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Clinical Characteristics and Independent Risk Factors for Early Reocclusion Following Endovascular Intervention in Patients with Diabetic Foot Complicated by Lower Extremity Atherosclerotic Occlusive Disease: A Retrospective Cohort Study

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Abstract

Objective

This study was designed to explore the independent risk factors for early post-intervention re-occlusion.

Methods

This retrospective comparative cohort study enrolled patients diagnosed with diabetic foot complicated by lower extremity atherosclerotic occlusive disease who received inpatient treatment at The Air Force Hospital of Eastern Theater of PLA between January 2024 and October 2025. Based on postoperative vascular patency, patients were divided into an early re-occlusion group and a late re-occlusion group (> 6 months). Baseline demographic characteristics, clinical characteristics, and laboratory parameters were compared. Multivariate logistic regression identified independent risk factors for early re-occlusion.

Results

A total of 129 patients were enrolled, 72 (55.8%) in the late re-occlusion group and 57 (44.2%) in the early re-occlusion group. Patients in the early re-occlusion group had higher of uremia (12% vs. 0%, $P = 0.003$) and smoking (30% vs. 8.3%, $P = 0.002$) compared with the late re-occlusion group. The early re-occlusion group exhibited elevated white blood cell count (9.90 vs. 7.70 × 10^9/L, $P = 0.013$), C-reactive protein (28.70 vs. 7.75 mg/L, $P < 0.001$), and higher hemoglobin (118.00 vs. 116.00 g/L, $P = 0.007$). Multivariate logistic regression analysis identified C-reactive protein (OR 1.047, 95% CI 1.017–1.078, $P = 0.002$), hemoglobin (OR 1.069, 95% CI 1.025–1.115, $P = 0.002$), creatinine (OR 1.005, 95% CI 1.001–1.010, $P = 0.026$), and left ventricular ejection fraction (OR 0.877, 95% CI 0.777–0.990, $P = 0.033$) as independent risk factors for early re-occlusion, while hypertension (OR 0.135, 95% CI 0.032–0.573, $P = 0.007$) and previous ipsilateral limb intervention (OR 0.254, 95% CI 0.067–0.962, $P = 0.044$) were identified as protective factors.

Conclusions

Complex interplay of inflammation, blood hyperviscosity, renal impairment, and cardiac insufficiency is associated with early re-occlusion following endovascular therapy in diabetic foot.

Introduction

Diabetes mellitus is a prevalent global metabolic disorder and an independent risk factor for the onset and progression of lower-extremity peripheral artery disease (PAD). As the most severe clinical subtype of PAD, chronic limb-threatening ischemia (CLTI) accounts for approximately 10% of all PAD cases and is characterized by intractable rest pain, non-healing wounds, and progressive tissue loss. Patients with diabetes mellitus-associated CLTI have a poor long-term prognosis, with a 1-year mortality rate as high as 22%[1]. For patients with diabetic foot ulcers (DFUs), concomitant PAD further increases amputation and mortality risks.

Endovascular intervention has become the primary revascularization strategy to restore limb perfusion in this population. Although percutaneous transluminal angioplasty (PTA) provides a minimally invasive approach with satisfactory short-term limb salvage outcomes, its long-term efficacy is frequently limited by post-procedural vessel

re-occlusion. Early re-occlusion, defined as vessel occlusion occurring within six months after intervention, remains a major clinical challenge. Despite a high technical success rate, nearly 19% of CLTI patients require reintervention within one year after successful revascularization, with a 1-year vessel patency rate of approximately 85%[2]. These data derived from general CLTI cohorts may underestimate the actual risk among DFU patients, as the diabetic prothrombotic and proinflammatory microenvironment synergistically promotes neointimal hyperplasia, rendering diabetic vessels more susceptible to early restenosis. Frequent early re-occlusion and repeated interventions lead to prolonged hospitalization, increased healthcare costs, impaired quality of life, and elevated major amputation risks.

Current studies regarding post-intervention reocclusion mainly focus on traditional atherosclerotic risk factors, including smoking, dyslipidemia, and glycemic control. However, these risk indicators show inconsistent predictive performance in complex DFU patients with multiple comorbidities. Most previous studies have not stratified reocclusion events by time, thereby failing to differentiate early reocclusion driven by acute vascular injury responses from late restenosis caused by chronic disease progression. In addition, existing research generally concentrates on single biological pathways, while the combined effects of systemic inflammation, metabolic derangement, renal dysfunction, and cardiac function on early reocclusion risk remain insufficiently clarified.

To address these gaps, this retrospective cohort study enrolled 129 DFU patients with PAD and stratified them by reocclusion timing (early ≤ 6 months vs. late > 6 months). We compared baseline characteristics, identified independent risk factors for early reocclusion, and explored potential mechanisms, aiming to provide evidence for postoperative risk stratification and individualized management.

