

**ROMANIA**

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**SURGICAL OPTIONS FOR PATIENTS UNDERGOING BREAST CANCER  
TREATMENT AND EVALUATION OF QUALITY OF LIFE  
SUMMARY OF THE THESIS**

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## CONTENTS

- **Introduction**
- **Part I: General Section**
  - **Chapter 1: Epidemiology of Breast Cancer**
    - 1.1 Global and national incidence and prevalence
    - 1.2 Incidence rates by age, ethnic/racial groups
    - 1.3 Socioeconomic factors
    - 1.4 Risk factors and causes of breast cancer
  - **Chapter 2: Biology and Pathology of Breast Cancer**
    - 2.1 Anatomy and physiology of the breast and axilla
    - 2.2 Types of breast cancer
    - 2.3 Molecular and genetic aspects
  - **Chapter 3: Diagnosis and Treatment of Breast Cancer**
    - 3.1 Screening techniques (e.g., mammography, ultrasound, MRI)
    - 3.2 Diagnostic methods (e.g., biopsy, histopathological analysis)
    - 3.3 Staging of breast cancer
    - 3.4 Biological markers and genetic tests
    - 3.5 Surgical treatment of breast cancer
    - 3.6 Systemic treatment of breast cancer
    - 3.7 Radiotherapy
  - **Chapter 4: Rare Diagnoses in Breast Pathology**
    - 4.1 Breast cancer during pregnancy
    - 4.2 Rosai-Dorfman disease with breast localization
    - 4.3 Anaplastic large cell lymphoma associated with breast implants (BIA-ALCL)
    - 4.4 Phyllodes tumor
  - **Chapter 5: Management and Survival in Breast Cancer**
    - 5.1 Prognostic factors
    - 5.2 Rehabilitation and quality of life after treatment
    - 5.3 Recurrence and prevention strategies

- 5.4 Psychosocial and economic implications of breast cancer diagnosis
      - 5.4.1 Psychosocial and economic impact of breast cancer
      - 5.4.2 Healthcare and health policies
      - 5.4.3 Role of education and public awareness
  - **Chapter 6: Conclusions and Recommendations**
    - 6.1 Summary of key findings
    - 6.2 Recommendations for future research
    - 6.3 Implications for clinical practice and health policies
- **Part II: Special Section**
  - 7. Introduction
  - 8. Aim
  - 9. Objectives
  - 10. Materials and Methods
    - 10.1 STUDY 1: Evaluation of the quality of life for patients diagnosed with breast cancer and the impact of genetic testing on patients diagnosed with breast cancer
    - 10.2 STUDY 2: Rare breast pathology and its implications in current practice
  - 11. Conclusions: Research novelty, limitations, new directions, and personal contributions

## **BIBLIOGRAPHY**

## **Introduction: Importance of the Issue, Hypotheses, Aims, and Objectives**

Breast cancer is the most common type of cancer among the female population worldwide. With a high mortality rate, especially in developing countries, this diagnosis poses a public health problem and remains a constant concern for medical professionals.

In recent years, specialists in the medical field have shown interest not only in improving the diagnosis and treatment of breast cancer but also in the social and emotional implications derived from such a diagnosis. It is known that a breast cancer diagnosis can have significant health consequences, up to and including life-threatening risks. However, it is a disease for which multiple treatments have proven effective over time. Therefore, the fact that it can also significantly impact psychosocial aspects is a current and much-studied concern in this field. The psycho-emotional consequences have also been shown to impact family, social, and cultural environments equally.

The aim of this thesis is to identify the medical and psychological mechanisms involved in the diagnosis and treatment of breast cancer at the Filantropia Clinical Hospital in Bucharest and the Nuffield University Hospital in Oxford, UK. The study aims to evaluate how quality of life is affected and what the most important psycho-emotional and social aspects are in the aftermath of such a diagnosis in both countries. Additionally, the existence of rare types of breast cancer, for which standard protocols do not fully apply, has generated special interest in the development of this work. Although recent advances in medical technology and the understanding of breast cancer biology have improved outcomes for many patients, increasing not only survival rates but also quality of life, there are still many challenges in this field. For example, identifying biomarkers for early diagnosis, developing targeted therapies, and especially identifying a strategy for standardizing the diagnosis, treatment, and subsequent socio-emotional support for patients diagnosed with breast cancer are important strategies that accompany oncology patients in the long term.

Quality of life is a complex, multifaceted concept that includes physical, emotional, social, and spiritual aspects. In the case of breast cancer, these dimensions can be influenced by the physical symptoms of the disease, the side effects of treatment, and the emotional impact of the diagnosis. Patients who receive a breast cancer diagnosis and undergo a quality-of-life evaluation during treatment and later in the follow-up period provide specialists with a comprehensive picture of the disease's impact on all levels of life.

Evaluating the quality of life and the socio-emotional impact of a breast cancer diagnosis thus becomes essential for providing comprehensive care tailored to patients' needs. Through understanding these aspects, healthcare professionals can develop treatment plans that not only combat the disease but also support patients in their journey toward recovery and reintegration into normal life, family, work, and, not least, society.

The novelty of this thesis lies in addressing specific aspects of breast cancer that are not well understood or sufficiently researched in Romania. This study aims to make a significant contribution to the evaluation of the quality of life of patients diagnosed with breast cancer in Romania and the psycho-emotional aspects that impact the lives of cancer patients in a country without a national breast cancer screening policy. Moreover, the evaluation of the quality of life in patients with breast cancer was assessed within an internal audit and at an oncology center in Europe, the Nuffield University Hospital, Oxford, UK, as part of a prospective study conducted over an 8-year period. Furthermore, this work aims

to present an evaluation of the genetic factors involved in the treatment and prognosis of patients diagnosed with breast cancer at Filantropia Hospital, given that there is no familial screening program and genetic testing can be a crucial pivot in the breast cancer treatment strategy.

This thesis also addresses the topic of rare breast cancers, for which studies still have much to reveal, such as anaplastic large cell lymphoma associated with breast implants or malignant Phyllodes tumors in pregnancy, and the treatment of breast cancer during pregnancy, which does not always follow standard treatment protocols and for which a multidisciplinary team's role is essential.

The studies conducted on patients in Romania are observational, cross-sectional, and retrospective, analyzing patients diagnosed with breast cancer who were included in genetic testing programs from January 2017 to December 2022. Additionally, the quality of life and psychosocial impact of patients diagnosed with breast cancer were analyzed using standardized, anonymized questionnaires. The patients were recruited from several oncology centers in Romania from January 2024 to March 2024, both online and at Filantropia Clinical Hospital. The study conducted at Nuffield University Hospital Oxford, UK, is an 8-year prospective study evaluating breast cancer patients who underwent conservative surgical intervention with partial breast reconstruction using the lateral thoracic artery perforator flap. Finally, a descriptive study of rare breast cancers was conducted based on cases encountered in current practice, describing the particularities of both diagnosis and treatment.

The multidisciplinary nature of this work is based on the fact that studies were conducted both locally and internationally, in collaboration with departments of oncologic surgery, oncology, radiotherapy, pathology, radiology, genetics, as well as with psychology specialists. The international character of the study reflects alignment with current international practice standards in the diagnosis and treatment of breast cancer.

The conclusions of the thesis confirm the importance of the multidisciplinary team in the diagnosis, treatment, and long-term follow-up strategy of breast cancer patients. Moreover, the studies confirm the importance of providing psycho-emotional support to breast cancer patients as an integral part of treatment to help improve quality of life both in the short and long term.

