TJVS Turkish Journal of Vascular Surgery

Turk J Vasc Surg.2025;34(3):197-203.
DOI: 10.9739/tjvs.2025.06.031

Available online at www.turkishjournalofvascularsurgery.org

Original Article

Association of serum uric acid/albumin ratio, C-reactive protein, and hemodynamic mismatch with arteriovenous fistula complications: A retrospective cohort study

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Received: June 18, 2025 Accepted: August 11, 2025 Published online: September 15, 2025

Abstract

Aim: Arteriovenous fistula (AVF) complications remain a major challenge in hemodialysis patients. This study aimed to evaluate the relationship between the serum uric acid/albumin ratio (UAR), C-reactive protein (CRP), and the development of AVF complications.
Material and Methods: This retrospective cohort study included 358 hemodialysis patients with functioning AVFs, divided into complication (n=120) and no-complication (n=238) groups. UAR, CRP, and Doppler ultrasound findings were compared between groups. Receiver operating characteristic (ROC) curve analysis evaluated the predictive value of UAR and CRP.
Results: AVF complications occurred in 33.5% of patients. Median UAR was significantly higher in patients with complications compared to those without (1.99 [IQR: 1.65–2.35] vs. 1.76 [IQR: 1.47–2.06], p<0.001). Mean CRP levels were also elevated in the complication group (6.5±2.1 mg/L vs. 3.2±1.8 mg/L, p<0.001). ROC analysis demonstrated that UAR had an AUC of 0.76, whereas CRP had an AUC of 0.70. Hemodynamic mismatch was significantly associated with higher complication rates (p=0.007).
Conclusion: Both UAR and CRP levels were independently associated with AVF complications, but UAR demonstrated superior predictive performance. UAR may therefore serve as a practical biomarker for the early identification of patients at risk of vascular access dysfunction, although further prospective studies are needed to validate these findings.

Keywords: Arteriovenous fistula, uric acid, serum albumin, C-reactive protein, renal dialysis

INTRODUCTION

Hemodialysis is the primary renal replacement therapy for patients with end-stage renal disease (ESRD), a condition affecting over 2 million individuals globally [1,2]. The arteriovenous fistula (AVF) is the preferred vascular access due to its superior long-term patency, lower infection rates, and reduced thrombosis risk compared to arteriovenous grafts and central venous catheters [3,4]. However, AVF dysfunction, which affects 20–40% of hemodialysis patients annually, is primarily driven by complications such as stenosis, thrombosis, and infection, compromising dialysis adequacy, increasing morbidity, and imposing substantial healthcare costs [5,6]. These challenges underscore the critical need for the early identification of at-risk patients to enable timely interventions and preserve vascular access functionality [7].

Current AVF monitoring often relies on invasive techniques, such as angiography, or indirect measures, like dialysis adequacy metrics, which often detect dysfunction only after significant clinical deterioration has occurred [8,9]. Recent research has prioritized non-invasive biomarkers to predict AVF complications preemptively, aiming to enhance outcomes and reduce intervention frequency [10,11].

CITATION
Guven H, Muduroglu A. Association of serum uric acid/albumin ratio, C-reactive protein, and hemodynamic mismatch with arteriovenous fistula complications: A retrospective cohort study. Turk J Vasc Surg.2025;34(3):197-203.

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The serum uric acid/albumin ratio (UAR) has emerged as a potential candidate, integrating serum uric acid, implicated in oxidative stress and endothelial dysfunction [12,13], and hypoalbuminemia, a marker of malnutrition and systemic inflammation prevalent in ESRD [14,15]. This composite metric reflects a state of oxidative stress and nutritional-inflammatory imbalance that may predispose patients to AVF dysfunction.

This study aims to evaluate the association between UAR, Creactive protein (CRP), and AVF complications in hemodialysis patients, addressing the problem of limited non-invasive biomarkers for early risk stratification. We hypothesize that elevated UAR, reflecting oxidative stress and inflammation-nutritional imbalance, is independently associated with higher AVF complication rates and may, therefore offer a practical tool for clinical monitoring.