Materials and Methods

1.1 Study Design and Ethics

This was a retrospective, single-center, comparative cohort study conducted at The Air Force Hospital of Eastern Theater of PLA, Nanjing, Jiangsu, China. The study protocol was approved by the Institutional Review Board of The Air Force Hospital of Eastern Theater of PLA, and the requirement for informed consent was waived due to the retrospective nature of the analysis. All procedures were performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

1.2 Study Population

This study retrospectively enrolled patients diagnosed with diabetic foot complicated by lower extremity atherosclerotic occlusive disease who received inpatient treatment The Air Force Hospital of Eastern Theater of PLA from January 2024 to October 2025.Eligible patients were those who required repeated ipsilateral endovascular intervention due to recurrent or aggravated limb ischemia after the initial procedure.

Inclusion criteria were

(1) age ≥ 18 years; (2) diagnosis of type 1 or type 2 diabetes mellitus; (3) presence of DFU (Wagner grade ≥ 1) with concomitant PAD confirmed by angiography; (4) history of at least one prior ipsilateral EVT; and (5) availability of complete baseline clinical and laboratory data.

Exclusion criteria were

(1) acute limb ischemia requiring emergency surgery; (2) prior ipsilateral bypass grafting; (3) coexisting malignancy or life-limiting comorbidities; (4) pregnancy or lactation; (5) Patients with inaccurate or missing records of

reocclusion time were excluded.;(6)loss to follow-up within 6 months after the last intervention.

1.2 Grouping and Definitions

This study adopted 6 months after the primary procedure as the cutoff for early and late reocclusion[3], consistent with prior literature on restenosis time windows.

- **Re-occlusion** was defined as recurrent or aggravated ipsilateral limb ischemia following initial EVT, confirmed by imaging evidence of vascular re-occlusion (duplex ultrasound or angiography), and necessitating repeat interventional revascularization.
- **Early re-occlusion** was defined as re-occlusion occurring within 6 months postoperatively.
- **Late re-occlusion** was defined as re-occlusion occurring beyond 6 months.

1.3 Observation Indicators

Demographic and clinical data were extracted from electronic medical records using a standardized case report form. The following variables were collected for each patient:

- **Demographics**: age, sex;
- **Clinical history**: diabetes duration, smoking status, hypertension, heart failure, uremia, prior ipsilateral limb intervention;
- **Laboratory parameters** (measured within 48 hours before the second intervention): white blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), hemoglobin, platelet-to-lymphocyte ratio (PLR), C-reactive protein (CRP), alanine aminotransferase (ALT), albumin, creatinine, uric acid, serum calcium, total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), monocyte-to-HDL ratio (MHR), D-dimer, fibrinogen;
- **Cardiac function**: left ventricular ejection fraction (LVEF) assessed by echocardiography.

All laboratory assays were performed at the central clinical laboratory of our institution using standard automated analyzers.

1.4 Endovascular Procedure

All endovascular interventions were performed by experienced vascular surgeons in a dedicated operating suite. The choice of revascularization strategy (e.g., balloon angioplasty, drug-coated balloon, stent placement, or atherectomy) was left to the discretion of the treating physician based on lesion morphology, location, and length, as well as vessel diameter and runoff status.

Technical success was defined as residual stenosis < 30% with restoration of straight-line flow to the foot, as confirmed by completion angiography. All patients received intraprocedural unfractionated heparin (70–100 IU/kg) to maintain activated clotting time > 250 seconds. Post-procedural antithrombotic regimens were prescribed according to the 2023 ESVS Clinical Practice Guidelines on Antithrombotic Therapy in Vascular Disease[4] and included dual antiplatelet therapy (aspirin plus clopidogrel) or a combination of aspirin/ clopidogrel and low-dose rivaroxaban, as clinically indicated.

1.5 Outcome Assessment

The primary outcome of this study was **early re-occlusion**, defined as target vessel re-occlusion requiring repeat ipsilateral endovascular intervention within 6 months after the primary procedure. Secondary outcomes included comparison of baseline characteristics and laboratory parameters between the early and late re-occlusion groups to identify potential risk factors.

1.6 Statistical Analysis

Data analysis was performed using SPSS version 26.0 software. Continuous variables are expressed as median (interquartile range) and were compared using the Wilcoxon rank-sum test. Categorical variables are presented as counts (percentages) and were compared using the Chi-square (χ^2) test. Multicollinearity was assessed using the Variance Inflation Factor (VIF) and correlation coefficients. Variables with $P < 0.05$ in the univariate analysis were included in the multivariate logistic regression model. P< 0.05 was considered statistically significant.

Results

2.1 Patient Disposition and Group Allocation

A total of 129 patients with diabetic foot ulcers (DFUs) and peripheral artery disease (PAD) who underwent repeated ipsilateral endovascular intervention were enrolled in this retrospective cohort study. According to the timing of re-occlusion, 72 patients (55.8%) were allocated to the late re-occlusion group (> 6 months), and 57 patients (44.2%) were allocated to the early re-occlusion group (≤ 6 months). The flow diagram of patient selection is presented in Fig. 1

2.2 Baseline Characteristics and Univariate Analysis

Baseline demographics, clinical characteristics, and laboratory parameters of the two groups are summarized in Table 1. The median age of the overall cohort was 74.0 years (IQR 67.0–78.0), with a male predominance (64.0%). No significant differences were observed between the two groups in terms of age, sex, hypertension, duration of diabetes, history of previous limb intervention, or cardiac function (all P > 0.05).