The limitations of this research include the difficulty in identifying and tracking patients, given that it is a retrospective, observational study. On the other hand, the international multidisciplinary nature creates discrepancies between the patient groups studied, and although the questionnaires used to assess quality of life and psycho-emotional aspects are internationally standardized, a parallel comparative study between the two patient populations could not be conducted. Furthermore, in Romania, there is no national breast cancer screening program, leading to more frequent diagnoses in advanced stages for many patients compared to those diagnosed in the UK, where they are subject to rigorous screening and benefit from early diagnosis and less aggressive oncologic treatments. Patients in Romania could benefit from conservative surgical treatment with or without oncoplastic techniques if they were more frequently diagnosed in the early stages of the disease. Enrolling patients in such studies can be challenging given the lack of unity and coherence between oncology centers both nationally and internationally, although all care provided in these centers adheres to international guidelines in

In Romania, breast cancer is also the most common form of cancer among women and the second most frequent type in the general population, after colorectal cancer. According to GLOBOCAN 2022 data, approximately 12,685 new cases of breast cancer were registered in Romania, representing 26.8% of all cancer cases in women. The incidence of breast cancer in Romania varies depending on different geographical regions. Urban areas, such as Bucharest, tend to have higher rates than rural areas, which may be attributed to access to diagnosis and lifestyle changes. On the other hand, breast cancer mortality ranks first in Romania as the leading cause of death among women. In 2022, 3,822 women died from breast cancer (15.8% of all cancer deaths in women), surpassing colorectal cancer (12.8%; 2,986 deaths) and lung cancer (11.9%; 2,787 deaths).

Breast cancer is a heterogeneous condition from a molecular and genetic standpoint, with multiple molecular subtypes that have significant implications for treatment, treatment response rates, and disease prognosis. Detailed immunohistochemical analysis complements histopathological examination to determine whether tumors express hormone receptors, including estrogen and progesterone receptors. Additionally, the differentiation grade of the tumor and Ki67 are determined (Ki67 is a nuclear protein associated with cellular proliferation, often used as a marker to assess the degree of cellular proliferation in tumor tissues, including breast cancer. Ki67 is present in the active phase of the cell cycle (G1, S, G2, and M phases), and its expression level reflects the rate of cell division in a particular tissue or tumor lesion. In breast cancer, evaluating Ki67 expression can be useful in determining the tumor's aggressiveness and predicting disease prognosis. Tumors with high Ki67 levels are often associated with faster tumor growth, a higher risk of recurrence, and a more reserved prognosis). HER2 gene expression is also assessed.

Based on these immunohistochemical details, the molecular classification of breast cancer is as follows:

- **Luminal A Subtype:** Characterized by the expression of estrogen (ER) and progesterone (PR) hormone receptors and the absence of HER2 overexpression. Patients with this molecular subtype typically have a more favorable prognosis compared to other subtypes.
- **Luminal B Subtype:** Similar to Luminal A but with lower hormone receptor expression or HER2 overexpression. This subtype has a more reserved prognosis and often requires more aggressive oncological therapies.
- **HER2-Positive Subtype (HER2 Amplified):** Characterized by overexpression of the HER2 receptor (human epidermal growth factor receptor 2). Targeted therapies such as trastuzumab have revolutionized the management of this subtype, significantly improving prognosis and patient survival.
- **Triple-Negative Breast Cancer:** Characterized by the absence of ER and PR hormone receptor expression and HER2 overexpression. It is associated with a more reserved prognosis and weaker responses to conventional therapies.

Genomic analyses and DNA sequencing have revealed various genomic abnormalities in breast cancer, including mutations in tumor suppressor genes (such as BRCA1 and BRCA2), HER2 gene amplification, and chromosomal rearrangements. These genetic abnormalities can serve as prognostic and predictive biomarkers, guiding personalized therapeutic choices.

A deep understanding of the molecular and genetic aspects of breast cancer has led to the development of targeted therapies and personalized treatment strategies. Targeted therapies, such as anti-HER2 therapy in HER2-amplified cases and PARP inhibitors in BRCA mutation cases, have revolutionized breast cancer management, significantly improving prognosis and patient survival. Future continued molecular and genomic research will enable the identification of new biomarkers and innovative therapies with the potential to further improve clinical outcomes in breast cancer.

Surgery remains the primary treatment for breast cancer in most cases. Although surgical techniques have undergone numerous modifications over time, studies have shown that the type of surgery should consider the tumor type, tumor size, location, extension to adjacent tissues, recurrence risk, patient preference, the opportunity for breast reconstruction, and the need for adjuvant treatments such as radiotherapy. All these factors should be carefully analyzed by a multidisciplinary team and together with the patient to make the most appropriate therapeutic decision, benefiting the patient both oncologically and in terms of quality of life after oncological treatments.

Breast-conserving surgery, also known as wide local excision, involves removing the tumor and a margin of healthy tissue around it while preserving as much of the breast as possible. This procedure is often combined with postoperative radiotherapy to reduce the risk of local recurrence. Clinical studies have shown that for many women with small, well-localized tumors, wide local excision followed by radiotherapy has similar oncological outcomes to mastectomy but with a superior cosmetic result and greater patient satisfaction.

Mastectomy is a surgical procedure involving the removal of the entire breast affected by cancer. There are several types of mastectomy, including simple (total) mastectomy, modified radical mastectomy, and skin-sparing and/or nipple-sparing mastectomy. Simple mastectomy involves removing the entire breast tissue without affecting the pectoral muscles. Modified radical mastectomy involves removing the entire breast and axillary lymph nodes while preserving the pectoral muscles. Skin-sparing or nipple-sparing mastectomy allows for immediate breast reconstruction, providing a better cosmetic outcome for patients.

Oncoplastic surgery is a revolution in breast cancer conservative surgery techniques, combining oncological principles of tumor excision with plastic surgery techniques to achieve superior aesthetic results and minimize post-operative breast deformities. This may include residual breast tissue reshaping techniques, breast reduction, or contralateral breast symmetrization. Oncoplastic techniques are particularly useful in cases where tumors are located in areas that could lead to significant cosmetic deformities after surgical excision. Studies have shown that oncoplastic techniques improve patient satisfaction with breast appearance and quality of life without compromising oncological outcomes.

Chemotherapy is one of the main systemic treatment methods for breast cancer, used in both early and advanced stages of the disease. This treatment involves using cytotoxic drugs to destroy cancer cells. Chemotherapy regimens often include combinations of drugs such as doxorubicin, cyclophosphamide, paclitaxel, and docetaxel. Chemotherapy can be administered in a neoadjuvant setting, given before surgery, potentially reducing tumor size and facilitating breast-conserving surgery. Adjuvant chemotherapy, administered postoperatively, aims to eliminate any residual cancer cells and reduce the risk of recurrence. Chemotherapy regimens are influenced by the type of breast cancer, the presence of genetic mutations, the stage of the disease, and the characteristics of each patient (age, medical history, associated pathologies).

Breast cancer during pregnancy is a rare diagnosis, but it is the most common malignancy diagnosed during pregnancy, accounting for 1 in 3 cancer cases associated with pregnancy. The incidence of breast cancer during pregnancy varies between 1 in 3,000 and 1 in 10,000 pregnancies.

