

Integrated Impact of Inflammation and Mineral Metabolism on Arteriovenous Fistula Stenosis and Repeated Intervention in Maintenance Hemodialysis: A Real-World Cross-Sectional Study

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**Integrated Impact of Inflammation and Mineral Metabolism on Arteriovenous
Fistula Stenosis and Repeated Intervention in Maintenance Hemodialysis: A Real-
World Cross-Sectional Study**

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Background

Arteriovenous fistula (AVF) dysfunction remains a major barrier to adequate dialysis delivery in patients undergoing maintenance hemodialysis (MHD), frequently resulting in repeated interventions and increased healthcare burden. Although chronic inflammation and mineral metabolism abnormalities are both implicated in vascular remodeling, their integrated clinical significance in AVF stenosis has not been well defined. Leveraging large-scale real-world data, this cross-sectional study aimed to comprehensively evaluate the associations of inflammatory indices and calcium–phosphate metabolism parameters with AVF stenosis and repeated percutaneous transluminal angioplasty (PTA).

Methods

In this single-center cross-sectional study, 683 MHD patients with AVF stenosis requiring PTA were enrolled as the case group, while 255 contemporaneous patients with normally functioning AVFs served as controls. Demographic characteristics, comorbidities, dialysis vintage, laboratory measurements, mineral metabolism markers, and inflammatory indices were collected. Inflammatory markers—including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR),

lymphocyte-to-monocyte ratio (LMR), neutrophil-to-high-density lipoprotein ratio (NHR), and systemic immune-inflammation index (SII)—were derived from peripheral blood counts. Multivariable logistic regression analyses were conducted to identify variables independently associated with AVF stenosis and repeated PTA within 12 months. Discriminatory performance was evaluated using receiver operating characteristic (ROC) curves, with subgroup analyses performed according to diabetes status and sex.

Results

Patients with AVF stenosis exhibited significantly higher serum phosphorus, intact parathyroid hormone (iPTH), calcium–phosphate product, NLR, PLR, and SII levels, alongside lower LMR and lymphocyte counts (all $P < 0.05$). Elevated iPTH, NLR, SII, calcium–phosphate product, and diabetes were independently associated with AVF stenosis. Among patients with established stenosis, higher NLR, diabetes, longer dialysis vintage, female sex, and lower serum albumin were independently associated with repeated PTA. Subgroup analyses suggested stronger associations with repeated interventions among diabetic and female patients. Notably, prediction models integrating inflammatory and mineral metabolism markers demonstrated superior discriminatory capacity compared with individual parameters.

Conclusion

Systemic inflammation and disordered mineral metabolism are both significantly associated with AVF stenosis in MHD patients, whereas inflammatory burden appears more closely linked to repeated interventions. A multidimensional risk assessment

strategy incorporating these markers may improve early identification of high-risk patients and support more targeted vascular access management.

Keywords:

Arteriovenous fistula stenosis; Neutrophil-to-lymphocyte ratio; Systemic immune-inflammation index; Parathyroid hormone; Calcium–phosphate product

Arteriovenous fistula (AVF) remains the preferred vascular access for patients undergoing hemodialysis due to its superior long-term patency and lower infection risk compared with arteriovenous grafts and central venous catheters ^[1]. Despite these advantages, AVF stenosis continues to represent a major clinical challenge, affecting up to 40% of patients within the first year after access creation ^{[2], [3]}. The pathogenesis of AVF stenosis is multifactorial, involving vascular injury, neointimal hyperplasia, and extracellular matrix remodeling. These processes are influenced not only by surgical and hemodynamic factors but also by systemic pathological conditions ^[4].

Chronic inflammation is a hallmark of end-stage kidney disease and maintenance hemodialysis and is increasingly recognized as a central driver of endothelial injury, vascular remodeling, and neointimal proliferation ^[5]. Persistent low-grade inflammation promotes the activation of neutrophils, monocytes, and platelets, leading to the release of pro-inflammatory cytokines and oxidative stress mediators that stimulate vascular smooth muscle cell proliferation and migration, thereby accelerating luminal narrowing at the venous segment of the AVF.

In recent years, inflammation-related indices derived from routine blood cell counts have attracted considerable attention because of their accessibility and cost-

effectiveness. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) are established markers reflecting the balance between inflammatory activation and immune regulation and have been associated with adverse outcomes across a range of conditions, including rheumatic diseases, malignancies, cardiovascular disorders, respiratory diseases, and dialysis-related complications [6], [7]. The systemic immune-inflammation index (SII), which integrates platelet counts with the NLR framework, may provide a more comprehensive representation of inflammatory burden, immune suppression, and thrombogenic potential. Emerging evidence suggests that SII may outperform single inflammatory markers in predicting vascular access patency, stenosis, and long-term survival [8], [9].