MATERIAL AND METHODS

This retrospective cross-sectional study, conducted at a local hospital in Bursa between January 2018 and March 2025, was initiated following the approval of the Ethics Committee of Mudanya University (Decision No: 2025-2/11, May 22, 2025).

A total of 358 adult patients receiving maintenance hemodialysis with a functional AVF were included in the study based on a retrospective review of medical records. This study was conducted in accordance with the Declaration of Helsinki and adhered to the STROBE guidelines to ensure transparency and methodological rigor.

Eligible participants were adults (≥18 years) who had been undergoing regular hemodialysis via a functional AVF for at least three months . Patients were excluded if they had an active infection at the time of data collection, had been hospitalized within the past three months, or had a diagnosis of malignancy, autoimmune diseases, or systemic inflammatory conditions. Patients using non-AVF vascular access such as tunneled catheters or synthetic grafts, and those with poor compliance to dialysis protocols, were also excluded (Table 1).

Table 1. Inclusion and exclusion criteria for the study

Category	Criteria
Inclusion criteria	Adults aged ≥18 years
	Receiving regular hemodialysis via a functional AVF for ≥3 months
Exclusion criteria	Active infection
	Hospitalization within the past 3 months
	Malignancy
	Autoimmune diseases
	Systemic inflammatory conditions
	Non-AVF vascular access
	Poor dialysis compliance

AVF: arteriovenous fistula

Demographic data including age, sex, and body mass index (BMI), along with clinical information such as dialysis duration, comorbidities (e.g., hypertension, diabetes mellitus), and AVF characteristics (e.g., location and duration of use), were retrieved from electronic medical records and dialysis center databases. Data on dialysis frequency, duration, and anticoagulant/antiaggregant use were not uniformly available in the retrospective records and were not included.

Venous blood samples collected during routine laboratory testing prior to hemodialysis sessions were used for biochemical analyses. Serum uric acid levels were measured using an enzymatic colorimetric method, and serum albumin levels were determined by the bromocresol green dye-binding method. Serum CRP levels were measured using a high-sensitivity nephelometric method. UAR was calculated by dividing the serum uric acid level (mg/dL) by the albumin level (g/dL). All laboratory analyses were performed at the hospital's certified central laboratory.

High-resolution Doppler ultrasonography (GE Logiq P9, 7.5–12 MHz linear probe) reports were retrospectively reviewed to assess AVF status. Fistula diameter (mm), blood flow volume (mL/min), presence of stenosis (≥50% vessel narrowing), thrombosis (complete or near-complete occlusion), and signs of infection (perivascular edema, abscess formation) were recorded. Hemodynamic mismatch was defined based on Doppler ultrasonography findings, with mismatch categorized as a fistula diameter of <6 mm with blood flow of >1000 mL/min, or a fistula diameter of >6 mm with blood flow of >1500 mL/min.

Due to the retrospective nature, preoperative Doppler ultrasound results were not uniformly available and thus were not included in the analysis.

The primary endpoint was the occurrence of AVF complications, defined as significant stenosis (≥50% vessel narrowing), thrombosis (complete or near-complete occlusion), or infection (perivascular edema, abscess formation), assessed via Doppler ultrasound and clinical records. As a retrospective observational study, no randomization was applied; patients were categorized into complication (n=120) and no-complication (n=238) groups based on Doppler ultrasound and clinical records.

A non-probability convenience sampling method was used, including all eligible patients with complete medical records from the study period. Due to the retrospective design, blinding of participants or investigators was not applicable. However, laboratory and Doppler ultrasound assessments were conducted by technicians unaware of the study's objectives to mitigate potential bias.

