Correlation analysis of patients with diabetic foot ulcers treated with tibial cortex transverse transport surgery and platelet-to-lymphocyte ratio and monocyte-to-neutrophil ratio

Sijie Yang[1,2,A–D], Kaixiang Pan[2,B,C], *Qikai Hua[2,D–F], Hongjie Su[1,B,C], Jun Hou[1,B], Kaibing Liu[2,B,C], *Jinmin Zhao[1,2,E,F]

[1] Department of Bone and Joint Surgery, The First Affiliated Hospital of Guangxi Medical University, Nanning, China
[2] Collaborative Innovation Centre of Regenerative Medicine and Medical Bioresource Development and Application Co-constructed by the Province and Ministry, Guangxi Medical University, Nanning, China

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

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Address for correspondence
Jinmin Zhao
E-mail: Zhaojinmin202309@163.com

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Conflict of interest
None declared

* Jinmin Zhao and Qikai Hua contributed equally to this work.

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Abstract

Background. Diabetic foot ulcers (DFUs) represent one of the most severe late-stage complications of diabetes. Tibial cortex transverse transport (TTT) surgery stands as the prevailing method for addressing DFUs. This surgical intervention holds the promise of expediting DFU wound healing and diminishing the rate of amputations, with the mitigation of inflammatory responses playing a pivotal role. In this study, we aim to explore the correlation between inflammation and TTT surgery, with the overarching goal of facilitating swift prognostic assessments in clinical practice.

Objectives. The correlation between the severity of DFUs and clinical test results remains ambiguous. A clinical prediction model was devised to explore the connection between DFU severity and the efficacy of TTT surgery, utilizing straightforward and efficient clinical indicators.

Materials and methods. Clinical data and examination results were gathered by tracking hospitalized DFU patients who underwent TTT surgery at the First Affiliated Hospital of Guangxi Medical University (Nanning, China). Indicators associated with DFU severity and wound healing time post-surgery were identified through logistic regression and least absolute shrinkage and selection operator (LASSO) regression analyses. Subsequently, a clinical prediction model was constructed. Finally, the intersection of these 2 sets of indicators revealed factors correlated with wound severity and post-operative healing duration.

Results. Our study was comprised of 202 patients who were categorized into 2 groups based on Wagner's grading classifications. Utilizing Student's t-tests, LASSO regression and logistic regression analyses, we identified 3 factors indicative of DFU severity: platelet-to-lymphocyte ratio (PLR), mixed lymphocyte reaction (MLR) and hemoglobin (HGB). Univariate COX regression analysis revealed 12 factors such as: white blood cells (WBC), neutrophils (NEUT), monocytes (MO), PLR, MLR, neutrophil-to-lymphocyte ratio (NLR), erythrocyte sedimentation rate (ESR), age, lymphocytes (LY), monocyte-to-neutrophil ratio (MNR), uric acid (UA), and albumin (ALB) associated with the postoperative healing duration. Ultimately, we identified 2 factors, PLR and MNR, at the intersection of these 2 datasets.

Conclusions. Platelet-to-lymphocyte ratio and MNR were identified as factors associated with both the severity of DFUs and the prognosis following TTT surgery.

Key words: platelet-to-lymphocyte ratio, diabetic foot ulcer, prognostic analysis, TTT surgery, monocyte-to-neutrophil ratio

Background

Diabetic foot ulcers (DFUs) are a severe late complication of diabetes and a public health problem.[1] Presently, the global morbidity of DFUs is about 6.3%.[2] Moreover, patients with DFU have a higher amputation rate and mortality. Around 1/4 of diabetic patients develop a DFU in their lifetime.[3] Many factors contribute to the occurrence and development of a DFU. Improper management of blood glucose levels, longer duration of diabetes, insulin use, foot ischemia, and ulcers have been proven to be important risk factors leading to foot ulcers,[4] and among these factors, infection plays an extremely important role.

The pathologic mechanism of DFUs is not completely understood. However, the role of the inflammatory response cannot be ignored in DFUs. The inflammatory stage is an important process in wound healing, which can directly affect the normal healing of the wound. However, a prolonged presence of inflammation is often cited as the primary reason for the failure of diabetic foot wounds to heal. Some studies have shown that chronic inflammation is associated with the pathogenesis of diabetes and the development of its complications.[5] In the past, clinical doctors have used simple laboratory tests to determine inflammation within the patient's body, such as white blood cell (WBC) count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). However, these test results cannot be analyzed separately and must be combined with others. Recent studies have demonstrated that alterations in the composition of circulating leukocytes serve as a more effective indicator of inflammation, enabling a swift and accurate determination of the inflammatory status in patients.[6,7]

The platelet-to-lymphocyte ratio (PLR) and monocyte-to-neutrophil ratio (MNR) are novel systemic inflammatory response markers that reflect the inflammatory status. Several studies have investigated these markers because they are easily determined from the peripheral blood.

The tibial cortex transverse transport (TTT) surgery is a novel and significantly effective surgery to treat DFUs.[8] It was developed based on Ilizarov technology. Qu et al. first reported the successful treatment of thromboangiitis obliterans (TAO) using TTT surgery.[9] Chen et al. first used TTT surgery to treat DFUs, achieving a good wound healing rate and limb salvage rate.[8] Yang et al. pointed out that TTT surgery can not only promote wound healing by enhancing vascular regeneration but also enhance wound immunity.[10] The immune system of the affected person determines the inflammatory state of the body. However, the correlation between DFUs after TTT surgery and PLR and MNR was not reported.

Objectives

To our knowledge, no research on predicting the prognosis of patients undergoing TTT surgery has been published. This study aimed to assess the correlation between PLR and MNR levels and the severity of DFUs. Additionally, we investigated the association between PLR, MNR and the prognosis of DFUs following TTT surgery.

Materials and methods

TTT surgery

The surgical procedure was conducted following the methodology outlined in a previous study,[8] and detailed research procedures are provided in Fig. 1.

The patients included in the study were diagnosed with diabetes based on the American Diabetes Association (ADA) criteria.[11] They were at least 18 years old and had 1 or more non-healing ulcers below the ankle for 6 months or more. All patients had previously undergone TTT surgery. They were excluded if they suffered from severe pulmonary, urinary tract, a systemic infection, or from severe dysfunction of the heart, lung, kidney, brain, or other organs. The participants were also excluded if they had used anticoagulation, antiplatelet, antibiotics, or other drugs known to affect the examination results in the previous months. In addition, patients were excluded if their clinical data were incomplete or if they had undergone amputation surgery or a repeat TTT surgery.