Although breast cancer treatment during pregnancy should follow existing guidelines as the standard, there are certain aspects that need to be considered, focusing not only on the diagnosed patient but also on the fetus and the implications for its health. A breast cancer diagnosis during pregnancy becomes much more complex in terms of both diagnosis and treatment. The complexity of this situation revolves around maintaining diagnostic and treatment standards for the mother while also preserving the fetus's health, considering that most oncological treatments can harm the fetus through toxicity.

The diagnosis of cancer during pregnancy has a significant psychological impact on the patient and her family. Therapeutic decisions are complex and must consider not only medical aspects but also the patient's personal preferences and values.

Treatment decisions must also integrate ethical considerations, the patient's preferences, and potential effects on the fetus. Studies show that psychological support and counseling are essential for managing the stress associated with this dual challenge. It is also vital to create evidence-based clinical guidelines to help standardize care and optimize outcomes for both mother and child.

Anaplastic large cell lymphoma associated with breast implants (BIA-ALCL) is a rare type of non-Hodgkin lymphoma that occurs in some women with breast implants, particularly those with textured surfaces. This condition develops in the periprosthetic space, manifesting as fluid accumulation, pain, or tumor formation around the implant. Diagnosis involves aspirating periprosthetic fluid and biopsying the capsule, followed by cytological and immunohistochemical analyses to detect CD30 and ALK markers. Primary treatment involves complete removal of the implant and surrounding capsule, and in some cases, chemotherapy or radiotherapy may be necessary, according to lymphoma treatment guidelines.

Phyllodes tumors are rare breast neoplasms, representing less than 1% of all breast tumors, characterized by mixed proliferation of stromal and epithelial components. These tumors can range from benign to malignant, with the potential for recurrence and metastasis in malignant cases. Malignant phyllodes tumors are rare breast neoplasms characterized by rapid proliferation and the potential for recurrence and metastasis. Management of these tumors requires a multidisciplinary approach involving surgeons, oncologists, and in some cases, radiotherapists. The primary treatment is surgical, but adjuvant strategies may be necessary depending on the malignancy grade and specific tumor characteristics. Clinically, they present as palpable and mobile breast masses that can rapidly increase in size. Diagnosis is based on biopsy, and primary treatment consists of wide excision with at least a 1cm margin to prevent recurrence. In cases where tumors are large or located in areas that do not allow for adequate margin excision, mastectomy may be considered. Breast-conserving surgery is possible and recommended if it is technically feasible to achieve surgical margins of at least 1cm for oncological safety without significant cosmetic compromise. Histological evaluation of margins is crucial to determine if excision was complete.



The survival rate for breast cancer has increased significantly in recent decades due to advances in diagnosis and treatment. Long-term survival depends on the stage of the disease at the time of diagnosis and the response to the treatments applied. Regular monitoring of patients after treatment is essential for the early detection of recurrences and the management of long-term side effects. Monitoring may include periodic clinical exams, follow-up imaging (mammograms, ultrasounds, MRI), and periodic evaluations of biomarkers. Long-term care must also address the psychosocial aspects of survival, offering support for quality of life and reintegration into normal life. The importance of a multidisciplinary team and a personalized care plan is crucial for optimizing long-term outcomes.

Physical rehabilitation is an essential aspect of post-treatment care for breast cancer survivors. Many patients experience long-term side effects of treatments, such as lymphedema, chronic pain, reduced shoulder mobility, and chronic fatigue. Rehabilitation programs include specialized physical exercises to improve strength and flexibility, physical therapy for managing lymphedema, and nutritional support to address weight-related side effects. Regular physical exercise is particularly beneficial, contributing to reduced fatigue, improved physical function, and an overall increase in quality of life.

Psychosocial support plays a crucial role in the rehabilitation of breast cancer survivors. The diagnosis and treatment of breast cancer can have a significant impact on mental health, leading to anxiety, depression, and post-traumatic stress. Psychological counseling, support groups, and group therapies are effective ways to help patients cope with these issues. Support from family and friends is also essential for emotional recovery. Psychosocial interventions not only improve mental health but can also enhance the positive effects of medical treatments, contributing to a faster and more complete recovery.

Sexual counseling and hormone therapy can help manage these side effects. It is also important for young patients to discuss fertility preservation options before starting treatment. Complete rehabilitation includes addressing these intimate and personal aspects to ensure the best possible quality of life after treatment.

The main goal of this doctoral thesis is to analyze the quality of life of patients treated for breast cancer in Romania, particularly in Filantropia Hospital, and to evaluate and compare the quality of life of another group of patients treated for breast cancer at the Nuffield University Hospital, Oxford, UK. Another important goal of this thesis is to assess the extent to which positive genetic testing for breast cancer susceptibility genes affects the treatment and prognosis of breast cancer patients treated at Filantropia Hospital, as well as to present cases of very rare breast pathology and their impact on current practice.

The objectives of the thesis are as follows:

1. Evaluate the impact of a breast cancer diagnosis and the consequences of this disease on quality of life, anxiety levels, resilience, and depression.
2. Evaluate the quality of life of breast cancer patients using oncoplastic techniques for breast reconstruction.

3. Analyze the impact of genetic testing for breast cancer susceptibility genes among patients diagnosed with breast cancer.
4. Describe particular and very rare cases in breast pathology, such as pregnancy-associated Phyllodes tumor and giant cell anaplastic lymphoma associated with breast implants.

To achieve these objectives, I have designed two studies: one containing two retrospective analyses and one prospective analysis, and another observational study that describes particular cases of breast pathology with a significant impact on patients and current medical practice for breast cancer.

**STUDY 1:** Evaluation of the quality of life of patients diagnosed with breast cancer according to the therapeutic options applied and the impact of genetic testing on patients diagnosed with breast cancer.

**Working Hypotheses:**

- Early detection of breast cancer can help de-escalate surgical (conservative surgery vs mastectomy) and oncological treatment.
- Functional scores and quality of life in breast cancer patients are influenced by the type of surgical treatment (conservative surgery vs mastectomy).
- There is a difference in resilience, anxiety, and depression scores between patients who undergo radical surgery and chemotherapy versus patients who have undergone conservative treatment and did not require chemotherapy.
- There is a positive correlation between anxiety, depression, and stress scores in women diagnosed with breast cancer.
- Social support moderates the relationship between quality of life and emotional conditions, so quality of life is positively influenced by social support and negatively by anxiety, depression, and stress levels in women with breast cancer.
- Resilience moderates the relationship between emotional conditions and quality of life so that women with higher resilience have lower levels of depression, anxiety, stress, and a better quality of life.
- Oncoplastic surgery techniques used in breast cancer patients improve their quality of life, considering overall satisfaction with physical appearance, sexual life, and functional scores (arm mobility, shoulder function).
- Oncoplastic surgery techniques can facilitate the avoidance of radical surgery in breast cancer for selected cases.
- Pathogenic variants of breast cancer susceptibility genes affect breast cancer treatment and long-term management.
- Positive genetic testing for breast cancer susceptibility genes in breast cancer patients can significantly impact screening and prophylaxis strategies.

## Objectives:

- Evaluate the impact of early breast cancer diagnosis on the type of surgical/oncological therapy.
- Evaluate anxiety, depression, resilience, and quality of life scores in breast cancer patients with a history of pregnancy/lactation.
- Analyze the impact of a breast cancer diagnosis on anxiety, depression, stress, resilience, and quality of life levels according to the method of diagnosis and type of treatment used.
- Evaluate the quality of life in breast cancer patients undergoing breast-conserving surgery using oncoplastic techniques (assessment of quality of life, satisfaction with physical appearance, self-esteem, impact on sexual life, and evaluation of arm/shoulder functional scores).
- Analyze the impact of genetic mutations on treatment and prophylaxis in patients diagnosed with breast cancer.

