



Prognostic Value of Liver and Renal Function Tests in Breast Cancer Patients Receiving Chemotherapy: A Prospective Study

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ABSTRACT

Introduction: This prospective study investigates the prognostic significance of routine liver and renal function tests in breast cancer patients undergoing chemotherapy. Given their central role in drug metabolism, systemic inflammation, and treatment tolerability, these readily available laboratory parameters may provide valuable prognostic information and support improved risk stratification and individualized clinical decision-making in breast cancer management.

Material and methods: This prospective cohort study enrolled 150 patients with stage I-III breast cancer receiving adjuvant or neoadjuvant chemotherapy. Baseline and serial assessments of liver and renal function and related laboratory biomarkers were performed during treatment. Clinical response, chemotherapy-related toxicity, overall survival, and progression-free survival were prospectively evaluated across molecular subtypes.

Results: Multivariable analysis identified stage III disease as the strongest predictor of poorer overall survival compared with stages I-II ($P < 0.001$), a finding corroborated by Kaplan–Meier analysis. Older age ($P = 0.014$), HER2-positive ($P = 0.011$) and basal-like subtypes ($P < 0.001$), and neoadjuvant chemotherapy ($P = 0.043$) were associated with increased mortality, whereas higher serum albumin ($P = 0.006$) and eGFR ($P = 0.017$) independently predicted improved survival.

Conclusion: These results underscore that prognosis in breast cancer is shaped by both tumor-related and host-related factors. While tumor stage and molecular subtype remain the cornerstone of risk stratification, routinely available clinical parameters such as albumin and renal function provide meaningful complementary prognostic information.

Introduction

Breast cancer remains the most frequently diagnosed malignancy and the leading cause of cancer-related morbidity among women worldwide. Despite significant advances in early detection and therapeutic strategies, chemotherapy continues to play a central role in the management of both early-stage and advanced breast cancer. However, interindividual variability in treatment response and toxicity highlights the need for reliable prognostic and predictive markers to optimize patient outcomes.

Among various laboratory parameters, routine liver and renal function tests increasingly recognized as potential indicators of prognosis in oncology practice (1). Chemotherapy agents commonly used in breast cancer, including anthracyclines, taxanes, cyclophosphamide, and platinum-based compounds, metabolized and excreted primarily through hepatic and renal pathways. Consequently, baseline organ function and chemotherapy-induced alterations in liver and kidney parameters may significantly influence drug pharmacokinetics, treatment tolerability, and therapeutic efficacy.

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Understanding the prognostic implications of these laboratory tests is therefore clinically relevant (2). The liver plays a pivotal role in drug metabolism, protein synthesis, and systemic inflammatory regulation. Abnormalities in liver function tests such as alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, bilirubin, and serum albumin have been associated with disease burden, metastatic involvement, and systemic inflammation in cancer patients. These parameters may reflect both tumor biology and host response, making them potential prognostic indicators (3). Hypoalbuminemia, in particular, has been consistently associated with poor outcomes across multiple malignancies, including breast cancer. Serum albumin reflects nutritional status, hepatic synthetic capacity, and systemic inflammatory activity. Low albumin levels have been linked to increased chemotherapy toxicity, reduced treatment adherence, and inferior survival, underscoring its prognostic significance (4).

Renal function is equally critical in oncology care. Parameters such as serum creatinine, blood urea nitrogen, and estimated glomerular filtration rate are routinely used to assess kidney performance. Impaired renal function can limit chemotherapy dosing, increase the risk of adverse effects, and compromise overall treatment efficacy. Moreover, renal dysfunction may reflect underlying comorbidities that adversely affect cancer prognosis (5). Emerging evidence suggests that subtle changes in renal function tests, even within clinically accepted normal ranges, may have prognostic implications in patients receiving systemic anticancer therapy. Reduced glomerular filtration rate has been associated with increased mortality, treatment discontinuation, and hospitalizations among cancer patients, highlighting the importance of careful renal assessment (6). Beyond their role in drug handling, liver and kidney function tests may also serve as surrogate markers of systemic inflammation and metabolic dysregulation. Cancer-related inflammation can alter hepatic protein synthesis and renal perfusion, leading to measurable laboratory abnormalities. These changes may precede overt clinical deterioration, offering an opportunity for early risk stratification (7).