Table 1
Comparison of baseline characteristics between the two groups

Variable	Total (N = 129)	Late Re-occlusion Group (N = 72)	Early Re-occlusion Group (N = 57)	Statistic	P-value
Age, years	74.00(67.00,78.00)	74.00(68.00,77.50)	74.00(64.00,79.00)	2137.50	0.686
Male, n(%)	82(64)	44(61)	38(67)	0.42	0.510
Heart failure, n(%)	41(32)	21(29)	20(35)	0.51	0.471
Uremia, n(%)	7(5.4)	0(0)	7(12)	9.35	*0.003*
Smoking, n(%)	23(18)	6(8.3)	17(30)	10.03	*0.002*
Hypertension, n(%)	80(62)	47(65)	33(58)	0.74	0.391
Duration of diabetes, years	20.00(10.00,23.00)	16.50(10.00,22.00)	20.00(15.00,24.00)	1785.50	0.205
Previous limb intervention, n(%)	49(38)	29(40)	20(35)	0.36	0.546
White blood cell, $\times 10^9$/L	8.50(6.50,11.20)	7.70(6.25,10.20)	9.90(6.70,11.50)	1526.50	*0.013*
NLR	4.13(2.89,5.45)	3.90(2.61,5.19)	4.30(3.00,6.00)	1688.00	0.085
Hemoglobin, g/L	117.00(99.00,129.00)	116.00(95.00,125.00)	118.00(109.00,134.00)	1487.00	*0.007*
PLR	145.00(95.56,190.00)	143.33(95.56,185.33)	145.00(86.09,192.31)	1983.50	0.747
CRP, mg/L	10.80(4.40,42.50)	7.75(3.90,18.05)	28.70(6.60,72.50)	1257.50	*< 0.001*
ALT, U/L	12.30(10.10,16.60)	11.65(10.00,14.95)	12.50(10.50,17.80)	1734.50	0.132
Albumin, g/L	35.40(33.00,37.30)	35.60(33.70,37.45)	35.00(31.40,36.80)	2353.00	0.154
Creatinine, μmol/L	86.40(61.70,144.90)	86.75(62.60,148.10)	75.30(59.70,141.70)	2134.00	0.699
Uric acid, μmol/L	302.10(236.20,359.70)	311.60(232.75,379.30)	291.30(238.60,320.70)	2345.50	0.165
Serum calcium, mmol/L	2.29(2.21,2.36)	2.30(2.22,2.36)	2.28(2.20,2.37)	2116.50	0.761
Total cholesterol, mmol/L	3.78(3.41,4.52)	3.86(3.53,4.66)	3.54(3.08,3.97)	2592.00	*0.010*
Triglyceride, mmol/L	1.39(0.95,1.67)	1.39(0.93,1.85)	1.39(0.96,1.67)	1994.50	0.786

Note: Continuous variables were presented as median (interquartile range) and compared using the Wilcoxon rank-sum test; categorical variables were expressed as n (%) and compared using the Chi-square test.

Variable	Total (N = 129)	Late Re-occlusion Group (N = 72)	Early Re-occlusion Group (N = 57)	Statistic	P-value
HDL-C, mmol/L	1.12(0.99,1.28)	1.12(1.00,1.34)	1.12(0.97,1.28)	2248.00	0.353
MHR	0.67(0.46,0.84)	0.67(0.46,0.87)	0.67(0.45,0.80)	2257.50	0.330
LDL-C, mmol/L	2.05(1.68,2.60)	2.27(1.91,2.65)	1.87(1.62,2.17)	2635.00	*0.006*
D-dimer, mg/L	0.78(0.44,1.16)	0.78(0.38,1.43)	0.78(0.51,1.11)	2185.50	0.528
Fibrinogen, g/L	4.50(3.60,6.10)	4.40(3.60,5.00)	4.50(3.60,7.00)	1677.00	*0.075*
LVEF, %	58.00(55.00,59.00)	58.00(55.50,60.00)	56.00(55.00,58.00)	2346.00	0.157

Note: Continuous variables were presented as median (interquartile range) and compared using the Wilcoxon rank-sum test; categorical variables were expressed as n (%) and compared using the Chi-square test.

Notably, patients in the early re-occlusion group had a significantly higher prevalence of uremia (12.0% vs. 0%, P = 0.003) and smoking (30.0% vs. 8.3%, P = 0.002) compared with the late re-occlusion group.

Regarding laboratory findings, the early re-occlusion group exhibited:

- Significantly elevated white blood cell count (median 9.90 vs. 7.70 × 10^9/L, P = 0.013) and C-reactive protein (median 28.70 vs. 7.75 mg/L, P < 0.001);
- Lower hemoglobin levels (median 118.00 vs. 116.00 g/L, P = 0.007);
- Lower total cholesterol (median 3.54 vs. 3.86 mmol/L, P = 0.010) and LDL-C (median 1.87 vs. 2.27 mmol/L, P = 0.006).

