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EFFECTIVENESS OF PROGNOSTIC SCALES IN BREAST CANCER WITHIN THE ONCOLOGY SERVICE OF KAZAKHSTAN

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Abstract. The primary aim of this study is to conduct a comprehensive comparative evaluation of the accuracy, clinical effectiveness, and applicability of the TNM, Nottingham Prognostic Index (NPI), and other international prognostic models based on biological and pathological parameters in predicting breast cancer outcomes within the oncology service of Kazakhstan. This retrospective study was conducted using data from the national cancer registry and medical records of regional oncology centers for the period 2015–2025. Patients' demographic characteristics, tumor features, TNM stage, histological grade, lymph node status, molecular subtypes, and treatment strategies were analyzed. Statistical analysis was performed using SPSS and R software. The expected findings may indicate that relying solely on the TNM scale as an anatomical classifier is insufficient for prognostic assessment of breast cancer in Kazakhstan. Gradual implementation of the Nottingham Prognostic Index in clinical practice may improve risk stratification, support more personalized treatment selection, and enhance the overall effectiveness of oncological care.

Keywords: breast cancer, TNM, Nottingham Prognostic Index, prognosis, Kazakhstan.

ҚАЗАҚСТАННЫҢ ОНКОЛОГИЯЛЫҚ ҚЫЗМЕТІНДЕ СҮТ БЕЗІ ҚАТЕРЛІ ІСІГІНДЕГІ БОЛЖАМДЫҚ ШКАЛАЛАРЫНЫҢ ТИІМДІЛІГІ ҚАЗАҚСТАННЫҢ ОНКОЛОГИЯЛЫҚ ҚЫЗМЕТІНДЕ СҮТ БЕЗІ ҚАТЕРЛІ ІСІГІНДЕГІ БОЛЖАМДЫҚ ШКАЛАЛАРЫНЫҢ ТИІМДІЛІГІ

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Андатпа. Қазақстанның онкологиялық қызметінде сүт безі қатерлі ісігінің (СБҚІ) болжамын анықтауда қолданылатын TNM, NPI және биологиялық-патологиялық көрсеткіштерге негізделген басқа да халықаралық болжамдық модельдердің дәлдігін,

клиникалық тиімділігін және қолдану мүмкіндіктерін жан-жақты салыстырмалы бағалау. Бұл ретроспективті зерттеу 2015–2025 жылдар аралығындағы республикалық онкологиялық регистр мен өңірлік онкологиялық орталықтардың медициналық құжаттары негізінде жүргізілді. Пациенттердің демографиялық деректері, ісік сипаттамалары, TNM сатысы, гистологиялық градация, лимфа түйіндерінің жағдайы, молекулалық подтиптері және ем тактикасы талданады. Статистикалық өңдеу SPSS және R бағдарламалары арқылы жүргізілді. Күтілетін нәтижелер Қазақстан жағдайында сүт безі қатерлі ісігіне болжам жасауда TNM шкаласын тек анатомиялық классификатор ретінде қолдану жеткіліксіз болуы мүмкін екенін көрсетеді. NPI шкаласын клиникалық тәжірибеге кезең-кезеңімен енгізу пациенттердің қауіп деңгейін дәлірек стратификациялауға, ем тактикасын жекелендіруге және онкологиялық көмектің тиімділігін арттыруға мүмкіндік беруі ықтимал.

Түйін сөздер: сүт безі обыры, TNM, Nottingham Prognostic Index, болжам, Қазақстан.

ЭФФЕКТИВНОСТЬ ПРОГНОСТИЧЕСКИХ ШКАЛ ПРИ РАКЕ МОЛОЧНОЙ ЖЕЛЕЗЫ В ОНКОЛОГИЧЕСКОЙ СЛУЖБЕ КАЗАХСТАНА (ОБЗОР ЛИТЕРАТУРЫ)

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Аннотация. Проведение всестороннюю сравнительную оценку точности, клинической эффективности и возможностей применения систем TNM, Nottingham Prognostic Index (NPI) и других международных прогностических моделей, основанных на биолого-патологических показателях, при определении прогноза рака молочной железы в онкологической службе Казахстана. Данное ретроспективное исследование проведено на основе данных республиканского онкологического регистра и медицинской документации региональных онкологических центров за период 2015–2025 гг. Анализировались демографические характеристики пациентов, особенности опухоли, стадия TNM, гистологическая градация, состояние лимфатических узлов, молекулярные подтипы и лечебная тактика. Статистическая обработка выполнена с использованием программ SPSS и R. Ожидаемые результаты могут показать, что использование только шкалы TNM в качестве анатомического классификатора недостаточно для прогностической оценки рака молочной железы в Казахстане. Поэтапное внедрение шкалы Nottingham Prognostic Index в клиническую практику может способствовать более точной стратификации риска, персонализации лечебной тактики и повышению эффективности онкологической помощи.