Mineral metabolism disorders are another common complication in patients with chronic kidney disease and are considered key determinants of vascular calcification progression [10]. Accumulating evidence indicates that abnormalities in phosphate homeostasis, calcium–phosphate product, and intact parathyroid hormone (iPTH) may contribute to AVF failure in hemodialysis populations [11]. Experimental studies further demonstrate that elevated PTH levels can induce endothelial dysfunction and upregulate adhesion molecule expression, thereby promoting vascular remodeling and stenosis [12].

To date, most investigations have focused on the independent effects of inflammatory markers or mineral metabolism disturbances on AVF dysfunction. However, the potential synergistic impact of these pathways on AVF patency remains insufficiently understood. Given the pivotal role of inflammation in vascular

remodeling and the high prevalence of mineral imbalance in dialysis patients, a comprehensive evaluation of their combined effects is warranted.

Therefore, the present study aimed to investigate the joint association of systemic inflammatory indices and mineral metabolism abnormalities with AVF dysfunction in patients undergoing maintenance hemodialysis, with the goal of improving risk stratification and informing strategies to prolong vascular access longevity.

2.METHOD

2.1 Study design and ethics approval

This single-center cross-sectional study was conducted at the Affiliated Hospital of North Sichuan Medical College. The study protocol was reviewed and approved by the Institutional Ethics Committee of the Affiliated Hospital of North Sichuan Medical College (Approval No.2026ER103-1). Given the retrospective nature of the study, the requirement for written informed consent was waived. The study adhered to the principles of the Declaration of Helsinki and was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

2.2 Study population

A total of 1,095 hemodialysis patients evaluated for vascular access dysfunction between January 2022 and December 2024 were retrospectively screened. After applying the eligibility criteria, 683 patients diagnosed with arteriovenous fistula (AVF) stenosis who underwent percutaneous transluminal angioplasty (PTA) were included in the stenosis group. The control group comprised 255 contemporaneous maintenance

hemodialysis (MHD) patients with normally functioning AVFs, thereby minimizing temporal bias.

All clinical and laboratory variables were collected at a single predefined time point—hospital admission for patients with AVF stenosis and routine clinical evaluation for controls—consistent with the cross-sectional design.

To identify determinants of recurrent vascular intervention, patients with AVF stenosis were categorized based on the number of PTA procedures within 12 months into a single-PTA group (one procedure, $n = 507$) and a repeated-PTA group (≥ 2 procedures, $n = 176$). This classification was derived from existing medical records without prospective follow-up.

Figure 1 illustrates the participant selection process.

Eligibility criteria

Inclusion criteria

Participants were eligible if they:

- (1) Had received hemodialysis via autologous AVF for ≥ 3 months
- (2) Underwent dialysis three times weekly
- (3) Had complete clinical and laboratory data.

Exclusion criteria

Patients were excluded for:

- (1) Non-autologous vascular access (e.g., tunneled catheters or grafts)
- (2) Poor dialysis adherence
- (3) Acute infection

- (4) Severe coagulation disorders and Recent major hemorrhage
- (5) Long-term systemic glucocorticoid therapy
- (6) Severe cardiopulmonary insufficiency
- (7) Active malignancy.

2.3 Definition and assessment of AVF stenosis

Ultrasound evaluations were performed by a single experienced vascular sonographer using a Mindray ultrasound system with a 16-MHz linear-array transducer, ensuring measurement consistency. Significant stenosis was defined as a $\geq 50\%$ reduction in luminal diameter compared with the adjacent normal vessel segment (stenosis ratio < 0.5), in accordance with established diagnostic criteria ^[13].

Percutaneous transluminal angioplasty procedure

All procedures were performed in the operating room of the Department of Nephrology at the Affiliated Hospital of North Sichuan Medical College. Percutaneous transluminal angioplasty (PTA) was conducted under ultrasound guidance by any two of three senior nephrologists (JZW, KY, and HPZ), each with at least five years of experience in interventional peripheral vascular procedures, ensuring procedural consistency and operator reliability.

2.4 Data collection and laboratory measurements

Baseline demographic and clinical data included age, sex, body mass index (BMI), dialysis vintage, presence of diabetes mellitus, and use of antiplatelet or anticoagulant medications.

Peripheral venous blood samples were obtained at study inclusion. Complete blood

counts were analyzed using the same automated hematology analyzer with routine calibration. Biochemical parameters—including serum creatinine, albumin, corrected calcium, phosphorus, and intact parathyroid hormone (iPTH)—were measured using standardized laboratory methods.

The calcium–phosphorus product ($\text{Ca} \times \text{P}$) was calculated as: corrected serum calcium $\times$ serum phosphorus $\times 12.4$.

