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ORIGINAL RESEARCH

Identification of Risk Factors for Poor Prognosis and Analysis of Their Correlation with Ulcer Severity in Diabetic Foot Patients Undergoing Digital Subtraction Angiography-Guided Intervention

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Objective: To identify risk factors for prognosis in diabetic foot patients undergoing digital subtraction angiography (DSA) intervention and analyze their correlation with ulcer severity.

Methods: This retrospective study analyzed 135 diabetic foot patients who underwent DSA-guided intervention between August 2023 and January 2025. Patients were classified good and poor prognosis groups based on 6-month outcomes. We compared demographic data and clinical laboratory indexes between groups. Statistically significant variables were analyzed using *Logistic* regression to identify independent risk factors. The receiver operating characteristic (ROC) curves and *Pearson* correlation analysis were employed to assess the diagnostic value of these factors and correlation with ulcer severity.

Results: The stratified diabetic foot ulcer risk score (SINBAD) was significantly higher in patients with poor prognosis (7.15±2.76) compared to those with good prognosis (3.24±1.81); Serum levels of procalcitonin (PCT), galactoagglutinin-3 protein (Gal-3), noncoding RNA molecule with circular structure (Hsa_circ_0057362), interleukin-6 (IL-6), and serum C-reactive protein (CRP) was significantly elevated in the poor prognosis group ($P < 0.05$). Pearson correlation analysis revealed positive corrections between these biomarkers and ulcer severity (r=0.283, 0.240,0.434, 0.370, 0.443, respectively; all $P < 0.05$); *Logistic* regression analysis identified PCT, Gal-3, Hsa_circ_0057362, IL-6, and CRP as independent influencing factors for poor prognosis in diabetic foot. Furthermore, ROC curve analysis demonstrated that each of these indicators possessed a certain degree of predictive value for poor prognosis following diabetic foot surgery.

Conclusion: A plethora of risk factors, including PCT, Gal-3, Hsa_circ_0057362, IL-6 and CRP, influence poor prognosis in diabetic foot patients undergoing DSA-guided intervention. These biomarkers demonstrate significant correlations with ulcer severity and hold substantial clinical utility in the predicting postoperative outcomes. Early identification of patients at risk for poor prognosis enables the implementation of targeted interventions, thereby effectively improving patient outcomes.

Keywords: digital subtraction angiography intervention, diabetic foot, ulcer severity, galactoagglutinin-3 protein

Introduction

Diabetes is a systemic metabolic disorder induced by defective insulin secretion or impaired biological function, and represents one of the most prevalent chronic diseases in China. According to estimates, the global prevalence of diabetes

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is projected to reach 10.00% by 2045, affecting approximately 693 million people.[1] In accordance with the International Diabetes Federation (IDF),[2] diabetes caused 4.2 million deaths in 2019, and up to 463 million adults aged 20–79 years had diabetes. These figures underscore that[3] diabetes not only severely impact patients' quality of life, physical and mental health, but also lead to serious complications such as diabetic foot ulcers (DFU), which exacerbate the disease and significantly increase mortality risk. DFU is a widespread global health issue, characterized by skin lesions and loss of epithelial tissue, progressing to affect the dermis and deeper layers, and in severe cases, even involving bone and muscle. Epidemiological studies have found[4] that DFU has been clinically categorized as a marker of high mortality in diabetic patients, which can range from 39.00% to 68.00% within 5 years after cut-off.

At this stage, the clinical treatment of diabetic foot is mainly through the improvement of microcirculation drugs, anti-infective drugs, hyperbaric oxygen, and hypoglycemic drugs, and a single program cannot fundamentally solve its pathological changes.[5] Imaging examination can effectively grasp the blood vessels, soft tissues and bone changes of patients, accurately determine their condition, and guide the smooth implementation of treatment. DSA-guided intervention can effectively improve the blood supply of diabetic foot patients, relieve symptoms, promote wound healing, reduce complications, and ultimately reduce the risk of amputation, mainly through precise vascular imaging assessment, accurate localization of lesions, and vascular intervention treatment and long-term outcome monitoring.[6] Related scholars' studies have confirmed[7] that vascular intervention can rapidly open occluded arteries, promote increased blood supply to the lower extremities, and accelerate wound healing. However, several studies have pointed out[8–10] that the risk of restenosis is highly susceptible after interventional procedures, increasing the incidence of poor prognosis. Although DSA-guided intervention can temporarily restore blood flow, vascular walls of diabetic patients are accompanied by different degrees of chronic inflammation, calcification and other pathologic changes, resulting in long-term poor blood flow, so that the therapeutic effect is poor. Coupled with poor blood supply, wound healing is more limited, which is very likely to cause restenosis, thus increasing the risk of poor prognosis. Currently, the clinical assessment of prognosis for DFU patients following DSA surgery primarily relies on traditional clinical scores, such as the stratified diabetic foot ulcer risk score (Site, Ischemia, Neuropathy, Bacterial infection, Area, Depth [SINBAD]), or single inflammatory biomarkers. However, these methods are limited by their subjectivity, lack of specificity, and insufficient coverage of the multifaceted pathological processes involved. This underscores the pressing clinical need for the development of more precise, multi-dimensional predictive tools.