**Material and Method:** The first part of the thesis is a descriptive, non-experimental study in which several hypotheses were tested during the period January-March 2024. Participants were recruited through online and social media announcements, and also a cohort of patients was included from Filantropia Clinical Hospital in Bucharest from the oncology and oncological surgery departments. Patients diagnosed with breast cancer were invited to participate in this study, and they completed a series of scientific questionnaires analyzing certain psychosocial aspects. All participants were included in the study voluntarily. The study also adhered to ethical standards, ensuring both data confidentiality and participant anonymity. The types of tools and procedures used in the study were non-invasive, aimed at avoiding additional stress for breast cancer patients.

Demographic data was collected from all patients, including age, hormonal status (pre/post-menopause), family history of cancer, personal history of associated pathologies, as well as information about the breast cancer diagnosis and the type of treatment used. Men diagnosed with breast cancer were excluded from the patient group, as most of the questionnaires are designed for female patients (especially those referring to body image, quality of sexual life, and psychosocial aspects of breast interventions).

In addition to this data, patients were asked to complete a series of standardized psychosocial questionnaires. The types of questionnaires included the following:

- EORTC QLQ-BR23 (quality of life questionnaires for breast cancer patients issued by the European Organization for Research and Treatment of Cancer) Romanian language module.
- Anxiety, depression, and stress levels were assessed using another standardized tool, the DASS 21-question scale (Depression, Anxiety, Stress Scale). This type of questionnaire assesses the level of psychological distress in breast cancer patients but is used in multiple populations with various medical conditions, whether we are talking about patients with chronic pain or patients with psychiatric conditions.
- The degree of resilience in breast cancer patients was assessed using the CD-RISC 10 questionnaire. This score is based on psychometric properties in both the general population

and certain populations with common characteristics, proving consistency and being validated over the years.

- To assess social support, we used a scale called MOS – the Social Support Scale, which was initially used and validated in a two-year study centered on patients with chronic conditions. It has been extensively validated and was designed to be used concretely to provide the necessary social support to patients with various conditions. [137] All these questionnaires are intended to provide a clear correlation between the type of diagnosis and the support modalities we can offer patients, both to improve the quality of life and to reduce the short-, medium-, and long-term side effects of treatment, and also to guide us towards measures that can be taken to reduce psychosocial distress in patients diagnosed with cancer.

Data analysis was performed in Python 3.7.4, using the pandas package for database processing (selecting variables, dividing into patient groups, extracting descriptive statistics) and the matplotlib and seaborn packages for graphical visualization of results.

## **Results and discussion**

### **Do patients diagnosed through screening have a higher chance of undergoing conservative surgery (avoiding radical mastectomy) and avoiding chemotherapy? Can early detection of breast cancer help de-escalate surgical and oncological treatment?**

From the group of patients included in the study, the majority underwent surgery, either conservative surgery (wide local excision) or radical surgery (mastectomy). Only two patients reported that they had not undergone surgery associated with their cancer diagnosis, either because they were undergoing neoadjuvant chemotherapy or because they were diagnosed at a locally advanced or metastatic stage. 42% of the patients had conservative surgery, 58% had radical surgery (mastectomy), and among them, 16% (28 patients) had breast reconstruction. Among the patients who discovered a lump through self-palpation, 73% required chemotherapy, a percentage similar to those diagnosed through screening mammography (71.2%), and the frequency of radiotherapy use was not influenced by the initial diagnostic method. Although data analysis shows that the group of patients diagnosed through screening mammography more frequently required conservative surgery, statistical analysis using the chi-square test shows that there is no statistically significant difference ( $p=0.548$ ).

### **Is there an impact on functional scores based on the type of surgery and the initial diagnostic method?**

Regardless of the type of surgery and diagnostic method, there are no differences in functional scores related to arm pain, shoulder function, and mobility in the group of patients included in this study. Therefore, the quality of life for this group of patients is not affected (ANOVA,  $p>0.5$ ) (Figure 21, Figure 24).

### **Do patients who underwent breast reconstruction have a better quality of life?**

The type of surgical treatment (mastectomy, mastectomy with reconstruction, or conservative surgery) was not associated with differences in perceived pain, body image, depression, anxiety, stress scores, or quality of life scores. Additionally, there were no differences in sexual function and pleasure between patients grouped by the type of surgical treatment.

Patients who believe that surgery had a negative impact on their quality of life have lower resilience scores and higher depression scores.

We also analyzed the group of patients who stated that surgery had a significant impact on their quality of life. These patients admitted that the impairment of quality of life was significantly due to surgery for breast cancer. We compared resilience, depression, anxiety, and stress scores for this group of patients. Statistical data confirmed that low quality of life is associated with low resilience and higher depression and stress scores. Based on this result, we validated another important positive correlation in the entire study group, namely, the relationship between depression, stress, and anxiety (for all patients included in the study, a positive correlation between depression, anxiety, and stress scores was demonstrated, thus confirming one of the hypotheses of this study).

Almost all physical symptoms (insomnia, loss of appetite, nausea and vomiting, constipation, arm symptoms, breast symptoms, fatigue, pain, dyspnea, etc.) as well as all psychological symptoms negatively correlate with the quality of life of patients. Moreover, quality of life negatively correlates with depression, stress, anxiety scores, and positively correlates with physical, social, and social support functioning scores. However, it is very difficult to assess causality between symptoms and quality of life, especially when different symptoms are themselves correlated, with some patients experiencing multiple symptoms with varying impacts on QoL. Thus, to further explore independent factors that predispose to decreased quality of life, we conducted a multinomial logistic regression analysis using quality of life above the median as the dependent variable. In this analysis, approximately 54% of the variability in quality of life (QoL) is explained by the independent variables included in the model. The proper training of the model was confirmed with a p-value of  $1.613e-13$  compared to a null model without predictors.

We conducted another prospective study on a group of patients treated at Nuffield University Hospital, Oxford, UK, over a period of 7 years. Patients who were diagnosed with breast cancer and surgically treated through oncoplastic surgery were included in this study to evaluate the quality of life after such a diagnosis and to also assess long-term outcomes regarding recurrence, aesthetic results, and quality of life. This study included patients who were diagnosed with ductal carcinoma in situ or invasive breast carcinoma and who underwent local wide excision of the lesion followed by partial breast reconstruction with a lateral thoracic artery perforator flap. This database was prospectively collected, and the oncological follow-up data (over 5 years) was collected from the hospital database to identify potential recurrences or metastatic cases. Additionally, an internal audit was conducted for these patients, who were asked to complete anonymized and standardized questionnaires (Breast-Q forms) regarding quality of life and its impact following a breast cancer diagnosis.

In this study, 105 patients who underwent breast cancer surgery over a 7-year period, between 2011 and 2018, at Nuffield University Hospital in Oxford, UK, in the dedicated breast surgery department, were prospectively included. All patients included in the study underwent wide local excision of the lesion and partial breast reconstruction with a lateral thoracic artery perforator flap. Clinical and biological data, as well as patients' history, comorbidities, risk factors, demographic data, and adjuvant treatments, were collected from the hospital database, which was subsequently updated during adjuvant treatments and scheduled follow-ups according to current standard guidelines. The team of surgeons was actively involved in the clinical evaluation during this follow-up period and also in

the evaluation of the physical and aesthetic postoperative outcome. Patient satisfaction with the aesthetic and functional outcome was evaluated through standardized, anonymized questionnaires.