BMI was calculated as weight (kg) divided by height squared (m^2).

Inflammatory indices

Inflammatory biomarkers were derived from peripheral blood counts: Neutrophil-to-lymphocyte ratio (NLR) = neutrophils / lymphocytes、Platelet-to-lymphocyte ratio (PLR) = platelets / lymphocytes、Lymphocyte-to-monocyte ratio (LMR) = lymphocytes / monocytes、Systemic immune-inflammation index (SII) = platelets $\times$ neutrophils / lymphocyte. These indices were selected due to their established value in reflecting systemic inflammation and immune imbalance.

All laboratory values were obtained at a single time point in accordance with the cross-sectional design.

2.5 Measures to reduce bias

Multiple methodological strategies were implemented to mitigate potential sources of bias. Consecutive patient enrollment reduced selection bias, contemporaneous controls minimized temporal confounding, and standardized laboratory procedures improved measurement consistency. Additionally, the use of predefined diagnostic criteria enhanced internal validity. However, residual

confounding inherent to observational research cannot be fully eliminated.

2.6 Statistical analysis

Statistical analyses were performed using SPSS version 23.0. Normality was assessed using the Shapiro–Wilk test. Normally distributed variables were expressed as mean $\pm$ standard deviation (SD) and compared using the independent-samples t-test. Non-normally distributed data were reported as median (interquartile range, IQR) and compared using the Mann–Whitney U test. Categorical variables were summarized as frequencies (percentages) and analyzed using the chi-square test or Fisher’s exact test. Variables with $P < 0.05$ in univariate analyses were entered into multivariable logistic regression models to identify independent factors associated with: AVF stenosis, Repeated PTA within 12 months. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Predictive performance was evaluated using receiver operating characteristic (ROC) curves, and the area under the curve (AUC) was calculated to compare discriminative ability between individual predictors and the combined model. All tests were two-sided, with $P < 0.05$ considered statistically significant.

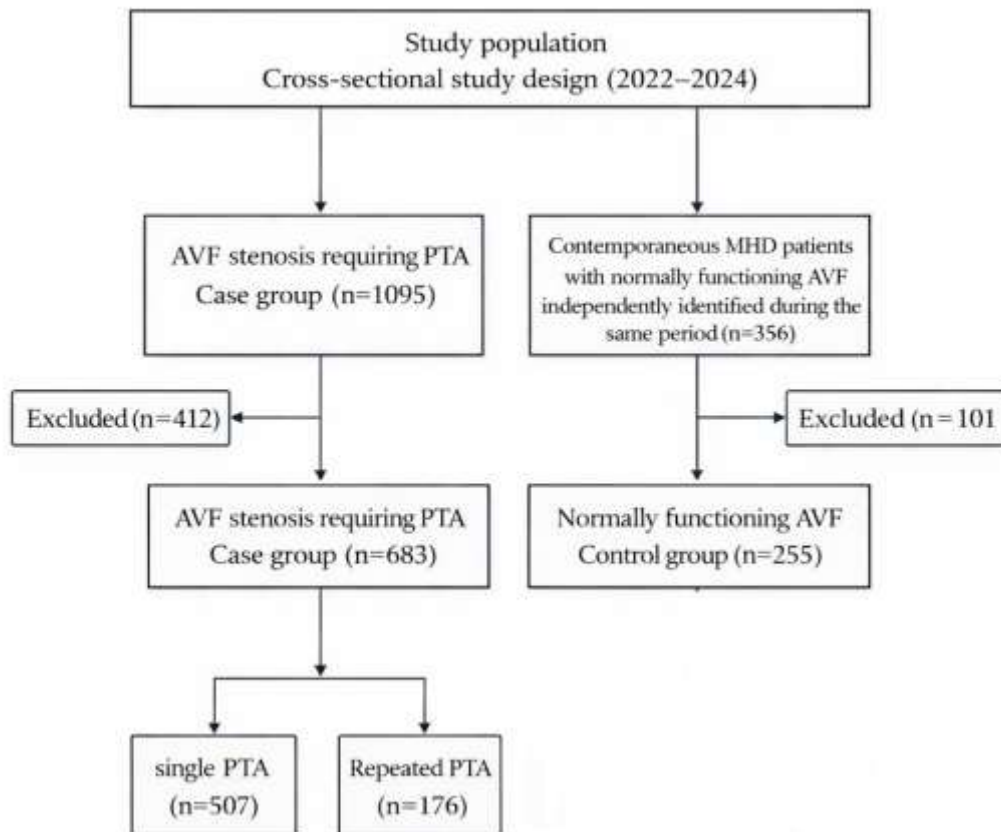


Figure 1. Flow diagram of participant selection. Patients with arteriovenous fistula (AVF) stenosis were screened from individuals evaluated for vascular access dysfunction, while contemporaneous maintenance hemodialysis patients with normally functioning AVF were independently identified as controls. Stenosis patients were further stratified according to the number of percutaneous transluminal angioplasty (PTA) procedures within 12 months.

