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Prognostic role of the serum uric acid-to-serum creatinine ratio in patients with st-elevation myocardial infarction and multivessel coronary artery disease

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Abstract

Background: *The aim of this study was to investigate whether serum uric acid to serum creatinine ratio (SUA/SCr) predicts the early major adverse cardiovascular and cerebrovascular events (MACCEs) in patients with ST elevation myocardial infarction (STEMI) and multivessel coronary artery disease (MVCAD).*

Methods: *This study was designed retrospectively and included 572 patients with a mean age of 61.9 ± 12.3 years who presented with STEMI and had MVCAD. The patients were divided into 2 groups as those with and without MACCEs, taking into account the 30-day follow-up period. Serum uric acid, and serum creatinine were obtained at admission. The SUA/SCr of all patients were calculated and evaluated the relationship of SUA/SCr with the 30-day MACCEs.*

Results: *During the mean 27.0 ± 7.7 day follow-up period, 58 (10.1%) patients died, and 84 patients (14.7%) suffered MACCEs. According to multivariable cox regression analysis, advanced age (HR: 1.020, p = 0.028), smoking (HR: 2.513, p = 0.001), lower left ventricular ejection fraction (HR: 0.962, p = 0.001), TIMI < 3 flow (HR: 0.425, p < 0.001), higher syntax score (HR: 1.067, p < 0.001), and higher SUA/SCr (HR: 1.1029, p = 0.011) independently predicted the 30-day MACCEs. The area under the curve for SUA/SCr was 0.606 with a p-value of 0.002. The Kaplan Meier curves represented that high-risk patients with SUA/SCr greater than 4.58 had significantly higher MACCEs than low-risk group during the follow up period after index hospitalization (p = 0.001).*

Conclusions: *Newly defined promising oxidative and inflammatory biomarker, SUA/SCr can be a potential predictor of MACCEs within 30 days and decision-making treatment in STEMI and MVCAD patients.* (Cardiol J 2025; 32, 6: 588–597)

Keywords: serum uric acid, serum creatinine, SUA/SCr ratio, ST elevation myocardial infarction, mortality

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Introduction

Approximately 40% to 50% of ST-elevation myocardial infarction (STEMI) patients who undergo primary percutaneous coronary intervention (pPCI) are diagnosed with multivessel coronary artery disease (MVCAD) [1–3]. Previous reports have suggested that MVCAD in patients with STEMI is associated with worse outcomes [4].

Serum uric acid (SUA) is the final oxidation product of purine metabolism; arising in conditions of impaired oxidative metabolism; it has been shown to be a modifiable risk factor for cardiovascular disease (CVD) [5, 6]. Hyperuricemia is frequently noted in patients with coronary artery disease (CAD) and has been associated with increased mortality. Additionally, increased SUA levels have been considered an independent predictor of death in patients at a high risk of CVD [6, 7]. Higher SUA levels are also found to be associated with CAD severity in patients with acute coronary syndrome (ACS) [8].

The concentration of endogenous SUA depends primarily on renal clearance function; particularly increasing with the deterioration of such function. However, some previous studies have ignored this effect. Therefore, renal function-normalized SUA (SUA-to-serum creatinine ratio [SUA/SCr]) has emerged as a new biomarker and is considered a superior indicator of net uric acid (UA) production [5]. Moreover, the SUA/SCr has been reported to be associated with several metabolic and CVDs and mortality [6, 9]. It has also been recently shown to be related to CAD severity in patients with chronic CAD [10]. According to available research, no studies have specifically evaluated the prognostic role of the SUA/SCr in individuals presenting with STEMI and diagnosed with MVCAD. Therefore, in the present study the aim was to investigate whether the SUA/SCr predicts early major adverse cardiovascular and cerebrovascular events (MACCEs) in individuals with STEMI and MVCAD.