Statistical analysis was conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Quantitative data were

summarized as mean±standard deviation (SD) for normally distributed variables (e.g., CRP) or median and interquartile range (IQR) for non-normally distributed variables (e.g., UAR), based on Shapiro-Wilk test results. Qualitative (categorical) data, such as AVF complication status or comorbidities, were summarized as frequencies and percentages. Statistical analyses tested the hypothesis that elevated UAR and CRP are associated with AVF complications. Normality of data distribution was assessed using the Shapiro-Wilk test. Based on the results, the non-normally distributed UAR values were analyzed using the Mann-Whitney U test, while the normally distributed CRP values were analyzed using an independent samples t-test. Chi-square tests were used to assess the independence of categorical variables, and Spearman's correlation was used to assess monotonic relationships. Receiver operating characteristic (ROC) analyses were used to evaluate predictive performance, with area under the curve (AUC) indicating discriminative ability.

Multivariable Analysis

Multivariable logistic regression was performed to assess the independent association of serum UAR and CRP levels with the presence of AVF complications. The model was adjusted for age, sex, dialysis duration, hypertension, diabetes mellitus, AVF type (brachiocephalic vs. radiocephalic), and presence of hemodynamic mismatch (defined as fistula diameter of <6 mm and blood flow of >1000 mL/min or diameter of >6 mm and flow of >1500 mL/min). Odds ratios (ORs) with 95% confidence intervals (CIs) and p-values were reported.

RESULTS

The study included 358 hemodialysis patients, predominantly male (55%), with a mean age of 59.4 years and dialysis duration of 6.8 years. Most had brachiocephalic AVFs (64.2%) and comorbidities such as hypertension (61.7%) and diabetes (39.1%), as detailed in Table 2.

Table 2. Demographic and clinical characteristics of the study population (N=358)

Characteristic	Mean±SD or %
Age (years)	59.4±13.2
Male gender (%)	55
Body mass index (kg/m²)	27.9±4.3
Dialysis duration (years)	6.8±4.2
Hypertension (%)	61.7
Diabetes mellitus (%)	39.1
AVF location: Brachiocephalic (%)	64.2
AVF location: Radiocephalic (%)	35.8

AVF: arteriovenous fistula

As detailed in Figure 1, patients who developed AVF complications exhibited significantly higher median UAR values (1.99 vs. 1.76, p<0.001) and mean CRP levels (6.5 mg/L vs. 3.2 mg/L, p<0.001) compared to those without complications (Figure 1).

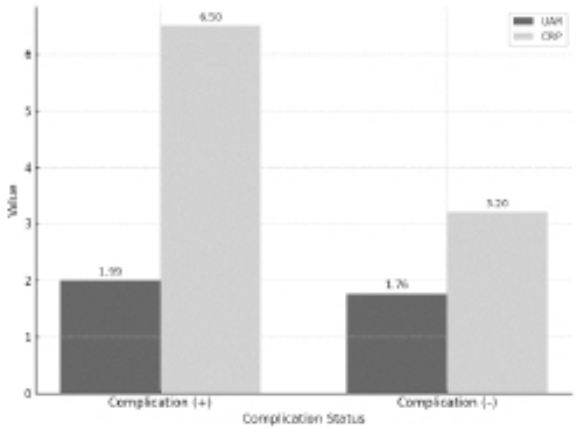

Figure 1. Comparison of UAR and CRP values between patients with and without AVF complications

The median serum UAR for the entire cohort was 1.84 (IQR: 1.54–2.17). AVF complications were identified in 120 patients (33.5%), including stenosis in 58 patients (16.2%), thrombosis in 34 patients (9.5%), and infection in 28 patients (7.8%). Subgroup analysis according to the type of AVF complication showed that mean UAR levels were highest in patients with thrombosis (2.02±0.24), followed by stenosis (2.00±0.23) and infection (1.91±0.23), whereas the mean UAR in patients without complications was 1.76±0.24 (p<0.001 by ANOVA) (Figure 2).