The research process is clearly shown in Fig. 1, including 2 main aspects of the research. First, based on the Wagner's grading of the selected patients, they were divided into 2 groups (Wagner's 2–3 and Wagner's 4). By comparing the differences in baseline data between the 2 groups, differential factors were obtained (Table 1). In order to identify differential factors related to the severity of DFU patients, least absolute shrinkage and selection operator (LASSO) and logistic regression analysis were employed. These factors are referred to as severity factors (SFs). Second, Cox regression analysis was used to analyze patients after TTT surgery and identify factors related to wound healing. We refer to these factors as TTT-prognosis-related factors (TTT-PFs). By intersecting these 2 datasets, factors that are both related to wound severity and can predict the prognosis after TTT surgery were obtained (TTT-SFs and PFs).

After the above screening, 202 DFU patients were included in the study from July 2016 to July 2021. These patients were divided into 2 groups based on the Wagner's grading stages. Their clinical data, such as age, sex and inspection results, are presented in Table 1. All the patients were followed up for at least 1 year.

Statistical analyses

Student's t-test was used to compare the means of the continuous variables between 2 groups and a one-way analysis of variance (ANOVA) test compared 3 or more groups. Logistic regression analysis screened for correlations between the variables. The Box–Tidwell test, variance influence factor (VIF) and Cook's distances were used to test the accuracy

Table 1. Baseline of patients based on Wagner's grade 2/3 (n = 135) and 4 (n = 67). The χ^2 test was used to test for gender differences. Student's t-test was used to compare the means of the continuous variables between 2 groups

Factors		Wagner's 2/3 (n = 135) (n/M ±SD)	Wagner's 4 (n = 67) (n/M ±SD)	Overall (n = 202) (n/M ±SD)	t/x^2	p-value
Sex	female	34	11	45	1.988	0.159
	male	101	56	157	–	–
Age		62.40 ±9.68	61.12 ±9.07	61.98 ±9.48	0.904	0.367
BMI		24.03 ±3.15	24.80 ±2.99	24.28 ±3.11	1.658	0.099
WBC		9.42 ±3.34	15.20 ±7.10	11.33 ±5.61	6.322	<0.001*
PLT		390.55 ±150.47	380.64 ±123.24	387.26 ±141.79	0.499	0.618
NEUT		6.43 ±3.01	12.66 ±6.77	8.49 ±5.46	7.184	<0.001*
LY		1.91 ±0.64	1.34 ±0.53	1.72 ±0.69	6.730	<0.001*
MO		0.75 ±0.29	1.00 ±0.50	0.83 ±0.39	3.850	<0.001*
PLR		229.86 ±125.96	318.94 ±132.08	259.41 ±134.44	4.582	<0.001*
MLR		0.43 ±0.21	0.84 ±0.44	0.56 ±0.36	7.278	<0.001*
MNR		0.13 ±0.06	0.08 ±0.03	0.12 ±0.06	7.438	<0.001*
NLR		3.74 ±2.27	11.13 ±7.09	6.19 ±5.67	8.320	<0.001*
HGB		104.8 ±20.51	94.93 ±25.95	101.04 ±22.81	2.726	0.007*
CR		100.84 ±101.73	181.62 ±247.46	127.63 ±168.70	2.567	0.012*
UA		327.27 ±109.08	311.44 ±157.08	322.02 ±126.84	0.741	0.461
CCR		70.77 ±27.92	63.93 ±31.12	68.50 ±30.20	1.422	0.158
ALB		33.81 ±5.83	30.53 ±6.21	32.72 ±6.16	3.686	<0.001*
ESR		70.2 ±30.38	89.63 ±34.16	76.52 ±32.92	4.142	<0.001*
TC		4.27 ±1.33	4.50 ±2.27	4.34 ±1.70	0.756	0.452
TG		1.53 ±0.93	1.68 ±1.03	1.58 ±0.97	1.060	0.291
HDL		0.90 ±0.31	0.89 ±0.46	0.90 ±0.36	0.214	0.831
LDL		2.62 ±1.04	2.75 ±1.60	2.66 ±1.25	0.582	0.562

Shapiro–Wilk test was used to test the normality of data; F-test was used to test the variance of 2 sets of data; *p ≤ 0.05; BMI – body mass index; SD – standard deviation; WBC – white blood cells; PLT – platelets; NEUT – neutrophils; LY – lymphocytes; MO – monocytes; PLR – platelet-to-lymphocyte ratio; MLR –mixed lymphocyte reaction; MNR – monocyte-to-neutrophil ratio; NLR – neutrophil-to-lymphocyte ratio; HGB – hemoglobin; CR – creatinine; UA – uric acid; CCR – creatinine reduction ratio; ALB – albumin; ESR – erythrocyte sedimentation rate; TC – total cholesterol; TG – thyroglobulin; HDL – high-density lipoprotein, LDL – low-density lipoprotein.

of the logistic regression model. Nagelkerke's R^2 was used to evaluate the goodness of fit in logistic regression analysis and to evaluate the interpretability of classification models. The "Lars" package of the R software (R Foundation for Statistical Computing, Vienna, Austria) was employed for the LASSO regression analysis and visualization. The "pROC" package computed the receiver operating characteristic (ROC) curves to assess the accuracy of the factors and nomogram.[12] A univariate Cox regression analysis was conducted to identify prognostic factors. The proportional risk hypothesis, logarithmic risk function and linear relationships between predictive factors were identified using Schoenfeld residuals. The goodness of fit of the Cox regression model was evaluated using the concordance index (C-Index). The survival package was used to perform a predictive analysis. In the absence of further specification, statistical significance was defined as a 2-sided probability value less than 0.05. The IBM SPSS v. 26 (IBM Corp., Armonk, USA) and R. 4.1.0 were employed in separate instances.

Results

PLR, MNR and HGB are associated with the severity of DFUs

Significant difference analyses were identified for 12 factors between the 2 groups (Table 1). The ROC curves indicated good accuracy of every factor (Fig. 2A,B). After the LASSO and logistic regression analysis, which identified 7 factors (LY, PLR, MLR, MNR, NLR, HGB, and CR) and 3 factors (PLR, MNR and HGB), respectively, by taking the intersection of the 2 sets, 3 factors factors (PLR, MNR and HGB) were identified as SFs (Table 2, Fig. 2C–F). Additionally, a nomogram was established based on these factors to describe DFU severity (Fig. 3A–C). Moreover, the ROC curve was determined to be accurate (Fig. 3B).