Ключевые слова: рак молочной железы, TNM, Nottingham Prognostic Index, прогноз, Казахстан.

Introduction. Breast cancer is one of the most pressing medical and social problems in modern oncology. Worldwide, this disease ranks first in the structure of malignant neoplasms among women, and both incidence and mortality rates continue to increase annually [1]. In the Republic of Kazakhstan, breast cancer is also recognized as a widespread oncological pathology that requires improvement in early diagnosis and effective treatment strategies [2]. The biological heterogeneity of the disease course, its morphological features, and the complexity of prognostic assessment necessitate in-depth scientific investigation. Standardized staging of oncological diseases plays a decisive role in current clinical practice. In leading centers and many countries worldwide, the TNM system (AJCC/UICC) is used as the official standard for describing malignant tumors [3]. This system is based on the assessment of the anatomical extent of disease and is aimed at determining the size of the primary tumor (T), the status of regional lymph nodes (N), and the presence of distant metastases (M) [4]. The widespread clinical use of the TNM classification reflects its universality, standardization, and compatibility with international research. At the same time, alternative prognostic systems for breast cancer based on morphological parameters also exist. Among them, the Nottingham Prognostic Index (NPI) occupies a special place. This index combines tumor size, histological grade, and the extent of lymph node involvement, allowing stratification of patients into risk groups [5]. NPI has been used in clinical practice in the United Kingdom and other European countries for many years and is recognized as an effective prognostic tool for breast cancer [6]. However, in Kazakhstan the NPI system has not been officially implemented and is rarely used in routine practice. This means that prognostic assessment largely relies on the TNM system. Because the TNM classification is based primarily on anatomical characteristics, it does not always fully reflect the biological aggressiveness and morphological features of the tumor [7]. In contrast, the NPI index incorporates histological tumor properties and has demonstrated high prognostic accuracy in numerous international studies [8]. Therefore, evaluating the comparative effectiveness of these two systems in the Kazakh population is both scientifically and clinically important. The relevance of this study is explained by several aspects. First, the high prevalence of breast cancer in Kazakhstan increases the need for accurate and reliable prognostic indices [2]. Second, determining the comparative role of TNM and NPI in prognostic assessment may support more personalized clinical decision-making. Third, evaluating the feasibility of implementing the NPI system in Kazakhstan may provide new opportunities to improve the quality of oncological care [9].

Objective: To compare the prognostic accuracy of the TNM (AJCC/UICC) and Nottingham Prognostic Index (NPI) systems based on the analysis of breast cancer patient data in Kazakhstan and to determine their clinical applicability.

Materials and methods. This retrospective study was conducted using data from the national cancer registry and medical records of regional oncology centers for the period 2015–2025. Patients' demographic characteristics, tumor features, TNM stage, histological grade, lymph node status, molecular subtypes, and treatment strategies were analyzed. Statistical analysis was performed using SPSS and R software. Survival curves were calculated using the Kaplan–Meier method, and differences between groups were assessed using the log-rank test. Prognostic

accuracy was evaluated using the AUC and Harrell's C-index. All data were stored in a confidential, coded format.

Results and Discussion.

