ANALYSIS OF THE RESULTS OF DIAGNOSIS AND TREATMENT OF BREAST CANCER IN YOUNG WOMEN

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ABSTRACT

This article presents a comprehensive analysis of the results from a detailed study focused on breast cancer (BC) in young women, a demographic with distinct clinical and biological challenges. The research entailed an in-depth examination of the clinical presentation, morphological characteristics, and biological profiles of tumors in this patient group. A key objective was to evaluate the efficacy of various contemporary treatment regimens employed in their management. Through rigorous statistical analysis, the study successfully identified critical factors that significantly impact both overall survival (OS) and recurrence-free survival (RFS). Building upon these findings, the article proposes refined and optimal treatment strategies that meticulously integrate the specific biological subtype of the tumor, such as hormone receptor status, HER2/neu amplification, and triple-negative phenotype, with the unique considerations

of the patient's age, including fertility preservation and long-term quality of life. The conclusions underscore the necessity of a personalized, multidisciplinary approach to improve prognostic outcomes and address the comprehensive needs of young women diagnosed with breast cancer.

Introduction

Breast cancer (BC) maintains its position as the most frequently diagnosed malignancy and the leading cause of cancer-related mortality among women globally, representing a paramount public health challenge of the 21st century [4]. The GLOBOCAN 2020 estimates starkly underscore the magnitude of this issue, with approximately 2.3 million new cases diagnosed and 685,000 deaths annually worldwide, meaning that one in every 8-10 women will develop BC during her lifetime [4]. This high incidence, however, is not uniform across all regions, with significant disparities observed between developed and developing nations. While mortality rates have been steadily declining in high-income countries due to advances in early detection through organized screening programs and access to modern, multidisciplinary therapeutics, the burden remains disproportionately high in low- and middle-income countries. In these regions, barriers such as limited access to screening, delayed diagnosis, and fragmented availability of effective treatments contribute to a higher proportion of women presenting with advanced, less curable disease.

In the specific context of Uzbekistan, as in many post-Soviet and Central Asian countries, the problem is particularly acute and multifaceted. Breast cancer consistently ranks as the foremost oncological disease among women, accounting for a significant portion of both cancer incidence and mortality [4, 9]. This high prevalence is compounded by unique challenges within the national healthcare system, including a higher frequency of later-stage diagnosis compared to Western nations, which profoundly impacts prognosis and survival outcomes. The socioeconomic impact of the disease on young, often economically active women who are integral to family structures and national productivity adds another layer of complexity. Therefore, developing, implementing, and optimizing evidence-based yet contextually adapted national diagnostic and treatment protocols tailored to the local population's genetic, cultural, and infrastructural needs is of paramount importance for improving cancer care outcomes [7, 10].

A particularly concerning and well-documented trend observed over the last two to three decades is the steady increase in the incidence of breast cancer among premenopausal women under the age of 40-45 [9]. This epidemiological shift is hypothesised to be multifactorial, driven by a complex interplay of evolving reproductive patterns (such as later age at first childbirth, fewer pregnancies, and reduced duration of breastfeeding), widespread exposure to environmental carcinogens, and lifestyle factors including dietary changes towards Westernized diets and increased physical inactivity. Furthermore, improved clinical awareness and diagnostic capabilities may also contribute to this rising incidence. A notable and critical aspect is the role of genetic predisposition; a higher prevalence of pathogenic germline variants in high-penetrance genes like BRCA1 and BRCA2 is consistently found in young-onset BC patients, which not only contributes to the aggressive nature of the disease in this demographic

but also has profound implications for genetic counseling and cascade testing within families [10].

The biological landscape of breast tumors in young women is distinctly more aggressive compared to those in their older counterparts, which directly influences therapeutic choices and prognosis. Young patients, particularly those under 40, present with a significantly higher frequency of biologically unfavorable and therapeutically challenging tumor phenotypes. Extensive research, including studies by Loibl et al. and guidelines from the ESMO-ESO International Consensus, indicates that tumors in this age group are more likely to be of the triple-negative (estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative) basal-like subtype or to exhibit HER2/neu gene amplification and protein overexpression [9, 10]. These subtypes are intrinsically associated with higher histological grade, increased proliferative activity as measured by markers like Ki-67 (>30%), and a greater propensity for visceral metastasis and early recurrence. Consequently, even when diagnosed at comparable stages, young women often face a worse prognosis, with lower rates of overall and disease-free survival, highlighting the critical and unmet need for more effective, age-specific therapeutic strategies and more robust prognostic biomarkers [8, 9].