Methods

The medical records of consecutive patients admitted to the Department of Cardiology were reviewed from Dr Siyami Ersek Thoracic and Cardiovascular Surgery Education Research Hospital and the University of Health Sciences Turkey from Jan. 2013 to Dec. 2017. Patients with MVCAD who were diagnosed with STEMI and underwent coronary angiography with pPCI were enrolled in the current study. Data on their baseline clinical and demographic characteristics including body mass index, hypertension, diabetes mellitus, family history, hyperlipidemia, smoking and vascular disease defined as a history of myocardial infarction (MI); peripheral arterial disease; and ischemic stroke (IS) or transient ischemic attack (TIA) due to thromboembolism in the carotid or vertebral arteries were obtained. Physical examination findings were also obtained.

The records of a total of 653 patients from the documented database were retrospectively reviewed and analyzed. Finally, 572 patients were enrolled in the study. Patients with a history of coronary artery bypass grafting (CABG) (n = 28); malignancy (n = 7); active infection (n = 5); connective tissue disorder (n = 6); end-stage renal disease or hemodialysis (n = 14); no significant CAD or other evident causes of coronary pain such as significant myocardial bridging or diffuse coronary spasm during angiography (n = 9); and any missing information (n = 12) were excluded from the study.

STEMI was diagnosed based on the symptoms; electrocardiographic findings; and other accessory examination findings in accordance with the American College of Cardiology/American Heart Association guidelines [11]. Presentation with acute chest pain or overwhelming shortness of breath with persistent ST elevation that was considered suggestive of STEMI, including true posterior MI. All patients were treated in accordance with the current guidelines.

Routine complete blood cell counts and blood evaluations for determining the blood glucose, creatinine, SUA, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglyceride levels were conducted using admission blood samples. The serum creatinine and SUA levels were measured using the Roche Diagnostics Cobas 8000 c502 analyzer (Indianapolis). The SUA/SCr was calculated as the ratio of the SUA level to the serum creatinine level. The estimated glomerular filtration rate was calculated by using the Modification of Diet in Renal Disease formula.

The angiograms of patients were evaluated by two experienced interventional cardiologists who were blinded to the current study. MVCAD was defined as significant stenosis (≥ 50%) in two or more major epicardial coronary arteries [12]. The coronary angiograms were analyzed by two experienced interventional cardiologists who were blinded to patients' clinical data. The anatomic

severity of coronary stenosis was quantitatively evaluated based on the anatomical SYNTAX score I (SxSI) using the downloaded version from https://syntaxscore.org.

The primary endpoint of the study was MACCEs; defined as cardiovascular death (i.e., MI, significant cardiac arrhythmia, heart failure, or stroke), additional endpoints include nonfatal MI; or nonfatal cerebrovascular accident (IS or TIA) within the 30-day follow-up period according to the Academic Research Consortium-2 consensus [13]. The national death notification system and hospital records were used to obtain information on mortality. The study population was divided into two groups according to the presence or absence of MACCEs.

Since the present study adopted a retrospective design, written informed consent from participants could not be obtained and the study protocol was approved by the local ethics committee at the documented hospital (Protocol number: E-28001928-604.01-253984079).

Statistical analysis

Continuous variables were reported as means ± ± standard deviations when the distribution was normal and as medians with interquartile ranges when the distribution was not. Categorical variables were reported as percentages. The chi-squared test was used to compare the categorical variables between the groups. The Kolmogorov––Smirnov test was conducted to assess whether the variables were normally distributed. The Student t-test or the Mann–Whitney U test was utilized to compare the continuous variables between the groups according to their data distribution. In determining the independent predictors of 30-day MACCEs; variables with a p-value of < < 0.05 in the univariable analysis were included in the multivariable Cox regression analysis; with the results reported as hazard ratios and 95% confidence intervals (CIs). Moreover, the area under the curve (AUC) or C-statistic was used as a measure of predictive accuracy and capacity to discriminate the SUA/SCr using a receiver-operating characteristic (ROC) curve analysis. The sensitivity and specificity of the SUA/SCr were evaluated and its cutoff value for predicting MACCEs in the ROC curve analysis using Youden's index [14]. The time-to-event data were presented graphically using Kaplan–Meier survival curves and analyzed using the log-rank test. The threshold of statistical significance was established at $p < 0.05$. All statistical analyses were performed using the Statistical Package for the Social Sciences version 24.0 (IBM Corp.; Armonk; NY; USA). The ROC curves of the models were compared using MEDCALC (MedCalc Software bv; Ostend; Belgium).