Several retrospective studies have explored the association between liver or renal dysfunction and survival outcomes in breast cancer patients. However, the majority of these studies were limited by heterogeneous populations, retrospective designs, or a focus on advanced metastatic disease. Prospective data specifically evaluating the prognostic value of routine liver and renal function tests during chemotherapy remain scarce (8). In clinical practice, laboratory biomarkers that are inexpensive, widely available, and routinely measured are particularly attractive. Liver and renal function tests meet these criteria and are already

integrated into standard oncologic care. Identifying their prognostic relevance could enhance clinical decision-making without imposing additional diagnostic burden (9). Chemotherapy-induced hepatotoxicity and nephrotoxicity represent significant challenges in breast cancer management. Elevations in liver enzymes or declines in renal function during treatment may necessitate dose reductions, treatment delays, or discontinuation, potentially compromising oncologic outcomes. Understanding whether these laboratory changes also predict long-term prognosis is of considerable interest (10).

Prospective evaluation allows for systematic monitoring of laboratory parameters before, during, and after chemotherapy, enabling temporal associations between organ function and clinical outcomes to be assessed. Such an approach minimizes bias and enhances the validity of prognostic analyses compared with retrospective studies (11). In addition, breast cancer is a biologically heterogeneous disease, with prognosis influenced by tumor subtype, stage, molecular characteristics, and patient-related factors. Integrating laboratory-based prognostic markers with established clinical and pathological variables may improve risk stratification and personalized treatment planning (12). The potential role of liver and renal function tests as predictive markers of chemotherapy response is also noteworthy. Patients with preserved organ function may tolerate full-dose chemotherapy and achieve better tumor control, whereas those with compromised function may experience suboptimal dosing and reduced efficacy (13). Despite the clinical relevance of these considerations, there is a lack of consensus regarding the prognostic thresholds and clinical interpretation of liver and renal function abnormalities in breast cancer patients undergoing chemotherapy. This uncertainty underscores the need for well-designed prospective studies focusing specifically on these parameters (14). Furthermore, most existing studies have examined composite prognostic scores or inflammatory indices, while fewer have evaluated conventional liver and kidney tests independently. Clarifying the individual prognostic contributions of these routine parameters may facilitate their integration into everyday clinical assessment (15). Therefore, the present prospective study aims to evaluate the prognostic value of liver and renal function tests in breast cancer patients receiving chemotherapy.

Material and methods

Study Design: This study is designed as a prospective cohort study conducted to evaluate the prognostic value of liver and renal function tests in patients with breast cancer undergoing chemotherapy. The study follows newly diagnosed patients longitudinally from baseline assessment

prior to chemotherapy initiation through the completion of treatment and subsequent follow-up. Data collection and patient monitoring were performed over a 12-month recruitment period, with extended outcome follow-up to assess survival endpoints.

Sample Size Estimation and Sampling Method: A total of 150 patients with breast cancer were enrolled in the study. The sample size was determined based on feasibility considerations, patient availability during the study period, and consistency with similar prospective oncologic cohort studies. Convenience sampling was applied, whereby all eligible patients presenting to the radiotherapy and chemotherapy outpatient clinics during the recruitment period were invited to participate until the target sample size was reached.

Inclusion and Exclusion Criteria: Eligible participants were adult female patients with histologically confirmed breast cancer stages I to III, who were candidates for chemotherapy, including adjuvant or neoadjuvant regimens. Patients were required to have classification into one of the recognized molecular subtypes, including Luminal A, Luminal B, HER2-positive, or Basal-like, and to provide informed consent prior to enrollment. Exclusion criteria included evidence of metastatic (stage IV) disease, prior chemotherapy or radiotherapy for breast cancer, known chronic liver or kidney disease unrelated to malignancy, concurrent malignancies, active infectious or inflammatory conditions affecting laboratory parameters, pregnancy or lactation, and incomplete baseline laboratory data.