No significant intergroup differences were found in neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), albumin, creatinine, D-dimer, fibrinogen, or LVEF (all P > 0.05).

2.3 Multicollinearity Test

Prior to multivariate logistic regression analysis, we assessed potential collinearity among the candidate independent variables by calculating the variance inflation factor (VIF) and tolerance. The results are presented in Table 2.

Table 2
Multicollinearity test results (VIF and Tolerance)

Variable	VIF	Tolerance
Age	2.993	0.334
Gender	1.521	0.658
Heart failure	1.452	0.689
Smoking history	1.335	0.749
Hypertension	1.421	0.704
Duration of diabetes	1.649	0.606
Previous limb intervention	1.257	0.796
White blood cell	3.170	0.315
NLR	4.179	0.239
Hemoglobin	1.952	0.512
PLR	4.098	0.243
CRP	3.820	0.261
ALT	1.923	0.519
Albumin	1.692	0.591
Creatinine	3.962	0.252
Uric acid	2.351	0.425
Serum calcium	2.136	0.468
Total cholesterol	9.285	0.107
Triglyceride	4.053	0.246
HDL-C	3.916	0.255
Fibrinogen	3.674	0.272
LVEF	1.704	0.586

Among all included variables, the VIF values ranged from 1.257 (previous limb intervention) to 9.285 (total cholesterol), and tolerance values ranged from 0.107 (total cholesterol) to 0.796 (previous limb intervention). The highest VIF value was observed for total cholesterol (VIF = 9.285, tolerance = 0.107), which approached but did not exceed the conventional threshold of 10 for VIF or 0.1 for tolerance. All other variables demonstrated VIF values well below 10 and tolerance values well above 0.1, indicating no significant multicollinearity among the covariates.

2.4 Multivariate Logistic Regression Analysis for Early reocclusion

To identify independent risk factors for early re-occlusion, we performed multivariate logistic regression analysis. Candidate variables with $P < 0.10$ in univariate analysis (uremia, smoking, white blood cell count, hemoglobin, C-

reactive protein, total cholesterol, and low-density lipoprotein cholesterol) were entered into the model. However, **uremia** could not be included in the final model because all cases of uremia occurred in the early re-occlusion group, resulting in zero events in the reference group and precluding estimation of the odds ratio. The final model also incorporated other clinically relevant covariates, including age, sex, heart failure, hypertension, duration of diabetes, previous limb intervention, NLR, PLR, ALT, albumin, creatinine, uric acid, serum calcium, triglycerides, HDL-C, MHR, D-dimer, fibrinogen, and LVEF. The full results are presented in Table 3.

Table 3
Multivariate logistic regression analysis of factors associated with early reocclusion

Variable	OR(95%CI)	P-value
Age	1.052 (0.961–1.152)	0.273
Female	5.434 (0.956–30.873)	0.056
Heart failure	1.076 (0.262–4.420)	0.920
Smoking	2.950 (0.507–17.167)	0.229
Hypertension	0.135 (0.032–0.573)	*0.007*
Duration of diabetes	0.951 (0.883–1.025)	0.188
Previous intervention	0.254 (0.067–0.962)	*0.044*
WBC	1.142 (0.828–1.576)	0.418
NLR	0.905 (0.607–1.352)	0.627
Hemoglobin	1.069 (1.025–1.115)	*0.002*
PLR	1.002 (0.990–1.015)	0.719
CRP	1.047 (1.017–1.078)	0.002
ALT	0.973 (0.907–1.045)	0.456
Albumin	0.837 (0.676–1.037)	0.104
Creatinine	1.005 (1.001–1.010)	*0.026*
Uric acid	0.994 (0.987–1.001)	0.112
Calcium	0.013 (0.000–6.809)	0.174
Total cholesterol	1.886 (0.871–4.084)	0.107
TG	0.758 (0.314–1.834)	0.539
HDL-C	0.141 (0.005–3.617)	0.237
MHR	0.491 (0.221–1.092)	0.081
D-dimer	0.951 (0.618–1.465)	0.821
Fibrinogen	0.749 (0.452–1.241)	0.261
LVEF	0.877 (0.777–0.990)	*0.033*

Among all included variables, the following factors were independently associated with early re-occlusion:

Factors associated with increased risk:

- **C-reactive protein (CRP)**: each 1 mg/L increase was associated with a 4.7% higher risk of early re-occlusion (OR 1.047, 95% CI 1.017–1.078, *P* = 0.002).
- **Hemoglobin**: each 1 g/L increase was associated with a 6.9% higher risk (OR 1.069, 95% CI 1.025–1.115, *P* = 0.002).
- **Creatinine**: each 1 μmol/L increase was associated with a 0.5% higher risk (OR 1.005, 95% CI 1.001–1.010, *P* = 0.026).
- **LVEF**: each 1% decrease was associated with a 12.3% higher risk (OR 0.877, 95% CI 0.777–0.990, *P* = 0.033).

Factors associated with decreased risk:

- **Hypertension**: OR 0.135 (95% CI 0.032–0.573, *P* = 0.007).
- **Previous ipsilateral limb intervention**: OR 0.254 (95% CI 0.067–0.962, *P* = 0.044).

