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Preoperative PIV and HALP: Correlation with Breast Cancer Pathology and Predictive Value for Microsatellite Status

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ABSTRACT

Breast cancer is a leading malignancy in women. Understanding its clinicopathological traits and microsatellite status is vital for prognosis and treatment planning. This study explored the links between preoperative pan-immune-inflammation value (PIV) and hemoglobin, albumin, lymphocyte, and platelet (HALP) score with breast cancer's pathological features and microsatellite status and assessed their predictive power for the latter.

This retrospective study analyzed data from 260 breast cancer patients who had surgery between 2022 and 2025. Researchers not involved in the patients' treatment collected and analyzed the data. HALP and PIV were calculated from preoperative blood tests. Patients were grouped based on the median values of these scores. Associations between the scores and clinicopathological characteristics were examined. Patients were also divided into microsatellite stable (MSS) and microsatellite instability-high (MSI-H) groups, and differences in HALP and PIV between these groups were compared. Receiver operating characteristic curves were used to evaluate the predictive accuracy of HALP and PIV for microsatellite status.

High PIV was linked to younger age and lower ER positivity. High HALP correlated with older age, a higher proportion of clinical stage I patients, and lower HER2 positivity. MSS patients had lower PIV and higher HALP than MSI-H patients. PIV and HALP showed significant correlations with microsatellite status. Both indicators had high AUC values (PIV: 0.867; HALP: 0.879), with 100% sensitivity, indicating strong predictive capabilities.

Preoperative PIV and HALP are closely tied to breast cancer's pathological features and microsatellite status. They offer high predictive value for microsatellite status, aiding in breast cancer diagnosis and treatment decisions.

Keywords: Breast neoplasms; Inflammation; Microsatellite instability; Nutritional status

INTRODUCTION

Significance and Innovation

The significance of this study lies in providing new potential indicators for the clinical diagnosis and prognostic assessment of breast cancer. By analyzing the relationships between pan-immune-inflammation value (PIV) and hemoglobin, albumin, lymphocyte, and

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platelet (HALP) score with tumor pathological characteristics and microsatellite status, it further refines the individualized treatment regimens for breast cancer and offers new evidence for the underlying mechanisms of immune inflammation in the development and progression of breast cancer. Moreover, this study innovatively explores the predictive value of both PIV and HALP for microsatellite status simultaneously and determines their optimal cutoff values. This provides a practical reference for preoperative clinical judgment of microsatellite status, which is conducive to optimizing precision treatment strategies for patients with breast cancer.

Currently, globally, 4 women are diagnosed with breast cancer every minute, and 1 woman dies from the disease, with this trend continuing to worsen.[1] Should present trends persist, the number of new global breast cancer cases is projected to escalate by 38% by 2050, accompanied by a 68% surge in annual deaths.[2] A study analyzed breast cancer stage distribution in 81 countries using data from over 2.44 million patients.[3] It found that sub-Saharan Africa had the highest rate of stage IV breast cancer diagnoses (5.6% to 30.6%), while North America had the lowest (0.0% to 6.0%). In China, the proportions of breast cancer cases at stages I, II, III, IV, and unknown stage were 30.6%, 31.1%, 12.8%, 5.8%, and 19.6%, respectively, with stages I and II accounting for 76.8% of cases.

Breast cancer is a highly heterogeneous malignant tumor, exhibiting significant differences in pathological characteristics, molecular biological behaviors, and clinical prognosis.[4] Therefore, accurately assessing the pathological features of breast cancer is of great importance for creating tailored treatment plans to boost patient survival and quality of life.[5] Traditionally, the pathological diagnosis of breast cancer has primarily relied on postoperative histopathological examination. However, this method has certain limitations, such as the inability to provide sufficient basis for treatment decisions before surgery and its invasive nature.[6] Consequently, the search for reliable preoperative predictive indicators has become an important topic in the field of breast cancer research. Recently, significant attention has been directed towards the association between inflammation and tumors.[7] Systemic immune-inflammatory markers reveal the body's overall immune-inflammatory status, providing a novel angle for tumor evaluation. PIV is a new systemic immune-inflammatory marker, derived from neutrophil, platelet, monocyte, and lymphocyte counts.[8] The PIV index integrates blood params, reflects inflammation and predicts advanced cancer outcomes.[9,10] The HALP scoring system is a tool for assessing nutritional status and immune responses based on preoperative hematological indicators of patients.[11] The HALP score combines anemia status reflected by hemoglobin, nutritional status indicated by albumin, immune function represented by lymphocytes, and the role of platelets in inflammation and tumor progression. It is closely related to postoperative complications and survival rates in cancer patients.[12,13]