Study Procedures: At baseline, prior to the initiation of chemotherapy, comprehensive demographic and clinical data were collected, including age, tumor stage, molecular subtype, and treatment plan. Blood samples were obtained to assess baseline laboratory parameters, including liver function tests (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, and serum albumin) and renal function tests (serum creatinine, blood urea nitrogen, and estimated glomerular filtration rate). Additional laboratory markers, including inflammatory markers, tumor markers, and anemia-related indices, were also recorded. During the chemotherapy course, patients were prospectively followed with periodic reassessment of laboratory parameters to monitor dynamic changes in liver and renal function. Treatment-related adverse effects, chemotherapy dose modifications, and clinical responses were

systematically documented. Patients were followed until the completion of chemotherapy, and treatment response was evaluated according to standard clinical and radiologic criteria. Long-term follow-up continued for up to two years to assess clinical outcomes, including overall survival (OS) and progression-free survival (PFS).

Statistical Analysis: Statistical analyses were performed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution, while categorical variables were reported as frequencies and percentages. Comparisons between groups were conducted using independent-sample t-tests or Mann–Whitney U tests for continuous variables and chi-square or Fisher’s exact tests for categorical variables. Survival outcomes were analyzed using the Kaplan–Meier method, with differences assessed by the log-rank test. Multivariable Cox proportional hazards regression models were applied to identify independent prognostic factors. A two-sided P value <0.05 was considered statistically significant.

Ethical Considerations: The study protocol was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences (Ethics Code: IR.TBZMED.FMD.REC.1404.297). All procedures were conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. Patient confidentiality was strictly maintained, and all data were anonymized and used exclusively for research purposes.

Results

Patients receiving neoadjuvant chemotherapy were significantly younger than those treated in the adjuvant setting (49.6 ± 9.8 vs. 54.1 ± 11.1 years, P=0.012) and more frequently presented with stage III disease (P<0.001). Basal-like and HER2-positive subtypes were more prevalent in the neoadjuvant group (P=0.021), whereas Luminal A tumors were predominant among adjuvant patients (P=0.034). Baseline liver function parameters, including ALT and AST, did not differ significantly between groups (P>0.05). However, serum albumin levels were modestly lower in the neoadjuvant group (3.91 ± 0.44 vs. 4.09 ± 0.39 g/dL, P=0.018). Renal function indices, including serum creatinine and eGFR, were comparable between groups (P>0.05), indicating similar baseline renal status prior to chemotherapy initiation (table 1).

Table 1. Baseline Demographic, Clinical, and Laboratory Characteristics of the Study Population (n=150)

Variable	Value
Age (years), mean ± SD	52.4 ± 10.8
Tumor stage, n (%)	
Stage I	38 (25.3)
Stage II	72 (48.0)

Stage III	40 (26.7)
Molecular subtype, n (%)	
Luminal A	54 (36.0)
Luminal B	46 (30.7)
HER2-positive	28 (18.7)
Basal-like (Triple-negative)	22 (14.6)
Chemotherapy setting, n (%)	
Adjuvant	94 (62.7)
Neoadjuvant	56 (37.3)
Baseline liver function tests, mean ± SD	
ALT (U/L)	27.6 ± 11.9
AST (U/L)	25.3 ± 9.7
ALP (U/L)	182.4 ± 54.1
Total bilirubin (mg/dL)	0.86 ± 0.31
Serum albumin (g/dL)	4.02 ± 0.42
Baseline renal function tests, mean ± SD	
Serum creatinine (mg/dL)	0.89 ± 0.21
eGFR (mL/min/1.73 m ²)	88.6 ± 16.4

