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# Uric Acid-to-High-Density Lipoprotein Cholesterol Ratio and Coronary Slow Flow: An Integrative Marker of Microvascular Dysfunction

## ABSTRACT

**Background:** Coronary slow flow (CSF) is an angiographic finding characterized by delayed distal vessel opacification despite normal epicardial coronary arteries. Its pathophysiology is multifactorial and involves microvascular dysfunction, endothelial impairment, and chronic inflammation. The uric acid-to-high-density lipoprotein (HDL) cholesterol ratio (UHR) has recently emerged as a novel composite biomarker reflecting both pro-oxidant and anti-inflammatory balance. This study aimed to evaluate the relationship between UHR and CSF.

**Methods:** In this retrospective cross-sectional study, 218 patients with normal or near-normal coronary arteries on angiography were analyzed. Patients were divided into 2 groups according to the presence of CSF based on thrombolysis in myocardial infarction (TIMI) frame count. Demographic, clinical, and laboratory parameters were compared between groups. Receiver operating characteristic (ROC) analysis was used to determine the discriminatory performance of UHR, and multiple logistic regression was performed to identify independent predictors of CSF.

**Results:** The mean UHR value was significantly higher in the CSF group compared with the control group (0.13 ± 0.04 vs. 0.09 ± 0.04, $P < .001$). Receiver operating characteristic analysis demonstrated that a UHR cut-off >0.107 predicted CSF with moderate discriminatory ability (area under the curve (AUC) = 0.733, 95% CI: 0.66-0.79, $P < .001$), with 73.5% sensitivity and 76.2% specificity. Multiple analyses suggested that UHR was independently associated with CSF (OR 1.20 per 0.01-unit increase, 95% CI 1.09-1.31, $P < .001$).

**Conclusion:** Elevated UHR was independently associated with CSF and may represent a readily available biomarker reflecting the metabolic-inflammatory balance contributing to coronary microvascular dysfunction. These findings should be interpreted as associative and hypothesis-generating.

**Keywords**: Coronary slow flow, endothelial dysfunction, inflammation, microcirculation, uric acid-to-HDL ratio

ORIGINAL INVESTIGATION

## INTRODUCTION

Coronary slow flow (CSF) is an angiographic phenomenon characterized by delayed contrast opacification of the distal coronary vasculature in the absence of obstructive epicardial coronary artery disease. It is reported in 1%-7% of patients undergoing coronary angiography and is now considered a form of coronary microvascular dysfunction (CMD).[1-3] CSF has been associated with recurrent angina, arrhythmias, and sudden cardiac death, emphasizing its clinical relevance.[4,5]

Although the exact mechanisms underlying CSF are not fully understood, studies suggest that endothelial dysfunction, increased inflammatory burden, oxidative stress, and microvascular autoregulatory abnormalities contribute to its pathophysiology.[6-9]

Serum uric acid, the final product of purine metabolism, reflects both oxidative and inflammatory status and is considered a mediator of endothelial injury.[10,11] Conversely, high-density lipoprotein cholesterol (HDL-C) exerts vasculoprotective effects through its antioxidant and anti-inflammatory properties.[12,13] A reduction

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in HDL-C levels has been linked to impaired endothelial function and atherosclerosis progression.[14]

The uric acid-to-HDL-C ratio (UHR) has emerged as a novel and integrated biomarker, capturing the detrimental influence of uric acid and the protective role of HDL-C. Uric acid-to-HDL-C ratio represents a balance between pro-oxidant uric acid and anti-inflammatory HDL-C, providing a composite index of vascular homeostasis. Recent literature has shown that UHR is associated with several conditions, including inflammation, insulin resistance, metabolic syndrome, and cardiovascular disease.[15,16]

However, the potential relationship between UHR and CSF has not been previously studied. Considering the pathophysiological overlap between the determinants of UHR and the mechanisms underlying CSF, it was hypothesized that an elevated UHR would be associated with the presence of CSF. Therefore, this study aimed to investigate the clinical utility of UHR as a potential biomarker in patients with CSF.