Breast cancer's pathology involves factors like histology, stage, lymph node spread, and differentiation. Different pathological types exhibit distinct biological behaviors and prognoses.[14] For instance, non-invasive carcinomas, such as ductal carcinoma in situ and lobular carcinoma in situ, generally have a better prognosis, whereas invasive carcinomas of no special type, like invasive ductal carcinoma and lobular carcinoma, tend to have a poorer prognosis.[15] Tumor size and lymph node metastasis are key factors affecting breast cancer prognosis. Bigger tumors and more lymph node metastases increase the risk of distant metastasis and worsen prognosis.[16] In-depth research into the correlations between preoperative PIV and HALP and these pathological characteristics is expected to provide more comprehensive and accurate information for preoperative assessment and treatment decision-making in breast cancer. Furthermore, the study of microsatellite status in breast cancer holds significant importance. Microsatellites are short tandem repeats widely distributed throughout the genome, and their stability is vital for maintaining genomic integrity. During tumorigenesis, due to defects in DNA mismatch repair (MMR) function, alterations in the length of microsatellite sequences, known as microsatellite instability (MSI), may occur.[17] This instability usually results from DNA replication errors, especially with MMR system defects. It causes insertions or deletions in microsatellite repeats, inducing a hypermutated genome.[18] MSI is found in many types of tumors and is strongly linked to their development, progression, prognosis and treatment response. In colorectal cancer, MSI status has become an important prognostic indicator and a biomarker for guiding immunotherapy. In breast cancer, although the incidence of MSI is relatively low,[19] studies have shown that patients with MSI-positive breast cancer may possess unique

clinicopathological characteristics and treatment responses.[20] Currently, the primary methods for detecting microsatellite status in breast cancer include immunohistochemical detection of MMR protein expression and direct detection of microsatellite locus instability through polymerase chain reaction or next-generation sequencing technologies. These methods typically require postoperative acquisition of tumor tissue samples for testing, and there is currently a lack of effective preoperative predictive methods.[21] Therefore, exploring preoperative indicators, such as PIV and HALP, that can effectively predict microsatellite status in breast cancer is of great clinical value for formulating reasonable treatment plans in advance, improving treatment efficacy, and enhancing patient prognosis.

This research explores the links between preoperative PIV and HALP and breast cancer's pathological traits and assesses their predictive power for microsatellite status. By collecting preoperative PIV and HALP data from 260 patients with breast cancer and combining them with postoperative pathological characteristics and microsatellite status detection results, we aim to unveil the intrinsic connections between PIV and HALP and the pathological characteristics of breast cancer and establish a predictive model for microsatellite status based on PIV and HALP. This study will provide new insights and methodologies for preoperative assessment and prognostic prediction of breast cancer and is expected to offer robust support for the formulation of more precise and individualized treatment plans in clinical practice, thereby enhancing the therapeutic effects and living standards of breast cancer patients.

MATERIALS AND METHODS

Research Design

This study is a retrospective clinical controlled study, with data collection and analysis conducted by researchers who were not involved in the patients' treatment. From March 2022 to March 2025, 260 patients with breast cancer who had surgery in our oncology department were included. HALP and PIV were calculated from preoperative lab data. Patients were divided into high/low HALP and high/low PIV groups by median values. The study analyzed the links between HALP/PIV and breast cancer clinicopathological traits. Based on microsatellite stability tests, patients were grouped into microsatellite stable (MSS) and microsatellite instability-high (MSI-H). HALP and PIV differences between these groups were compared. Receiver operating characteristic (ROC) curves were used to assess HALP and PIV's predictive value for microsatellite status. See Figure 1 for the study flowchart.

Inclusion Criteria

Patients diagnosed with breast cancer through pathological examination who underwent mastectomy or breast-conserving surgery, completed peripheral blood tests within 1 month before surgery, were aged older than 18 years old, and had complete clinical data records, including pathological type and tumor stage, were included in the study

Exclusion Criteria

Exclusion criteria included (1) patients with other primary malignant neoplasms, (2) patients suffering from hematologic disorders, autoimmune conditions, or acute/chronic inflammatory illnesses, (3) those with severe impairment of vital organs like the heart, liver, or kidneys, (4) patients who received blood transfusions or used medications that might affect immune and inflammatory indicators before surgery, (5) patients with incomplete preoperative peripheral blood test data, making it impossible to calculate PIV and HALP, (6) patients with incomplete postoperative pathological reports, making it impossible to determine microsatellite status, or (7) pregnant or lactating women.