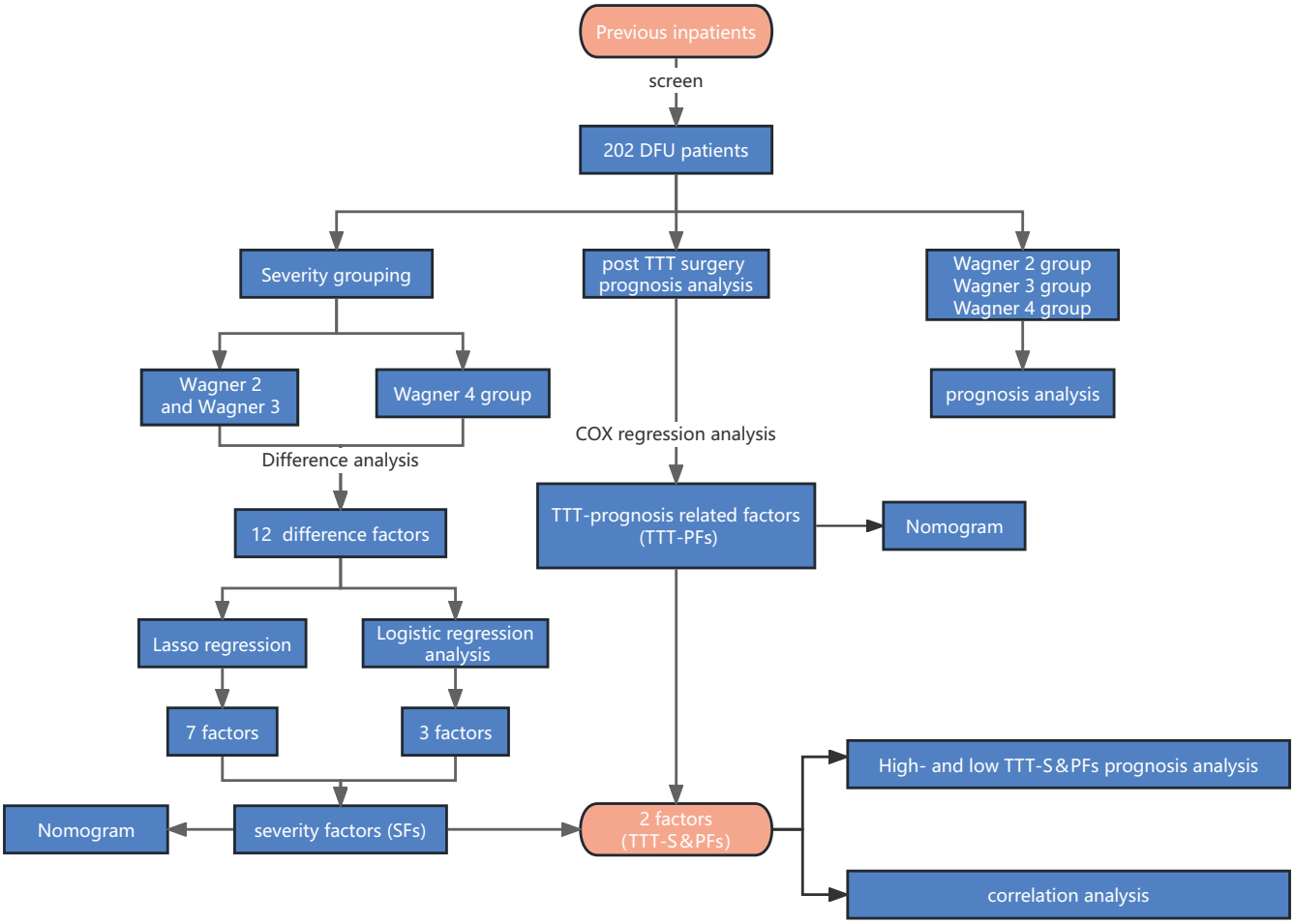

Fig. 1. Research process of this study. This study is mainly divided into 3 parts, all based on 202 diabetic foot ulcer (DFU) patients who underwent tibial cortex transverse transport (TTT) surgery. Through differential analysis and correlation analysis of the patients, TTT-S and PFs were identified, and a survival analysis of wound healing in patients was conducted

TTT-S and PFs – TTT-severity and prognosis related factors.

Table 2. Binary logistic regression analysis based on 11 factors

Factors	Wald	p-value	OR	95% CI low	95% CI up
WBC	0.907	0.341	0.528	0.142	1.963
NEUT	0.592	0.442	1.752	0.420	7.313
MO	0.204	0.652	4.300	0.008	2,423.260
PLR	7.254	0.007*	0.856	0.745	0.928
MLR	1.753	0.185	107.882	0.106	110,233.896
MNR	4.581	0.032*	0.032	0.015	0.079
NLR	0.251	0.616	1.147	0.671	1.959
HGB	6.455	0.011*	0.903	0.824	0.997
CR	0.265	0.607	1.008	0.971	1.128
ALB	0.007	0.932	0.987	0.905	1.174
ESR	0.097	0.756	0.995	0.953	1.083

*$p < 0.05$. WBC – white blood cells; PLT – platelets; NEUT – neutrophils; LY – lymphocytes; MO – monocytes; PLR – platelet-to-lymphocyte ratio; MLR –mixed lymphocyte reaction; MNR – monocyte-to-neutrophil ratio; NLR – neutrophil-to-lymphocyte ratio; HGB – hemoglobin; CR – creatinine; UA – uric acid; CCR – creatinine reduction ratio; ALB – albumin; ESR – erythrocyte sedimentation rate; TC – total cholesterol; TG – thyroglobulin; HDL – high-density lipoprotein, LDL – low-density lipoprotein; 95% CI – 95% confidence interval; OR – odds ratio.

Nomogram for prognosis-related factors for DFU patients

Univariate Cox regression analysis identified 12 TTT-PFs related to wound healing in DFU patients after TTT surgery (Fig. 4A). Among them, 7 factors (WBC, NEUT, MO, PLR, MLR, NLR, and ESR) negatively affected the recovery of DFUs. Conversely, 5 factors (age, LY, MNR, UA, and ALB) predicted a better prognosis for DFUs (Fig. 4A). The prediction nomogram was established from these 12 factors (Fig. 4B)

By taking the intersection of SFs and TTT-PFs, 2 factors (PLR and MNR) were considered to be TTT-S and PFs (Fig. 4C) and the nomogram was accurately predicted (Fig. 4D).