## METHODS

### Study Design and Population

This retrospective cross-sectional study included 218 consecutive patients who underwent coronary angiography between January 2023 and January 2025 at a tertiary referral center due to typical angina or positive noninvasive ischemia tests. Patients with angiographically normal or near normal epicardial coronary arteries were eligible. Exclusion criteria were significant coronary artery stenosis (>50%), prior myocardial infarction, valvular heart disease, left ventricular systolic dysfunction (LVEF <50%), cardiomyopathy, chronic kidney disease (defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 $m^2$), liver disease, active infection, systemic inflammatory or autoimmune disease, malignancy, and use of drugs known to affect uric acid or lipid metabolism, including uric acid–lowering therapies (e.g., allopurinol), diuretics known to increase uric acid levels, or lipid-lowering therapy initiated within the last 3 months. Estimated glomerular filtration rate was calculated using the MDRD equation based on serum creatinine, age, and sex.

## HIGHLIGHTS

- Coronary slow flow (CSF) represents a manifestation of coronary microvascular dysfunction and low-grade inflammation.
- The uric acid-to-HDL cholesterol ratio (UHR) integrates pro-oxidant burden and reduced vasoprotective capacity.
- Uric acid-to-HDL cholesterol ratio levels were significantly higher in patients with CSF compared with controls.
- Uric acid-to-HDL cholesterol ratio remained independently associated with CSF after multiple logistic regression adjustment.
- Uric acid-to-HDL cholesterol ratio may serve as a simple, low-cost biomarker reflecting microvascular dysfunction.

### Angiographic Assessment

Coronary angiography was performed via the femoral or radial approach using the standard Judkins technique. Angiograms were acquired using the Siemens Artis Zee angiography system (Siemens Healthineers, Germany) at 15 frames per second. Coronary slow flow (CSF) was defined using the corrected thrombolysis in myocardial infarction (TIMI) frame count (cTFC) method. The angiographic system in the laboratory recorded at 15 frames per second (fps); therefore, all measured TIMI frame counts were multiplied by 2 to ensure comparability with the conventional 30 fps reference values, consistent with the original definitions of Gibson et al. Patients were classified as CSF if cTFC exceeded 27.6 for LAD, 22.6 for LCx, and 20.4 for RCA. Coronary contrast was administered manually with an iodinated contrast agent at an estimated rate of 3-4 mL/s, in line with previous reports emphasizing the importance of injection speed and volume standardization for reliable TIMI frame count assessment. Thrombolysis in myocardial infarction frame counts were evaluated by 2 experienced interventional cardiologists who were blinded to the patients' clinical data and group allocation. In cases of uncertainty, consensus was reached by the 2 observers. Because independent duplicate measurements were not performed, intra- and inter-observer variability could not be formally assessed.

### Biochemical Analysis

Blood samples were obtained after at least 12 hours of fasting. Serum uric acid, HDL cholesterol, and other routine biochemical parameters were measured using standard enzymatic methods (Roche Diagnostics, Germany). The UHR was calculated by dividing the serum uric acid level (mg/dL) by the HDL cholesterol level (mg/dL).

### Statistical Analysis

Continuous variables were tested for normality using the Kolmogorov–Smirnov test. Data were presented as mean ± standard deviation (SD) or median (interquartile range, IQR) for continuous variables, and as numbers (percentages) for categorical variables. Comparisons between groups were performed using Student's *t*-test or Mann–Whitney *U*-test for continuous variables and chi-square test for categorical variables. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive ability of UHR for CSF, and the area under the curve (AUC) with 95% CI was calculated using the bootstrap method (2000 resamples). Logistic regression analyses were performed to identify predictors of CSF. Variables with $P < .10$ in univariate analysis were included in the multiple logistic regression model. The multiple logistic regression model was adjusted for age, sex, smoking status, triglyceride levels, and hypertension. A 2-tailed *P* value <.05 was considered statistically significant. A post-hoc power analysis was performed based on the observed discriminative performance of UHR (AUC = 0.733). At a 2-sided $\alpha$ level of .05, the sample size of the present study provided greater than 85% statistical power to detect significant differences between groups. Multicollinearity was assessed using variance inflation factors (VIF). Analyses were performed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA).