Sample Size Calculation

The Rosner method was used to estimate the sample size,[22] and G*Power software was used for calculations to compare differences in clinicopathological characteristics of breast cancer between the high PIV group and the low PIV group. When the effect size was set at a moderate level (effect size=0.25), the significance level (α) was set at 0.05, and power was set at 0.95, the total required sample size was calculated to be 210 individuals. The final sample size determined for this study was 260 individuals. This sample size significantly exceeds the minimum estimated requirement, thereby providing higher statistical power for the study and further ensuring the reliability and robustness of the results.

Data Collection

This study systematically collected clinical and pathological data from patients who underwent breast

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cancer surgery between March 2022 and March 2025. The data specifically included basic information, such as patients' age, body mass index (BMI), past medical history, and family history, imaging examination results, tumor marker detection data, and preoperative needle biopsy findings. Postoperative pathological reports provided detailed records of key information, including pathological type, tumor grade, immunohistochemical results, and microsatellite status. In addition, particular emphasis was placed on collecting laboratory test indicators from patients one week before surgery, including complete blood count, blood biochemistry (hemoglobin, albumin), and other relevant indicators. These data were used to calculate preoperative PIV and HALP and to analyze their relationships with the pathological characteristics and microsatellite status of breast cancer.

Grouping of research subjects

Based on the calculated PIV[23] and HALP[24] values, patients were divided into corresponding high HALP/low HALP groups and high PIV/low PIV groups using the median values of these two indicators. The median HALP value was 46, with patients having a HALP ≥46 classified into the high HALP group (n=130) and those with a HALP <46 into the low HALP group (n=130). Similarly, the median PIV value was 302, with patients having a PIV ≥302 classified into the high PIV group (n=130) and those with a PIV <302 into the low PIV group (n=130). Furthermore, breast cancer patients were categorized into the MSS group (n=252) and the MSI-H group (n=8) based on the results of microsatellite stability testing.

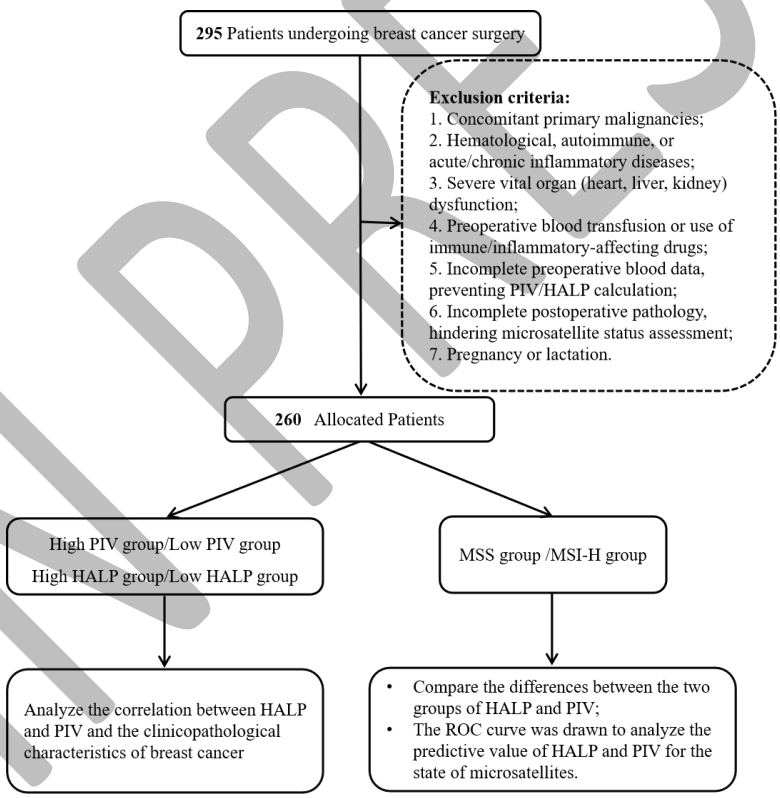

Figure 1. Research process

Statistical Analysis

SPSS 25.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Normally distributed data were shown as mean ± standard deviation and compared using *t* tests. Categorical data such as tumor stage were presented as n (%) and compared using the χ^2 test. Pearson correlation analysis assessed the relationship between preoperative PIV and HALP and breast cancer microsatellite status. ROC curve analysis evaluated the predictive value of preoperative PIV and HALP for microsatellite status. $p<0.05$ was statistically significant.

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RESULTS

Comparison of clinicopathological data (PIV)

Table 1 shows the comparison results of the clinicopathological data of patients in the high PIV group and the low PIV group. The high PIV group's mean age was 47.85 ± 6.73 years, significantly lower than the low PIV group's 52.88 ± 7.45 years [95% CI, −6.766 to −3.296; t=−5.710; p<0.001]. No significant differences were found in tumor stage, lymph node stage, or clinical stage between groups (p>0.05). However, the high PIV group had a lower ER positivity rate than the low PIV group (χ^2=4.091; p=0.043), hinting at a possible link between PIV and breast cancer endocrine status. Other factors like BMI, histological type, PR status, HER2 status, Ki-67 expression, menopausal status, and histories of diabetes and hypertension showed no significant differences (p>0.05).