Multivariable Cox regression analysis demonstrated that advanced tumor stage was a strong independent predictor of poorer overall survival, with stage III disease conferring a significantly higher risk compared with stages I-II (HR=2.41, P<0.001). Older age was also associated with increased mortality risk (HR per 10-year increase = 1.28, P=0.014). Compared with Luminal A tumors, HER2-positive (HR=1.94, P=0.011) and basal-like subtypes (HR=2.63, P<0.001) showed significantly worse survival, whereas Luminal B subtype was not

independently associated with outcome (P=0.152). Patients receiving neoadjuvant chemotherapy experienced a higher mortality risk than those treated in the adjuvant setting (HR=1.46, P=0.043). Higher baseline serum albumin levels were significantly protective (HR=0.58, P=0.006), while preserved renal function, reflected by higher eGFR, was associated with improved survival (HR=0.82, P=0.017). In contrast, baseline ALT levels were not significantly associated with overall survival (P=0.183) (table 2).

Table 2. Multivariable Cox Proportional Hazards Analysis of Prognostic Factors for Overall Survival

Variable	Hazard Ratio (HR)	95% Confidence Interval	P value
Age (per 10-year increase)	1.28	1.05 – 1.56	0.014
Tumor stage (III vs. I–II)	2.41	1.48 – 3.92	<0.001
Molecular subtype			
Luminal B vs. Luminal A	1.37	0.89 – 2.11	0.152
HER2-positive vs. Luminal A	1.94	1.16 – 3.24	0.011
Basal-like vs. Luminal A	2.63	1.54 – 4.51	<0.001
Chemotherapy setting (Neoadjuvant vs. Adjuvant)	1.46	1.01 – 2.12	0.043
Serum albumin (per 1 g/dL increase)	0.58	0.39 – 0.86	0.006
ALT (per 10 U/L increase)	1.09	0.96 – 1.24	0.183
eGFR (per 10 mL/min/1.73 m ² increase)	0.82	0.70 – 0.96	0.017

Figure 1 summarizes the multivariable Cox regression analysis for overall survival, demonstrating clear between-group differences across clinic pathological and biochemical factors. Patients with stage III disease exhibited a significantly higher mortality risk compared with those with stage I-II tumors (P<0.001). Increasing age was associated with worse survival (P=0.014). When molecular subtypes were compared with Luminal A tumors, both HER2-positive (P=0.011) and basal-like subtypes (P<0.001) showed

significantly poorer outcomes, whereas no significant difference was observed for Luminal B tumors (P=0.152). Patients treated with neoadjuvant chemotherapy had inferior survival compared with those receiving adjuvant therapy (P=0.043). In contrast, higher serum albumin levels were associated with significantly improved survival (P=0.006), and better renal function, reflected by higher eGFR, was likewise protective (P=0.017). Baseline ALT levels did not differ significantly between survival outcomes (P=0.183).

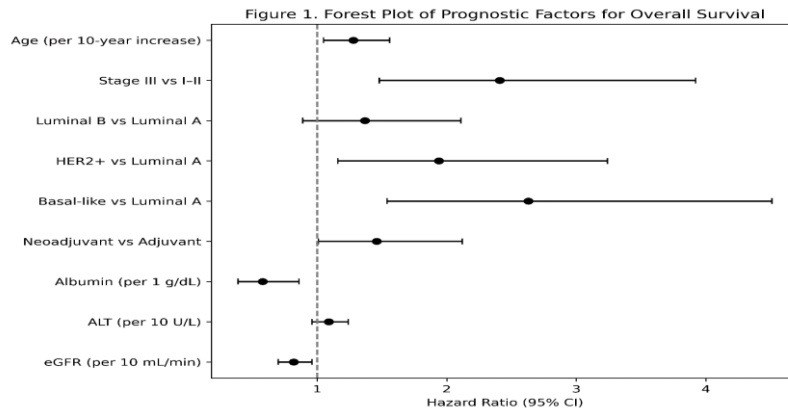


Figure 1. Forest Plot of Multivariable Cox Regression for Overall Survival

Figure 2 illustrates the Kaplan Meier analysis of overall survival stratified by tumor stage, revealing a pronounced divergence between the two groups over time. Patients diagnosed with stage III breast cancer experienced significantly poorer overall survival compared with those with stage I-II disease (log-rank test, $P < 0.001$). The survival curves

separated early during follow-up and continued to diverge throughout the observation period, indicating a persistent adverse effect of advanced stage on mortality risk. In contrast, patients with early-stage tumors maintained higher survival probabilities across all time points, underscoring the prognostic advantage of earlier disease stage.