**Ethical Considerations** This study was conducted as a retrospective analysis under an existing ethics approval obtained for a broader investigation of coronary slow flow and related clinical and laboratory parameters. The present analysis represents a predefined secondary evaluation focusing on the UHR as a metabolic–inflammatory marker. All data were collected retrospectively from anonymized clinical records and handled in accordance with the principles of the Declaration of Helsinki. The requirement for informed consent was waived by the Institutional Ethics Committee due to the retrospective design of the study (Decision No: 280118606,429; Date: June 25, 2025).

## RESULTS

### Patient Characteristics

A total of 218 patients were included, of whom 113 (51.8%) had CSF and 105 (48.2%) had normal coronary flow. There were no significant differences in diabetes mellitus or hyperlipidemia between the 2 groups, whereas hypertension was less frequent among patients with CSF (30.5% vs. 15.9%, $P = .034$) (Table 1). This finding likely reflects the younger age and male predominance of the CSF group rather than a true protective effect of hypertension. Age was significantly lower in the CSF group (49.1 ± 11.2 vs. 55.1 ± 11.0, $P < .001$) in univariate comparisons; however, in the multivariate model it showed only a borderline association with CSF ($P = .091$). Male sex and smoking were significantly more prevalent among patients with CSF (71.7% vs. 47.6%, $P < .001$; and 41.6% vs. 25.7%, $P = .001$, respectively). Regarding laboratory parameters, patients with CSF had significantly higher serum uric acid levels and lower HDL-C concentrations (both $P < .001$). Consequently, the UHR was markedly elevated in the CSF group ($P < .001$) (Table 2).

### Thrombolysis in Myocardial Infarction Frame Count Standardization

Because the angiography system used in the study recorded at 15 frames per second, TIMI frame counts were multiplied by 2 to standardize them to the conventional 30 fps reference values. Using the standard diagnostic thresholds defined by Gibson et al[13] (LAD > 27.6, Cx > 22.6, and RCA > 20.4), 52 patients (23.9%) had LAD-CSF, 36 (16.5%) had Cx-CSF, and 50 (22.9%) had RCA-CSF (Table 3). These findings confirm that the CSF classification remained consistent after technical standardization.

### Receiver Operating Characteristic Analysis

Receiver operating characteristic curve analysis demonstrated that UHR had a moderate discriminatory power for predicting CSF (AUC = 0.733, 95% CI: 0.66-0.79, $P < .001$). The optimal cutoff value of 0.107 yielded 73.5% sensitivity and 76.2% specificity (Figure 1). Boxplot analysis further confirmed that UHR values were significantly higher in the CSF group compared with controls (Figure 2).

### Regression Analyses

In univariate logistic regression analysis, UHR was significantly associated with the presence of CSF ($P < .001$). In the multiple logistic regression model (Table 4), adjusted for age, sex, smoking status, triglyceride levels, and hypertension, UHR remained an independent predictor of CSF (OR = 1.20 per 0.01-unit increase; 95% CI: 1.09-1.31; $P < .001$). Model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test, which indicated good calibration of the multiple logistic regression model ($P > .05$). Age showed a borderline association with the presence of CSF (OR = 0.97; 95% CI: 0.93-1.00; $P = .091$), while sex, smoking, triglyceride levels, and hypertension were not independently associated with CSF. Sensitivity analyses were performed after excluding patients with diabetes mellitus and current smokers to assess the robustness of the findings. In these analyses, UHR remained independently associated with CSF.