Results

A total of 572 patients with a mean age of 61.9 ± ± 12.3 years diagnosed with STEMI and MVCAD were included in the study. In terms of adverse events at the end of the 30-day follow-up period; 58 patients (10.1%) died of cardiovascular causes; and 84 patients (14.7%) developed MACCEs. Detailed demographic and clinical characteristics of patients with and without MACCEs are summarized in Table 1. Considering the biochemical and hematological parameters, there was no significant difference between the groups in terms of parameters other than SUA/SCr ($p > 0.05$ for all). Conversely, the SUA/SCr was significantly higher in the MACCEs group than in the non-MACCEs group (5.73 ± 2.1 vs. 5.0 ± 1.9; $p = 0.002$). The laboratory parameters of all participants and their between-group comparisons are further detailed in Table 2.

Regarding the angiographic and procedural parameters; the MACCEs group had more extensive and severe CAD based on the anatomical SxSI than the others ($p < 0.001$). In this study, all patients underwent pPCI for their culprit lesions. The procedure failed in 38 patients (6.6%); and the failure rate was significantly higher in the MACCEs group than in the non-MACCEs group (22.6% vs. 3.9%; $p < 0.001$). The rate of poor postprocedural thrombolysis in myocardial infarction (TIMI) flow (grade < 3) was also higher in the MACCEs group ($p < 0.001$). Percutaneous coronary intervention (PCI) was also performed on non-culprit lesions (NCLs) in a total of 92 patients. In particular; ad hoc PCI was conducted in 26 patients and elective PCI in 66 patients. CABG was performed in the remaining patients. The failure rate for the NCLs procedures was higher in the MACCEs group than in the non-MACCEs group ($p = 0.034$). During the follow-up period, no patients without MACCEs required revascularization, while 14 patients with MACCEs (16.7%) required revascularization ($p < 0.001$).

In order to determine the independent predictors of 30-day MACCEs; multivariable cox regression analysis was performed by the included variables that exhibited statistically significant relations in the univariable analysis. Since uric acid and SCr are components of SUA/SCr they were not included

Table 1. Demographic and clinical parameters of the study population and those patients with and without MACCEs