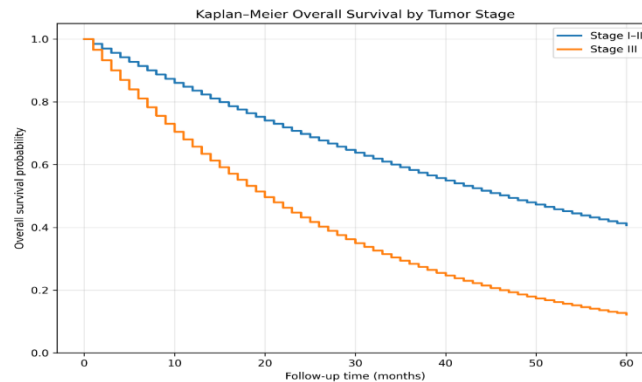


Figure 2. Kaplan Meier Overall Survival Curves According to Tumor Stage

Discussion

This prospective cohort study highlights that survival outcomes in patients with non-metastatic breast cancer are determined by an integrated interaction between tumor burden, intrinsic molecular characteristics, treatment context, and host biological condition. Advanced disease stage, older age, aggressive molecular phenotypes, and receipt of neoadjuvant chemotherapy were associated with poorer survival, whereas preserved nutritional status and renal function emerged as protective factors. In contrast, baseline hepatic enzyme levels did not appear to exert a meaningful influence on long-term outcomes, underscoring the differential prognostic value of routinely assessed biochemical parameters.

Tumor stage emerged as the dominant determinant of overall survival, reflecting the fundamental role of disease extent in shaping prognosis. Advanced stage disease is typically associated with a higher likelihood of lymph vascular invasion, nodal dissemination, and occult micro metastatic spread, all of which contribute to increased recurrence risk

and cancer-related mortality. Moreover, patients with more advanced tumors often require more intensive multimodal treatment, which may be associated with cumulative toxicity, treatment delays, or dose reductions that further compromise outcomes. The persistent survival disadvantage observed over time suggests that the biological and clinical consequences of advanced stage disease are not fully offset by contemporary therapeutic strategies (16).

Increasing age was independently associated with worse survival, emphasizing the prognostic relevance of host factors beyond tumor-specific characteristics. Aging is accompanied by immunosenescence, reduced physiological reserve, and a higher prevalence of comorbid conditions, all of which may limit treatment tolerance and recovery. Older patients may also be less likely to receive optimal systemic therapy due to concerns regarding toxicity or functional decline. Importantly, the association between age and survival persisted after adjustment for stage and subtype, suggesting that age captures clinically

meaningful vulnerability that is not fully explained by tumor biology alone (17).

Molecular subtype analysis demonstrated significantly inferior survival among patients with HER2-positive and basal-like tumors compared with Luminal A disease, reinforcing the central role of intrinsic tumor biology in breast cancer prognosis. Basal-like tumors are characterized by high proliferative activity, genomic instability, and limited targeted treatment options, leading to early relapse and poor long-term outcomes. Although HER2-positive breast cancer outcomes have improved substantially in the era of targeted therapy, real-world cohorts may still experience inferior survival due to advanced presentation, treatment heterogeneity, or incomplete access to anti-HER2 agents (18).

In contrast, the Luminal B subtype was not independently associated with overall survival in the adjusted model, highlighting the biological heterogeneity within this group. Luminal B tumors encompass a broad spectrum of proliferative indices and endocrine responsiveness, and their prognosis may be substantially modified by appropriate systemic therapy. The lack of an independent association may also reflect overlap with other subtypes and the effectiveness of combined chemotherapy and endocrine treatment in mitigating adverse biological features. These findings suggest that Luminal B disease should not be uniformly categorized as high-risk without consideration of additional clinic pathological factors (19).