**Table 1. Baseline Demographic and Clinical Characteristics of the Study Population**

| Variables | CSF (−) | CSF (+) | *P* |
|---|---|---|---|
| Age (years) | 55.1 ± 11.0 | 49.1 ± 11.2 | <.001 |
| Male, n (%) | 50 (47.6) | 81 (71.7) | <.001 |
| Hypertension, n (%) | 32 (30.5) | 18 (15.9) | .034 |
| Diabetes Mellitus, n (%) | 27 (25.7) | 22 (19.5) | .308 |
| Hyperlipidemia, n (%) | 42 (40.0) | 54 (47.8) | .275 |
| Smoking, n (%) | 27 (25.7) | 47 (41.6) | .001 |
| Glucose (mg/dL) | 114.08 ± 41.38 | 108.96 ± 33.48 | .022 |
| Creatinine (mg/dL) | 0.86 ± 0.34 | 0.86 ± 0.23 | .251 |
| Uric Acid (mg/dL) | 4.8 ± 1.63 | 5.46 ± 1.42 | <.001 |
| CRP (mg/L) | 3.94 ± 3.14 | 3.70 ± 2.85 | .570 |
| Total Cholesterol (mg/dL) | 186.83 ± 38.78 | 178.5 ± 38.56 | .036 |
| HDL-C (mg/dL) | 58.6 ± 14.2 | 46.4 ± 11.4 | <.001 |
| LDL-C (mg/dL) | 104.4 ± 32.97 | 98.3 ± 30 | .152 |
| Triglyceride (mg/dL) | 140.6 ± 78.1 | 177.1 ± 101.7 | .007 |
| AST (U/L) | 25 ± 10.1 | 30.1 ± 33.1 | .188 |
| ALT (U/L) | 23.74 ± 11.88 | 33.23 ± 44.31 | .033 |
| Sodium (mmol/L) | 136.72 ± 11.95 | 138.76 ± 2.52 | .019 |
| Potassium (mmol/L) | 4.38 ± 0.44 | 4.25 ± 0.42 | .034 |
| WBC ($10^3$/μL) | 7.85 ± 2.22 | 8.36 ± 2.43 | .104 |
| Hemoglobin (g/dL) | 14.1 ± 1.54 | 14.7 ± 1.79 | .006 |
| Platelets ($10^3$/μL) | 255.54 ± 72.35 | 243.98 ± 65.96 | .630 |
| eGFR (mL/min/1.73 $m^2$) | 86.99 ± 22.48 | 92.99 ± 25.90 | .069 |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CSF, coronary slow flow; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; WBC, white blood cell.

**Table 2. Comparison of UHR and Coronary TIMI Frame Counts Between Groups**

| Variables | CSF (−) (n = 105) | CSF (+) (n = 113) | *P* |
|---|---|---|---|
| Uric acid to HDL cholesterol ratio (UHR) | 0.09 ± 0.04 | 0.13 ± 0.05 | <.001 |
| LAD TIMI frame count | 16.45 ± 3.46 | 27.56 ± 13.56 | <.001 |
| Cx TIMI frame count | 9.30 ± 1.68 | 14.54 ± 7.36 | <.001 |
| RCA TIMI frame count | 9.97 ± 1.73 | 20.12 ± 8.03 | <.001 |

Cx, circumflex artery; LAD, left anterior descending artery; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction; UHR, uric acid-to-HDL cholesterol ratio.

**Table 3. Adjusted TIMI Frame Count Values (Standardized to 30 fps) and CSF Positivity Rates**

| TIMI Variables | Threshold (30 fps) | Mean ± SD | CSF Positive (n, %) |
|---|---|---|---|
| LAD TIMI (adjusted) | >27.6 | 44.41 ± 22.94 | 52 (23.9) |
| Cx TIMI (adjusted) | >22.6 | 24.03 ± 12.03 | 36 (16.5) |
| RCA TIMI (adjusted) | >20.4 | 30.37 ± 15.53 | 50 (22.9) |

As the angiography system operates at 15 frames per second, all measured TIMI frame counts were multiplied by 2 to align with the standard 30 fps-based thresholds. Coronary slow flow (CSF) was defined using the classical thresholds proposed by Gibson et al[13]: LAD > 27.6, Cx > 22.6, and RCA > 20.4 (all in 30 fps terms).

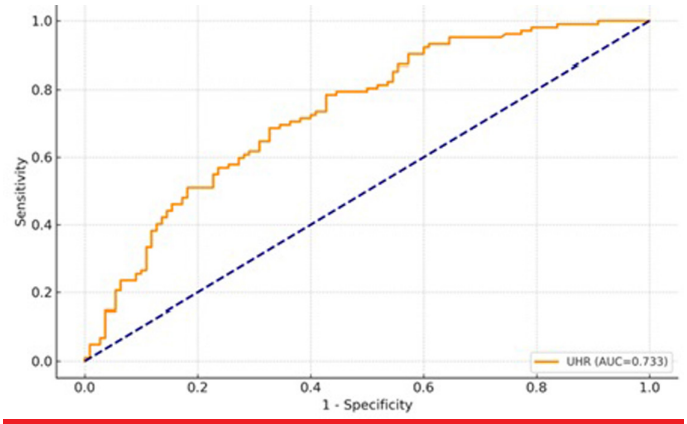


**Figure 1. Receiver operating characteristic (ROC) curve of the uric acid-to-HDL cholesterol ratio (UHR) for predicting coronary slow flow (CSF). The area under the curve (AUC) was 0.733 (95% CI: 0.66-0.79). UHR, uric acid-to-HDL cholesterol ratio; CSF, coronary slow flow.**