Variables	All population	No MACCEs (n = 488; 85.3%)	MACCEs (n = 84; 14.7%)	p-value
Male gender, n [%]	457 (79.9)	396 (81.1)	61 (72.6)	0.072
Age, years	61.9 ± 12.3	60.3 ± 11.5	64.8 ± 13.4	0.002
BMI, [kg/m^2]	26.4 ± 3.0	26.3 ± 2.9	26.4 ± 3.4	0.740
Hypertension, n [%]	129 (22.6)	111 (22.7)	18 (21.4)	0.790
Diabetes mellitus, n [%]	90 (15.7)	71 (14.5)	19 (22.6)	0.061
Hyperlipidemia, n [%]	293 (51.2)	246 (50.4)	47 (56.0)	0.348
Smoking, n [%]	80 (14.0)	61 (12.5)	19 (22.6)	0.014
Family history, n [%]	232 (40.6)	191 (39.1)	41 (48.8)	0.095
Heart Failure, n [%]	37 (6.5)	28 (5.7)	9 (10.7)	0.087
CAD history, n [%]	72 (12.6)	60 (12.3)	12 (14.3)	0.611
MI history, n [%]	51 (8.9)	42 (8.6)	9 (10.7)	0.531
PCI history, n [%]	61 (10.7)	52 (10.7)	9 (10.7)	0.987
PAD history, n [%]	7 (1.2)	5 (1.0)	2 (2.4)	0.296
CVA history, n [%]	9 (1.6)	7 (1.4)	2 (2.4)	0.520
CRF, n [%]	16 (2.8)	11 (2.3)	5 (6.0)	0.058
COPD, n [%]	7 (1.2)	4 (0.8)	3 (3.6)	0.034
Medications, n [%]				
Acetylsalicylic acid	75 (13.1)	62 (12.7)	13 (15.5)	0.487
P2Y12 inhibitors	11 (1.9)	9 (1.8)	2 (2.4)	0.741
RAS Blockers	71 (12.4)	56 (11.5)	15 (17.9)	0.101
Beta Blockers	81 (14.2)	65 (13.3)	16 (19.0)	0.164
Statins	80 (14.0)	63 (12.9)	17 (20.2)	0.074
Antianginals	23 (4.0)	19 (3.9)	4 (4.8)	0.708
OADs	84 (14.7)	66 (13.5)	18 (21.4)	0.059
Insulin	18 (3.1)	14 (2.9)	4 (4.8)	0.359
High Killip class, n [%]	53 (9.3)	39 (8.0)	14 (16.7)	0.011
LVEF %	45.5 ± 10.3	46.5 ± 9.7	39.5 ± 11.5	< 0.001
Cardiogenic Shock, n [%]	10 (1.7)	4 (0.8)	6 (7.1)	< 0.001
CPA on admission, n [%]	26 (4.5)	11 (2.3)	15 (17.9)	< 0.001
Admission diagnosis, n [%]				
Anterior MI	224 (39.2)	182 (37.3)	42 (50.0)	0.028
High Lateral MI	17 (3.0)	16 (3.3)	1 (1.2)	0.663
Posterior MI	39 (6.8)	32 (6.6)	7 (8.3)	0.554
Inferior MI	318 (55.6)	279 (57.2)	39 (46.4)	0.067
Acute heart Failure, n [%]	38 (6.6)	12 (2.5)	26 (31.0)	< 0.001
Rehospitalization, n [%]	61 (10.7)	28 (5.7)	33 (39.3)	< 0.001
Nonfatal MI, n [%]	16 (2.8)	0 (0.0)	16 (19.0)	< 0.001
Stroke, n [%]	13 (2.3)	0 (0.0)	13 (15.5)	< 0.001
30-days mortality, n [%]	58 (10.1)	0 (0.0)	58 (69.0)	< 0.001

BMI — body mass index; CAD — coronary artery disease; COPD — chronic obstructive pulmonary disease; CPA — cardiopulmonary arrest, CRF — chronic renal failure; CVA — cerebrovascular accident; LVEF — left ventricular ejection fraction; MI — myocardial infarction; OADs — oral antidiabetik drugs; PAD — peripheral artery disease;; PCI — percutaneous coronary intervention; RAS — renin-angiotensin system

Table 2. Biochemical and hematologic parameters of all study population and the patients with and without major adverse cardiovascular and cerebrovascular events (MACCEs)

Variables	All population	No MACCEs (n = 488; 85.3%)	MACCEs (n = 84; 14.7%)	p-value
Glucose [mg/dL]	134.0 ± 56.8	133.4 ± 57.0	138.5 ± 56.8	0.434
Creatinine [mg/dL] IQR	1.03 [0.85–1.10]	1.04 [0.86–1.11]	0.96 [0.80–1.05]	0.305
eGFR [mL/min/1.73 m^2]	72.2 [62.0–89.6]	71.8 [62.0–88.4]	75.2 [63.3–95.4]	0.207
SUA [mg/dL]	4.98 ± 1.5	4.90 ± 1.5	5.12 ± 1.4	0.241
SUA/SCr ratio	5.13 ± 1.9	5.0 ± 1.9	5.73 ± 2.1	0.002
Total cholesterol [mg/dL]	206.5 ± 47.0	206.4 ± 46.4	207.5 ± 52.5	0.834
LDL-C [mg/dL]	128.3 ± 44.3	127.9 ± 44.2	130.4 ± 44.8	0.637
HDL-C [mg/dL]	41.2 ± 8.4	41.1 ± 8.4	42.0 ± 8.7	0.362
Triglyceride [mg/dL] IQR	166.0 [117.8–245.0]	170.0 [120.5–244.5]	159.0 [107.8–255.5]	0.654
Hemoglobin [g/dL]	13.8 ± 1.5	13.8 ± 1.6	13.7 ± 1.5	0.773
White blood count [10^9/L]	8.4 ± 2.2	8.4 ± 2.1	8.5 ± 2.0	0.852
Platelet [10^9/L]	270.2 ± 67.8	270.0 ± 70.2	270.4 ± 52.0	0.979

eGFR — estimated glomerular filtration rate; IQR — interquartile range; LDL-C — low-density lipoprotein cholesterol; HDL-C — high-density lipoprotein cholesterol; SUA — serum uric acid; SUA/SCr — serum uric acid to serum creatinine ratio