Discussion

PAD, particularly when complicated by DFUs, represents a severe manifestation of systemic atherosclerosis that significantly impairs limb viability and patient quality of life[5]. Despite advances in endovascular revascularization, the post-intervention course in this population is frequently marred by restenosis or re-occlusion, a critical event that undermines the durability of treatment and often necessitates repeat interventions[6]. The risk of such adverse outcomes is notably amplified in the presence of comorbidities such as end-stage renal disease, which further complicates the post-procedural vascular healing process and portends a poor prognosis[7, 8]. Consequently, elucidating the specific clinical and biological determinants that drive early vessel failure is paramount to improving limb salvage rates in this high-risk cohort.This retrospective study enrolled 129 eligible patients and divided subjects into early and late re-occlusion groups based on reintervention time. The baseline clinical and laboratory indicators of these patients were compared and independent risk factors for early re-occlusion were screened. The results revealed that elevated CRP, increased hemoglobin and serum creatinine, as well as decreased LVEF were independent influencing factors. Early postoperative vascular failure was jointly affected by systemic inflammation, hemorheological changes, renal and cardiac function, rather than merely determined by conventional atherosclerotic risk indicators (Figure 2:*Mechanisms of Early Re-occlusion after Lower Extremity Intervention in Diabetic Patients: Independent Contributions of Inflammation, Hemorheology, Renal-Vascular Axis, and Hemodynamics*).

A cornerstone finding of the present analysis is that elevated CRP levels emerged as an independent risk factor for early re-occlusion following endovascular intervention in diabetic foot patients with lower extremity atherosclerotic disease. From a mechanistic perspective, CRP is not merely a passive biomarker of systemic inflammation; it actively promotes vascular injury by activating the complement cascade, upregulating endothelial cell adhesion molecules such as ICAM-1 and VCAM-1[9], and directly inducing a pro-thrombotic state through tissue factor expression on monocytes. These processes collectively impair endothelial healing and accelerate neointimal hyperplasia following angioplasty. This observation is particularly salient in the context of diabetes, where hyperglycemia and insulin resistance synergistically amplify CRP production and its downstream effects, thereby magnifying the inflammatory milieu beyond what is typically observed in non-diabetic populations with PAD[10, 11]. Indeed, previous work has demonstrated that diabetic patients exhibit a more robust CRP response to vascular injury, which is associated with a higher incidence of adverse limb events[12, 13]. While the predictive value of CRP is well-established in coronary artery disease, our data underscore its specific and independent role in the early failure of infrainguinal

revascularization, suggesting that the inflammatory burden is a critical determinant of short-term patency in this unique cohort. Thus, heightened systemic inflammation, as reflected by elevated CRP, fundamentally compromises vascular repair processes and constitutes a primary driver of early re-occlusion.

Further expanding the risk profile, a higher hemoglobin level was independently associated with early re-occlusion, a finding that diverges from the traditional focus on anemia in vascular disease. The potential mechanism may be related to changes in hemorheology. A higher hemoglobin concentration can increase blood viscosity and slow microcirculatory flow, leading to a hypercoagulable state at sites of endothelial injury. These alterations may promote local thrombosis and impair vascular repair, thereby elevating the risk of early re-occlusion [14]. Accordingly, elevated hemoglobin may act as an independent prothrombotic factor for early vessel failure following lower extremity revascularization.

The independent contribution of renal dysfunction, as signified by elevated creatinine levels, to early re-occlusion underscores the critical role of the kidney-vascular axis. Uremic toxins, such as indoxyl sulfate and p-cresol, which accumulate in renal impairment, are known to directly induce endothelial dysfunction, promote vascular smooth muscle cell proliferation, and accelerate vascular calcification, thereby creating a hostile environment for post-intervention vessel repair[15]. This effect is particularly pronounced in the diabetic population, where diabetic nephropathy often co-exists with advanced atherosclerosis, creating a synergistic pathological loop. The risk of reocclusion attributed to renal impairment appears to be independent of traditional glycemic control metrics, as previous large-scale studies have shown that while HbA1c is a risk factor for peripheral artery disease, chronic kidney disease (CKD) itself remains a potent and independent predictor of adverse limb outcomes[12, 16].This distinction is clinically critical, as it suggests that managing uremic milieu, rather than simply optimizing glucose, may be paramount in preventing early restenosis. Furthermore, the presence of CKD complicates post-procedural management, as it limits the safe use of certain antithrombotic agents and contrasts agents, potentially leading to suboptimal pharmacotherapy. In essence, impaired renal function constitutes a powerful, independent risk factor for early reocclusion by fostering a uremic, pro-inflammatory, and pro-calcific vascular environment.