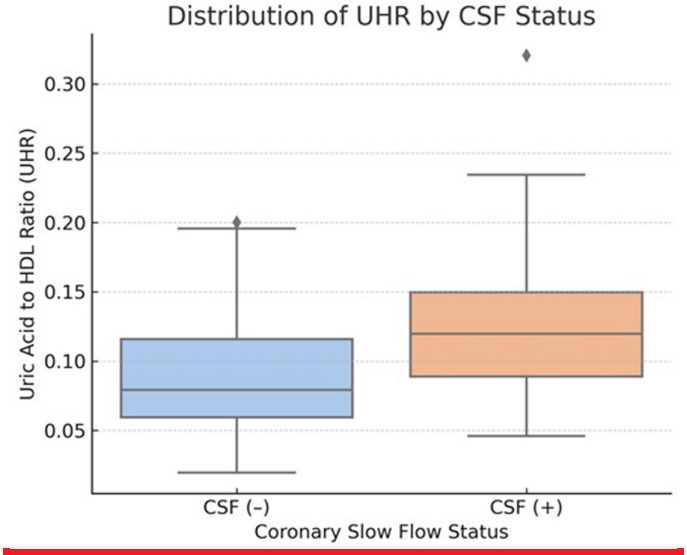


**Figure 2. Boxplot showing the distribution of UHR in patients with CSF and in controls with normal coronary flow. UHR was significantly higher in the CSF group ($P < .001$).**

## DISCUSSION

In this study, the relationship between UHR and CSF were investigated, an angiographic phenomenon characterized by delayed opacification of the distal coronary vasculature in the absence of obstructive epicardial coronary artery disease. The findings showed that UHR levels were significantly higher in patients with CSF compared with those with normal coronary flow. Furthermore, UHR demonstrated a moderate discriminatory ability for predicting CSF in ROC analysis (AUC = 0.733, 95% CI: 0.66-0.79, $P < .001$) and remained independently associated with CSF in multiple logistic regression analysis after adjustment for age, sex, smoking status, triglyceride levels, and hypertension. These findings suggest a statistically significant but modest association between UHR and CSF.

**Table 4. Multiple Logistic Regression for Predictors of Coronary Slow Flow**

| Variables | OR | 95% CI (Lower) | 95% CI (Upper) | *P* |
|---|---|---|---|---|
| UHR (per 0.01 unit) | 1.20 | 1.09 | 1.31 | <.001 |
| Age (per year) | 0.97 | 0.93 | 1.00 | .091 |
| Sex: male vs. female (reference) | 1.55 | 0.75 | 3.21 | .239 |
| Smoking: yes vs. no (reference) | 0.79 | 0.35 | 1.75 | .554 |
| Triglycerides (per mg/dL) | 1.00 | 1.00 | 1.00 | .825 |
| Hypertension: yes vs. no (reference) | 0.64 | 0.30 | 1.37 | .250 |

The multiple logistic regression model was adjusted for age, sex, smoking status, triglyceride levels, and hypertension. Odds ratios are presented with 95% CI. The UHR odds ratio is expressed per 0.01-unit increase to provide clinically interpretable effect sizes given the relatively small numerical range of UHR. UHR, uric acid-to-HDL cholesterol ratio

Coronary slow flow is a manifestation of microvascular dysfunction, low-grade inflammation, and endothelial impairment. Although first described by Tambe et al in 1972, its pathophysiological mechanisms remain incompletely understood.[14] Inflammation, increased oxidative stress, and altered rheological properties of blood have been implicated. In particular, studies have demonstrated that impaired endothelial nitric oxide production and microvascular constriction significantly contribute to CSF development. Furthermore, inflammatory cytokines such as CRP and IL-6 are frequently elevated in patients with CSF.[15-18]