Table 3. Angiographic and procedural parameters of the whole study population and the patients with and without major adverse cardiovascular and cerebrovascular events (MACCEs)

Variables	All population	No MACCEs (n = 488; 85.3%)	MACCEs (n = 84; 14.7%)	p-value
Two vessel disease, n [%]	328 (57.3)	295 (60.5)	33 (39.3)	< 0.001
Three vessel disease, n [%]	243 (42.5)	192 (39.5)	51 (60.7)	< 0.001
Syntax Score I	21.5 ± 5.6	20.9 ± 5.5	24.7 ± 5.1	< 0.001
Culprit lesion, n [%]				0.533
LAD and side branches	228 (39.9)	190 (38.9)	38 (45.2)	
Cx and side branches	99 (17.3)	85 (17.4)	14 (16.7)	
RCA and side branches	237 (41.4)	207 (42.4)	30 (35.7)	
Undetermined	8 (1.4)	6 (1.2)	2 (2.4)	
LMCA disease, n [%]	17 (3.0)	12 (2.5)	5 (6.0)	0.082
CTO; n (%)	14 (2.5)	13 (2.7)	1 (1.2)	0.418
PCI for NCL, n [%]	92 (16.1)	84 (17.2)	8 (9.5)	0.076
Ad hoc PCI	26 (4.5)	20 (4.1)	6 (7.1)	0.216
Elective PCI	66 (11.5)	64 (13.1)	2 (2.4)	0.004
CABG for other vessels, n [%]	473 (82.7)	399 (81.8)	74 (88.1)	0.156
OMT; other vessels, n [%]	6 (1.0)	4 (0.8)	2 (2.4)	0.195
Procedure, n [%]				0.266
POBA	5 (0.9)	3 (0.6)	2 (2.4)	
BMS	214 (37.4)	182 (37.3)	32 (38.1)	
DES	353 (61.7)	303 (62.1)	50 (59.5)	
Failure of PCI for culprit vessel	38 (6.6)	19 (3.9)	19 (22.6)	< 0.001
Failure of PCI for NCL	7 (1.2)	4 (0.8)	3 (3.6)	0.034
TIMI < 3 flow in culprit vessel	100 (17.5)	67 (13.7)	33 (39.3)	< 0.001
Stent thrombosis, n [%]	7 (1.2)	6 (1.2)	1 (1.2)	0.974
Requiring revascularization, n [%]	14 (2.4)	0 (0.0)	14 (16.7)	< 0.001

BMS — bare metal stent; CABG — coronary artery by-pass graft surgery; CTO — chronic total occlusion; Cx — Circumflex artery; DES — drug-eluting stent; LAD — left anterior descending artery; LMCA — left main coronary artery; NCL — non-culprit lesion; OMT — optimal medical therapy; PCI — percutaneous coronary intervention; POBA — plain old balloon angioplasty; RCA — right coronary artery; TIMI — thrombolysis in myocardial infarction

Table 4. Factors that were found to be independently associated with the major adverse cardiovascular and cerebrovascular events (MACCEs in univariable and multivariable cox regression analysis models (model 1 and 2)