Prognostic analysis

Patients were separated into 3 groups based on the Wagner's grading (Fig. 5A). The prognosis analysis results showed that patients with a Wagner's grade 4 ulcer had a lower healing rate and took a longer time to heal. In contrast, patients

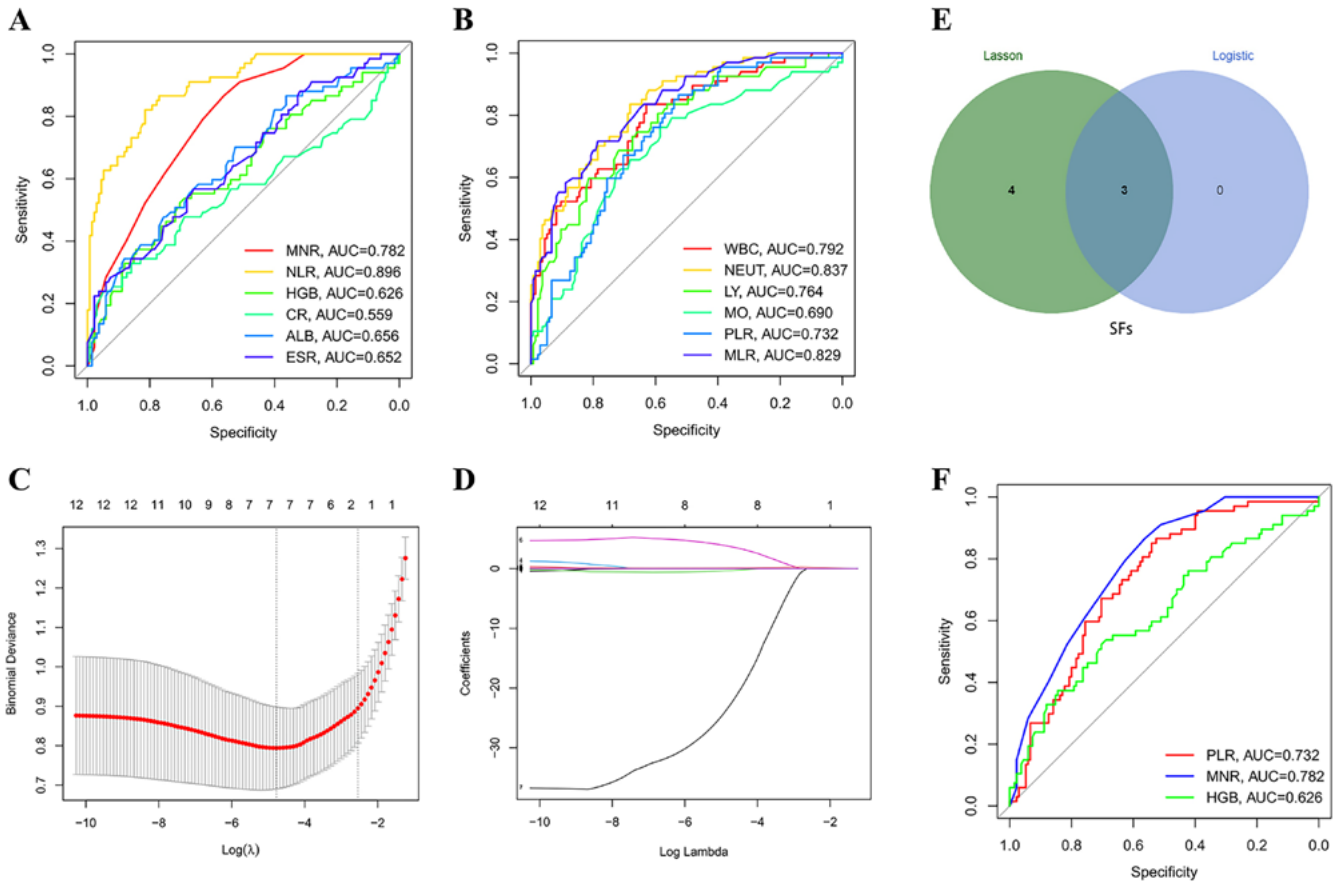

Fig. 2. Identification of SFs. A,B. ROC curves of the 12 differential factors; C. Least absolute shrinkage and selection operator (LASSO) coefficient profiles of the 7 characteristics; D. 1000-fold cross-validation was used to generate the optimal penalty parameter lambda; E. Identification of SF Venn diagrams. After LASSO and logistic regression analysis of the 12 differential factors, 3 SFs were discerned, identifying the point of intersection; F. ROC curves for the 3 SFs

SFs – severity factors; ROC curve – receiver operating characteristic curve; AUC – area under the ROC curve; WBC – white blood cells; PLT – platelets; NEUT – neutrophils; LY – lymphocytes; MO – monocytes; PLR – platelet-to-lymphocyte ratio; MLR –mixed lymphocyte reaction; MNR – monocyte-to-neutrophil ratio; NLR – neutrophil-to-lymphocyte ratio; HGB – hemoglobin; CR – creatinine; UA – uric acid; CCR – creatinine reduction ratio; ALB – albumin; ESR – erythrocyte sedimentation rate.

with Wagner's grades 2 and 3 exhibited a higher healing rate and a shorter healing time (Fig. 5A). When we divided patients into high- and low-groups based on the optimal cutoff values for PLR and MNR values, their survival analysis results showed different outcomes. The high-MNR group had a higher healing rate and shorter healing time (Fig. 5B). In contrast, the PLR group exhibited the opposite trend (Fig. 5C). When analyzing the PLR and MNR values of patients with different Wagner's grades, we found that as the Wagner's grade increased, the MNR values tended to decrease (Fig. 6A). However, the PLR values exhibited the opposite trend (Fig. 6B). In other words, the PLR increased, and the MNR decreased as the Wagner's grade increased. Correlation analysis also showed that PLR was negatively related to MNR (R = −0.44; p = 3.5e-11 (Fig. 6C,D).