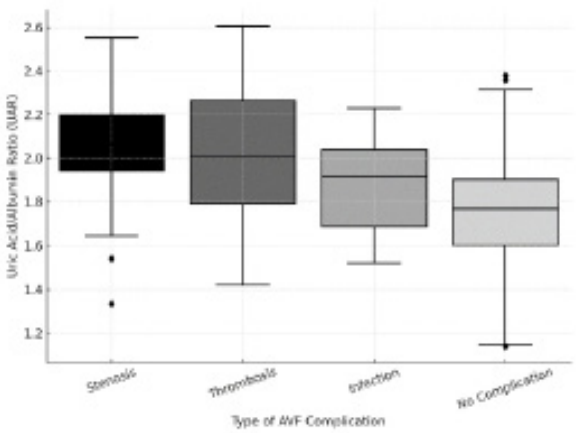

Figure 2. Comparison of UAR among different types of AVF complications

Hemodynamic mismatch analysis revealed that patients with fistula diameter of <6 mm and blood flow of >1000 mL/min had a complication rate of 59.5%, while those with diameter of >6 mm and flow of >1500 mL/min had a complication rate of 52.6%. In contrast, the complication rate among patients without hemodynamic mismatch was 27.3% (p=0.007) (Figure 3).

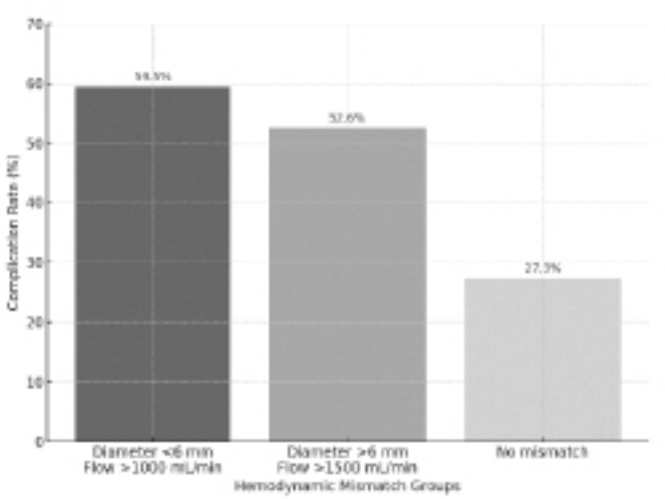

Figure 3. Complication rates according to hemodynamic mismatch status based on AVF diameter and blood flow criteria

Spearman's correlation analysis revealed a positive and significant association between serum UAR levels and AVF complications (r=0.328, p<0.001). Additionally, a significant positive correlation was found between serum CRP levels and AVF complications (r=0.290, p<0.001). When stratified according to UAR thresholds, patients with UAR >2.0 exhibited a complication rate of 58.2%, compared to 23.7% in those with UAR ≤2.0 (p<0.001).

ROC curve analysis demonstrated that the AUC for UAR in predicting AVF complications was 0.76, indicating good discriminative ability. For CRP, the AUC was 0.70, suggesting a moderate yet lower predictive value compared to UAR (Figure 4).