Regarding patient satisfaction, the aesthetic, functional, and quality of life evaluation for these patients was conducted through an internal audit that involved the use of Breast-Q and BIS (Body Image Scale) questionnaires. The response rate to these questionnaires was 70%, and the quality of life (pre- and postoperative), body image, sexual life, shoulder and arm functionality, mobility, pain, and the surgical team's evaluation were assessed. Patients' responses revealed that there was 80% satisfaction regarding the aesthetic aspect, and also, 95% satisfaction with the surgical team.

If we analyze the patients who responded to the Breast-Q questionnaires, we observe that there is 75% satisfaction regarding the general well-being among the patients in the study, 80% also affirm a good quality of life from a psychosocial perspective, and only 60% state that they have satisfactory sexual quality of life. On the other hand, this last percentage, which refers to aspects of quality of life in relation to sexual life, is similar to the percentages recorded preoperatively, which means that the impairment of sexual life was not due to the surgery itself, but rather to the background of the diagnosis and other preexisting factors. 73% of patients had excellent scores regarding discomfort, pain, and mobility of the neck, shoulder, and arm, and over 80% affirmed an excellent quality of life regarding the scar on the posterior thoracic area concerning shoulder mobility.

We also conducted a retrospective evaluation of a group of breast cancer patients who required genetic testing and for whom breast cancer management and follow-up were modified as a result of genetic testing. Thus, we conducted a retrospective analysis at Filantropia Hospital over a period of 6 years, between 2017 and 2022, and included in this study patients who required genetic testing following a breast cancer diagnosis, according to international recommendations and guidelines. The majority of patients were tested for pathogenic variants of BRCA1 and BRCA2, but the testing was extended for some patients, including the evaluation of genes such as PALB2, CHEK2, POLE, TERC, TMEM127, BRIP1, RAD50, APC, MSH, KRAS, and TP53. It is also important to note that genetic testing in Romania is not covered by the public health system, and testing was recommended for patients diagnosed with breast cancer before the age of 50, patients with triple-negative breast cancer, men diagnosed with breast cancer, and also relatives of these patients.

More than half of the patients in the study group tested positive for a pathogenic or potentially pathogenic variant of the BRCA1 or BRCA2 genes (53% of patients), while the remaining patients tested positive for genes such as PALB2, Chek2, KRAS, TP53, POLE, MSH, and RAD51.

We also analyzed in our group the types of treatments and their sequencing. Treatment recommendations were in line with current guidelines and the recommendations of the multidisciplinary team, considering the stage of the disease, molecular subtype, and genetic testing for these patients. In the study group, the majority of patients received neoadjuvant chemotherapy due to staging and molecular subtype (62% of patients). The remaining 31% had surgery as the first therapeutic step for the same reasons related to staging, and especially the molecular subtype, considering that a significant number of patients had Luminal A/B subtype.

In this group of patients, we analyzed the types of prophylactic surgery recommended and performed. Apart from cases of bilateral breast surgery with prophylactic contralateral mastectomy performed for 16% of patients, prophylactic interventions on the ovaries were also recommended and carried out in

our group. Specifically, 7% of patients underwent bilateral adnexectomy via laparoscopy as part of preventive management for patients carrying genes with pathogenic or potentially pathogenic variants for breast cancer susceptibility. For all patients, considering the predominantly fertile age in our group, thorough counseling was provided regarding prophylactic strategies, whether surgical or medical, as well as counseling on fertility and the patients' desire to have pregnancies in the future.

## **10.2 STUDY 2: Rare Breast Pathology and Its Implications in Current Practice**

The existence of rare breast pathology, which does not always conform to the criteria of current guidelines, has garnered special interest among medical specialists. Whether discussing Phyllodes tumors, which can be benign, borderline, or malignant, or anaplastic large cell lymphoma associated with breast implants, these pathologies do not always follow the known treatment steps.

When it comes to diagnostic stages, these are similar in terms of imaging and clinical examination, with patients undergoing clinical examination as well as mammography/ultrasound. However, the treatment perspective changes when dealing with sarcomatous pathology or with conditions requiring treatment from the field of hematological oncology, such as anaplastic large cell lymphoma associated with breast implants.

In this case, the first patient, a 36-year-old woman, presented to the doctor with a rapidly developing right breast tumor, with a sudden increase in size noticed by the patient over the last 3-4 months. At the time of the medical consultation, the patient was 19 weeks pregnant. The patient's personal history includes a full-term spontaneous birth, the excision of a right breast fibroadenoma 18 years ago, and no reported family history of oncological or other clinically significant pathology.

Clinical examination revealed a large right breast tumor approximately 10 cm in size, located in the upper outer quadrant of the right breast, with no pathological skin changes, no nipple or skin retraction, and the tumor was painless, mobile, and well-demarcated. Considering the patient's age and current pregnancy, the next recommended investigation was a breast ultrasound, which revealed a large breast tumor approximately 10 cm in the central quadrant and towards the upper outer quadrant of the right breast, as well as a few clinically insignificant cystic areas.

Following the clinical and ultrasound examination, a suspicion of Phyllodes tumor (PT) was raised, and a core needle biopsy was performed under local anesthesia to obtain a definitive diagnosis and safely proceed with the necessary therapeutic steps for both the patient and the fetus. The initial biopsy result diagnosed a benign PT with a rapid growth pattern, without borderline or malignant features. Therefore, considering the pregnancy and the tumor's rapid growth, the decision was made to surgically excise the tumor according to current guidelines.

Conservative surgery was performed under general anesthesia with careful monitoring of both the patient and the fetus. The postoperative aesthetic result was excellent, with an arched incision in the upper outer quadrant, and no postoperative complications were recorded. The patient's recovery was excellent, and the pregnancy was not affected by the surgery.

Histopathological examination revealed a borderline PT with 1 mm resection margins, and subsequent immunohistochemical tests confirmed a malignant PT (with sarcomatous heterologous differentiation). Given the diagnosis, clinical context, and ongoing pregnancy, the case was discussed by a multidisciplinary team to determine the subsequent therapeutic approach. Considering the malignant PT

diagnosis, the large tumor size of 10 cm, the resection margin without safety margins, and the ongoing pregnancy, surgical intervention was recommended to achieve safe margins. Additionally, constitutional factors and the ratio between the breast tissue to be excised and the remaining breast tissue were considered, leading to the recommendation for mastectomy, as an aesthetically satisfactory result could not be achieved.

The patient was appropriately informed, taking into account the diagnosis, pregnancy, and the multidisciplinary team's recommendations. The risks and benefits of further surgery, as well as the risk of recurrence and metastasis, were explained. However, at 25 weeks pregnant, the patient refused the surgery to achieve safe margins, opting instead for close clinical and imaging follow-up. She did not want additional breast surgery due to the advanced state of her pregnancy and did not want to risk preterm birth associated with the surgical risks. Thus, close clinical and ultrasound follow-up was conducted every 4 weeks in the subsequent period.