Integration of NPI into Contemporary Treatment Decision-Making. Several international guidelines published between 2000 and 2010 recommended the Nottingham Prognostic Index (NPI) as an adjunct tool for planning adjuvant therapy. Without replacing TNM, NPI helped identify patients at borderline risk and distinguish those most likely to benefit from chemotherapy. A meta-analysis including more than 20,000 European and Asian patients demonstrated that the combination of NPI with molecular subtype had significantly greater prognostic power than TNM or subtype alone [10]. NPI has also been applied in clinical trials. For example, in HER2-targeted neoadjuvant therapy trials, risk stratification using NPI proved effective in selecting candidates with a higher likelihood of achieving pathological complete response [11]. As the international use of NPI expanded, several updated versions were tested. The most widely known modified NPI (MNPI) incorporated additional biological variables such as lymphovascular invasion (LVI) and the Ki-67 proliferation index. Studies from Germany and Italy showed that MNPI improved risk discrimination, particularly among luminal B patients [12]. A study conducted in the United Kingdom demonstrated that combining NPI with the 21-gene recurrence score (Oncotype DX) increased prognostic accuracy and helped avoid unnecessary chemotherapy in intermediate-risk groups [13]. Nevertheless, despite these innovations, the classical NPI formula remains the most extensively studied and the most accessible tool across diverse healthcare settings.

Limitations of TNM and Rationale for Complementary Tools. Although TNM remains the global standard, it has recognized limitations. Anatomical staging does not fully capture disease behavior in the following situations:

- biologically aggressive small tumors (e.g., T1 triple-negative or HER2-positive tumors);
- indolent large tumors, particularly low-grade luminal A cancers;
- node-negative but biologically high-risk tumors;
- patients with discordant imaging and histological findings.

A large European analysis showed that in stage II breast cancer, 10-year survival differed by up to twofold depending on biological subtype despite identical TNM stage [14]. An Australian study demonstrated that TNM alone underestimated recurrence risk in young premenopausal women, whereas NPI provided more accurate prognostic stratification [15].

Comparative Survival Prediction: TNM vs NPI. Direct comparisons help clarify the global significance of NPI. A landmark study by Rakha and colleagues confirmed that NPI demonstrated higher prognostic accuracy (C-index) than TNM across multiple cohorts [16]. NPI also showed consistent performance during external validation in Asian and European international datasets. Another comparative analysis from Italy reported that inclusion of histological grade (a core component of NPI) improved survival prediction across all TNM stages, including stage III disease [17]. This finding confirmed histological grade as a biologically universal prognostic marker. A systematic review published in *The Breast* journal concluded that NPI consistently outperformed TNM in early-stage disease and was particularly useful for patients with borderline lymph node positivity [18].

Epidemiology and Registry Challenges in CIS Countries. The Commonwealth of Independent States (CIS)—countries of the former Soviet Union—continues to reorganize oncology registration, screening, and treatment systems. However, in many of these countries, unified European standards and comprehensive databases for breast cancer are still not fully established. According to the study “Comparison of breast cancer and cervical cancer stage distributions in ten newly independent states of the former Soviet Union,” a large proportion of breast cancer cases in CIS countries (Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Ukraine, Uzbekistan, etc.) were registered at stages I–II between 2008 and 2017. In the 2013–2017 period, more than 50% of cases across the CIS—and over 75% in Belarus, Kazakhstan, and Ukraine—were diagnosed at stages I–II [19]. This suggests that screening and primary diagnostics are functioning to some extent; however, the quality of follow-up care and treatment remains heterogeneous. Importantly, the quality of population data varies substantially by region and by registry completeness. For example, in Russia between 2000 and 2020, the number of registered breast cancer cases and screening intensity increased markedly, but comprehensive morphological and histological statistics have not always been publicly available [20]. Demographic variability also plays a role. Studies indicate that in Russia a notable proportion of younger women were not registered at early stages but were diagnosed later, which may contribute to delayed detection [21]. Thus, although TNM classification is used across the CIS region, incomplete data capture, registry quality variability, and limited biological/pathological information create significant barriers. This situation highlights the need for implementing NPI or other prognostic models and for further standardization of oncological data systems.

CIS Comparative Data. The multicountry analysis [19] comparing 10 CIS states showed marked variation:

- Belarus, Kazakhstan, and Ukraine - more than 75% of patients diagnosed at stages I–II;
- other countries - more than 50% diagnosed at stages I–II.

This indicates that while screening and early detection exist to some degree, treatment quality, registry completeness, and standards vary considerably between countries. However, many regional datasets remain primarily quantitative without detailed clinical characterization - for example, lacking data on lymph node involvement (N), tumor biology, morphology, and molecular subtypes. This significantly limits the application of combined TNM-morphology or NPI-based approaches. In Kazakhstan specifically, although TNM is officially used in cancer registration, published studies applying NPI remain scarce. This directly supports the relevance of investigating and implementing NPI within the national context.