2. Results

2.1 Baseline characteristics of the study population

A total of 938 patients receiving maintenance hemodialysis were included in this study, comprising 683 patients with arteriovenous fistula (AVF) stenosis (case group)

and 255 patients with functionally normal AVF (control group). The two groups were comparable in terms of age and sex distribution.

Compared with the control group, patients with AVF stenosis exhibited significantly higher levels of serum phosphorus, intact parathyroid hormone (iPTH), calcium–phosphorus product ($\text{Ca}\times\text{P}$), and inflammatory indices, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), and systemic immune-inflammation index (SII) (all $P < 0.05$). In addition, significant differences were observed in neutrophil and lymphocyte counts between the two groups. The prevalence of diabetes was also significantly higher among patients with AVF stenosis ($P < 0.05$) (Table 1).

Table 1. Baseline data between AVF group and control group.

Variable	AVF group (n=683)	Control group (n=255)	<i>P</i> -value
Age (Y)	58.84±13.32	57.22±14.51	0.103
Kt/V	1.32±0.08	1.32±0.03	0.408
Dialysis age (m)	35.00 (21.00-68.00)	38.00 (21.00-79.00)	0.144
Gender (Male, %)	383 (56.80%)	141 (55.29%)	0.830
Diabetes (n, %)	231 (33.82%)	62 (24.31%)	0.005
ANC ($\times 10^9/\text{L}$)	4.72 (3.76-6.12)	4.25 (3.43-5.12)	0.000
ALC ($\times 10^9/\text{L}$)	1.04 (0.77-1.34)	1.16 (0.94-1.49)	0.000
AMC ($\times 10^9/\text{L}$)	0.38 (0.29-0.50)	0.37 (0.30-0.46)	0.460
RBC ($\times 10^{12}/\text{L}$)	3.74 (3.15-4.15)	3.68 (3.23-4.14)	0.769
Hb (g/dl)	110.00 (95.00-124.00)	108.00 (96.00-122.00)	0.622

PLT ($\times 10^9/L$)	166.00 (125.00-208.00)	154.00 (124.00-203.00)	0.084
Albumin (g/d)	40.70 (37.50-43.70)	41.10 (38.50-43.40)	0.146
cCa (mmol/l)	2.25 (2.11-2.38)	2.24 (2.13-2.37)	0.603
P (mmol/l)	1.83 (1.46-2.30)	1.68 (1.38-2.04)	0.004
iPTH (pg/ml)	252.00 (138.90-455.00)	225.00 (147.40-348.40)	0.043
NLR	4.56 (3.28-6.44)	3.51 (2.77-4.45)	0.000
PLR	155.55 (118.04-215.13)	134.61 (91.72-174.11)	0.000
LMR	2.75 (1.94-3.67)	3.18 (2.47-4.16)	0.000
SII	738.70 (484.43-1175.52)	524.77 (370.96-756.16)	0.000
Ca $\times$ P (mg^2/dL^2)	50.13 (40.60-63.58)	46.48 (39.06-56.24)	0.003
Scr ($\mu mol/l$)	787.20 (638.62-977.45)	825.70 (678.70-1007.00)	0.150
TC (mmol/l)	3.66 (3.08-4.30)	3.59 (3.20-4.16)	0.486
HDL-C (mmol/l)	1.03 (0.83-1.29)	1.04 (0.82-1.27)	0.914

AVF: arteriovenous fistula; Ktv: ; ANC: absolute neutrophil count; ALC: absolute lymphocyte count; AMC: absolute monocyte count; RBC: red blood cell; Hb: hemoglobin; PLT: platelet; cCa: corrected calcium; P: phosphate; iPTH: intact parathyroid hormone; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; SII: systemic immune-inflammation index; Ca-P product: Calcium – Phosphate product; Scr: serum creatinine; TC: total cholesterol; HDL-C: high density lipoprotein cholesterol.

2.2 Univariate and multivariate logistic regression analyses for AVF stenosis

In the univariate logistic regression analysis, serum phosphorus, intact parathyroid hormone (iPTH), calcium–phosphorus product (Ca $\times$ P), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), and diabetes were significantly associated with AVF stenosis (all $P < 0.05$). Variables that achieved statistical significance in the univariate analysis were subsequently entered into the

multivariate logistic regression model.

After adjustment for potential confounders, iPTH, NLR, SII, calcium–phosphorus product, and diabetes remained independently associated with AVF stenosis (all $P < 0.05$) (Table 2).