At 9 weeks after the initial surgery, ultrasound examination revealed local recurrence and disease progression. At least 6 lesions were identified in the right breast, the largest measuring approximately 3 cm. No lesions were identified in the contralateral breast or other suspicious lesions in the axilla. The clinical and imaging findings were typical of local recurrence of malignant PT, given the close resection margins in the first surgery and the patient's refusal to complete surgery within oncological safety margins.

At 35 weeks pregnant, the patient underwent curative surgery, resulting in a right mastectomy without axillary dissection. There were no perioperative complications, the pregnancy progressed physiologically without associated effects on the fetus, and the patient was closely monitored by a team consisting of an oncological surgeon, obstetrician, oncologist, and radiologist.

Postoperative recovery was very good, with both the patient and fetus being monitored in the standard manner. The final histopathological result of the mastectomy specimen revealed multiple malignant PTs with heterogeneous sarcomatous differentiation, the largest tumor measuring 4/2 cm. Subsequently, the patient gave birth spontaneously, at term, to a normal-weight baby, without peripartum complications, with excellent recovery.

Postpartum, the patient underwent a control CT scan of the head, chest, abdomen, and pelvis to exclude metastases. The CT examination showed no distant metastases. The case was rediscussed by the multidisciplinary team, and the patient was recommended and subsequently underwent adjuvant chemotherapy, with 6 cycles of Doxorubicin and adjuvant radiotherapy to prevent recurrence and achieve local disease control.

Follow-up was conducted according to the standard protocol within the multidisciplinary team. Four years after the diagnosis, the patient continues to be monitored, showing no signs of local recurrence or distant metastasis. During the follow-up period, the patient also underwent right breast reconstruction with an excellent aesthetic and functional outcome. The patient continues to be monitored in the oncology and oncological surgery department.

Malignant PTs associated with pregnancy are extremely rare, and the management of these cases is based on reports of similar cases in the medical literature. Although the general recommendation for surgical excision with at least 1 cm margins remains the gold standard in treatment



recommendations for malignant PTs (with those associated with pregnancy being no exception), when this is not technically possible due to local or constitutional factors, recommendations for adjuvant oncological treatment (chemotherapy and radiotherapy) can reduce the risk of local recurrence and metastasis. What becomes more challenging in cases of malignant PTs associated with pregnancy is synchronizing treatment with the gestational age to minimize fetal impact, as well as calculating the probable time of delivery and avoiding radiotherapy until after birth. Although chemotherapy can be safely administered during pregnancy with selected therapies that have minimal effects on the fetus, this is most commonly recommended during the second trimester, with a period of approximately 3-4 weeks between the last chemotherapy session and delivery to allow the fetus to recover its cell lines. Of course, personalized treatment may also include earlier delivery if the risk of recurrence is high and radiotherapy should not be delayed. This decision is not only made by a multidisciplinary team that includes the entire care team for a breast cancer patient but also requires a team of experienced obstetricians and a neonatology team prepared to care for a potentially premature newborn after the mother's chemotherapy treatment. The implications are significant for both the mother and the fetus, and the care and treatment efforts involve the entire team.

The second case of rare breast pathology involves a patient diagnosed with anaplastic large cell lymphoma associated with breast implants (BIA-ALCL). The particularity of this case is that the diagnosis was made in a young patient who had textured implants for aesthetic purposes placed 11 years ago, and her diagnosis revealed advanced local disease involving regional lymph nodes. Cases reported in the medical literature confirm that most BIA-ALCLs are diagnosed at a stage limited to the implant, and surgical excision of the implant and its capsule cures the patient. However, locally advanced cases are extremely rare, this being the first case diagnosed at the Nuffield University Hospital in Oxford, UK.

A 48-year-old female patient presented to the Nuffield University Hospital in Oxford with a history of bilateral submuscular breast implants for breast augmentation 11 years ago. The implants were textured Allergan implants, containing silicone, with a volume of 295 ml, type ST110. The records from the initial surgery were retrieved, showing no perioperative complications, and the follow-up visits were routine, with no notable events. The patient presented to the hospital in August 2017, reporting a lump in the left breast for approximately six weeks. Her personal history includes the detection of a right breast fibroadenoma, for which a biopsy was performed in the past for confirmation, but no surgical intervention was required.

The patient also had a family history of breast cancer, with her mother being diagnosed at age 65, post-menopause. Physiological history revealed that the patient had two pregnancies and did not breastfeed, and she used progesterone-based contraception for five years.

Clinical examination detected a significant tumor mass in the upper-inner quadrant of the left breast, without signs of implant rupture. No capsular contracture or other clinical signs related to the breast implant were noted during the examination. Subsequent imaging investigations were performed, considering the clinical picture, history, and patient's age. Mammography did not reveal any suspicious images. Ultrasound evaluation reconfirmed the presence of the right breast fibroadenoma, and multiple tumor masses were described in the upper-inner quadrant of the left breast, raising suspicion of giant cell lymphoma. No fluid collection or other ultrasound abnormalities were detected at the implant site. An ultrasound-guided biopsy was performed during the examination to obtain a definitive diagnosis.

As part of the diagnostic investigations, a bilateral breast MRI was also performed, describing a poorly defined, lobulated tumor mass measuring 46/35/40 mm in the upper-inner quadrant of the left breast, located anterior and superior to the implant capsule, in close contact with the pectoral muscle. A minimal fluid layer around the left breast implant was also identified. To complete the investigations, a PET-CT was performed, which described, in addition to the tumor mass in the upper-inner quadrant of the left breast, a 6-7 cm mass and a few suspicious-looking nodes in the left axilla and a small suspicious node in the internal mammary chain. The PET-CT ruled out the spread of the disease to other organs. Subsequently, a core biopsy was performed on the suspicious left axillary lymph node.

The histopathological result identified neoplastic giant cells with multiple mitoses, a few small lymphocytes, and eosinophils. Immunohistochemistry confirmed that the tumor was intensely positive for CD30 and CD45 and positive for CD2, CD4, CD5, and Granzyme B; the background of this biopsy consisted of reactive small T cells. The neoplastic cells were confirmed to be ALK-1 negative, CD56 negative, CK7 and AE1/3 negative, and the MIB1 proliferation index was 80%. All this information, correlated later with the positive biopsy for the axillary lymph node, led to the diagnosis of BIA-ALCL with invasion of the axillary lymph nodes, stage IIB.

With a definitive diagnosis confirmed by histological and immunohistochemical analyses, the case was discussed in a multidisciplinary committee, including a hematologist, hemato-oncologist, breast surgeon, hematopathologist specializing in hematologic and breast pathology, and a radiologist.

Considering the diagnosis, stage of the disease, and preoperative evaluation, which indicated a risk of incomplete resection even with the assistance of a thoracic surgeon, neoadjuvant chemotherapy with six cycles every two weeks consisting of cyclophosphamide, doxorubicin, vincristine, and prednisone was considered, followed by surgical intervention and adjuvant consolidation radiotherapy.

The patient underwent neoadjuvant chemotherapy without significant adverse effects and with good tolerance. A control PET-CT was performed post-chemotherapy, showing a complete imaging response both in the left breast and left axillary lymph nodes and in the internal mammary chain nodes.

After completing the six cycles of chemotherapy, surgery was performed to remove both breast implants en bloc with their capsules under general anesthesia. Intraoperatively, no tumor masses or other pathological aspects were identified, but given that the implant was removed en bloc with its capsule, subsequent analysis was carried out through histopathological examination. At the level of the pectoral muscle, where an intimate adhesion between the tumor mass and the muscle was initially described, no specific aspect was identified intraoperatively. Macroscopically and comparatively, the capsule of the left breast implant, affected by BIA-ALCL, was thicker and more adherent to the implant. The surgical intervention was limited to the bilateral breast implants, and no surgery was recommended at the level of the axillary lymph nodes, given the preoperative PET-CT result, which showed a complete imaging response.