Comparison of clinicopathological data (HALP)

Table 2 shows the comparison results of the clinicopathological data of patients in the high HALP group and the low HALP group. For HALP grouping, the high HALP group had a mean age of 51.64 ± 7.45 years, significantly higher than the low HALP group's 49.08 ± 7.40 years (95% CI, 0.739 to 4.368; t=2.772; p=0.006). No significant differences were found in tumor stage, lymph node stage, or BMI (p>0.05). However, the high HALP group had a higher proportion of clinical stage I breast cancer (χ^2=7.050; p=0.030) and a lower HER2 positivity rate (χ^2=4.055; p=0.044). This implies HALP may be related to breast cancer's clinical stage and HER2 expression. Other factors like histological type, ER/PR status, Ki-67 level, menopausal status, and history of diabetes or hypertension showed no significant differences (p>0.05).

Comparison results of PIV between the MSS group and the MSI-H group

Table 3 compares the preoperative PIV values between breast cancer patients in the MSS group (n=252) and the MSI-H group (n=8). The results indicate that the PIV value in the MSS group was significantly lower than that in the MSI-H group (307.54 ± 88.16 vs 411.38 ± 27.78, t=3.321, p=0.001), with a 95% CI of −165.421 to −42.258. This demonstrates a statistically significant difference in PIV between the two groups, suggesting a potential correlation between PIV and the microsatellite status of breast cancer.

Comparison results of HALP between the MSS group and the MSI-H group

Table 4 compares the preoperative HALP between breast cancer patients in the MSS group and the MSI-H group. The HALP value in the MSS group was significantly higher than that in the MSI-H group (46.56 ± 13.31 vs 28.38 ± 3.34, t=3.853, p<0.001), with a 95% CI of 8.892 to 27.478. This indicates a statistically significant difference in HALP between the two groups, suggesting a potential association between HALP and microsatellite instability status.

Table 1. Comparison of clinicopathological data (PIV)

Variables	High PIV group (n=130)	Low PIV group (n=130)	95% CI		Effect size	*p*
			Lower	Upper		
Age, y	47.85 ± 6.73	52.88 ± 7.45	−6.766	−3.296	−5.710	<0.001[a]
Tumor stage						
T1	46 (35.38)	47 (36.15)	-	-	0.647	0.886[b]
T2	68 (53.31)	71 (54.62)				
T3	8 (6.15)	6 (4.62)				
T4	8 (6.15)	6 (4.62)				
Node stage						
N0	59 (45.38)	65 (50.00)	-	-	0.744	0.863[b]
N1	36 (27.69)	35 (26.92)				
N2	22 (16.92)	18 (13.85)				
N3	13 (10.00)	12 (9.23)				
Clinical stage						
I	26 (20.00)	32 (24.62)	-	-	2.516	0.284[b]
II	63 (48.46)	68 (52.31)				
III	41 (31.54)	30 (23.08)				
BMI, kg/m^2	23.22 ± 2.51	22.89 ± 2.68	−0.294	0.974	1.055	0.292[a]
Histological type						
Invasive ductal carcinoma	110 (84.62)	109 (83.85)	-	-	0.029	0.865[b]
Others	20 (15.38)	21 (16.15)				
ER status						
Positive	83 (63.85)	98 (75.38)	-	-	4.091	0.043[b]
Negative	47 (36.15)	32 (24.62)				
PR status						
Positive	79 (60.77)	85 (65.38)	-	-	0.595	0.441[b]
Negative	51 (39.23)	45 (34.62)				
HER2 status						
Positive	39 (30.00)	38 (29.23)	-	-	0.019	0.892[b]
Negative	91 (70.00)	92 (70.77)				
Ki-67						
>14%	62 (47.69)	57 (43.85)	-	-	0.387	0.534[b]
≤14%	68 (52.31)	73 (56.15)				
Menopause status						
Positive	69 (53.08)	66 (50.77)	-	-	0.139	0.710[b]
Negative	61 (46.92)	64 (49.23)				
Diabetes						
no	113 (86.92)	117 (90.00)	-	-	0.603	0.438[b]
yes	17 (13.08)	13 (10.00)				
Hypertension						
no	106 (81.54)	108 (83.08)	-	-	0.106	0.745[b]
yes	24 (18.46)	22 (16.92)				

BMI: body mass index; CI: confidence interval; ER: estrogen receptor; HER2: human epidermal growth factor receptor 2; PIV: pan-immune-inflammation value; PR: progesterone receptor.