Discussion

Diabetes is a major chronic disease, with the number of affected individuals continuously growing. In 2015, it reached 450 million.[13,14] Diabetic foot ulcers are a significant complication of diabetes, affecting about 25% of people with diabetes.[2,15] Diabetic foot ulcers are mainly associated with peripheral neuropathy and lower extremity arterial disease.[16] However, despite extensive research, the precise mechanism of DFUs remains unclear. Diabetes causes systemic effects on the patient's immune function and alters the state of inflammation. Diabetic foot ulcers are prone to co-infection, which can lead to complications such as gangrene, osteomyelitis and the progression to severe DFUs. Patients with DFUs have a higher mortality and amputation rate than the general diabetic population.

Treatment of DFUs, especially severe DFUs, is a worldwide challenge. Conventional surgical treatment includes debridement and revascularization. These treatments help avoid amputations in some patients and heal the ulcer. However, the rate of recurrence remains high.[15] Tibial cortex transverse transport surgery is effective for treating severe and recalcitrant DFUs. Tibial cortex transverse transport surgery has been shown to result in a higher rate of wound healing and limb salvage, as well as a lower recurrence rate.

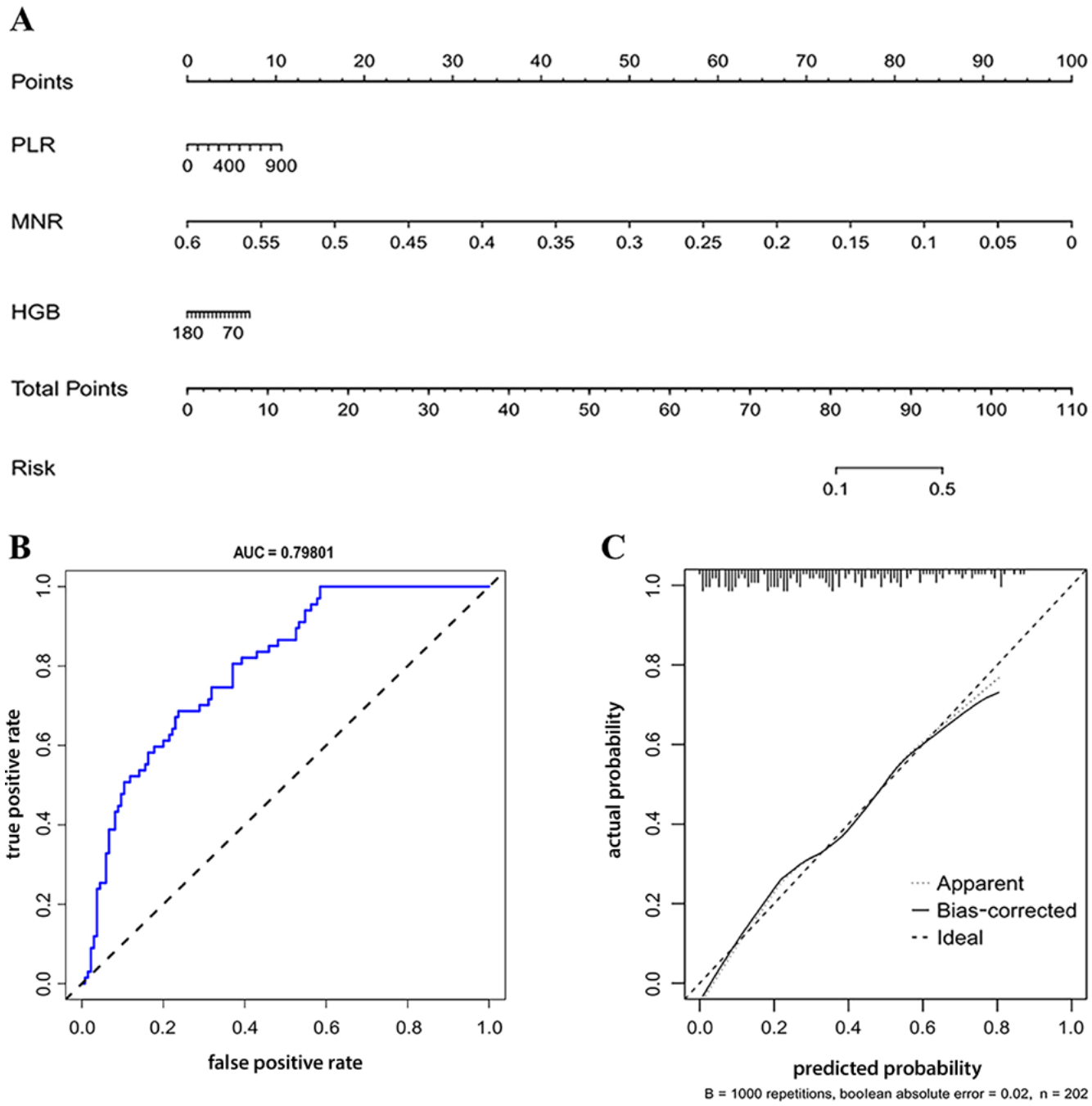

Fig. 3. Establishing a nomogram based on SFs. A. The nomogram is used to identify the severity of DFUs; B. ROC curve of the nomogram; C. Calibration curves for predicting DFU severity

SFs – severity factors; ROC curve – receiver operating characteristic curve; DFU – diabetic foot ulcer; AUC – area under the ROC curve; PLR – platelet-to-lymphocyte ratio; HGB – hemoglobin.

This surgical approach has also been shown to enhance angiogenesis and immunomodulation in patients.[17]

In this study, we proposed the concept of TTT-S and PFs for the first time, which had not been explored in previous research. Our study identified 2 TTT-S and PFs, PLR and MNR, which were correlated with the Wagner's grading of DFUs. Additionally, these factors predicted the prognosis of DFU patients treated with TTT surgery. Platelet-to-lymphocyte ratio is an inflammatory index that has been linked to both the diagnosis and prognosis of diabetes.[17–20] In the present study, PLR showed a positive correlation with the severity of the DFU, as indicated by the Wagner's DFU grading system. These findings are consistent with previous research, indicating the reliability of our results. At the same time, PLR was associated with the prognosis of wound healing in DFU patients treated with TTT surgery. A higher PLR predicted a longer time to heal after TTT surgery. This correlation has not been reported