The patient's postoperative recovery was favorable, with no postoperative complications. The final histopathological result showed no malignant cells in the implant capsule, demonstrating a complete pathological response after neoadjuvant chemotherapy, as anticipated by preoperative imaging evaluation.

## **11. Conclusions, Research Innovation, Limitations, New Directions, and Personal Contributions**

The quality of life of patients during and after a breast cancer diagnosis has become an extremely important concern for medical professionals. This is due to the evolution of oncological medical therapies and surgical interventions that have proven their effectiveness over time through highly valuable randomized studies. Additionally, patients undergoing breast cancer diagnosis have the chance of curing the disease. However, their quality of life can be significantly influenced in the short and medium term by oncological treatment and in the long term by the consequences of oncological treatment: early menopause, absence of a breast, body image, sexual life, self-esteem, functional aspects related to shoulder/arm mobility, social stigmatization, anxiety, or depression, etc. All these factors, individually or together, often have an irreversible impact on the lives of breast cancer patients.

This study aimed to analyze how breast cancer treatment can positively or negatively influence the quality of life of breast cancer patients. The comparative study between different types of oncological or surgical therapies shows significant differences for patients. Thus, patients who underwent conservative surgery, innovative oncoplastic surgery techniques, were spared from radical surgery, and those who underwent breast reconstruction had a better quality of life. However, it is also significant that patients who preserved their breasts through one technique or another still have a better quality of life even than patients who underwent mastectomy with reconstruction, with significantly better scores regarding resilience, anxiety, stress, and post-oncological treatment depression. Regarding self-image and quality of sexual life, it has been proven that limited surgery leads to better results in improving the quality of life. Practically, patients who benefited from conservative surgical interventions reported a generally better quality of life, especially regarding the perception of body image and functional aspects (sexual life, pain, or dysfunction of the arm/shoulder on the operated side). The results of this study suggest that breast preservation significantly contributes to better psychological well-being and faster social and physical reintegration into daily activities.

In the current study, we observe that patients who underwent radical mastectomy-type interventions generally report a higher degree of postoperative anxiety and depression, correlated with the diagnosis, the complete loss of the breast, and the significant change in body image. However, some patients in this category report greater psychological calm, especially regarding the perceived risk of breast cancer recurrence, emphasizing once again the importance and complexity of treatment choice and the need for thorough counseling to manage the expectations and fears of each patient.

The current study also highlights the significant impact of oncoplastic surgery on the quality of life of breast cancer patients. For patients who underwent oncoplastic surgery, the benefits observed included both aesthetic outcomes and psychological well-being. These patients reported increased satisfaction with the appearance of their breasts post-surgery, leading to an improved body image, greater self-confidence, and enhanced quality of life, including sexual well-being and social reintegration. This demonstrates that using oncologic surgery principles combined with plastic surgery techniques significantly reduces the negative psychological impact associated with post-operative breast deformation. It proves that integrating oncoplastic surgery into routine practice for breast cancer patients offers not only the standard oncological safety benefits according to breast cancer protocols but also significantly improved aesthetic results compared to conventional surgical techniques. Oncoplastic techniques allow for the customization of surgical treatment according to each patient's aesthetic and psychological needs, further emphasizing the role of a specialized multidisciplinary team in breast cancer

treatment. Integrating oncoplastic surgery into regular practice is thus essential to ensuring optimal outcomes, both in terms of oncological treatment and improving quality of life after a breast cancer diagnosis.

This thesis further underscores the importance of considering the long-term impact on the quality of life of breast cancer patients when choosing between conservative and radical surgery. The multidisciplinary approach here involves not just oncologists, surgical oncologists, radiologists, pathologists, or geneticists, but also highlights the importance of specialized counselors and psychologists who can assess and treat oncological patients, ensuring not only the best chances for breast cancer diagnosis but also the best quality of life post-treatment for these patients.

Additionally, conducting a study on the impact of genetic testing in breast cancer patients demonstrates another pivotal aspect in the personalization of treatment and the management of familial risk. Identifying genetic mutations in breast cancer susceptibility genes allows for an important assessment of the risk of recurrence or the development of other cancers, contributing significantly to the adoption of both therapeutic and preventive strategies that are as well-adapted as possible. These patients benefit from proactively and therapeutically well-tailored surgical options, such as contralateral prophylactic mastectomy or bilateral adnexectomy. Moreover, more frequent monitoring than the standard can significantly reduce patient anxiety related to the risk of recurrence or the development of new cancers, clearly improving long-term quality of life.

These patients also benefit from appropriate genetic counseling and psychosocial support tailored to them and their families, which generally aids in decision-making regarding prophylactic surgery or preventive strategies for both themselves and their family members. This integrated approach increases awareness and education among families predisposed to breast cancer, leading to the adoption of effective prevention strategies accompanied by adapted and effective emotional support. In practice, genetic testing not only improves clinical outcomes but supports a comprehensive, personalized care model for each patient, which is essential in addressing the complexities of breast cancer diagnosis.

Case studies on rare pathologies, such as malignant Phyllodes tumor during pregnancy, BIA-ALCL, and Rosai-Dorfman disease, emphasize the importance of early diagnosis and a personalized approach. These pathologies, due to their rarity, present significant challenges for clinicians, including diagnostic difficulties and a lack of clear treatment guidelines. Accurate and prompt identification of these conditions is essential to provide patients with the best chances of recovery and to minimize long-term complications.

In the case of malignant Phyllodes tumor during pregnancy, the approach must balance the need for the mother's oncological treatment with the protection of the fetus. Personalized therapeutic decisions, which consider the gestational age and tumor aggressiveness, are crucial for optimizing maternal and fetal outcomes. For BIA-ALCL, a rare condition associated with breast implants, personalized treatment typically involves complete surgical excision of the implant capsule, often combined with adjuvant therapies such as chemotherapy or radiotherapy, depending on the stage of the disease. A personalized approach, based on a comprehensive evaluation of each case, is crucial to ensuring that patients receive the most appropriate and effective care, minimizing the risk of recurrence and maximizing quality of life. These case studies highlight the ongoing need for research and

interdisciplinary and multidisciplinary collaboration to develop clearer and more effective guidelines for managing rare pathologies.

The present study shows that there are still many aspects concerning the diagnosis and holistic treatment of breast cancer. Numerous factors can be adjusted to improve the quality of life of breast cancer patients. It is essential to emphasize that, in addition to the medical aspects of breast cancer treatment, there are also extremely important psychological factors that must be considered, as they have a significant impact on breast cancer patients.

There are several future directions aimed at improving the quality of life for breast cancer patients, and future research could provide valuable insights in these areas.