Elevated uric acid levels can promote endothelial dysfunction, vascular smooth muscle proliferation, and oxidative stress, whereas low HDL cholesterol levels are known to impair reverse cholesterol transport and antioxidant defense.[19-22] Thus, UHR may provide a composite measure of pro-inflammatory and atherogenic burden. Previous studies have linked hyperuricemia[19] and low HDL-C[20] to CSF separately, but the combined use of these parameters as a ratio may provide additional pathophysiological insight into the metabolic–inflammatory milieu underlying microvascular dysfunction. UHR may serve as a pragmatic integrative biomarker reflecting both pro-oxidant burden and reduced vasoprotective capacity. However, the present study did not formally evaluate whether UHR provides incremental predictive value beyond its individual

components, and UHR should therefore be interpreted as a pragmatic composite index rather than a statistically validated superior marker.

In addition to biochemical markers, the findings also revealed that male sex and smoking were significantly more prevalent among patients with CSF. These demographic and behavioral patterns are consistent with previous reports, which have identified the male sex as a predisposing factor due to sex-related differences in endothelial function and vascular reactivity.[5,14]Similarly, cigarette smoking has been shown to promote oxidative stress, impair nitric oxide bioavailability, and induce microvascular dysfunction, all of which are central to the pathogenesis of CSF.[6,18] The additive impact of smoking on uric acid levels and HDL metabolism may further potentiate the pro-inflammatory milieu captured by UHR, amplifying microvascular compromise.

Recently, UHR has gained attention as a novel biomarker for cardiovascular risk stratification. Studies have shown its association with metabolic syndrome, atherosclerotic cardiovascular disease, arterial stiffness, and adverse outcomes in patients with acute coronary syndrome. Furthermore, elevated UHR levels are associated with increased coronary artery calcium scores and subclinical atherosclerosis in asymptomatic individuals. [23-27]

The optimal cut-off value for UHR in predicting CSF was determined to be 0.107 in the study, with a sensitivity of 73.5% and specificity of 76.2%. This supports the notion that UHR may be a useful non-invasive biomarker for identifying patients at risk for CSF, although further studies are needed to compare its performance with its individual components. The association of UHR with CSF may reflect the dual contribution of uric acid–induced oxidative stress and impaired HDL-mediated vasoprotection in microcirculation.

A corrected TIMI frame count methodology was applied because the angiographic acquisition rate in the catheterization laboratory was 15 frames per second (fps), which differs from the standard 30 fps used in most prior studies. To ensure compatibility with published diagnostic thresholds, the measured TIMI frame counts were adjusted by multiplying them by 2. This allowed a direct comparison with the standard reference values reported in the literature, namely >27.6 for LAD, >22.6 for CX, and >20.4 for RCA.[13] Importantly, the threshold values themselves were not altered, as they were already established based on a 30 fps acquisition rate. This methodological correction enhanced the precision of the CSF classification and ensured the validity and comparability of the results with those of previous research.

The study included a relatively modest but comparable sample size to previous investigations of CSF, together with detailed laboratory profiling. The higher uric acid levels and lower HDL-C concentrations observed in the CSF group are consistent with previous findings and support the use of UHR as a synthesized inflammatory/metabolic marker. Moreover, the ROC and regression analyses confirmed a statistically significant association between UHR and CSF.

The multiple logistic regression analysis suggested that UHR was independently associated with CSF, even after adjustment for age, sex, smoking, triglycerides, and hypertension (Table 4). An OR of approximately 1.20 per 0.01-unit increase underscores the potential clinical relevance of UHR, warranting further prospective investigation in the context of microvascular dysfunction. This effect size represents a statistically significant but modest association, suggesting that small variations in UHR within the observed clinical range may be associated with differences in the likelihood of CSF. The absence of significant multicollinearity (all VIF values <10) supports the robustness of this association.