[a]Independent samples *t* test

[b]χ^2 test

Table 2. Comparison of clinicopathological data (HALP)

Variables	High HALP group (n=130)	Low HALP group (n=130)	95% CI		Effect size	*p*
			Lower	Upper		
Age, y	51.64 ± 7.45	49.08 ± 7.40	0.739	4.368	2.772	0.006[a]
Tumor stage						
T1	50 (38.46)	47 (36.15)	-	-	0.268	0.966[b]
T2	69 (53.08)	70 (53.85)				
T3	6 (4.62)	7 (5.38)				
T4	5 (3.85)	6 (4.62)				
Node stage						
N0	77 (59.23)	74 (56.92)	-	-	0.151	0.985[b]
N1	33 (25.38)	35 (26.92)				
N2	15 (11.54)	16 (12.31)				
N3	5 (3.85)	5 (3.85)				
Clinical stage						
I	39 (30.00)	21 (16.15)	-	-	7.050	0.030[a]
II	62 (47.69)	73 (56.15)				
III	29 (22.31)	36 (27.69)				
BMI, kg/m^2	23.15 ± 2.49	22.96 ± 2.71	−0.442	0.829	0.600	0.549[b]
Histological type						
Invasive ductal carcinoma	112 (86.15)	113 (86.92)	-	-	0.033	0.856[b]
Others	18 (13.85)	17 (13.08)				
ER status						
Positive	94 (72.31)	90 (69.23)	-	-	0.298	0.586[b]
Negative	36 (27.69)	40 (30.77)				
PR status						
Positive	81 (62.31)	80 (61.54)	-	-	0.016	0.898[b]
Negative	49 (37.69)	50 (38.46)				
HER2 status						
Positive	46 (35.38)	62 (47.69)	-	-	4.055	0.044[b]
Negative	84 (64.62)	68 (52.31)				
Ki-67						
>14%	84 (64.62)	85 (65.38)	-	-	0.017	0.897[b]
≤14%	46 (35.38)	45 (34.62)				
Menopause status						
Positive	62 (47.69)	65 (50.00)	-	-	0.139	0.710[b]
Negative	68 (52.31)	65 (50.00)				
Diabetes						
No	112 (86.15)	109 (83.85)	-	-	0.272	0.602[b]
Yes	18 (13.85)	21 (16.15)				
Hypertension						
No	110 (84.62)	108 (83.08)	-	-	0.029	0.865[b]
Yes	20 (15.38)	22 (16.92)				

BMI: body mass index; CI: confidence interval; ER: estrogen receptor; HALP: hemoglobin, albumin, lymphocyte, and platelet score; HER2: human epidermal growth factor receptor 2; PR: progesterone receptor.

[a]Independent samples *t* test

[b]χ^2 test

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Table 3. Comparison of PIV between the MSS group and the MSI-H group of patients

Group	n	PIV
MSS group	252	307.54 ± 88.16
MSI-H group	8	411.38 ± 27.78
Test		Independent samples *t* test
95% CI		
Lower		−165.421
Upper		−42.258
Effect size		3.321
p		0.001

CI: confidence interval; MSI-H: microsatellite instability-high; MSS: microsatellite stable; PIV: pan-immune-inflammation value.

Table 4. Comparison of HALP between the MSS group and the MSI-H group

Group	n	HALP
MSS group	252	46.56 ± 13.31
MSI-H group	8	28.38 ± 3.34
Test		Independent samples *t* test
95% CI		
Lower		8.892
Upper		27.478
Effect size		3.853
p		<0.001

CI: confidence interval; HALP: hemoglobin, albumin, lymphocyte, and platelet score; MSI-H: microsatellite instability-high; MSS: microsatellite stable.

Correlation analysis of preoperative PIV and HALP with Microsatellite status of breast cancer

Table 5 shows that through Pearson correlation analysis, the correlation coefficient between PIV and the microsatellite status of breast cancer was found to be 0.202 (p=0.001), while the correlation coefficient between HALP and the microsatellite status was −0.233 (p<0.001). These results suggest that PIV and HALP may play a certain role in the formation or expression of microsatellite status in breast cancer.

Predictive value of preoperative PIV for the microsatellite status of breast cancer

Figure 2 illustrates the predictive value of preoperative PIV in determining the microsatellite status of breast cancer. The study results indicate that the area under the curve (AUC) for PIV reached 0.867, demonstrating high predictive accuracy. The sensitivity of PIV was 100.00%, meaning that all actually positive samples were correctly identified, while the specificity was 73.81%, indicating that 73.81% of all actually negative samples were correctly identified. The optimal cutoff value was determined to be 375 (p<0.001).