A growing number of studies have gradually begun to focus on the prognostic risk factors affecting patients with interventional diabetic foot surgery and its potential association with ulcer severity, further suggesting that patients with diabetic foot are usually accompanied by peripheral vasculopathy, vascular stenosis, and occlusion of blood vessels severely which affecting blood circulation in the lower extremities and exacerbating the risk of poor prognosis. Therefore, exploring the risk factors for prognosis and their correlation with ulcer severity in diabetic foot patients undergoing DSA-guided intervention is crucial for elucidating the pathophysiological mechanisms of the disease and informing novel therapeutic strategies. The early identification of high-risk patients prone to poor outcomes post-DSA allows for the implementation of intensified monitoring, adjunct therapies, or individualized treatment plans. This approach is instrumental in enhancing therapeutic efficacy, reducing unnecessary medical interventions, and optimizing resource allocation.

Information and Methodology

General Information

Clinical data of 135 patients with diabetic foot under DSA-guided intervention were retrospectively selected from August 2023 to January 2025. They were categorized into a good prognosis group and a poor prognosis group based on their 6-month prognosis status. The study was approved by our Ethics Committee, and all procedures were conducted in accordance with the ethical standards of the 1964 *Declaration of Helsinki* and its subsequent amendments. The study was retrospective in nature and there was concealment of patient identifying information, therefore informed consent from patients and their families was not required.

Inclusion and Exclusion Criteria

Inclusion criteria: (1) all patients with diabetes met the diabetes-related diagnostic criteria in *2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD;*[11] (2) all patients with diabetic foot met the diagnostic criteria for diabetic foot in *Guidelines on the prevention of foot ulcers in persons with diabetes;*[12] (3) complete clinical data were available, including but not limited to demographic characteristics, disease-related features, laboratory parameters, and follow-up records; (4) first visit and the cause of which is diabetes; (5) infections such as septic arthritis, abscesses, onychomycosis, osteomyelitis at below-ankle sites of patients.

Exclusion criteria: (1) cancerous ulcers; (2) inflammation and infection in other parts of the body other than the foot; (3) coagulation dysfunction; (4) severe cardiac, hepatic, and renal insufficiency; (5) respiratory, urinary, and gastrointestinal infections.

Data Collection

As a retrospective study, all data of patients were collected through the medical record system including gender, body mass index [BMI=weight (kg)/height squared (m^2)], place of residence, smoking history (≥100 cigarettes in the past 1 year), drinking history (≥1 drink in per week for 5 consecutive months), duration of diabetes, ulcer size, previous ulcers history, hypertension (meeting the diagnostic criteria related to hypertension in *Blood pressure and the diagnostic criteria related to hypertension in the new ACC/AHA hypertension guidelines*[13]), neuropathy, retinopathy, white blood cell count, hemoglobin, fasting glucose, glycosylated hemoglobin, serum procalcitonin (PCT), galactin-3 protein (Gal-3), noncoding RNA molecule with circular structure (Hsa_circ_0057362), interleukin-6 (IL-6) and serum C-reactive protein (CRP).