Table 2. Univariate and multivariate logistic regression analyses for AVF stenosis.

Variable	Univariate analysis		Multivariate analysis	
	OR (95%CI)	<i>P</i> -value	OR (95%CI)	<i>P</i> -value
Diabetes	1.591 (1.147-2.206)	0.005	1.476(1.048-2.081)	0.001
ANC	1.273 (1.161-1.395)	0.000		
ALC	0.443 (0.317-0.619)	0.000		
P	1.306 (1.050-1.624)	0.016		
iPTH	1.001 (1.000-1.002)	0.000	1.001 (1.000-1.002)	0.001
NLR	1.343 (1.235-1.461)	0.000	1.241 (1.124-1.369)	0.000
PLR	1.006 (1.004-1.008)	0.000		
LMR	0.817 (0.743-0.898)	0.000		
SII	1.001 (1.001-1.001)	0.000	1.000 (1.000-1.001)	0.024
Ca-P product	1.010 (1.003-1.018)	0.009	1.009 (1.001-1.017)	0.032

AVF: arteriovenous fistula; ANC: Absolute Neutrophil Count; ALC: Absolute Lymphocyte Count; P: Phosphate; iPTH: intact parathyroid hormone; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; SII: systemic immune-inflammation index; Ca-P product: Calcium – Phosphate product.

2.3 Risk factors for repeated PTA among patients with AVF stenosis

Among the 683 patients with AVF stenosis, participants were further categorized according to the number of percutaneous transluminal angioplasty (PTA) procedures

performed within 12 months into a single-PTA group (one procedure, $n = 507$) and a repeated-PTA group (≥ 2 procedures, $n = 176$).

Univariate logistic regression analysis demonstrated that sex, dialysis vintage, diabetes, serum albumin level, and neutrophil-to-lymphocyte ratio (NLR) were significantly associated with the need for repeated PTA within 12 months (all $P < 0.05$). After multivariate adjustment, NLR, diabetes, dialysis vintage, sex, and serum albumin remained independent predictors of repeated PTA interventions (all $P < 0.05$) (Table 3).

Table 3. Univariate and multivariate logistic regression analyses for repeated PTA in patients with AVF stenosis.

Variable	Univariate analysis		Multivariate analysis	
	OR (95%CI)	<i>P</i> -value	OR (95%CI)	<i>P</i> -value
Dialysis age (m)	1.004 (1.000-1.008)	0.038	1.005(1.000-1.009)	0.028
			1.005 (1.000-1.009)*	0.022*
Albumin (g/L)	0.968 (0.937-1.000)	0.048	0.959 (0.928-0.992)	0.015
			0.958 (0.926-0.991)*	0.014*
NLR	1.062 (1.026-1.100)	0.001	1.069 (1.030-1.110)	0.000
			1.181 (1.103-1.263)*	0.000*
Gender (F/M)	1.138 (1.055-1.227)	0.013	1.911(1.314-2.777)	0.001
			1.854 (1.267-2.714)*	0.001*
Diabetes	3.905 (2.727-5.593)	0.000	4.373 (3.001-6.371)	0.000
			4.525 (3.079-6.650)*	0.000

PTA: percutaneous transluminal angioplasty; AVF: arteriovenous fistula; NLR: neutrophil-to-lymphocyte ratio.

*: Adjust for iPTH, SII, Ca-P product and age.

2.4 Subgroup analyses

(1) Stratification by diabetes status (Figure 2A)

Subgroup analysis among patients with AVF stenosis demonstrated that individuals with diabetes had a significantly higher risk of requiring repeated PTA procedures within 12 months compared with those without diabetes. This finding suggests that diabetes may accelerate the progression of AVF stenosis and increase the likelihood of repeated vascular interventions.

(2) Stratification by sex (Figure 2B)

When stratified by sex, female patients with AVF stenosis exhibited a significantly greater risk of undergoing repeated PTA within 12 months than male patients. This observation indicates that sex-related biological characteristics or vascular differences may influence long-term AVF patency.