- I believe that educating the population can increase awareness of the rising incidence of breast cancer, especially in countries like Romania, where breast cancer screening policies have not yet been properly implemented. Patients need to understand that early detection of breast cancer improves their chances of recovery, overall quality of life, and helps them reintegrate more quickly into their social and professional lives.
- Treatment decisions should be well-balanced and accompanied by thorough patient counseling, considering that the type of surgical intervention can leave a significant mark on the quality of life of breast cancer patients, not just in the short and medium term, but also in the long term (given that breast cancer currently generally has a good prognosis, with multiple successful treatment options available). Patients should be carefully counseled and educated so that they understand they are active participants in the therapeutic decision-making process, allowing therapies to be adapted to their needs.
- Although there are international guidelines for the diagnosis and treatment of breast cancer, in countries like Romania, there is a lack of screening programs and standardized national guidelines. Such standardization would lead to greater coherence in making therapeutic decisions as personalized and adapted as possible to the diagnostic type of each patient. Clinical outcomes and quality of life are significantly better when therapeutic management is personalized and adapted to the needs of each patient.

I emphasize, first and foremost, that the social aspect is extremely important when conducting studies among patients diagnosed with cancer. In Romania, there is a significant issue of stigmatization and shame felt by patients diagnosed with breast cancer. Additionally, these patients, who undergo such a diagnosis, experience multiple bodily changes, have difficulty talking about these changes, the impact on their sexual life, or other challenges associated with this diagnosis. All these factors only serve to accentuate stigmatization and social isolation, making it more difficult to accept such a diagnosis and its consequences.

Another major challenge for patients in Romania is the lack of education regarding preventive medicine and recommended types of screening. Since there is no national screening program, patients are unaware of the need to undergo specific imaging investigations, and the lack of information and low interest in population education leads to late-stage diagnoses that often require more aggressive treatments, more radical surgery, and result in a significantly affected quality of life in both the short and long term. A patient diagnosed at an early stage could benefit from conservative surgery, possibly even

oncoplastic surgery; moreover, they could potentially avoid chemotherapy if the diagnosis is made early in an initial stage. On the other hand, there is a tendency to make extreme decisions when faced with such a diagnosis. The psychosocial impact can be so significant that patients opt for radical therapeutic decisions, preferring radical interventions out of a desire for cure and fear of possible recurrence. However, most patients are unaware of the long-term implications of such a decision, and for those who are eventually considered cured of breast cancer, regret over the radical decision often arises, given the statistical similarity between mastectomy and conservative surgery accompanied by adjuvant radiotherapy in terms of survival and recurrence risk.

The existence of a national guideline, alongside heterogeneity and laxity in therapeutic decisions, and the absence of multidisciplinary teams in many medical units treating breast cancer patients, leads to a lack of unity in therapeutic decisions, which is primarily a disadvantage for patients. It remains important to emphasize that individualizing treatment is the key and the future in optimizing clinical outcomes and improving the quality of life for breast cancer patients.

The limitations of this study include, first and foremost, the sample size, especially when compared to the samples in the existing literature. Moreover, the Romanian sample cannot be directly compared to that of the UK, given the different study designs, one being retrospective and the other prospective. Additionally, the study conducted on Romanian patients was over a short period of time, compared to the UK study; the data collected may be incomplete or inconsistent, as it is based on patient responses rather than the evaluation of their medical records. Furthermore, our study sample is relatively heterogeneous, considering that it was addressed to all breast cancer patients who had access to the online questionnaire, leading to the inclusion of patients from different oncological centers. Additionally, there is no concrete medical data, as the questionnaire is based on patients' reports (which is why such data was not requested).

The strengths to mention include, first and foremost, the fact that standardized international questionnaires were used in all studies evaluating quality of life. This allows for correlation and interpretation within a broader context and comparison with other groups of patients treated at other oncology centers for breast cancer. Furthermore, this study provides important information on the impact of a cancer diagnosis on emotional well-being and the socio-emotional impact on breast cancer patients in Romania.

The study's results can be leveraged in two ways: first, to help specialists in the field recognize the importance of personalized treatment and integrating patients into therapeutic decision-making; and second, to contribute to the development of screening programs and support for emotional disorders that exist or are associated with a cancer diagnosis, particularly in breast cancer patients. The integration of specialists, such as psychotherapists or psychiatrists, could offer a significant advantage in the holistic care of breast cancer patients, with the ultimate goal not only to treat the disease itself but also to improve the quality of life for breast cancer patients during treatment and in the long term after diagnosis.

This study is also useful in guiding the formation of support groups for breast cancer patients, the development of group therapies, or even the creation of emotional support strategies for professionals dedicated to breast cancer patients. This could translate into not only an improvement in the quality of life for breast cancer patients but also a significant social impact by facilitating the reintegration of these patients into society after diagnosis and minimizing their stigmatization.

The results of this study demonstrate that surgical intervention for breast cancer has a significant impact on the quality of life of patients diagnosed with breast cancer. Pain and chronic fatigue are also significant factors in evaluating the quality of life for these patients, as they are among the most frequently mentioned symptoms that have a negative impact. The assessment of these patients' quality of life has shown that social support and increased resilience have positive effects on breast cancer patients' perceptions and quality of life. Patients who have adequate social and familial support and higher resilience also enjoy a better quality of life.

The type of surgical intervention has a particularly significant long-term impact, as studies show that a conservative intervention has a lesser impact on body image, self-esteem, and sexual life. The development of oncoplastic surgical techniques has increased the number of patients who can benefit from conservative surgical interventions, providing the possibility of better quality of life both in the short and long term. Integrating patients into therapeutic decision-making, involving a multidisciplinary team, and incorporating psychotherapy specialists could lead to greatly improved clinical and psychosocial outcomes for breast cancer patients.

Rare cases in breast pathology also have a significant impact on patients and professionals in the field, representing not only a clinical-surgical challenge but also, given the lack of clear guidelines for these extremely rare pathologies, the multidisciplinary team becomes an essential pivot in subsequent therapeutic decisions for optimal patient outcomes. Pregnancy-associated breast cancer is becoming more frequently diagnosed due to the fact that many patients choose to conceive at an older age than a few decades ago. Although there are guidelines for breast cancer detected during pregnancy, the challenge for clinicians and surgeons is the timing of the diagnosis relative to the gestational age and the fact that there are often two patients requiring special care in the oncological context: the expectant mother and the fetus.

On the other hand, the widespread use of plastic surgery techniques for breast augmentation has also led to an increased long-term risk of developing very rare diseases, such as anaplastic large cell lymphoma associated with breast implants. This pathology remains important not only for the impact on patients who receive this diagnosis but also as an ethical issue in the future use of textured implants.

All of this leads to the development of better screening techniques, the active integration of patients into therapeutic decisions, and the inclusion of psychology specialists to offer real support to women undergoing a breast cancer diagnosis.

### **Future Directions**

- Personalized treatment and strategies to actively improve the quality of life for patients undergoing surgical interventions/aggressive oncological treatments
- Reducing the rate of radical surgical interventions through early detection of breast cancer
- Reducing the side effects of oncological treatment, both in terms of physical symptoms and by providing adequate emotional support
- Increasing public awareness of screening and the importance of this condition, which is common among the female population in general
- Identifying real strategies to increase resilience among patients diagnosed with breast cancer

- Identifying protective/risk factors regarding psycho-emotional disorders such as stress, anxiety, and depression among women with breast cancer
- Assessing the impact of a breast cancer diagnosis and effectively treating psycho-emotional disorders to offer breast cancer patients emotional well-being
- Identifying effective strategies to reduce psycho-emotional disorders and improve the quality of life for breast cancer patients by integrating specialists who can provide their expertise and the necessary support to patients
- Integrating and specializing oncological surgeons in oncoplastic surgery to offer patients the best and safest therapeutic options, both oncologically and aesthetically, which can significantly improve the quality of life and their perception of surgical intervention in general.

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