Serum Indicator Tests

Within 24 hours prior to surgery, 5mL of fasting peripheral venous blood was collected from each patient. Of this volume, 3 mL was placed in an EDTA anticoagulant tube and centrifuged for 15 min at 3,500 r/min. The resulting supernatant was then collected and preserved. The remaining 2 mL was placed in a standard coagulant tube, allowed to stand at room temperature for 30 minutes, and subsequently centrifuged at 3,000 r/min for 15 minutes to separate the serum. All aliquoted samples were stored at −80 °C for subsequent analysis, with repeated freeze-thaw cycles avoided. IL-6 and CRP were determined by enzyme-linked immunosorbent assay (ELISA), and chemiluminescence immunoassay was chosen to detect PCT, with the assay kit purchased from Shanghai Guangrui Bio-technology Co. Ltd.; serum Gal-3 level was tested by ELISA, with the operation strictly according to the instruction manual of the kit (ZK-H1734, Shenzhen ZiKe Bio-technology Co. Ltd).; Hsa_circ_0057362 was measured by real-time fluorescence quantitative polymerase chain reaction (RT-PCR) technique using an ABI7500 fluorescence quantitative PCR instrument. Forward primer: 5′-CCTGGTGGT AAAGGCGAAAT′, reverse primer: 5′-TAGCCTGCGAGTCCTCCTAC-3′, with the reaction conditions as denaturation at 95°C for 30s, annealing at 60°C for 30s, and extension at 72°C for 60s, for a total of 40 cycles. Glyceraldehyde 3-phosphate dehydrogenase was used as the internal reference gene (forward primer: 5′-TCA CATGCTGTCTAGAGAGACT-3′, reverse primer: 5′-ACT GAGGGCACTGCTACCAT-3′), and the 2-ΔΔCt method was adopted to calculate the level of Hsa_circ_0057362, with the glycerol tris-phosphate dehydrogenase (GAPDH) selected as the internal reference gene because of its stable expression.

All assays were performed by two experienced laboratory technicians. Each batch included standard curves, blank controls, and quality control samples to ensure all results complied with the manufacturer's specifications.

SINBAD Score

Within 24 hours prior to surgery, the severity of foot ulcers was assessed using the SINBAD[14] score by a specialized wound ostomy nurse. The assessment result was independently verified by an attending vascular surgeon. The SINBAD score comprises six dimensions: Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth. The total score categorizes ulcer severity as follows: 0–3 indicates mild, 4–6 indicates moderate, and a score of 7 or above indicates severe diabetic foot. A higher score denotes a greater severity of the ulcer.

Prognostic Criteria

Two experienced attending vascular surgeons independently reviewed the 6-month follow-up data for all diabetic foot patients, guided by relevant literature,[15] to assess the prognosis. Good prognosis was defined as ulcer heating with clinical improvement and no evidence of in-stent restenosis. Poor prognosis was defined as non-healed ulcers, clinical deterioration, and the presence of >50% in-stent restenosis or >50% stenosis within 5 mm of the stent edges, compared to the distal native vessel. In case of any discrepancy between the two assessors, a third senior vascular surgeon with the rank of associate chief physician or higher served as an arbiter to reach a final consensus.

Statistical Processing

IBM SPSS 27.0 (IBMCorp, Armonk, N.Y., USA) statistical software was employed to analyze the data, and the count data were expressed as n with the χ^2 test adopted; the normal distribution test was carried out using the Shapiro–Wilk method for the measurement data, with those not conforming to the normal distribution expressed using median and interquartile spacing [M (P_{25}, P_{75})], and those conforming to the normal distribution expressed as ($\bar{x} \pm$ s) by t test. Differences were considered statistically significant at $P < 0.05$. The items that differed between the two groups were brought into a *Logistic* regression equation to analyze the risk factors affecting the occurrence of poor prognosis in patients with diabetic foot after surgery, using interventional surgical treatment under DSA as the dependent variable, and clinical data as the independent variable, with P=0.05 as the criterion for gradual screening of variables.

Results

Comparison of Postoperative Prognostic Conditions of Patients

In this study, 135 patients with diabetic foot undergoing DSA-guided intervention were included with their prognostic status assessed at 6 months postoperatively, of which a total of 30 cases (22.22%) had poor prognosis with a SINBAD score of (7.15±2.76), and a total of 105 cases (77.78%) had good prognosis with a SINBAD score of (3.24±1.81).

Comparison of Clinical Data

As shown in Table 1, there was no statistically significant comparison between the two groups in terms of gender, BMI, place of residence, smoking history, drinking history, duration of diabetes, ulcer size, previous ulcers history, hypertension, neuropathy, retinopathy, white blood cell counts, hemoglobin, fasting blood glucose, and glycosylated hemoglobin ($P > 0.05$). The difference of PCT, Gal-3, Hsa_circ_0057362, IL-6, and CRP between the poor prognosis group and good prognosis group was statistically significant ($t1$ value = 21.335, $t2$ value = 8.512, $t3$ value = 5.557, $t4$ value = 8.402, $t5$ value = 10.380, $P < 0.05$), suggesting that PPCT, Gal-3, Hsa_circ_0057362, IL-6, and CRP was predictors of poor prognosis after diabetic foot intervention.