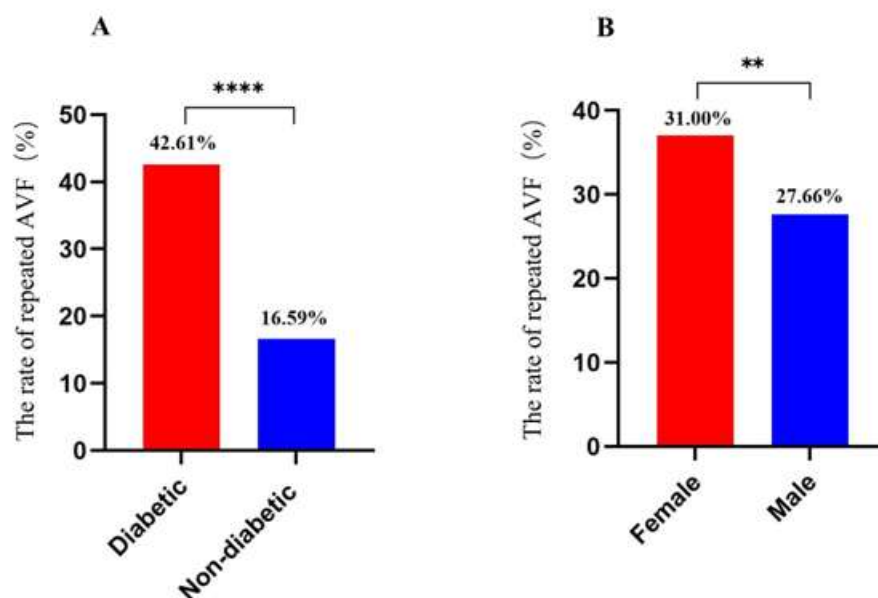


Figure2. The rate of repeated AVF in diabetic and non-diabetic patients, and by sex. (A) The rate of repeated AVF was significantly higher in diabetic patients compared to non-diabetic patients (42.61% vs 16.59%, **** $p < 0.0001$).

(B) Female patients had a significantly higher rate of repeated AVF compared to male patients (31.00% vs 27.66%, $**p < 0.05$).

2.5 Receiver operating characteristic analysis for AVF stenosis

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of independent risk factors identified in the multivariate logistic regression model, including intact parathyroid hormone (iPTH), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), calcium-phosphorus product ($\text{Ca} \times \text{P}$), and diabetes, for AVF stenosis. Each individual parameter demonstrated moderate discriminatory ability. Notably, the combined predictive model incorporating all five variables yielded a higher area under the curve (AUC) than any single parameter, indicating superior performance in identifying AVF stenosis (Figure 3A).

2.6 Receiver operating characteristic analysis for repeated PTA

ROC curve analysis was further conducted to assess predictors of repeated PTA among patients with AVF stenosis. Independent variables identified through multivariate analysis—including NLR, diabetes, dialysis vintage, sex, and serum albumin—were evaluated both individually and in combination. The composite predictive model achieved a higher AUC compared with each individual predictor, suggesting improved risk stratification for repeated AVF interventions (Figure 3B).

Figure 3. ROC curve analysis for predicting AVF stenosis and repeated PTA interventions.