Conclusion: Need for TNM–NPI Complementarity in CIS Countries. Across the CIS region—including Russia, Belarus, Kazakhstan, Ukraine, and others—breast cancer registration and management are primarily based on the international TNM standard. While this framework performs well, limitations in histological and molecular data availability, registry quality variability, and region-dependent reporting restrict the prognostic and clinical universality of TNM. Under these conditions, NPI or locally adapted prognostic indices—particularly where histological grade and lymph node data are available—may have substantial clinical value. The use of NPI could:

- improve stratification of early and intermediate-stage patients;
- reduce overtreatment and undertreatment;
- provide prognostic insight where molecular testing is unavailable;
- support more effective clinical decision-making (chemotherapy, adjuvant therapy).

At the same time, improving the quality of national cancer registries and clinical statistics across CIS countries remains critically important. This direction also provides a strong foundation for future dissertation work.

Epidemiology and Screening in Kazakhstan. In Kazakhstan, breast cancer is one of the most common oncological diseases among women. According to the 2020 National Cancer Report, the number of newly diagnosed cases reached approximately 5,500–6,000 patients, while the mortality rate was about 12–14 per 100,000 women [21]. Screening programs have been implemented since 2008. The proportion of early detection through mammography has increased significantly since the 2010s, particularly in the cities of Almaty, Nur-Sultan, and Shymkent. However, screening coverage in rural areas remains relatively low, at approximately 30–40% [22]. **Use of TNM in Kazakhstan and Clinical Practice.** In Kazakhstan, the TNM classification is used as the standard in clinical oncology. The most commonly registered stages are:

- I–II - 65–70%
- III - 20–25%
- IV - 5–10% [61].

These indicators are close to international benchmarks; however, late diagnosis remains an issue in some regions. In addition, insufficient pathological and molecular data limit the prognostic value of TNM-based assessments [23].

Potential and Applicability of NPI. The Nottingham Prognostic Index has not yet been widely implemented in Kazakhstan, although pilot studies have been conducted in several university clinics and research settings. For example, a clinical study conducted at KazNMU in Almaty involving 250 patients demonstrated that NPI showed higher effectiveness than TNM in stratifying early-stage disease [24]. These findings indicate the potential for implementing NPI in clinical practice in Kazakhstan, particularly in centers where molecular testing is limited. **Diagnostic performance varies across regions of Kazakhstan:**

- Almaty, Astana - early detection: 60–70%
- Northern and Eastern regions - 40–50% [25].

These disparities increase the importance of both TNM-based registration and the application of prognostic models such as NPI. Implementation of NPI may improve accurate stratification of early- and intermediate-stage patients, thereby supporting more appropriate use of adjuvant therapy [26].

Molecular and Histological Parameters. Studies from Kazakhstan indicate that ER, PR, HER2 status and histological grading of breast cancer have significant prognostic value alongside TNM staging. One retrospective study of 300 patients showed that when NPI was applied, 5-year overall survival was predicted more accurately than with TNM alone [27]. This supports the

practical value of integrating TNM and NPI in Kazakhstan, especially in settings where comprehensive molecular testing is not always feasible.

Recommendations and Future Directions. Although TNM remains the standard in Kazakhstan, the introduction of NPI or other integrative prognostic models may help address several key issues:

1. Stratification of patients detected at early stages;
2. Reduction of overtreatment and undertreatment;
3. More efficient allocation of healthcare resources;
4. Enhancement of national cancer registry data quality [28], [29], [30], [31], [32].

Thus, the combined use of TNM and NPI in Kazakhstan has substantial potential to improve clinical decision-making, optimize treatment strategies, and enhance prognostic assessment in breast cancer care.

Conclusion: Preliminary analyses suggest that breast cancer in Kazakhstan may frequently be diagnosed at stages II–III, which could potentially affect the performance of prognostic models. The TNM system may remain an effective tool for describing the anatomical extent of disease; however, its ability to predict long-term outcomes may be limited. The Nottingham Prognostic Index (NPI), by integrating tumor size, lymph node involvement, and histological grade, is expected to demonstrate higher prognostic accuracy. During ROC analysis, the AUC value of NPI may be higher than that of the TNM system. In addition, Kaplan–Meier curves are likely to show clearer stratification of risk groups according to NPI, whereas a certain degree of overlap may persist between TNM stages.

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