Table 1 Comparison of Clinical Data Between Groups (n=135)

Clinical Data		Poor Prognosis Group (n=30)	Good Prognosis Group (n=105)	χ^2/t	*P*
Gender	Male	18	62	0.009	0.925
	Female	12	43		
Age (years)		63.06±2.43	62.85±2.47	0.412	0.681
BMI (kg/m^2)		22.14±0.58	22.12±0.61	0.160	0.873
Place of residence	Town	20	60	0.877	0.349
	Countryside	10	45		
Smoking history	Yes	14	50	0.009	0.927
	No	16	55		

(*Continued*)

Table 1 (Continued).

Clinical Data		Poor Prognosis Group (n=30)	Good Prognosis Group (n=105)	χ^2/t	*P*
Drinking history	Yes	8	21	0.615	0.433
	No	22	84		
Duration of diabetes (years)		9.25±1.63	9.33±1.25	0.288	0.774
Ulcer size (cm^2)		42.38±9.31	42.76±9.28	0.198	0.844
Previous ulcers history	Yes	12	37	0.229	0.632
	No	18	68		
Hypertension	Yes	11	35	0.115	0.734
	No	19	70		
Neuropathy	Yes	12	40	0.036	0.850
	No	18	65		
Retinopathy	Yes	16	65	0.714	0.398
	No	14	40		
White blood cell counts ($\times10^9$/L)		11.28±3.25	11.17±3.34	0.160	0.873
Hemoglobin (g/L)		113.27±10.88	112.17±10.83	0.490	0.495
Fasting blood glucose (mmol/L)		9.63±3.64	10.27±3.56	0.864	0.389
Glycosylated hemoglobin (%)		9.62±2.63	9.24±2.72	0.680	0.498
PCT (pg/mL)		501.25±60.25	458.25±61.25	3.403	0.001
Gal-3 (ng/mL)		6.27±2.68	5.14±1.63	2.850	0.005
Hsa_circ_0057362		4.81±1.98	2.84±1.63	5.557	<0.001
IL-6 (pg/mL)		118.25±21.36	98.47±20.63	4.596	<0.001
CRP (mg/L)		12.25±3.63	8.45±3.11	5.682	<0.001

Abbreviations: PCT, procalcitonin; Gal-3, galactoagglutinin-3 protein; Hsa_circ_0057362, noncoding RNA molecule with circular structure; IL-6, interleukin-6; CRP, serum C-reactive protein.

Correlation Analysis of PCT, Gal-3, Hsa_circ_0057362, IL-6, and CRP with Ulcer Severity

A *Pearson* correlation model was constructed to analyze the relationship of PCT, Gal-3, Hsa_circ_0057362, IL-6 and CRP with ulcer severity, and the results showed that PCT, Gal-3, Hsa_circ_0057362, IL-6, and CRP were positively correlated with the ulcer severity (r=0.283, 0.240,0.434, 0.370, 0.443, $P < 0.05$ Figure 1).

Multifactorial Logistic Regression Analysis Affecting the Poor Prognosis of Patients with Diabetic Foot Under DSA-Guided Intervention

In Table 2, with difference items calculated by *Logistic* regression equation, the results presented that PCT, Gal-3, Hsa_circ_0057362, IL-6, and CRP were the influencing factors on poor prognosis of diabetic foot, in which PCT (*OR*=1.012, 95% CI=1.004~1.019, *P*=0.002), Gal-3 (*OR*=1.357, 95% CI=1.087~1.693, *P*=0.007), Hsa_circ_0057362 (*OR*=1.873, 95% CI=1.423~2.465, *P*<0.001), IL-6 (*OR*=1.047, 95% CI=1.023~1.072, *P*<0.001), and CRP (*OR*=1.415, 95% CI=1.219~1.642, *P*<0.001) were risk factors for poor prognosis after diabetic foot surgery.