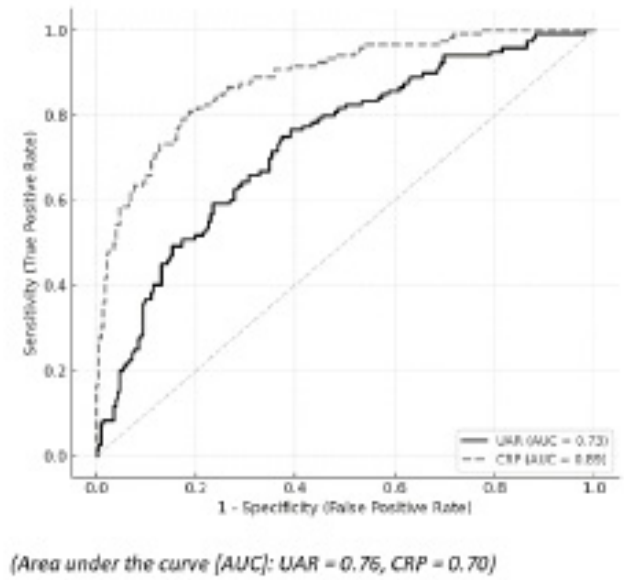

Figure 4. ROC curves for predicting AVF complications using UAR and CRP

Subgroup analysis by AVF type showed no significant difference in UAR (median 1.86 [IQR: 1.55–2.19] for brachiocephalic vs. 1.82 [IQR: 1.53–2.15] for radiocephalic, p=0.45, Mann-Whitney U test), CRP (mean 4.8±2.0 mg/L for brachiocephalic vs. 4.6±1.9 mg/L for radiocephalic, p=0.38, t-test), or complication rates (34.8% for brachiocephalic vs. 31.2% for radiocephalic, p=0.51, chi-square test) between brachiocephalic and radiocephalic fistulas (Table 3).

Table 3. Subgroup analysis of UAR, CRP, and complication rates by AVF type (N=358)

Characteristic	Brachiocephalic (n=230)	Radiocephalic (n=128)	p-value
UAR, median (IQR)	1.86 (1.55–2.19)	1.82 (1.53–2.15)	0.45*
CRP (mg/L), mean±SD	4.8±2.0	4.6±1.9	0.38†
Complication rate (%)	34.8% (80/230)	31.2% (40/128)	0.51‡

* Mann-Whitney U test, † t-test, ‡ Chi-square test

Multivariable Logistic Regression Analysis

In the multivariable logistic regression model, higher UAR levels were independently associated with increased odds of AVF complications (OR=2.47, 95% CI: 1.62–3.77, p<0.001), even after adjusting for age, sex, dialysis duration, hypertension, diabetes mellitus, AVF type, and hemodynamic mismatch. CRP was also a significant but weaker independent predictor of AVF complications (OR=1.21, 95% CI: 1.01–1.44, p=0.041). Among the covariates, hemodynamic mismatch remained a strong predictor (OR=2.85, 95% CI: 1.70–4.76, p<0.001), while age, sex, dialysis duration, hypertension, diabetes, and AVF type were not significantly associated with complications in the multivariable model (all p>0.05). The model showed acceptable discrimination (AUC=0.76) and good calibration based on the Hosmer-Lemeshow test (p=0.45) (Table 4, Figure 5).

Table 4. Multivariable logistic regression for predictors of AVF complications

Variable	Odds ratio (OR)	95% CI	p-value
UAR (per unit increase)	**2.47**	**1.62–3.77**	**<0.001**
CRP (per mg/L increase)	**1.21**	**1.01–1.44**	**0.041**
Age (per year)	1.01	0.99–1.03	0.28
Male sex	1.08	0.70–1.68	0.73
Dialysis duration (years)	1.04	0.98–1.10	0.18
Hypertension	1.22	0.78–1.91	0.38
Diabetes mellitus	1.17	0.74–1.85	0.50
AVF type (brachiocephalic)	1.14	0.74–1.76	0.54
Hemodynamic mismatch	**2.85**	**1.70–4.76**	**<0.001**

Note: Bolded variables are statistically significant; The 'radiocephalic' AVF type was used as the reference category