For the substantial proportion (approximately 50-60%) of young women with hormone receptor-positive (HR+) disease, which remains the most common subtype even in this age group, endocrine therapy (ET) is the cornerstone of adjuvant treatment to mitigate the risk of recurrence. The landmark meta-analyses by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) firmly established that 5 years of tamoxifen therapy reduces the annual breast cancer recurrence rate by nearly half and mortality by 31% over a 15-year follow-up [1]. However, the management of premenopausal women with HR+ BC is a rapidly evolving and nuanced field. The optimal duration and intensity of endocrine manipulation—specifically, the addition of ovarian function suppression (OFS) to either tamoxifen or an aromatase inhibitor—remain areas of active research and intense clinical debate, as the benefits must be carefully weighed against the significant toxicity profile [2, 5, 6]. The seminal SOFT and TEXT trials demonstrated that for women at sufficient risk of recurrence (e.g., those with high-grade tumors, extensive nodal involvement, or high Ki-67), the combination of OFS with exemestane provides superior disease control compared to tamoxifen alone or OFS plus tamoxifen, though invariably at the cost of increased menopausal symptoms and a detrimental impact on quality of life [2, 5, 6]. The recent long-term follow-up of these trials has further refined our understanding of which patients derive the greatest absolute benefit from these more intensive strategies [5].

Beyond the paramount goals of survival and disease control, the comprehensive management of breast cancer in young women demands a unique and dedicated focus on long-term quality-of-life issues, with fertility preservation and sexual health being paramount concerns. A vast number of young patients have not yet initiated or completed their families at the time of diagnosis, and gonadotoxic cytotoxic chemotherapy and prolonged endocrine therapy can induce iatrogenic premature ovarian insufficiency and irreversible infertility, leading to significant psychological distress [3, 10]. This profound desire to preserve fertility significantly influences treatment decisions and necessitates a proactive, multidisciplinary approach involving medical oncologists, reproductive endocrinologists, fertility specialists, and psychologists early in the treatment planning process. Recent pioneering studies, such as the

positive trial, have begun to provide much-needed prospective data on the safety of temporarily interrupting adjuvant endocrine therapy to attempt pregnancy, offering hope and tangible options for young survivors without compromising their oncological outcomes [3]. Furthermore, the extensive psychosocial sequelae, including concerns about body image after surgery, sexual dysfunction, genetic risk to offspring, and economic stability, are more pronounced and poorly addressed in this population, necessitating integrated supportive care services and rehabilitation programs throughout the cancer care continuum from diagnosis to long-term survivorship [10]. International guidelines, such as the ESMO Clinical Practice Guidelines and the BCY4 Consensus, now strongly recommend that fertility and family planning discussions are a standard and mandatory part of the initial treatment consultation for every young patient [7, 10].

The aim of the study was to improve the results of diagnosis and treatment of BC in young women by analyzing the clinical, morphological, and biological characteristics of tumors, as well as by developing optimal treatment algorithms.

Materials and methods.

The study included 80 patients diagnosed with BC aged 18 to 45 years who underwent treatment at the Tashkent City Faculty of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology (TGΦ RSNPMCOandR) from 2017 to 2023. The average age was 35±6.2 years. Diagnosis included mammography, ultrasound, MRI, PET, and morphological verification of the tumor. Staging was performed according to the TNM system.

Distribution of patients by disease stage: stage 0 (TisN0M0) – 6 patients (7.5%), stage I (T1N0M0) – 16 patients (20%), stage II (T2N0M0/T1N1M0) – 30 patients (37.5%), stage III (T3N1M0/T2N2M0/T4N2M0) – 18 patients (22.5%), stage IV (M1) – 10 patients (12.5%).

Histological Type	Number of Patients (n)	Proportion (%)
Invasive ductal carcinoma	56	70%
Invasive lobular carcinoma	8	10%
Tubular carcinoma	4	5%
Mucinous (colloid) carcinoma	3	4%
Medullary carcinoma	2	3%
Papillary / Micropapillary / Metaplastic carcinoma	2	3%
Paget's disease of the nipple	1	2%
Inflammatory breast cancer	2	3%

Table 1. Distribution by Histological Types

Table 1 shows the distribution of the 80 enrolled breast cancer patients according to the histological types of their tumors. Invasive ductal carcinoma was the most prevalent type, accounting for 70% of cases (n=56), followed by invasive lobular carcinoma (10%, n=8). Other histological subtypes, including tubular, mucinous, medullary, papillary/micropapillary/metaplastic carcinomas, Paget's disease of the nipple, and inflammatory breast cancer, were less frequently observed, collectively comprising the remaining 20% of cases.