ROC Analysis of Factors Predicting the Occurrence of Poor Prognosis in Postoperative Diabetic Foot Patients

By the ROC curves, it could be seen that AUC values of PCT (AUC=0.696), Gal-3 (AUC=0.646), Hsa_circ_0057362 (AUC=0.776), IL-6 (AUC=0.744), CRP (AUC=0.785), and the co-diagnosis (AUC=0.919) were all over 0.6, thus indicating that each of the above indicators had a degree of predictive value for the occurrence of adverse prognostic outcomes in postoperative patients with diabetic foot (Figure 2).

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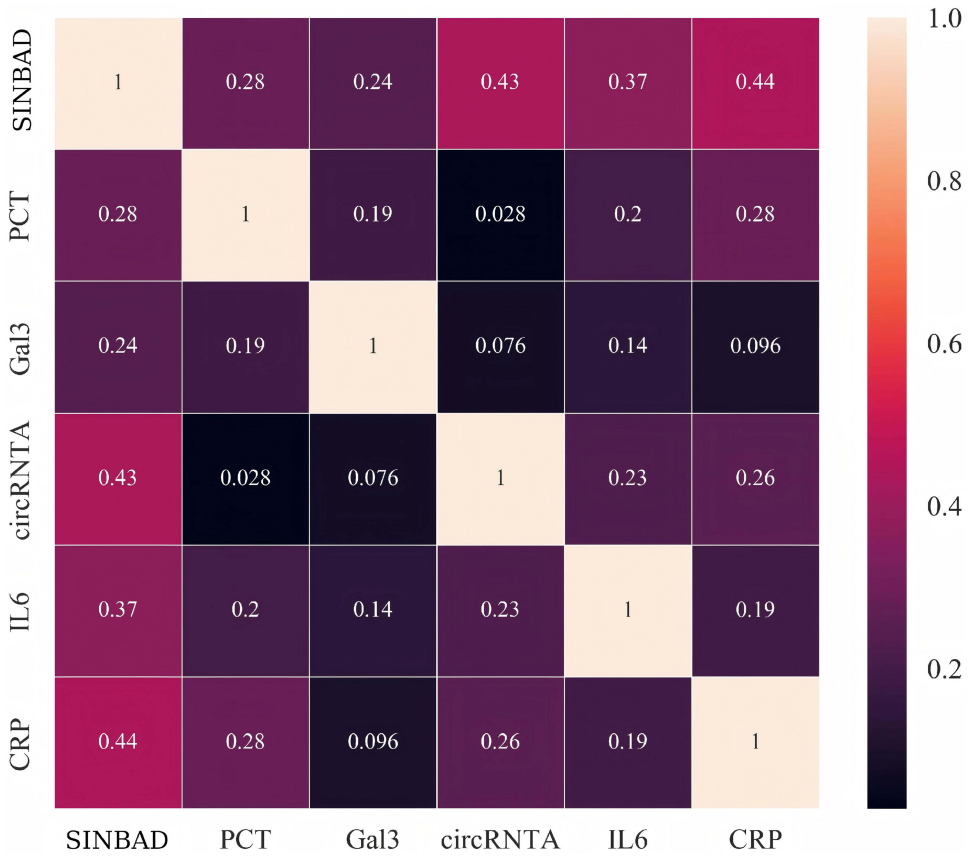

Figure 1 Correlation analysis of PCT, Gal-3, Hsa_circ_0057362, IL-6, and CRP with ulcer severity.
Abbreviations: PCT, procalcitonin; Gal-3, galactoagglutinin-3 protein; Hsa_circ_0057362, noncoding RNA molecule with circular structure; IL-6, interleukin-6; CRP, serum C-reactive protein.

Discussion

The ulcer severity in diabetic foot patients has become a key factor affecting the prognosis of procedures under DSA. More severe ulcers are usually accompanied by different degrees of vasculopathy, which makes the local blood supply abnormal and directly increases the difficulty coefficient of postoperative healing. Related scholars have found[16] although DSA-guided intervention can obtain high therapeutic value, it is still prone to face a high risk of slow wound healing, postoperative infection and recurrent ulcers, thus increasing the incidence of poor prognosis.