Variables	Univariable		Model 1		Model 2	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.026 (1.008–1.044)	0.004	1.020 (1.002–1.038)	0.028	1.022 (1.004–1.041)	0.014
Smoking	1.798 (1.078–2.997)	0.025	2.513 (1.491–4.236)	0.001	2.483 (1.469–4.196)	0.001
Anterior MI	1.595 (1.040–2.447)	0.032	0.940 (0.590–1.499)	0.796	0.996 (0.628–1.581)	0.987
LVEF	0.948 (0.929–0.967)	< 0.001	0.962 (0.939–0.985)	0.001	0.962 (0.939–0.985)	0.001
High Killip class	1.958 (1.103–3.476)	0.022	1.392 (0.741–2.617)	0.304	1.441 (0.765–2.714)	0.259
TIMI < 3 flow	3.377 (2.179–5.234)	< 0.001	2.353 (1.472–3.761)	< 0.001	2.327 (1.452–3.728)	< 0.001
Syntax score I	1.073 (1.049–1.099)	< 0.001	1.067 (1.036–1.099)	< 0.001	1.067 (1.036–1.098)	< 0.001
Uric acid	1.091 (0.945–1.259)	0.233	–	–	–	–
SCr	0.351 (0.134–0.918)	0.033	–	–	0.502 (0.212–1.185)	0.116
SUA/SCr	1.144 (1.044–1.253)	0.004	1.129 (1.028–1.239)	0.011	–	–

*variables with a p-value of less than 0.05 in the univariate analysis were incorporated into the multivariable cox regression analysis by using the enter method; CI — confidence interval; HR — hazard ratio; LVEF — left ventricular ejection fraction; MI — myocardial infarction; SCr — serum uric acid; SUA/SCr — serum uric acid to serum creatinine ratio; TIMI — thrombolysis in myocardial infarction

in the analysis Table 3, where SUA/SCr is included (model 1). A separate multivariable analysis (model 2) was performed without including SUA/SCr to test whether SCr values predicted the development of MACCEs; considering that SCr may have an impact on the significant relationship between SUA/SCr and MACCEs. Moreover, since uric acid was not found to be associated with MACCEs in the univariable analysis ($p > 0.05$), it was not evaluated in the multivariable analysis. Both models revealed that: older age, smoking, lower LVEF, poor TIMI flow, and higher anatomical SxSI were found to be independent predictors of the worst 30-day cardiovascular outcomes. Furthermore, higher SUA/SCr independently predicted 30-day MACCEs whereas SCr levels did not show the same significant association with the development of MACCEs (Tab. 4). Also, to test the discriminatory ability and diagnostic performance of the SUA/SCr in determining the 30-day MACCEs; a ROC curve analysis was performed. The AUC of the SUA/SCr was 0.606 (95% CI = 0.540–0.671; $p = 0.002$) (Fig. 1). An SUA/SCr of > 4.58 was determined as the cutoff value based on the Youden's index; with a 75% sensitivity and a 44% specificity for the prediction of MACCEs. The Kaplan–Meier survival curves indicated that high-risk patients (patients with an SUA/SCr of > 4.58) had a significantly higher prevalence of MACCEs than the low-risk patients (patients with an SUA/SCr of ≤ 4.58) during the follow-up period after index hospitalization ($p = 0.001$) (Fig. 2).

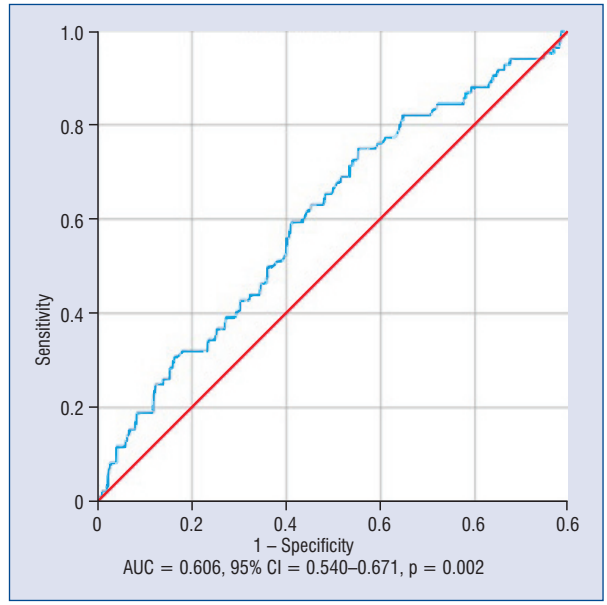


Figure 1. Predictive performance of serum uric acid to serum creatinine ratio (SUA/SCr) in determining the 30-day major adverse cardiovascular and cerebrovascular events (MACCEs); AUC — area-under-the-curve; CI — confidence interval; ROC — receiver operating characteristic curve