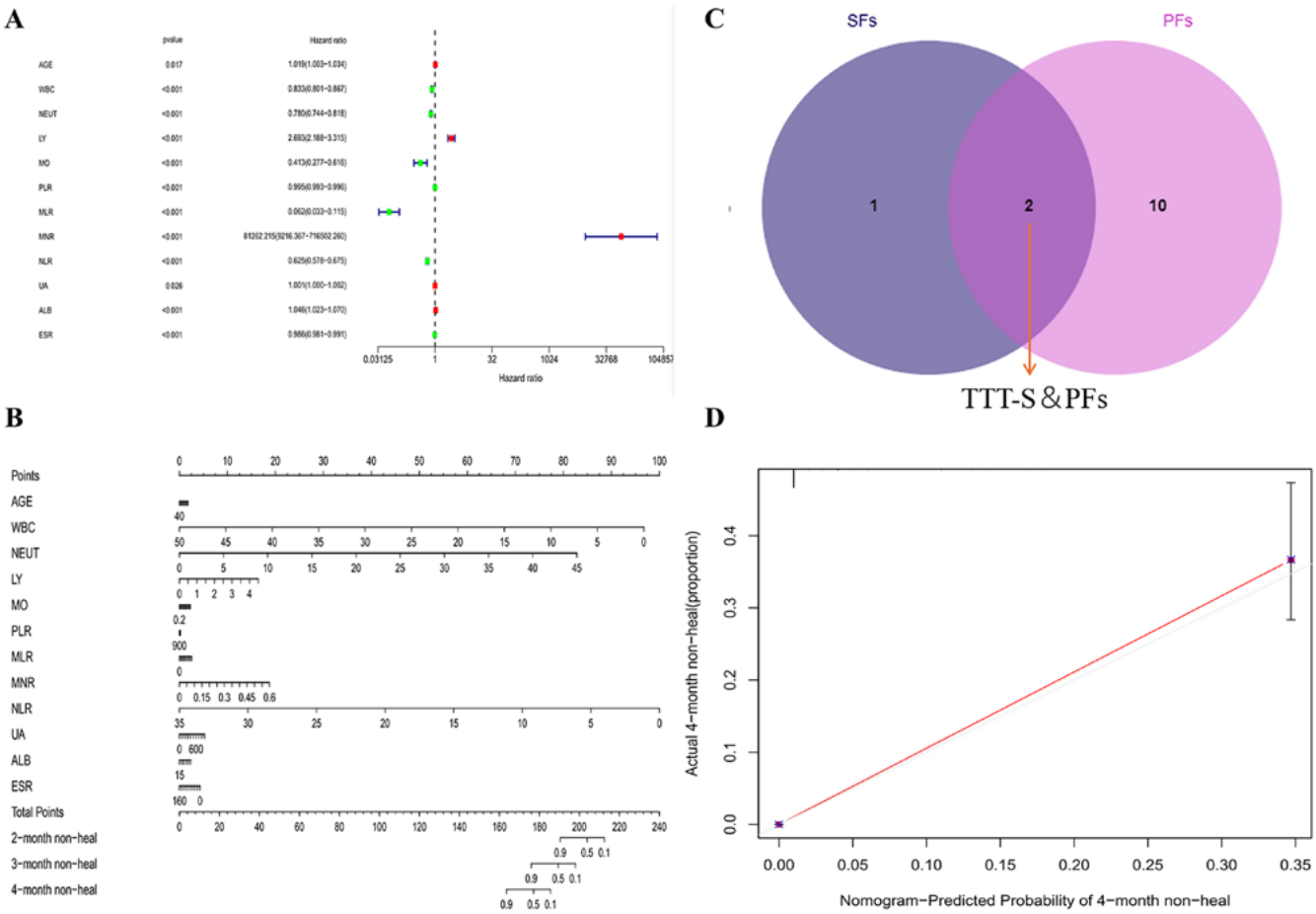

Fig. 4. Identification of TTT-S and PFs and establishment of a nomogram related to wound healing after tibial cortex transverse transport (TTT) surgery. A. Univariate Cox regression analysis identified TTT-PFs; B. Nomogram established based on TTT-PFs; C. Venn diagram shows the intersection of severity factors (SFs) and TTT-PFs to derive TTT-S and PFs; D. Calibration curves for predicting the possibility of 4-month non-healing after TTT surgery based on the nomogram

TTT-PFs – wound prognosis relative factors post TTT surgery; AGE – advanced glycation end products; WBC – white blood cells; PLT – platelets; NEUT – neutrophils; LY – lymphocytes; MO – monocytes; PLR – platelet-to-lymphocyte ratio; MLR –mixed lymphocyte reaction; MNR – monocyte-to-neutrophil ratio; NLR – neutrophil-to-lymphocyte ratio; HGB – hemoglobin; CR – creatinine; UA – uric acid; CCR – creatinine reduction ratio; ALB – albumin; ESR – erythrocyte sedimentation rate.

earlier. Therefore, PLR can serve as a simple clinical index for predicting the time required for wound healing after TTT surgery.

Diabetes creates a chronic inflammatory state in patients. Therefore, detecting inflammation indicators can provide insights into the severity of diabetes and the associated risk of complications.[21–23] One of the main causes of a DFU is linked to peripheral arterial disease (PAD).[24,25] Patients with DFUs and PAD are at higher risk of experiencing unhealed wounds, requiring amputations and facing increased mortality rates.[26,27] Additionally, PAD serves as a predictive factor for the risk of amputation in DFU patients.[28] Previous studies have reported the association between increased PLR and critical limb ischemia (CLI) and PAD.[29] Chronic inflammation over a long period impairs immune function and reduces the number of lymphocytes. Chronic inflammation over a long period leads to an elevation in platelets and inflammatory factors. This process damages the vascular endothelium and contributes to the development of atherosclerosis, which is the pathological basis for the further PAD formation.[30]

The MNR is a ratio of peripheral blood cells and serves as a novel indicator reflecting the level of inflammation. Related studies have demonstrated that MNR represents a combination of thrombosis and inflammation.[31] The current study revealed that monocytes and neutrophils negatively impact healing in DFU patients treated with TTT surgery, whereas MNR exhibits the opposite effect. However, these findings are not contradictory. Monocytes are the primary cells of innate immunity and play a central role in initiating and resolving inflammatory responses to pathogens. Several studies have shown that monocytes are functionally impaired in diabetic patients, with reduced anti-inflammatory capacity and immune differentiation.[32,33] Monocytes maintain a balance between pro-inflammatory and anti-inflammatory responses. Inflammatory development is stronger in the early stages of wound healing when the M1 phenotype dominates