In the cohort, hyperlipidemia tended to be more frequent in patients with CSF, consistent with previous reports, although without reaching statistical significance. Conversely, hypertension and diabetes mellitus were less common among CSF patients, likely reflecting the younger age and male predominance of this group rather than a true protective effect. These findings indicate that CSF can occur even in patients with relatively few conventional cardiovascular risk factors, underscoring the role of alternative mechanisms such as inflammation and microvascular dysfunction. Interestingly, UHR remained associated with CSF even among patients with fewer traditional cardiovascular risk factors, supporting its potential role as a non-traditional metabolic indicator of microvascular dysfunction.

Despite these contributions, several limitations should be acknowledged. This study had a retrospective, observational, cross-sectional, and single-center design, which inherently limits causal inference and the generalizability of the findings. The relatively modest sample size may have limited the statistical power of the study, although it was comparable to previous CSF investigations. Waist circumference data were unavailable; therefore, formal diagnosis of metabolic syndrome could not be established. Although several metabolic components (fasting glucose, triglycerides, HDL-C, and hypertension) were available and considered in the analyses, residual confounding related to metabolic syndrome cannot be fully excluded. Potential confounders such as dietary habits, serum insulin, or medication use (e.g., diuretics, statins) that could influence uric acid or HDL levels were not assessed. Although recently initiated lipid-lowering therapy was an exclusion criterion, long-term stable statin use was allowed and may represent a potential residual confounder. A single measurement of laboratory parameters was relied on, and did not evaluate longitudinal outcomes such as recurrent angina or cardiovascular events. Thrombolysis in myocardial infarction frame counts were assessed by 2 blinded interventional cardiologists in consensus; since independent duplicate measurements were not performed, intra- and inter-observer variability could not be calculated. Furthermore, mechanistic assays to directly evaluate oxidative stress and endothelial dysfunction were not performed, and the observed associations remain observational. Finally, although the cohort was homogeneous and carefully selected, the results may not be generalizable to other populations without external validation.

From a mechanistic standpoint, the findings are consistent with contemporary evidence indicating that CSF represents a state of increased microvascular resistance, reflected by elevated cTFC, and is closely linked to systemic inflammation and endothelial dysfunction. Although recent analyses have shown that angiographic CSF is an imperfect surrogate for invasively measured CMD, the application of standardized imaging protocols and validated cTFC thresholds continues to support its role as a clinically relevant phenotype of microvascular disease.[28-31]Consistent with the findings, Lu et al demonstrated that endothelial dysfunction–related biomarkers are closely associated with coronary heart disease, supporting the biological plausibility of integrative indices such as the uric acid–to–HDL cholesterol ratio in coronary microvascular disorders.[32]

From a clinical perspective, UHR constitutes a readily available, low-cost composite biomarker integrating the prooxidant burden (uric acid) with diminished vasoprotective function (HDL-C). Large-scale, population-based cohorts have consistently demonstrated that higher UHR levels are associated with an increased incidence of cardiovascular disease, as well as with both all-cause and cardiovascular mortality, particularly among individuals with diabetes or prediabetes.[33,34] These converging data reinforce the observation that elevated UHR parallels the presence of CSF. They also provide a rationale for prospective investigations to determine whether UHR-guided risk stratification or longitudinal surveillance could improve outcomes in patients with suspected microvascular angina.

## CONCLUSION

This study introduces UHR as a novel, simple, and easily accessible biomarker that is significantly associated with CSF. The moderate association between UHR and CSF highlights the intertwined role of low-grade inflammation and metabolic imbalance in the pathophysiology of slow coronary flow. Future multicenter and prospective studies are needed to validate these findings and to determine whether UHR may complement existing clinical risk models for risk stratification and treatment monitoring in patients with CSF.

**Ethics Committee Approval:** This study was approved by the Local Ethics Committee of Batman Training and Research Hospital (Approval No: 280118606,429; Date: June 26, 2025).

**Informed Consent:** Informed consent was waived by the institutional ethics committee due to the retrospective design of the study.

**Peer-review:** Externally peer-reviewed.

**Data Availability:** The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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**Author Contributions:** Concept – R.A., E.E.; Design – R.A., E.E.; Supervision – R.A., E.İ.; Resources – R.A., E.E.; Materials – R.A., E.E.; Data Collection and/or Processing – R.A., E.E., Analysis and/or Interpretation – R.A., E.E.; Literature Search – R.A., E.E.; Writing – R.A.; Critical Review – R.A., E.İ.

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