The predictive value of preoperative HALP for microsatellite status of breast cancer

Figure 3 demonstrates the predictive value of preoperative HALP in determining the microsatellite status of breast cancer. The study results indicate that the AUC for HALP reached 0.879, showing high predictive accuracy. The sensitivity of HALP was 100.00%, meaning that it was able to identify all MSI-H cases without any missed diagnoses. The specificity was 76.59%, indicating a high proportion of correctly identified MSS cases by HALP. The optimal cutoff value was determined to be 35 (p<0.001).

Table 5. Correlation between preoperative PIV and HALP and the microsatellite status of breast cancer

	PIV	HALP
Pearson r	0.202	−0.233
p	0.001	0.000

HALP: hemoglobin, albumin, lymphocyte, and platelet score; PIV: pan-immune-inflammation value.

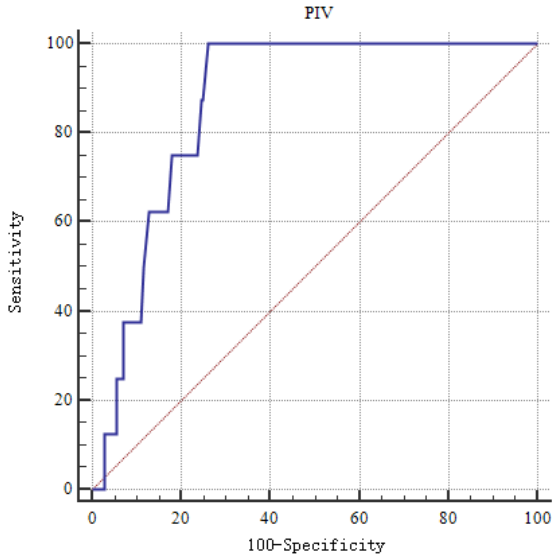

Figure 2. The receiver operating characteristic curve of preoperative pan-immune-inflammation value (PIV) in predicting the microsatellite status of breast cancer

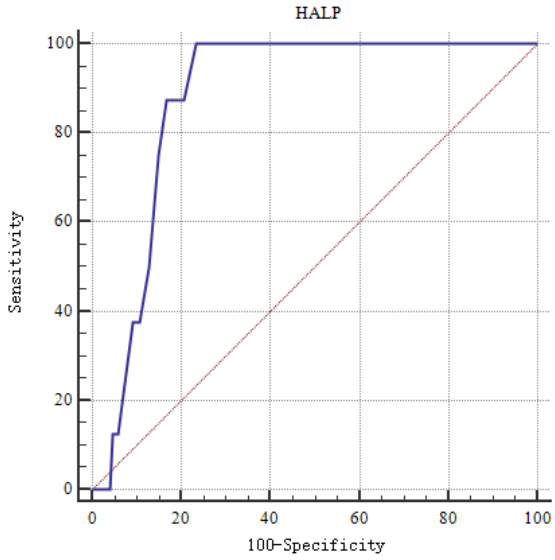

Figure 3. The receiver operating characteristic curve of preoperative hemoglobin, albumin, lymphocyte, and platelet (HALP) score for predicting the microsatellite status of breast cancer.

DISCUSSION

Breast cancer is a highly common malignancy in women worldwide, marked by high incidence and mortality rates.[25] The prognosis and treatment options for breast cancer patients depend not only on traditional clinicopathological characteristics, but are also closely related to the molecular features of the tumor.[26] MSI serves as a crucial molecular marker in breast cancer, and MSI-H patients typically show improved response to immune checkpoint inhibitors.[27] Therefore, in the context of precision medicine, accurately identifying the microsatellite status is of great significance for optimizing treatment strategies.