135 patients with diabetic foot who underwent DSA-guided intervention were included in this study with their prognostic status evaluated at 6 months postoperatively, among which 30 cases with poor prognosis accounted for 22.22%, implying that patients with diabetic foot were prone to poor prognosis after the surgery, which should be highly emphasized by clinic. DSA is a class of commonly used clinical auxiliary examination techniques, and applicable to

Table 2 Multifactorial *Logistic* Regression Analysis Affecting Poor Prognosis of Diabetic Foot Patients Under DSA Intervention

Factor	*B* value	*SE*	*Z* value	*P* value	*OR* value	*OR* value 95% CI
PCT	0.012	0.004	3.147	0.002	1.012	1.004~1.019
Gal-3	0.305	0.113	2.697	0.007	1.357	1.087~1.693
Hsa_circ_0057362	0.627	0.140	4.474	0.000	1.873	1.423~2.465
IL-6	0.046	0.012	3.869	0.000	1.047	1.023~1.072
CRP	0.347	0.076	4.563	0.000	1.415	1.219~1.642

Abbreviations: PCT, procalcitonin; Gal-3, galactoagglutinin-3 protein; Hsa_circ_0057362, noncoding RNA molecule with circular structure; IL-6, interleukin-6; CRP, serum C-reactive protein.

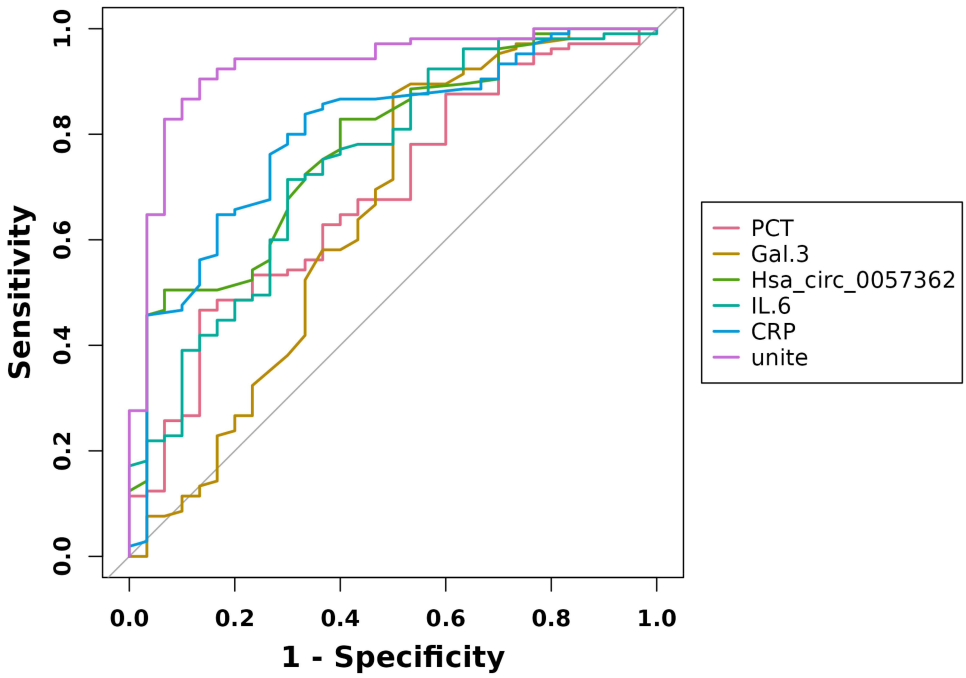

Figure 2 ROC of factors predicting the occurrence of poor prognosis in postoperative diabetic foot patients.
Abbreviations: PCT, procalcitonin; Gal-3, galactoagglutinin-3 protein; Hsa_circ_0057362, noncoding RNA molecule with circular structure; IL-6, interleukin-6; CRP, serum C-reactive protein.

clinical diagnosis and treatment for a variety of diseases, which can effectively and accurately reflect the area and extent of vascular lesions. Ding HX and other[17] scholars found that interventional procedures were prone to restenosis and increased the risk of poor prognosis, further confirming the findings of this study. This study found that PCT was one of the independent risk factors for the occurrence of poor prognosis after diabetic foot interventions, which had a strong association with ulcer severity. Omar J et al[18] scholars found that serum PCT levels gradually increased as the degree of diabetic foot infection aggravated (from mild to severe). PCT is a class of precursor proteins secreted by thyroid C-cells also a common marker of susceptibility for bacterial infections; its synthesis is susceptible to factors such as interleukins and intracellular toxins, and PCT levels are abnormally elevated in patients with poor prognosis. The higher the serum PCT level, the more pronounced the tissue damage of organism, making the endothelial damage in vessel more severe, thus triggering restenosis and increasing the risk of poor prognosis. Relevant scholars have found[19] that PCT level increase directly reflects the systemic inflammatory response, after diabetic foot surgery, the wound is susceptible to bacterial infection, especially drug-resistant bacterial infection. When bacteria invade through the wound, it is very easy to induce local and systemic immune response, the level of PCT, as a marker of bacterial infection, is significantly increased and aggravates the inflammatory reaction, leading to different degrees of tissue necrosis, sepsis and other complications, which suppresses the immune system response and further aggravates ulcer severity.