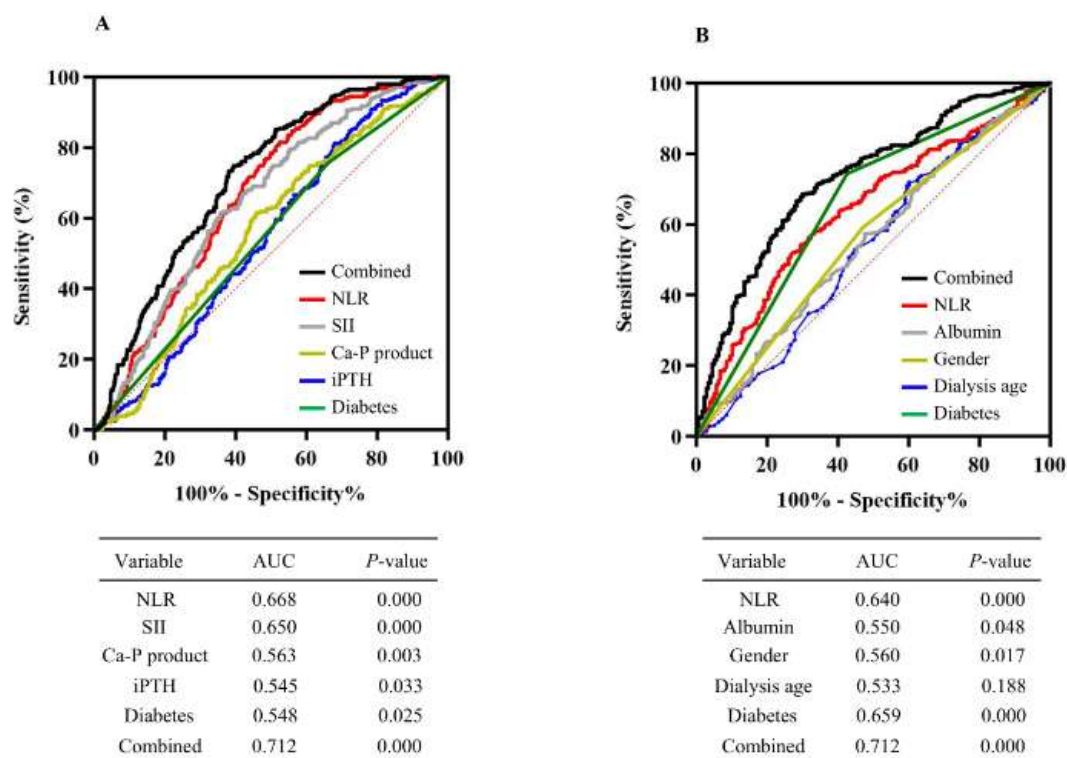


Figure3. ROC curve analysis for predicting AVF stenosis and repeated PTA interventions. (A) ROC analysis for AVF stenosis showed that the combined model (black line) including PTH, NLR, SII, calcium–phosphate product, and diabetes had a superior AUC compared to individual parameters, indicating better discriminatory power. (B) ROC analysis for repeated PTA in AVF stenosis patients demonstrated that the combined model, including NLR, diabetes, dialysis vintage, sex, and serum albumin, achieved a higher AUC than individual predictors, suggesting improved risk stratification for repeated interventions. Table below shows the AUC and P-values for each variable.

3. Discussion

Arteriovenous fistula (AVF) remains the preferred vascular access for maintenance hemodialysis; however, stenosis and access dysfunction continue to compromise dialysis adequacy and long-term patient outcomes. The present study provides a comprehensive evaluation of inflammatory burden and mineral metabolism abnormalities in relation to AVF dysfunction using real-world clinical data from a large cohort. Notably, our findings highlight the complementary roles of systemic inflammation and disordered mineral metabolism in shaping vascular vulnerability,

thereby offering clinically actionable insights for early risk stratification.

Inflammation is increasingly recognized as a central driver of AVF remodeling, influencing endothelial integrity, extracellular matrix turnover, and neointimal formation throughout the lifespan of the access ^[14]. In this context, we identified both NLR and SII as independent correlates of AVF stenosis, with the combined model demonstrating superior discriminatory capacity compared with individual markers. NLR reflects an imbalance between innate inflammatory activation and adaptive immune regulation; neutrophil-derived proteolytic enzymes and reactive oxygen species may directly injure the vascular endothelium, whereas lymphopenia signals chronic physiological stress ^[15]. Prior studies have similarly linked elevated NLR to AVF maturation failure and access dysfunction ^[16]. Importantly, our study extends these observations by demonstrating that NLR also predicts repeated PTA, suggesting that persistent systemic inflammation may predispose patients to maladaptive vascular repair following intervention.

SII further integrates platelet activity into the inflammatory framework, capturing the interplay between immune activation and thrombogenic potential. Beyond hemostasis, platelets amplify leukocyte recruitment and promote smooth muscle cell migration, thereby accelerating vascular remodeling ^[17]. The independent association between SII and AVF stenosis observed in our cohort supports the concept that composite inflammatory indices may outperform single biomarkers when characterizing the complex vascular microenvironment.

Mineral metabolism disorders represent another fundamental pathway

contributing to vascular pathology in dialysis populations. Intact parathyroid hormone (iPTH), once viewed primarily as a regulator of calcium-phosphate homeostasis, is now recognized as an active mediator of vascular calcification. Experimental evidence suggests that excess PTH can induce osteogenic differentiation of vascular smooth muscle cells via ERK1/2 and NF- κ B signaling pathways ^{[10] , [18]}. Clinically, elevated iPTH levels have been associated with an increased risk of AVF thrombosis ^[19]. Consistent with these findings, our analysis identified iPTH as an independent correlate of AVF stenosis.

Similarly, the calcium-phosphate product ($\text{Ca} \times \text{P}$) functions as an integrated indicator of mineral imbalance. Current KDIGO recommendations emphasize maintaining $\text{Ca} \times \text{P}$ below $55 \text{ mg}^2/\text{dL}^2$ to mitigate vascular calcification risk. Mechanistically, excess calcium-phosphate promotes osteogenic transition of vascular smooth muscle cells, increases arterial stiffness, and impairs adaptive vascular remodeling ^{[20], [21]}. Previous clinical work has also identified elevated $\text{Ca} \times \text{P}$ as a predictor of AVF reoperation^[22]. Together, these data reinforce the structural contribution of mineral dysregulation to AVF susceptibility.

Interestingly, although both iPTH and $\text{Ca} \times \text{P}$ were associated with stenosis, neither independently predicted repeated PTA. This divergence suggests that mineral metabolism abnormalities may primarily influence the initiation of structural vascular injury, whereas post-stenotic progression appears to be more dynamically governed by inflammatory activity and reparative responses.