Finally, a reduced LVEF was identified as a forth independent predictor, establishing a direct link between cardiac pump function and the fate of lower extremity vascular interventions. The primary mechanism is hemodynamic: a diminished cardiac output results in reduced perfusion pressure and flow velocity to the distal limb, which promotes local stasis, activates the coagulation cascade, and impairs the washout of pro-thrombotic factors[17–19]. This low-flow state also compromises the endothelial shear stress required for the maintenance of a healthy intimal layer and for the re-endothelialization of the injured vessel segment post-angioplasty. This finding aligns with data demonstrating that coronary heart disease and cerebrovascular disease are independent risk factors for peripheral artery disease in diabetic populations, highlighting the systemic nature of the atherosclerotic burden[16]. Furthermore, in diabetic patients, the presence of diabetic cardiomyopathy—often characterized by diastolic dysfunction and reduced vascular reserve—can exacerbate this vulnerability even with a relatively preserved LVEF. Our data extend these observations by showing that overt systolic dysfunction is a powerful and independent risk factor specifically for early, rather than late, reocclusion, emphasizing the critical importance of adequate forward flow in the immediate post-procedural period. In summary, impaired cardiac systolic function creates a low-flow, pro-thrombotic state in the lower extremities, which directly and independently accelerates the process of early arterial reocclusion after intervention.

In conclusion, this study identifies a novel, integrative risk profile for early reocclusion in diabetic foot patients with lower extremity arterial disease post-intervention, comprising elevated CRP, hemoglobin, creatinine, and reduced LDL-C and left ventricular EF. This multi-system model underscores that early reocclusion is a consequence of intertwined

inflammatory, metabolic, renal, and cardiac dysfunction, moving beyond traditional single-factor paradigms. Future research should prioritize prospective validation of a predictive model incorporating these variables and investigate targeted interventions, such as anti-inflammatory strategies and optimized cardiorenal management, to translate these findings into improved clinical outcomes.

Limitations

The study has several limitations that warrant consideration. First, the retrospective, single-center design with a relatively small sample size (n = 129) may introduce selection bias and limit the generalizability of our findings to broader populations, such as those with different ethnic backgrounds or healthcare systems. Second, the lack of detailed data on post-procedural medication adherence (e.g., antiplatelet agents, statins) and precise glycemic control metrics precludes a comprehensive assessment of how these critical management factors confound the observed associations, particularly the paradoxical finding of low LDL-C, which may be influenced by unmeasured statin use or underlying inflammatory cachexia.

Declarations

Disclosure of interest

The authors declare that there are no conflicts of interest.

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Author Contribution

Chenyang Lu: Conceptualization, Methodology, Investigation, Writing – original draft, Visualization.Guangyuan Xiang: Data curation, Formal analysis, Investigation, Software, Writing – review & editing.Lei Wang: Methodology, Validation, Investigation, Writing – review & editing.Huijuan Qin: Data curation, Formal analysis, Investigation, Visualization.Xinjuan Sun: Conceptualization, Methodology, Supervision, Project administration, Funding acquisition, Writing – review & editing.Jinan Chen: Conceptualization, Methodology, Supervision, Resources, Writing – review & editing.All authors contributed to the article and approved the submitted version. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data Availability

The datasets generated and/or analysed during the current study are not publicly available due to patient confidentiality and institutional ethics regulations, but are available from the corresponding author on reasonable request and subject to appropriate ethical approval.

References

1. S. CALLEGARI, G. ROMAIN, A. AGGARWAL et al., Diabetes status and long-term mortality and major amputation outcomes following revascularization in chronic limb-threatening ischemia [J]. J. Vasc Surg. **82**(4), 1401–11e5 (2025)
2. X. LUO, K. HUANG, B. HUANG et al., Single-Center Experience of Treating Chronic Limb-Threatening Ischemia of Lower Limbs Combined with Diabetes [J]. Sichuan Da Xue Xue Bao Yi Xue Ban. **53**(6), 988–992 (2022)
3. R. FITRIDGE, V. CHUTER, J. MILLS et al., (eds.), 's Choice - The Intersocietal IWGDF, ESVS, SVS Guidelines on Peripheral Artery Disease in People With Diabetes Mellitus and a Foot Ulcer [J]. Eur J Vasc Endovasc Surg, 2023, 66(4): 454 – 83
4. A.B.O.Y.A.N.S.V. TWINE C P, KAKKOS S K et al., (eds.), 's Choice - European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on Antithrombotic Therapy for Vascular Diseases [J]. European journal of vascular and endovascular surgery: the official journal of the European Society for Vascular Surgery, 2023, 65(5): 627 – 89
5. C.H.U.N.G.J. COOK I O, Contemporary Medical Management of Peripheral Arterial Disease [J]. Cardiovasc. Drugs Ther. **39**(2), 357–371 (2025)
6. B. ZHAO, X. YANG, J. JIANG et al., Comprehensive evaluation of combined AngioJet and drug-coated balloon therapy for diabetic foot ulcers with lower extremity arterial occlusive disease [J]. Am. J. Transl Res. **17**(8), 6166–6179 (2025)
7. H. HSU, J. CHAN, CHENG Y T et al., Diabetic Foot Preservation in End-Stage Renal Disease with Combined Angioplasty and Free Flap Reconstruction [J]. Plast. Reconstr. Surg. **157**(5), 763e–73e (2026)
8. H.M. THAI D Q, JUNG Y K, HAHN et al., Factors affecting the outcome of lower extremity osteomyelitis treated with microvascular free flaps: an analysis of 65 patients [J]. J. Orthop. Surg. Res. **16**(1), 535 (2021)
9. J. ZELLER, J. LOSEFF-SILVER, K. KHOSHMANESH et al., Shear-Sensing by C-Reactive Protein: Linking Aortic Stenosis and Inflammation [J]. Circ. Res. **135**(11), 1033–1047 (2024)
10. H. GONG, Y. REN, Z. LI et al., Clinical characteristics and risk factors of lower extremity amputation in the diabetic inpatients with foot ulcers [J]. Front. Endocrinol. (Lausanne). **14**, 1144806 (2023)
11. M. SIBIANU, SLEVIN M. The Pathogenic Role of C-Reactive Protein in Diabetes-Linked Unstable Atherosclerosis [J]. Int. J. Mol. Sci., 2025, **26**(14)
12. B. REN, B. LI, T. PAN et al., Risk factors for at-risk foot and peripheral artery disease among the population with diabetes: A multicommunity-based cross-sectional study [J]. Diabetes Res. Clin. Pract. **203**, 110869 (2023)
13. T. ALNIMA, MEIJER R I, SPRONK H M, H et al., Diabetes- versus smoking-related thrombo-inflammation in peripheral artery disease [J]. Cardiovasc. Diabetol. **22**(1), 257 (2023)
14. J.R. BYRNES, A.S. WOLBERG, Red blood cells in thrombosis [J]. Blood. **130**(16), 1795–1799 (2017)
15. M. KILIC, N. OLGUN, M. DUNDAR et al., Prevalence, risk level and risk factors of diabetic foot ulcer among adult individuals with diabetes in the Southeastern Anatolia Region of Turkiye [J]. J. Tissue Viability. **34**(1), 100839 (2025)