Gal-3 is a family of glycoconjugate albumin, with 15 members have been isolated and recognized at this stage, which plays a key role in the inflammatory response, the immune system, vascular disease and other pathological processes. Formed by macrophage secretion and collagen fusion, it has the function of regulating cell proliferation, apoptosis, adhesion and migration, which is involved in a variety of molecular activities, such as participating in the inflammatory response as a multi-class inflammatory factor, and serving as important receptor for the end-products of glycosylation on surface of cell. Gal-3 has been playing a crucial role in the process of diabetes mellitus and its complications, so that this index has a higher diagnostic value in the assessment of diabetic foot. Relevant scholars have found[20] that due to the long-term hyperglycemic state of patients in the diabetes group, Gal-3 is directly involved in the inflammatory response of body, causing a large number of macrophages secretions, promoting endothelial cell differentiation and vascular neonatology, which actively participates in the formation and progression of peripheral arterial vascular disease, so as to

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effectively determine the ulcer severity, and to predict the prognosis of its condition. In this study, Gal-3 was found to be one of the independent risk factors for the development of poor prognosis after intervention in diabetic foot patients, which had a strong association with ulcer severity. Ohkura T et al[21] scholars have found that serum Gal-3, as a serological marker for vascular disease, is expressed at high levels in patients and strongly associated with the severity of complications. Relevant scholars have found[20] that due to the long-term hyperglycemic state of patients in the diabetes group, Gal-3 is directly involved in the inflammatory response of body, causing a large number of macrophages secretions, promoting endothelial cell differentiation and vascular neonatology, which actively participates in the formation and progression of peripheral arterial vascular disease, so as to effectively determine the ulcer severity, and to predict the prognosis of its condition.

It was found in this study that circ_0057362 is one of the independent risk factors for the occurrence of poor prognosis after intervention in diabetic foot patients, which has a strong association with ulcer severity. Peripheral blood circular RNA is a class of single-stranded non-coding RNAs, and directly involved in the onset and development of diabetes and its complications, which can provide a new direction for the early diagnosis and treatment of type 2 diabetes and its complications. CHEN Z J et al[22] scholars have found that Hsa_circular RNA is energetically involved in oxidative stress, inflammatory response regulation, with a key role in the development of diabetic foot and wound healing process, which further confirmed the findings of this study. Hsa_circular RNA is a class of RNA molecules with multiple biological functions, with highly stable expression and conserved evolution, and widely distributes in eukaryotes. Its abnormal expression is directly involved in the proliferation, migration, and apoptosis of keratinocytes, which interferes with the wound repair function of stromal cells, thus playing a pivotal role in the onset and development of diabetic foot and determining the ulcer severity and predicting the prognosis of diabetic foot effectively.[23]

IL-6 is a common pro-inflammatory cytokine that activates the inflammatory response in the body and promotes the infiltration of inflammatory cells, exacerbating the inflammatory response in the ulcerated area. In chronic hyperglycemia, the level of this indicator is usually located in a high state, which directly aggravates the formation of diabetic foot ulcers and inhibits the wound healing because it affects the proliferation and migration of the fibroblasts and keratinocytes, which cells play an important role in the wound healing process.[24] Another scholar's studies have found[25] that elevated IL-6 levels suggest a strong local or systemic inflammatory response, which increases the risk of infection in diabetic foot ulcers, making healing more difficult, and even incrementing the risk of amputation. In this study, it was found that IL-6 was an independent risk factor for the development of poor prognosis after intervention in diabetic foot patients, and there was a strong association with ulcer severity. Xu S et al[26] scholars found that serum IL-6 levels were positively correlated with the ulcer severity in diabetic foot, which meant in patients with severe ulcers, IL-6 levels were significantly elevated, suggesting that elevated levels of IL-6 might drive the progression of disease, thereby increasing the risk of poor prognosis. This study also found that CRP was a common risk factor for poor prognosis after interventional surgery in patients with diabetic foot, and there was a close relationship with the ulcer severity. Gülcü A et al[27] scholars found that elevated CRP levels were associated with poor prognosis and treatment failure in diabetic foot ulcers, further confirming the findings of this paper. CRP is a class of acute-phase proteins synthesized by liver, and its level increases rapidly during the inflammatory response. As a commonly used clinical inflammatory marker, this index is usually applied to determine the acute and chronic inflammatory state. In patients with diabetic foot, elevated CRP levels usually reflect the presence of a strong local or systemic inflammatory response, and after the occurrence of diabetic foot ulcers, factors such as tissue damage, infection and ischemia are prone to cause local inflammatory response, which leads to an increase of CRP levels.[28] Another scholarly study found[29] that elevated CRP levels were positively correlated with ulcer severity, and higher postoperative CRP levels were indicative of a slower healing process and poorer quality of healing, thus increasing the incidence of poor prognosis.[30]