Dialysis vintage emerged as another independent determinant of repeated

intervention. Rather than serving merely as a temporal measure, prolonged dialysis exposure likely reflects cumulative vascular injury. Chronic exposure to abnormal shear stress promotes endothelial dysfunction and neointimal hyperplasia—the principal mechanism underlying AVF restenosis ^[23]. These findings underscore the progressive nature of vascular remodeling in long-term dialysis patients.

We additionally observed that diabetes and female sex were associated with higher risks of repeated PTA. Hyperglycemia-induced endothelial dysfunction and impaired vascular repair may partly explain the adverse impact of diabetes ^[24]. Sex-related differences in vessel diameter, hormonal influences, and susceptibility to neointimal proliferation have also been proposed. ^{[25] [26]}

Hypoalbuminemia independently predicted repeated intervention, further supporting the pathogenic synergy between malnutrition and inflammation. As a surrogate marker of the malnutrition-inflammation complex, low albumin reflects impaired tissue repair capacity and heightened inflammatory stress, both of which may accelerate vascular failure ^{[27] [28]}.

Limitations and future directions

Several limitations should be acknowledged. First, this was a single-center study with a cross-sectional case–control design, which precludes causal inference and limits generalizability to broader hemodialysis populations. Although consecutive inclusion and contemporaneous controls were applied to reduce selection and temporal bias, residual confounding inherent to observational research cannot be fully excluded. Second, detailed data on thrombosis events, anatomical characteristics of the fistula,

and quantitative stenosis severity were not systematically available, which may have constrained mechanistic interpretation. Third, inflammatory and mineral metabolism parameters were assessed at a single predefined time point; therefore, dynamic fluctuations over time and their temporal relationship with AVF dysfunction could not be evaluated. Finally, external validation of the composite predictive model was not performed.

Future multicenter prospective cohort studies with larger and more diverse populations are warranted to validate our findings and enhance external applicability. Incorporation of longitudinal biomarker measurements, imaging-derived vascular parameters, and time-to-event analyses would provide deeper insight into causal pathways and progression patterns. In addition, integrating inflammatory and mineral biomarkers into risk prediction tools alongside clinical and hemodynamic variables may refine individualized surveillance strategies. Such efforts may ultimately facilitate earlier identification of high-risk patients, optimize timing of intervention, and contribute to prolonging vascular access longevity in the maintenance hemodialysis population.

Conclusion

This study confirms that inflammatory responses and mineral metabolism disorders play a key role in the occurrence of AVF dysfunction. NLR, SII, PTH and calcium-phosphorus product were important independent correlates with AVF stenosis, and the combined model had better risk identification ability than a single index. In patients with AVF stenosis, NLR, diabetes, dialysis age, gender, and serum albumin

were significantly associated with repeat PTA, suggesting that multidimensional risk assessment could help optimize the identification of high-risk populations. Since the above indicators are derived from routine laboratory testing, the integrated evaluation strategy constructed in this study has good clinical feasibility, which may promote the transformation of vascular access management from passive intervention to active risk stratification. In the future, multicenter prospective studies are still needed to further validate and improve the prediction model to improve the vascular access outcomes of maintenance hemodialysis patients.

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Abbreviations

AVF: Arteriovenous fistula

MHD: Maintenance hemodialysis

PTA: Percutaneous transluminal angioplasty

NLR: Neutrophil-to-lymphocyte ratio

PLR: Platelet-to-lymphocyte ratio

LMR: Lymphocyte-to-monocyte ratio

SII: Systemic immune-inflammation index

PTH: Parathyroid hormone

KDIGO:Kidney Disease: Improving Global Outcomes

Author Contributions

YK conceived and designed the study, conducted the statistical analyses, interpreted the data, and drafted the manuscript. YK had full access to the data and takes responsibility for the integrity and accuracy of the analysis. ZHP and IIAAS provided overall supervision of the project, contributed to the study methodology, and critically revised the manuscript for important intellectual content. LJL, WJZ, ZHP, and YK performed the interventional procedures, ensured procedural standardization, and maintained operative quality control. QM and TD carried out patient screening, eligibility assessment, and primary data acquisition. ZT and TJC were responsible for data validation, database management, and implementation of quality assurance protocols. PWX contributed to data interpretation and critically revised the manuscript to improve scientific clarity and academic rigor. All authors meet the authorship criteria of the International Committee of Medical Journal Editors, approved the final version of the manuscript, and agree to be accountable for all aspects of the work.

Conflict of Interest

The authors declare that they have no competing interests.

Data Availability

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

Ethics Approval

This retrospective study was approved by the Institutional Ethics Committee of the

Affiliated Hospital of North Sichuan Medical College (Approval No. 2026ER103-1).

The requirement for informed consent was waived due to the retrospective nature of the study. All procedures involving human participants were conducted in accordance with the ethical standards of the institutional research committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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