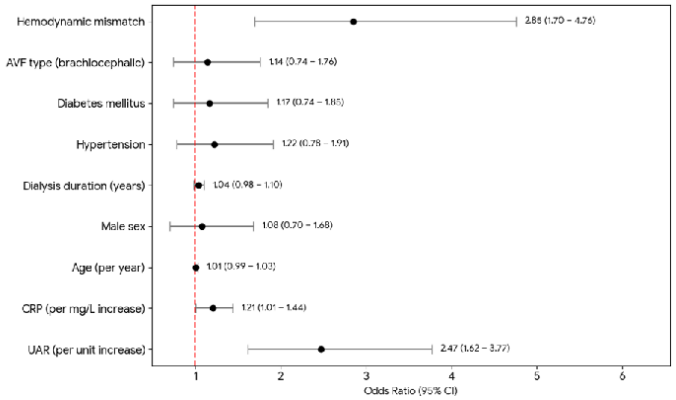

Figure 5. Multivariable logistic regression for predictors of AVF complications

DISCUSSION

This retrospective cohort study demonstrated that elevated serum UAR and CRP levels were significantly associated with an increased risk of AVF complications in hemodialysis patients. Patients with AVF complications exhibited higher median UAR values (1.99 [IQR: 1.65–2.35] vs. 1.76 [IQR: 1.47–2.06], p<0.001) and mean CRP levels (6.5±2.1 mg/L vs. 3.2±1.8 mg/L, p<0.001) compared to those without complications. These preliminary findings suggest that UAR, as a composite marker of oxidative stress and inflammation-nutritional status, may hold promise as a potential predictor of vascular access dysfunction, potentially offering advantages over CRP alone.

The observed AVF complication rate of 33.5%, with stenosis (16.2%), thrombosis (9.5%), and infection (7.8%) as primary contributors, aligns with reported epidemiology [5,6]. Stenosis and thrombosis, driven by intimal hyperplasia and endothelial dysfunction, are well-documented outcomes of oxidative stress and inflammation [16-18]. Elevated UAR likely reflects these processes, as uric acid promotes vascular smooth muscle proliferation and oxidative damage [12,13], while hypoalbuminemia signals chronic inflammation and malnutrition prevalent in ESRD [14,15].

Compared to other biomarkers, UAR's strength lies in its derivation from routinely measured parameters, enhancing its feasibility for clinical application. For instance, CRP is widely studied but can be influenced by non-vascular factors such as infections [19,20]. Other markers, such as fibrinogen, are associated with thrombotic events but lack specificity for AVF dysfunction; D-dimer reflects coagulation but is non-specific [21], and VEGF, while linked to neointimal hyperplasia, is often cost-prohibitive for routine use [22].

Although various biomarkers such as CRP, fibrinogen, D-dimer, and VEGF have been investigated for their potential to predict vascular access complications in AVF patients, their routine clinical utility remains limited due to issues of low specificity, high cost, and restricted availability [21-23]. In contrast, meta-analyses have demonstrated significant associations between UAR and CRP levels with adverse vascular outcomes in the contexts of hemodialysis and percutaneous coronary interventions [24,25]. Within this framework, the integration of hemodynamic mismatch parameters alongside UAR in the present study may offer a more comprehensive approach to risk stratification specific to AVF-related complications.

These considerations highlight UAR's broader clinical relevance, especially when benchmarked against existing inflammatory biomarkers. However, UAR's discriminative ability (AUC 0.76) compared to CRP (AUC 0.70) suggests it captures a broader pathophysiological spectrum, although these potential advantages require prospective validation [19]. Additionally, the multivariable logistic regression model, incorporating UAR, CRP, and other covariates, demonstrated an acceptable discrimination with an AUC of 0.76, indicating a robust overall predictive performance within the commonly accepted range of 0.7–0.8, where values between 0.8 and 0.9 are considered good and those above 0.9 are considered excellent [26]. This value, derived from the analysis of Table 4 and Figure 5, reflects the model's ability to distinguish between patients with and without AVF complications across all included variables, further supporting the clinical relevance of UAR and hemodynamic mismatch as key predictors. A UAR threshold of >2.0 was associated with a higher complication rate (58.2% vs. 23.7% for UAR ≤2.0), suggesting potential utility for risk stratification. This threshold aligns with studies linking elevated UAR to adverse cardiovascular outcomes in non-dialysis populations [24,25], but its application in hemodialysis warrants prospective confirmation to establish clinical reliability.

Hemodynamic mismatch further increased complication rates, with 59.5% in patients with fistula diameter of <6 mm and flow of >1000 mL/min, and 52.6% in those with diameter of>6 mm and flow of >1500 mL/min, compared to 27.3% in those without mismatch (p=0.007). These findings are consistent with evidence that abnormal flow dynamics exacerbate intimal hyperplasia and thrombosis risk [10,11].

