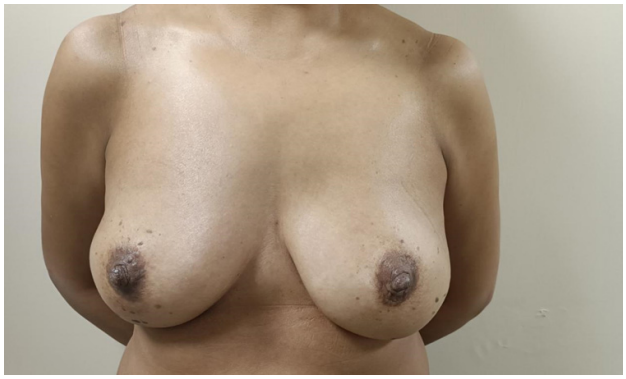

*Photo 2 : Bilateral Nipple Sparing Mastectomy at 12th mounth*

# DISCUSSION

Since the 1990s, with the first identification of the BRCA 1 and BRCA 2 hereditary mutation, genetic tests for breast cancer have been developing significantly. Thanks to these tests, it is ensured that genes with risk for breast or other cancer types are detected in a timely manner. With the expansion of these evaluated genes, the need to elaborate clinical management has increased (10). With this genetic mutation analysis, time was saved for patients. However, clinical information is scarce for patients with pathological variants detected in these large genetic panels, so there are not many clinics to guide. With this study, we aimed to help guide in this regard. Besides the BRCA 1 and BRCA 2 gene, TP53, PTEN, CDH1, and PALB2 are included in the guideline as high-risk genes associated with breast cancer. Prophylactic mastectomy operations can be recommended for these patients (11,12).

It is stated in international guidelines that the benefit of prophylactic mastectomy in reducing the risk of breast cancer in patients with high-risk genetic mutations is great. However, these guidelines are inconsistent with insurance policies (13). The lifetime risk of developing breast cancer in patients with BRCA1 or BRCA2 mutations is in the range of 60-90%, and it has been documented that this risk is reduced by > 90%, with thanks to prophylactic mastectomy surgery (14). The lifetime risk of developing breast cancer in patients with TP53 and PTEN gene mutations is 90%, and prophylactic mastectomy is recommended for these patients (15). There is a life-time risk of developing breast cancer between 35-50% in CDH1 and STK11 genes, and prophylactic mastectomy is not recommended in patients with this mutation (16). Although prophylactic mastectomy in high-risk genes is still controversial in some guidelines, other risk-reducing options such as regular screening and chemoprevention can be recommended to patients (17). At the same time, there are additional complications of performing contralateral breast surgery in patients diagnosed with breast cancer.

As in any operation, there are risks such as additional anesthesia time, bleeding, wound infection. At the same time, side effects and complications related to mastectomy can also be observed. The most common of these is seroma, and the others are capsular contracture, skin flap necrosis, nipple necrosis, postoperative pain, lymphedema, and limitation of arm movements. such complications are more common in bilateral mastectomy than in unilateral mastectomy, and their frequency varies between 5 and 35% (17). In our series, the complication rate was 40% and the necessity for reoperation was evaluated as 26.6%. Our patients underwent reconstructive surgery and we supported the finding of a higher incidence of complications than unilateral mastectomy, together with other articles in the literature. In addition, none of these complications delayed the patients' time to receive adjuvant treatment and did not go beyond oncological principles.

There are deficiencies in our study due to the relatively low number of patients. On the other hand, the flow rate is high since all patients underwent prophylactic mastectomy. We aim to contribute to the literature with the tumor free survival and overall surveillance times of the patients being 100%. Wide-panel genetic testing is an important advance in guiding treatment today. Physicians' guidance on the treatment of patients should be completely based on the person. With this article, we aimed to reveal the advisability of prophylactic mastectomy.

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