This study innovatively addresses the need for prognostic assessment in diabetic foot patients undergoing DSA-guided intervention. Its novelty is threefold. First, it is the first to integrate PCT, Gal-3, Hsa_circ_0057362, IL-6, and CRP into a multi-factor prognostic model. This combined model achieved a superior predictive AUC of 0.919, significantly outperforming any single biomarker and overcoming the limitation of limited pathological coverage inherent to single-marker approaches. Second, Hsa_circ_0057362 has been scarcely investigated in the DFU field; our study is the first to identify it as an independent risk factor for poor postoperative outcomes, thereby proposing a novel molecular target for DFU prognosis.

We also objectively acknowledge that its clinical translation remains exploratory. Finally, by combining these biochemical markers with the SINBAD clinical ulcer severity score, we constructed a dual-dimensional assessment tool. This integrated approach effectively mitigates the subjectivity of clinical scores while compensating for the inability of molecular markers to directly reflect wound status, thereby enhancing the tool's clinical applicability and value. However, there were still several limitations. The sample size was relatively small and sourced from a single center, comprising 30 patients with poor prognosis and 105 patients with good prognosis selected based on specific research needs, which may affect the reliability and the generalizability of the findings. Potential influences from factors such as individual patient variations, laboratory conditions, and technical expertise on the accuracy of the observed indicators were not fully accounted for. Furthermore, as non-specific biomarkers, IL-6 and CRP levels could be confounded by other systemic conditions, potentially limiting the model's specificity. Although this study confirms the predictive value of the five biomarkers and their combined model for prognosis following DSA-guided intervention in DFU patients, these findings remain preliminary. Future research should adopt a multi-center, large-sample, prospective design with strictly controlled inclusion and exclusion criteria to further validate the predictive efficacy of these biomarkers. Efforts should also focus on identifying DFU-specific molecular markers and integrating them with IL-6 and CRP to develop more precise predictive models. Additionally, risk stratification based on biomarker profiles should be explored to inform personalized management strategies and thoroughly evaluate their impact on improving clinical outcomes.

In summary, there are various risk factors affecting the occurrence of poor prognosis in diabetic foot patients undergoing DSA-guided intervention, such as PCT, Gal-3, Hsa_circ_0057362, IL-6, and CRP, which have close correlation with the ulcer severity, with a high value of application in the prediction of the occurrence of poor prognosis in patients with diabetic foot. By identifying patients with poor postoperative prognosis at an early stage and adopting targeted intervention programs, the prognosis of patients can be effectively improved.

Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethics Approval and Consent to Participate

This retrospective study was reviewed and approved by the Ethics Committee of Longhua Hospital (NO.2025LCSY082). As the research involved no more than minimal risk and all patient identifying information was permanently anonymized prior to analysis, the need for obtaining informed consent from participants was waived by the aforementioned Ethics Committee. All procedures were conducted in accordance with the ethical standards of the Declaration of Helsinki. The confidentiality of patient data was rigorously maintained throughout the study.

Author Contributions

Xuanyu Wang: Conceptualization, Data Curation, Formal Analysis, Methodology, Writing – Original Draft.

Zhichang Pan: Conceptualization, Data Curation, Formal Analysis, Methodology, Writing – Original Draft.

Huafa Que: Formal Analysis, Supervision, Funding Acquisition, Writing – Review & Editing, Resources.

Jianjie Rong: Validation, Project Administration, Writing – Review & Editing.

All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. Xuanyu Wang and Zhichang Pan contributed equally to this work and share first authorship.

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Disclosure

No potential conflict of interest was reported by the authors.

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