Patients treated with neoadjuvant chemotherapy exhibited worse survival compared with those receiving adjuvant therapy, a finding that is most plausibly explained by confounding by indication. Neoadjuvant treatment is preferentially administered to patients with larger tumors, nodal involvement, or aggressive molecular subtypes, all of which inherently confer poorer prognosis. Furthermore, failure to achieve a pathological complete response following neoadjuvant therapy is a well-established marker of chemoresistance and adverse outcome. Thus, the observed association likely reflects underlying disease aggressiveness rather than a detrimental effect of neoadjuvant chemotherapy itself (20).

Baseline serum albumin was strongly associated with improved survival, underscoring the prognostic importance of nutritional and systemic inflammatory status in breast cancer. Albumin serves as an integrated marker of protein reserves, chronic inflammation, and overall physiological resilience. Hypoalbuminemia has been linked to impaired immune function, reduced tolerance to systemic therapy, and increased susceptibility to treatment-related complications. Conversely, higher albumin levels may reflect preserved metabolic homeostasis and enhanced capacity to withstand the

physiological stress imposed by both malignancy and anticancer treatment (21).

Preserved renal function, as reflected by higher estimated glomerular filtration rate, was likewise associated with superior survival. Adequate kidney function is essential for optimal drug metabolism, prevention of treatment-limiting toxicity, and maintenance of systemic homeostasis. Renal impairment may lead to chemotherapy dose modifications, increased adverse events, and treatment interruptions, all of which can negatively impact oncologic outcomes. In addition, chronic kidney dysfunction is associated with systemic inflammation and vascular disease, which may further contribute to adverse prognosis in cancer patients (22).

In contrast to albumin and renal function, baseline alanine aminotransferase levels were not significantly associated with survival. This finding suggests that mild variations in hepatic transaminase levels, in the absence of overt liver disease or metastasis, may not meaningfully influence long-term outcomes in breast cancer. Unlike albumin, which reflects chronic systemic processes, ALT primarily indicates acute hepatocellular injury and may lack sensitivity as a prognostic biomarker in this context. The substantial functional reserve of the liver may further attenuate the clinical impact of modest enzyme elevations (23).

The Kaplan–Meier analysis demonstrated early and persistent divergence in survival between patients with early and advanced stage disease, reinforcing the clinical relevance of stage at diagnosis. These findings emphasize the importance of early detection strategies and timely initiation of treatment to improve long-term outcomes (24).

Conclusion

Collectively, these results underscore that prognosis in breast cancer is shaped by both tumor-related and host-related factors. While tumor stage and molecular subtype remain the cornerstone of risk stratification, routinely available clinical parameters such as albumin and renal function provide meaningful complementary prognostic information. Incorporating these markers into clinical assessment may facilitate more refined risk stratification and individualized treatment planning. Future studies should explore whether targeted interventions aimed at optimizing nutritional and physiological status can translate into improved survival across diverse breast cancer subtypes.

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Conflicts of interest

The authors declare that they have no competing interests.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