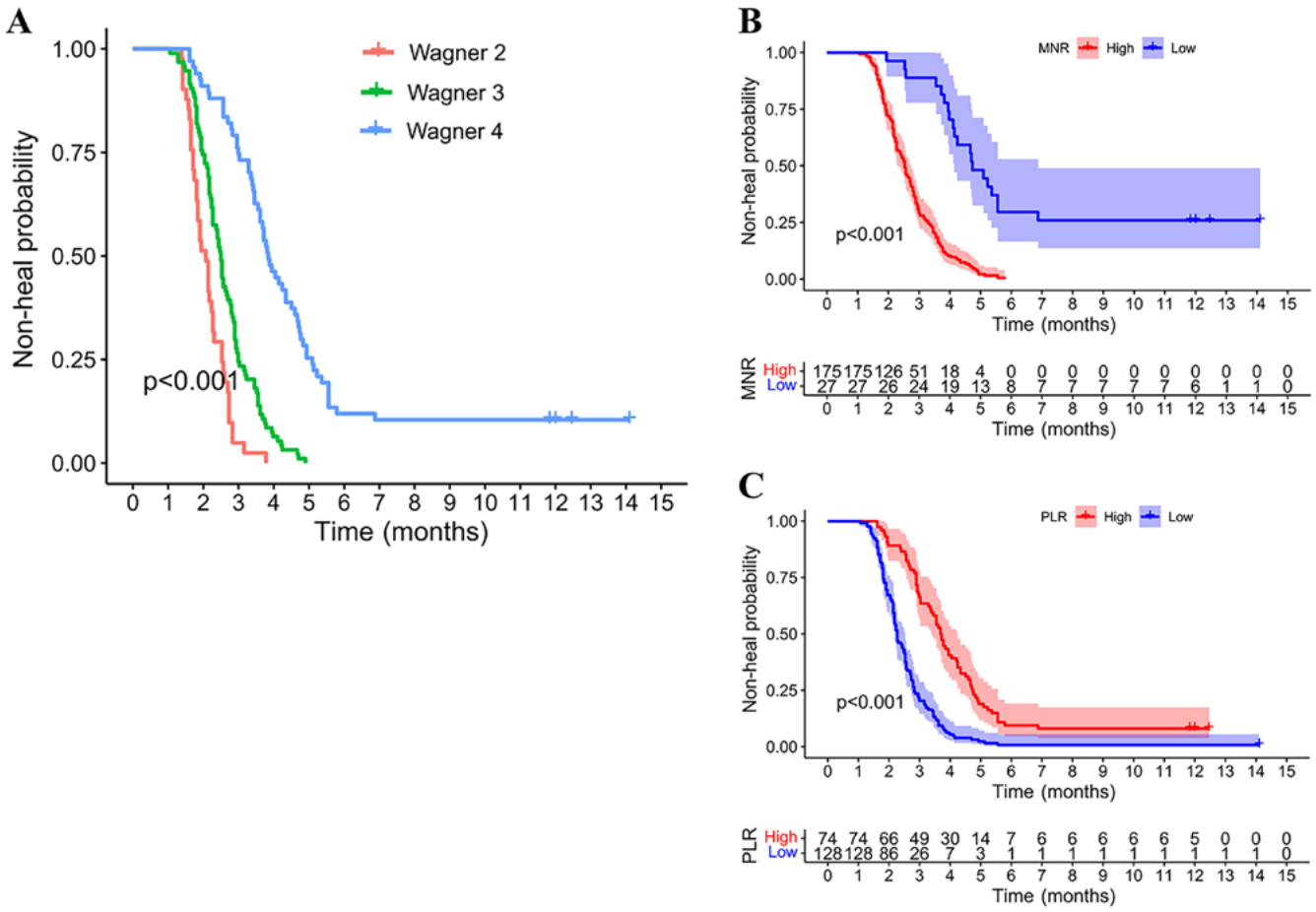

Fig. 5. Kaplan–Meier curve analysis for wound prognosis. A. Prognostic analysis of wound healing in diabetic foot ulcer (DFU) patients with the Wagner's grades 2/3 group and Wagner's 4 group after tibial cortex transverse transport (TTT) surgery ($\chi^2 = 96.207$); B. Prognostic analysis of wound healing in DFU patients with high- and low-monocyte-to-neutrophil ratios (MNRs) after TTT surgery ($\chi^2 = 74.918$); C. Prognostic analysis of wound healing in DFU patients with high- and low-platelet-to-lymphocyte ratios (PLRs) after TTT surgery ($\chi^2 = 65.214$)

monocytes. In the later stages of wound healing, the state of inflammation decreases, and the M2 phenotype predominates. Diabetic foot ulcers are persistent non-healing wounds in a state of chronic inflammation, with a predominant M1 phenotype for the mononuclear cells. These wounds have been in the early stages of healing for a long time, with an increased number of mononuclear cells and delayed healing. Elevated WBC counts in patients with impaired glucose tolerance increase the neutrophils.[34,35] The neutrophil elevation is more pronounced in DFU patients with co-infection, suggesting a significant inflammatory response. The MNR increases as inflammation decreases during wound healing. The observation is consistent with the present finding. This study also observed reduced MNR in patients with high Wagner's grades. The possible reason could be a greater severity of wound infections and higher levels of inflammation in these patients. Therefore, the detection of these inflammatory indicators can provide us with some strategies for the early prediction of wound healing after TTT surgery.

It is evident that certain baseline data (such as gender, age and body mass index (BMI)) in this study do not show significant differences across different Wagner's grades. While some studies indicate an association between baseline data and the severity of DFUs, others present conflicting findings.[36,37] Thus, there remains controversy regarding the relationship between gender, age, BMI, and the severity of DFUs, necessitating further research for deeper exploration. Additionally, in the context of blood tests, the focus primarily lies on immune-related cells correlating with the Wagner's classification of DFUs, aligning precisely with the pathophysiological processes of DFUs. Furthermore, certain inflammatory markers, such as ESR, also correlate with DFUs. It is evident that the healing of DFUs is a highly complex process.[38] Hence, the mere elevation or reduction of a single indicator cannot entirely predict the healing of DFUs. Therefore, a comprehensive analysis of various indicators is crucial for predicting the healing of DFUs. Our research findings precisely support this viewpoint, highlighting the urgency of further refining comprehensive indicators for predicting DFU healing.