Alterations in tumor-associated inflammatory cells mirror the intensity of the tumor's inflammatory reaction, with a more pronounced inflammatory response typically indicating a poorer prognosis. Inflammation can influence the tumor microenvironment by inducing immunosuppression, and individuals with immunosuppression often face an increased risk of tumor progression.[28] As the primary defense against cancer, immunity is a focal point in current cancer research, and immunotherapy has gradually emerged as an important treatment modality for cancer. Monocyte-to-lymphocyte, platelet-to-lymphocyte ratio, and neutrophil-to-lymphocyte ratios, as commonly used peripheral blood immune-inflammatory indicators, have been confirmed to be associated with the clinicopathological characteristics and prognosis of various malignant tumors, including colorectal cancer, endometrial cancer, and gastric cancer.[29-32] In 2020, Fucà et al[33] integrated NLR, platelet count, and monocyte count to develop a novel IIB, namely the prognostic inflammatory and nutritional index (PIV). As a comprehensive indicator reflecting the body's immune-inflammatory status, an elevated PIV may suggest a more active immune-inflammatory response state, which could be associated with rapid proliferation and invasion of tumor cells.[34] Tumor cells can promote their own progression by secreting inflammatory mediators. Meanwhile, the excessive production of inflammatory factors can activate systemic inflammatory responses, affecting the body's immune balance and tissue repair capabilities. This immune imbalance can notably raise PIV values. Our research shows that breast cancer patients in the high PIV group are younger and have a lower ER positivity rate than those in the low PIV group. Thus, PIV is closely tied to patients' age and hormone receptor status. Younger breast cancer patients often exhibit more aggressive tumor biological behaviors, with faster tumor cell proliferation and stronger invasive capabilities, which may be associated with the activation of immune-inflammatory responses. Demir et al[35] conducted a study focusing on breast cancer patients under 40 years old and found that patients in the high PIV group were younger and had poorer survival rates, which is generally consistent with our findings. Therefore, for younger patients with high PIV, more aggressive treatment strategies may need to be considered. Additionally, ER-negative breast cancer typically has a poorer prognosis, and the biological behavior of its tumor cells is more complex. The elevation of PIV may reflect the special interactions of these tumor cells within the immune microenvironment. The elevation of PIV may be related to tumor cell-induced immune cell infiltration and the release of inflammatory factors, thereby influencing tumor growth and invasion. Tumor cells can induce immune cell infiltration through various mechanisms, such as secreting chemokines to attract lymphocytes, monocytes, and other immune cells into tumor tissues.[36] Once activated in the tumor microenvironment, these immune cells release large amounts of inflammatory factors, such as interleukins and tumor necrosis factors, which not only directly act on tumor cells to promote their growth and invasion but also regulate other cellular components in the tumor microenvironment, such as fibroblasts and endothelial cells, further promoting tumor progression.[37] Therefore, as an indicator reflecting the body's immune-inflammatory status, an elevated PIV may reflect immune-inflammatory activity in the tumor microenvironment, closely tied to tumor cell behavior. Several studies have examined the link between PIV and breast cancer prognosis. Provenzano et al[38] demonstrated that among triple-negative breast cancer patients receiving first-line platinum-based chemotherapy, elevated PIV was linked to poorer overall survival (OS) and progression-free survival (PFS) compared to those with low PIV. This suggests that PIV may provide important references for treatment strategies in breast cancer patients. In addition to having good predictive value for traditional chemotherapy regimens, PIV has also been confirmed as a predictive indicator for the efficacy of neoadjuvant chemotherapy in breast cancer. Şahin et al[39] investigated 743 breast cancer patients receiving neoadjuvant chemotherapy and identified PIV as an independent prognosticator of

neoadjuvant chemotherapy efficacy in this cancer type. Lower PIV was linked to better prognosis. Furthermore, Tong et al[40] demonstrated that, compared to other inflammatory indicators, an elevated PIV value was an independent risk factor for axillary lymph node metastasis in breast cancer cases. This finding further highlights the important role of PIV in the prognosis of breast cancer and is expected to provide clinicians with more precise prognostic assessments and treatment decision support. In clinical practice, it is necessary to comprehensively consider the level of PIV along with other clinicopathological characteristics to develop personalized treatment plans.