References

- [1] Slamon, D., J., et al. (1987). Human breast cancer: Correlation of relapse and survival with amplification of the HER-2/neu oncogene. *Science*, 235, 177-182.
- [2] Liu, Y., et al. (2018). Targeting 17q23 amplicon to overcome the resistance to anti-HER2 therapy in HER2+ breast cancer. *Nature Communications*, 9, 4718.
- [3] Jia, Y., et al. (2021). Th1 cytokine interferon gamma improves response in HER2 breast cancer by modulating the ubiquitin proteasomal pathway. *Molecular Therapy*, 29, 1541-1556.
- [4] Moasser, M., M., & Krop, I., E., (2015). The evolving landscape of HER2 targeting in breast cancer. *JAMA Oncology*, 1, 1154-1161.
- [5] Perez, E. A., et al. (2017). Trastuzumab etamine with or without pertuzumab versus trastuzumab plus taxane for human epidermal growth factor receptor 2-positive, advanced breast cancer: Primary results from the phase III MARIANNE study. *Journal of Clinical Oncology*, 35, 141-148.
- [6] Gianni, L., et al. (2011). Treatment with trastuzumab for 1 year after adjuvant chemotherapy in patients with HER2-positive early breast cancer: A 4-year follow-up of a randomized controlled trial. *Lancet Oncology*, 12, 236-244.
- [7] Slamon, D., et al. (2011). Adjuvant trastuzumab in HER2-positive breast cancer. *New England Journal of Medicine*, 365, 1273-1283.
- [8] Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of cancer: The next generation. *Cell*, 144, 646-674.
- [9] Yu, L., R., et al. (2018). Immune response proteins as predictive biomarkers of doxorubicin-induced cardiotoxicity in breast cancer patients. *Experimental Biology and Medicine (Maywood)*, 243, 248-255.
- [10] Liu, M., et al. (2020). Prognostic significance of PD-L1 expression on cell-surface vimentin-positive circulating tumor cells in gastric cancer patients. *Molecular Oncology*, 14, 865-881.
- [11] Ding, N., et al. (2020). Roles of neutrophil/lymphocyte ratio in prognosis and in differentiation of potential beneficiaries in HER2-

positive breast cancer with trastuzumab therapy. *BMC Cancer*, 20, 235.

- [12] Hoenicke, L., & Zender, L., (2012). Immune surveillance of senescent cells Biological significance in cancer- and non-cancer pathologies. *Carcinogenesis*, 33, 1123-1126.
- [13] Huang, H., et al. (2019). Prognostic value of preoperative systemic immune-inflammation index in patients with cervical cancer. *Scientific Reports*, 9, 3284.
- [14] Sun, Y., et al. (2019). Increased systemic immune-inflammation index independently predicts poor survival for hormone receptor-negative, HER2-positive breast cancer patients. *Cancer Management and Research*, 11, 3153-3162.
- [15] Li, W., et al. (2021). Systemic immune-inflammation index is a prognostic factor for breast cancer patients after curative resection. *Frontiers in Oncology*, 11, 570208.
- [16] Hua, X., et al. (2020). Prognostic value of preoperative systemic immune-inflammation index in breast cancer: A propensity score-matching study. *Frontiers in Oncology*, 10, 580.
- [17] Gu, Q., Zhao, J., Liu, Y., Chen, H., & Wang, L. (2023). Association between the systemic immune-inflammation index and the efficacy of neoadjuvant chemotherapy, prognosis in HER2 positive breast cancer A retrospective cohort study. *Gland Surgery*, 12, 609-618.
- [18] Jiang, L., Fang, J., & Ding, J. (2020). High systemic immune-inflammation index predicts poor survival in patients with human epidermal growth factor receptor-2 positive breast cancer receiving adjuvant trastuzumab. *Cancer Management and Research*, 12, 475-484.
- [19] Zhu, L., et al. (2016). A new prognostic score based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. *OncoTargets and Therapy*, 9, 4879-4886.
- [20] Domon, H., et al. (2021). Proteolytic cleavage of HLA class II by human neutrophil elastase in pneumococcal pneumonia. *Scientific Reports*, 11, 2432.
- [21] Hsu, B. E., Shen, Y., & Siegel, P. M. (2020). Neutrophils: Orchestrators of the malignant phenotype. *Frontiers in Immunology*, 11, 1778.
- [22] Partl, R., et al. (2023). The pre-treatment platelet-to-lymphocyte ratio as a prognostic factor for loco-regional control in locally advanced rectal cancer. *Diagnostics*.
- [23] Granja, T. F., et al. (2022). Platelets and the cybernetic regulation of ischemic inflammatory responses through PNC formation regulated by extracellular nucleotide metabolism and signaling. *Cells*.
- [24] Klement, G. L., et al. (2009). Platelets actively sequester angiogenesis regulators. *Blood*, 113, 2835-2842.