Limitations

This study has several limitations that should be acknowledged. First, there may be some information bias

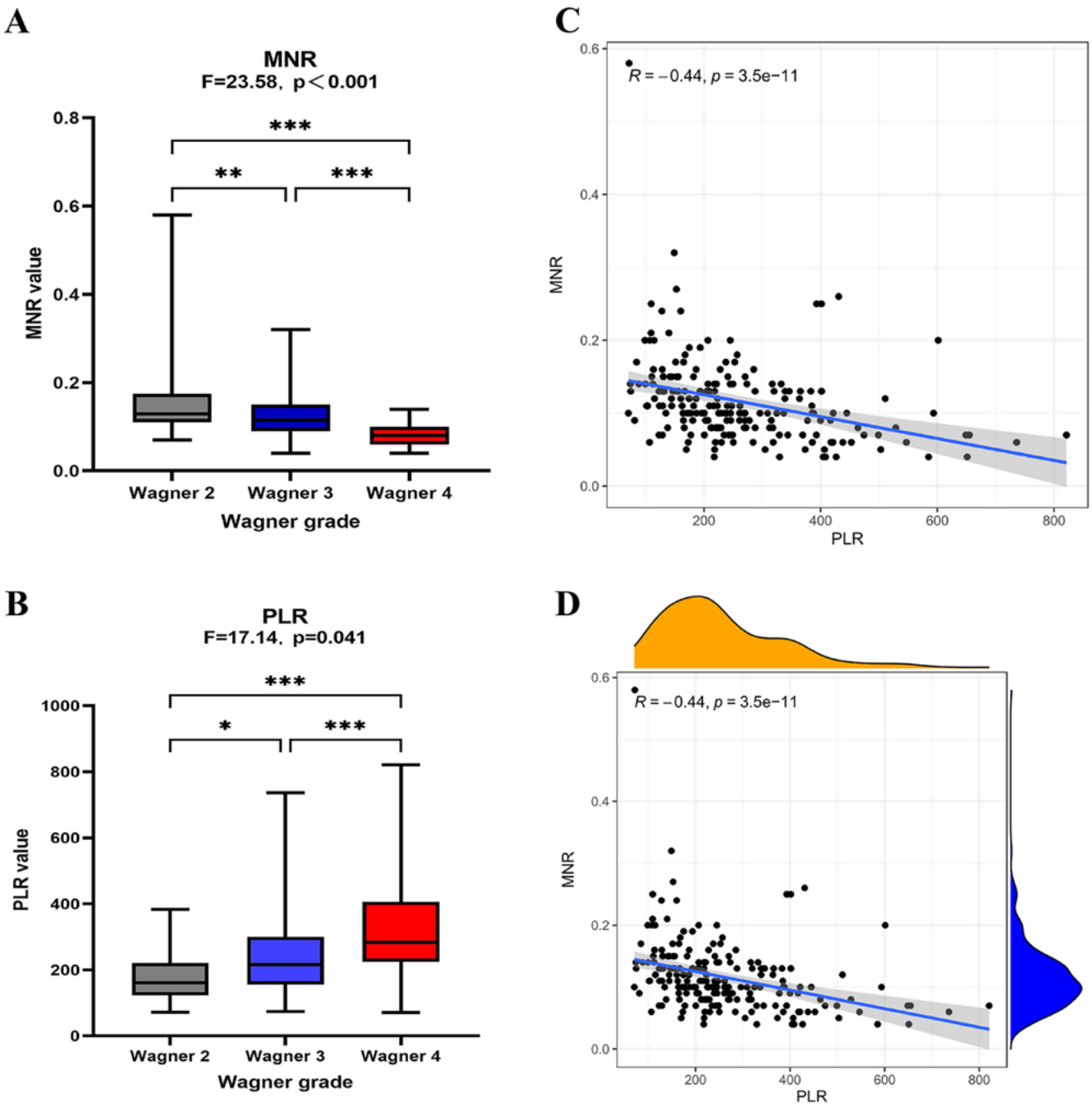

Fig. 6. Correlation analysis between platelet-to-lymphocyte ratio (PLR) and monocyte-to-neutrophil ratio (MNR). A. Comparison of MNR values in patients with different Wagner's grades. The MNR value decreased as the Wagner's level increased; B. Comparison of PLR values in patients with different Wagner's grades. The PLR value increased as the Wagner's level increased; C,D. Correlation analysis of the PLR and MNR (Spearman's analysis)

because it is a retrospective study. Additionally, the study only analyzed a limited number of influencing factors. It did not examine all indicators associated with DFU severity and healing after receiving TTT surgery for DFUs. Furthermore, although the ROC curve showed good accuracy, the developed nomogram model was not sufficient for use in clinical practice. Follow-up studies are needed to refine the diagnostic model. Therefore, a multicenter and more extensive cohort study is required. In the future, the model can be updated for better accuracy and improved prediction to help guide the treatment of DFUs.

Conclusions

The present study provides a comprehensive summary of the risk factors associated with the severity of DFUs and their prognosis. Platelet-to-lymphocyte ratio and MNR are critical predictors of DFU severity and prognosis after TTT surgery. The results of this study can guide risk stratification and inform preoperative prevention strategies for DFU patients. Additionally, they can contribute to a better prognosis for patients undergoing TTT surgery.

Supplementary data

The supplementary materials are available at https://doi.org/10.5281/zenodo.10952319. The package includes the following files:

Supplementary Fig. 1. A scatter plot illustrating the Cook's distance based on a binary logistic regression analysis established from 202 samples. Each point represents the Cook's distance for a sample When the Cook's distance is greater than 1, it indicates an extreme outlier, which should be excluded from the model.

Supplementary Fig. 2. The Schoenfeld residuals of 12 models in a univariate Cox regression analysis. It is evident that the residuals of all models show no trend over time, indicating that the professional hazards assessment of the Cox regression is valid.

Supplementary Table 1. Box–Sidewell test for validation linear relationship between predictors and the logit of the response variable.

Supplementary Table 2. VIF and tolerance are used to analyze the collinearity of logistic regression analysis models. Setting tolerance greater than 0.1 and VIF less than 5 is considered a perfect result.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

ORCID iDs

Sijie Yang https://orcid.org/0000-0002-4856-8717
Hongjie Su https://orcid.org/0000-0001-7685-6970
Jun Hou https://orcid.org/0009-0001-4437-9580

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