For clinical integration, UAR could potentially be measured monthly alongside routine bloodwork in hemodialysis patients, with values of >2.0 prompting targeted ultrasound evaluations to assess fistula health. Clinicians could use these data to prioritize high-risk patients for early interventions, such as angioplasty for stenosis or anti-inflammatory therapies to mitigate oxidative stress, potentially reducing complication rates [27]. A proposed protocol might involve integrating UAR into dialysis unit electronic health records, with automated alerts for elevated values triggering multidisciplinary reviews by nephrologists and vascular surgeons. For example, patients with UAR >2.0 could be scheduled for Doppler ultrasound within 1–2 weeks, and those with confirmed stenosis could be referred for

preemptive angioplasty, aligning with guideline-recommended proactive surveillance [10]. However, standardized protocols for UAR monitoring and intervention thresholds require further development through prospective studies.

Subgroup analysis revealed UAR levels were the highest in patients with thrombosis (2.02±0.24), followed by stenosis (2.00±0.23) and infection (1.91±0.23), compared to those without complications (1.76±0.24, $p<0.001$). This pattern supports the role of oxidative stress and inflammation in thrombotic and stenotic processes, consistent with mechanistic studies on AVF failure [16-18]. UAR's strength lies in its accessibility, leveraging routine laboratory tests to provide a cost-effective tool for risk assessment, unlike more specialized markers such as VEGF [22].

Limitations

This study has several limitations. The retrospective design may introduce selection bias or incomplete data capture, although standardized data collection and robust statistical methods were implemented to mitigate these risks. Heterogeneity in AVF duration post-surgery may influence complication rates, as longer durations could increase cumulative risk exposure. Single-point measurements of UAR and CRP fail to account for temporal variability, which may influence predictive accuracy. The absence of additional inflammatory markers, such as interleukin-6 or tumor necrosis factor-alpha, limits insights into the broader inflammatory milieu. The single-center design restricts generalizability, necessitating multicenter studies to confirm findings across diverse populations. The absence of preoperative Doppler ultrasound data limits insights into baseline vascular characteristics that may predispose patients to AVF complications. The absence of data on dialysis frequency, duration, and anticoagulant/antiaggregant use limits the ability to control for these potential confounders.

Future Research Directions

Prospective, longitudinal studies are needed to validate UAR's predictive utility and establish standardized clinical thresholds. Future studies should incorporate preoperative Doppler ultrasound to assess baseline vessel characteristics and their impact on AVF outcomes. Incorporating additional biomarkers, such as fibrinogen, D-dimer, or VEGF, could clarify their synergistic roles in AVF dysfunction. Combining UAR with advanced imaging, such as Doppler ultrasound or magnetic resonance angiography, may enhance predictive accuracy. Interventional trials targeting UAR, such as allopurinol to reduce uric acid or nutritional support to improve albumin levels, could explore its modifiability and impact on AVF outcomes. These studies should prioritize large, diverse cohorts with follow-up periods of at least 12 months to assess long-term predictive value and clinical impact. Prospective studies should standardize AVF duration to assess its impact on complication rates.

CONCLUSION

This study demonstrates a significant association between elevated UAR and CRP levels and AVF complications in hemodialysis patients, with UAR showing preliminary promise as a predictive tool. By integrating oxidative stress and inflammation-nutritional status, UAR offers a cost-effective, non-invasive approach that may complement existing biomarkers such as CRP, fibrinogen, or VEGF. Hemodynamic mismatch underscores the need for comprehensive monitoring strategies combining biomarkers and ultrasonography. Despite limitations, the study's robust methodology and the novel application of UAR highlight its potential to inform vascular access management. Prospective, multicenter trials are essential to validate these findings and develop standardized protocols for UAR integration, potentially improving AVF longevity and patient outcomes.

Ethics Committee Approval: This study was approved by the Ethics Committee of Mudanya University (Decision No: 2025-2/11, dated May 22, 2025).

Patient Consent for Publication: Not necessary for this manuscript.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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