Also patients were classified according to immunohistochemical (IHC) subtypes, and the proportion of patients receiving appropriate treatment for each subtype was calculated. Distribution outlines the distribution of patients based on immunohistochemical (IHC) subtypes, which are critical for determining therapeutic strategies. The Luminal A subtype was the most common (40%, n=32), followed by Triple-negative (20%, n=16), Luminal B (25%, n=20), and HER2-positive (15%, n=12) subtypes. The table also details the primary treatment approach for each subtype and shows a high rate of treatment adherence, with coverage ranging from 88% for the triple-negative subtype to 100% for the Luminal A subtype (table 2).

Table 2. Distribution by Immunohistochemical Subtypes

IHC Subtype	Number of Patients (n)	Proportion (%)	Main Treatment	Received Treatment (%)
Luminal A (ER+, PR+, HER2–, Ki-67 < 20%)	32	40%	Endocrine therapy ± radiotherapy	100%
Luminal B (ER+, HER2+/–, Ki-67 ≥ 20%)	20	25%	Endocrine therapy + chemotherapy; if HER2+ → anti-HER2 therapy	95%
HER2-positive (ER–, PR–, HER2+)	12	15%	Anti-HER2 therapy + chemotherapy	90%
Triple-negative (ER–, PR–, HER2–)	16	20%	Chemotherapy (anthracyclines, taxanes)	88%

Note: Luminal A subtype represents the most favorable prognosis group and all patients received endocrine therapy. Luminal B subtype required combined systemic treatment, with HER2-positive cases additionally receiving targeted therapy. HER2-positive and triple-negative cancers were treated with chemotherapy-based regimens, with high treatment coverage rates.

Results

Data analysis showed that early stages (0–I) were more common in younger women, while stages III–IV predominated in patients over 35 years old. Overall survival and recurrence-free survival directly depended on the disease stage and the hormonal status of the tumor. Thus, the 5-year survival rate for stages 0–I was over 90%, while for stage IV it was less than 40%.

A comparative analysis of the effectiveness of various treatment methods was additionally conducted. It was found that the use of combined regimens, including chemotherapy, hormone therapy, and targeted drugs, provided higher overall survival rates. For example, in patients with HER2-positive tumors, adding trastuzumab to standard chemotherapy increased the 5-year survival rate from 55% to 78%. In patients with a triple-negative phenotype, the best results were achieved with neoadjuvant chemotherapy followed by surgery and adjuvant radiation.

It was revealed that the frequency of local recurrences directly depended on the type of surgical intervention. Radical mastectomy provided the lowest risk of local recurrence (12%), while this figure was 24% for organ-preserving operations. However, organ-preserving interventions positively impacted the quality of life, especially when using reconstructive surgery. Separate attention was paid to the analysis of factors affecting prognosis. Age, menstrual status, family history of BC, expression of hormone receptors, and Ki-67 were independent prognostic indicators. A high level of Ki-67 (>30%) was associated with worse recurrence-free survival, regardless of the stage and treatment conducted.

The role of ovarian suppression in patients under 40 was additionally investigated. The combination of tamoxifen with LHRH analogs reduced the risk of recurrence by 34% compared to tamoxifen monotherapy. In the subgroup of patients with preserved fertility, an analysis of the treatment's impact on menstrual function and the possibility of pregnancy was conducted. It was found that when using regimens with ovarian suppression, up to 60% of women retained the ability to conceive 2–3 years after completing therapy. Quality of life was assessed using the EORTC QLQ-C30 and FACT-B scales. Patients who received comprehensive treatment involving a psychologist and a physical rehabilitation program demonstrated higher rates of emotional and physical well-being (table 3).

Table 3. Association between clinicopathological characteristics, treatment modalities, and clinical outcomes.

Parameter / Factor	Findings / Outcome Measure	Notes / Subgroups
Stage at Diagnosis	Early stages (0-I) more common in younger women (<35 yrs); Stages III-IV predominated in patients >35 yrs.	—
5-Year Overall Survival (OS)	Stage 0-I: >90%	Directly dependent on disease stage and hormonal status.
	Stage IV: <40%	
Treatment Efficacy (HER2+)	5-year OS with Chemotherapy (CT) alone: 55%	Demonstrates the significant impact of targeted therapy.
	5-year OS with CT + Trastuzumab: 78%	

Surgical Outcome (Local Recurrence)	Radical Mastectomy: 12%	Organ-preserving surgery associated with better quality of life, especially with reconstruction.
	Organ-Preserving Surgery: 24%	
Endocrine Therapy (HR+ <40 yrs)	Recurrence Risk Reduction: Tamoxifen + LHRH analogs vs. Tamoxifen monotherapy: 34% risk reduction	Beneficial for higher-risk premenopausal patients.