Nutritional status and immune-inflammatory responses are linked to breast cancer occurrence and progression. Cancer-related inflammation is common in many malignancies and tied to tumor pathology. It also suppresses treatment responses to a certain extent and affects survival outcomes. In 2015, Chen et al[41] established the HALP score based on preoperative values of hemoglobin, albumin, lymphocytes, and platelets. They found that it demonstrated strong predictive power in the prognosis of gastric cancer and was significantly correlated with clinicopathological features such as tumor diameter and T stage, serving as a comprehensive indicator for assessing the body's immune and nutritional status. Our research revealed that the high HALP group had significantly older patients and a higher proportion of clinical stage I cases, but a lower HER2 positivity rate compared to the low HALP group. This suggests a close link between HALP and the age, clinical stage, and HER2 status of breast cancer patients. Older breast cancer patients often exhibit slower tumor growth rates and relatively better prognoses, which may be associated with the relatively stable immune function of the body. An elevation in HALP may reflect a relatively normal state of immune function, which could help inhibit tumor growth and invasion by enhancing immune surveillance and regulatory mechanisms, thereby delaying disease progression. Additionally, breast cancer patients at clinical stage I have smaller tumor burdens and relatively weaker invasive capabilities of tumor cells. An elevation in HALP may suggest that the body's immune system can better control tumor progression.[42] HER2-positive breast cancer typically has higher proliferative capacity, stronger invasiveness, and a higher risk of recurrence and metastasis. A decrease in HALP may reflect a relative deficiency in immune function, which is unable to effectively inhibit tumor growth and invasion.[43] Recent studies have shown that HALP levels are closely related to the prognosis of breast cancer patients. Jiang et al[44] found that the 5-year OS and PFS rates were 94.3% vs 90.8% and 87.5% vs 83.2% for the high HALP group and the low HALP group respectively. Zhao et al[45] likewise revealed that a low HALP score was notably linked to shorter relapse-free survival in early-stage breast cancer patients and elevated the recurrence risk. Changes in HALP levels during breast cancer treatment may provide important references for clinical decision-making. For example, in chemotherapy and targeted therapy, an elevation in HALP may suggest relatively normal immune function of the body, enabling better tolerance to the side effects of treatment and thus improving treatment efficacy. However, an elevation in HALP may also suggest the presence of a relatively stable immune microenvironment within the tumor. This stable immune microenvironment may not be conducive to the action of certain immunotherapy drugs, thereby affecting treatment outcomes. Therefore, in clinical practice, treatment plans should not be solely based on HALP levels. Instead, HALP levels should be comprehensively considered along with other clinicopathological characteristics, such as tumor stage, HER2 status, and hormone receptor status, to develop more precise and personalized treatment plans, thereby improving patient survival rates.

Expensive detection and scarce resources restrict MSI testing in breast cancer patients.[46,47] The results of this study reveal that MSI-H patients tend to exhibit low HALP levels and high PIV values. The correlation coefficient between PIV and microsatellite status is 0.202 (p=0.001), while that between HALP and microsatellite status is −0.233 (p<0.001). This indicates a strong association between both PIV and HALP and microsatellite status. Low HALP levels may reflect a compromised immune and nutritional state in MSI-H patients, whereas high PIV values may suggest an elevated level of inflammation. These disparities could be linked to the tumor's biological characteristics of MSI-H patients, such as a higher mutation load, lower metastatic potential, and sensitivity to immunotherapy. In terms of predicting microsatellite status, PIV shows an AUC of 0.867, with 100.00% sensitivity, 73.81% specificity, and an optimal cutoff value of 375 (p<0.001). HALP has an AUC of 0.879, with 100.00% sensitivity, 76.59% specificity, and an optimal cutoff

value of 35 (p<0.001). This highlights the high predictive value of both PIV and HALP for microsatellite status. Therefore, we propose that for patients for whom obtaining tissue specimens is difficult and MSI testing is challenging, calculating HALP and PIV could serve as an alternative approach to assess microsatellite status, thereby providing a reference for selecting clinical treatment plans. For patients predicted to be in the MSI-H state, immunotherapy or combination treatment strategies could be prioritized to improve treatment outcomes.

LIMITATIONS

This study is a single-center retrospective study, potentially subject to selection bias. The findings' generalizability and representativeness need further validation. Future research could adopt a prospective study design, strictly controlling the selection of study subjects and the data collection process to minimize the impact of bias. The sample size in this study is also relatively limited, which may affect the stability and generalizability of the results. Given the low incidence rate of microsatellite instability and the fact that there were only 8 MSI-H patients in this study, the research conclusions are somewhat influenced. Larger sample size studies are needed for validation in the future. Additionally, future research could further explore the mechanisms of action of PIV and HALP in the occurrence and development of breast cancer. Through in vitro cell experiments and animal model studies, the interaction mechanisms between PIV and HALP and tumor cells, as well as their regulatory roles in the tumor microenvironment, could be investigated in depth. This will contribute to further refining the immune-inflammatory theory of breast cancer and providing theoretical basis for the development of new therapeutic targets.

This study shows that preoperative PIV and HALP are closely related to breast cancer's clinicopathological features and microsatellite status, and both have high predictive value for microsatellite status. By measuring preoperative PIV and HALP levels, it is possible to make a preliminary assessment of a patient's microsatellite status before surgery, thereby providing a reference basis for selecting clinical treatment plans.

STATEMENT OF ETHICS

This study follows ethical guidelines like the Declaration of Helsinki. It was approved by the Ethics Committee of Hongqi Hospital Affiliated to Mudanjiang Medical University. All patients gave written consent after learning about the study. During the research process, patient privacy and data confidentiality were rigorously protected. All data were analyzed and stored in an anonymized format to ensure that personal identification information could not be traced.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

AI ASSISTANCE DISCLOSURE

No AI tools were used in the preparation of this manuscript.

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