16. J. LIU, X. YUAN, J. LIU et al., Risk Factors for Diabetic Peripheral Neuropathy, Peripheral Artery Disease, and Foot Deformity Among the Population With Diabetes in Beijing, China: A Multicenter, Cross-Sectional Study [J]. Front. Endocrinol. (Lausanne). **13**, 824215 (2022)
17. K. VAHIDKHAH, M. ABBASI, M. BARAKAT et al., Effect of reduced cardiac output on blood stasis on transcatheter aortic valve leaflets: implications for valve thrombosis [J]. EuroIntervention. **13**(7), 811–819 (2017)
18. U.S. GURBEL P A, TANTRY, Antiplatelet and anticoagulant agents in heart failure: current status and future perspectives [J]. JACC Heart Fail. **2**(1), 1–14 (2014)
19. L. HE, Q. ZHANG C L, CHEN et al., Endothelial shear stress signal transduction and atherogenesis: From mechanisms to therapeutics [J]. Pharmacol. Ther. **235**, 108152 (2022)

Figures

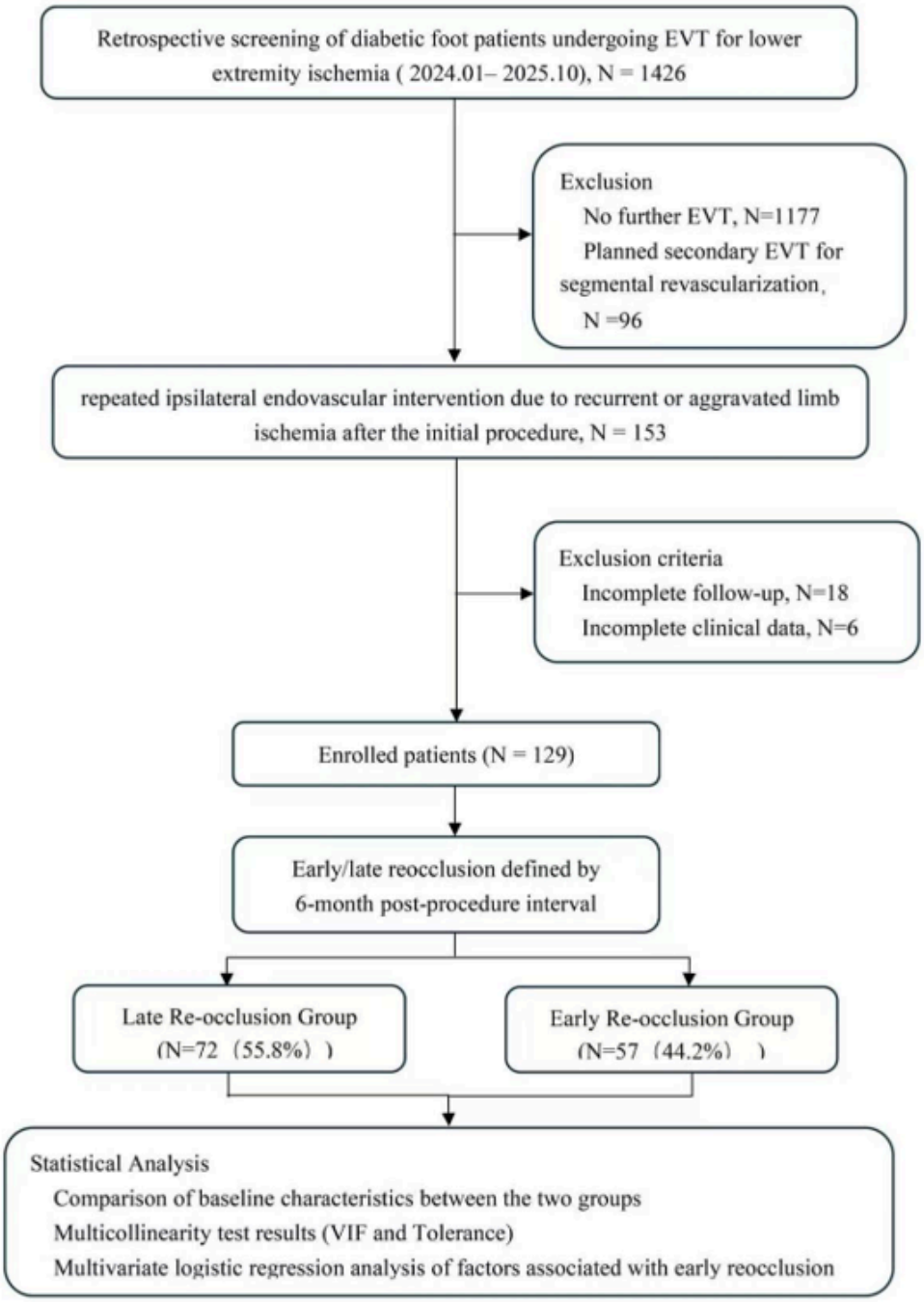


Figure 1

The flow diagram of patient selection

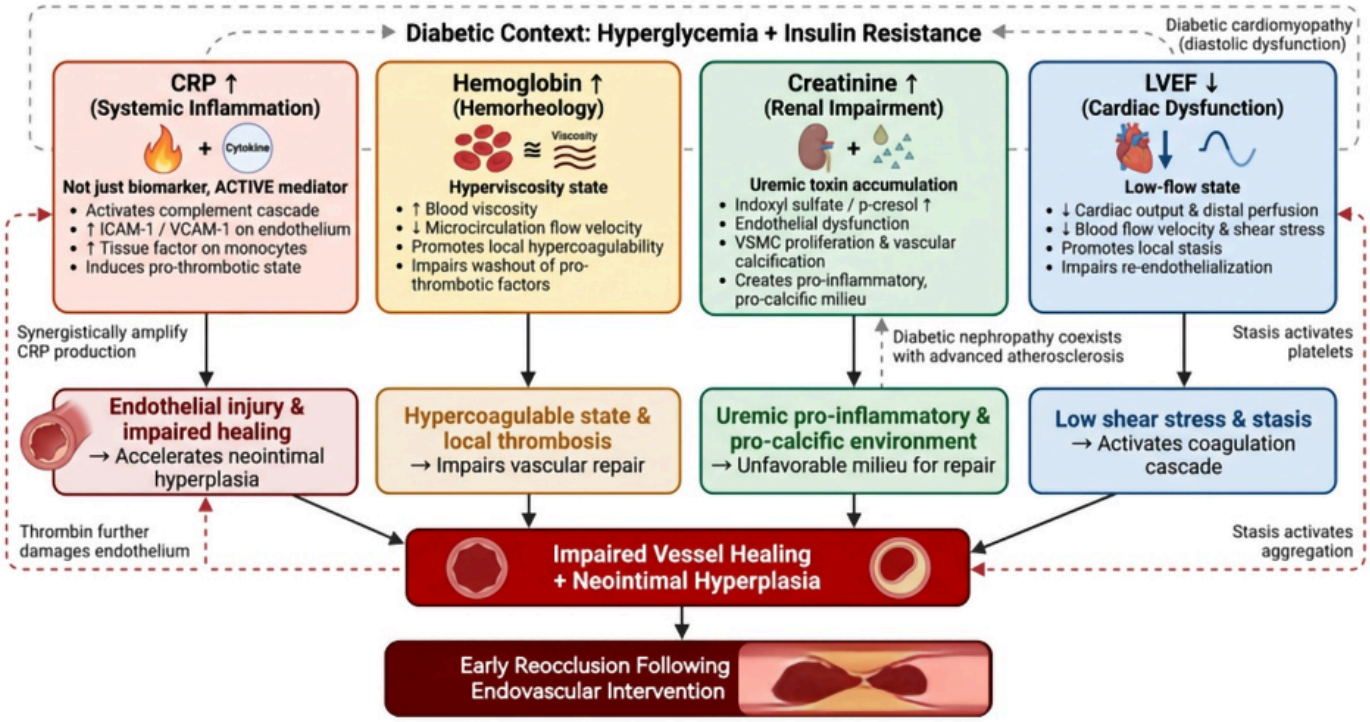


Figure 2

Mechanisms of Early Re-occlusion after Lower Extremity Intervention in Diabetic Patients: Independent Contributions of Inflammation, Hemorheology, Renal-Vascular Axis, and Hemodynamics