Discussion

The findings of our study are in strong agreement with the body of international research, which consistently underscores the more aggressive clinical behavior and distinct biological profile of breast cancer diagnosed in young women. The data obtained, demonstrating a higher prevalence of advanced stages in patients over 35 and a direct correlation between tumor stage/hormonal status and survival outcomes, reaffirm the challenging nature of this disease in a younger demographic. The predominance of biologically aggressive subtypes, specifically the triple-negative phenotype and HER2-positive tumors, which our analysis confirmed, provides a clear pathophysiological explanation for the observed worse prognosis and lower survival rates in this patient cohort compared to older women. These subtypes are intrinsically linked to higher proliferative activity, as evidenced by high Ki-67 levels in our cohort, and a greater propensity for early recurrence and distant metastasis.

The comparative analysis of treatment efficacy conducted in our study yields critical insights for optimizing therapeutic strategies. The superior outcomes achieved with combined modality regimens—integrating chemotherapy, hormone therapy, and targeted agents—validate the necessity of a multifaceted approach. The significant improvement in 5-year survival from 55% to 78% with the addition of trastuzumab in HER2-positive disease mirrors the transformative impact of targeted therapy seen in global trials. Similarly, the observed benefit of neoadjuvant chemotherapy followed by surgery and radiotherapy in triple-negative breast cancer aligns with international guidelines aimed at maximizing pathological response and improving long-term disease control. Our investigation into surgical outcomes, which found a lower risk of local recurrence after radical mastectomy but a better quality of life with organ-preserving techniques, highlights the ongoing need to balance oncological radicality with the preservation of body image and psychosocial well-being, particularly in this age group.

A pivotal aspect of our discussion revolves around the management of hormone receptor-positive disease, which constitutes a substantial proportion of cases even in young women. The 34% reduction in recurrence risk observed with the combination of tamoxifen and LHRH agonists (ovarian function suppression) compared to tamoxifen alone is a finding of considerable clinical importance. This result strongly supports the evidence from landmark trials, indicating that for premenopausal women at higher risk of recurrence, escalating endocrine therapy by adding ovarian suppression provides superior disease control. However, this benefit must be carefully contextualized within the patient's individual risk profile and personal priorities, given the associated side effects that can impact quality of life and adherence.

Furthermore, our study places significant emphasis on the paramount importance of addressing fertility and long-term quality of life, which are integral components of comprehensive care for young women with breast cancer. The analysis revealing that up to 60% of women retained the potential for conception 2-3 years after completing ovarian-suppressive therapy is an encouraging finding that can inform patient counseling. It reinforces the emerging data from studies like the positive trial, which provides reassurance regarding the relative safety of temporary treatment interruption for pregnancy attempts in selected patients. The higher scores on quality-of-life scales among patients who received integrated support from psychologists and rehabilitation specialists underscore the indispensable role of supportive care services. This holistic approach is crucial for mitigating the profound psychosocial sequelae of the disease and its treatment, including concerns about body image, sexual health, and genetic risk to offspring.

In conclusion, the data from our study collectively advocates for a highly personalized and multidisciplinary management strategy. This strategy must seamlessly integrate robust, biology-driven adjuvant therapies with proactive, patient-centered discussions about fertility preservation, family planning, and long-term survivorship issues. The results substantiate the need to adapt and implement modern, evidence-based clinical protocols that are tailored to the specific epidemiological and sociocultural context of regions like Uzbekistan, with the ultimate goal of improving both survival and the overall quality of life for young women facing a breast cancer diagnosis.

Conclusion

Breast cancer in young women is characterized by an aggressive course and requires a comprehensive approach to diagnosis and treatment. Optimizing treatment regimens considering the biological characteristics of the tumor and the age of the patients can increase survival and quality of life. The results of the study can be used to improve clinical protocols, develop screening and rehabilitation programs for young women with BC. Further research is needed to develop personalized treatment algorithms and preserve fertility.

Thus, the obtained data indicates the need for treatment individualization considering the biological characteristics of the tumor, age, and reproductive plans of the patients. The application of a comprehensive approach ensures a significant improvement in outcomes and quality of life.

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