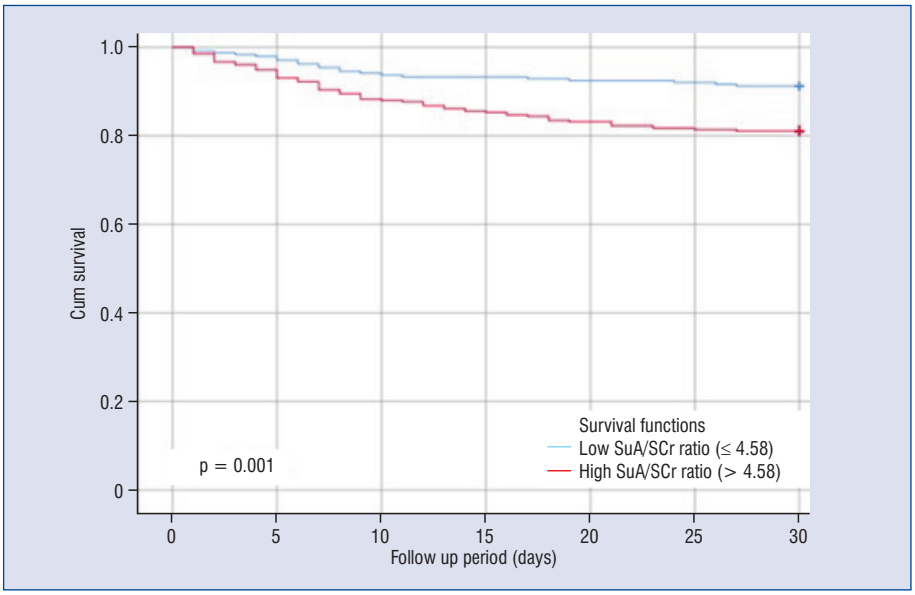


Figure 2. The Kaplan–Meier curve exhibited that patients with a high SUA/SCr ratio (> 4.58) had a poor prognosis compared to those with a low SUA/SCr ratio (≤ 4.58); SUA/SCr — serum uric acid to serum creatinine ratio

Discussion

The main findings of this study are as follows: (1) Preprocedural elevated SUA/SCr, lower LVEF, smoking, postprocedural TIMI flow of < < 3 and higher anatomical SxSI were found to be independent predictors of early MACCEs among the patients with STEMI and MVCAD. This relationship remained significant even after adjusting for other confounding factors in the univariate and multivariate logistic regression analyses. (2) An SUA/SCr of > 4.58 predicted MACCEs with a 75% sensitivity and a 44% specificity. (3) Based on the Kaplan–Meier survival curves; the patients with an SUA/SCr of > 4.58 had a significantly worse prognosis than those with an SUA/SCr of ≤ 4.58.

Oxidative stress (OS) plays an important role in the initiation and progression of atherosclerosis by causing endothelial dysfunction due to oxidative damage in vascular endothelial cells [15]. OS has also been closely associated with the extent and severity of CAD as well as stabilization of atherosclerotic plaques and ACS [15–19]. UA is the end product of purine metabolism; produced by the action of xanthine oxidase. It is also thought to be associated with endothelial dysfunction through the formation of free radicals and high OS; thus, playing a role in the pathophysiology of CVD [20, 21]. Several previous studies have reported an association between SUA and CVD including hypertension, metabolic syndrome, ACS, chronic CAD, cerebrovascular disease and future unfavourable cardiovascular outcomes [20–22]. Moreover, beyond being related to fatal and non-fatal ACSs; SUA has also been associated with the extent and severity of CAD in patients with ACS [7, 20, 23]. A study by Zhang et al. [8] demonstrated that as the levels of SUA increased, the severity of CAD also increased. The authors concluded that hyperuricaemia is an independent risk factor for 1-year total major adverse cardiovascular events and MVCAD in patients with ACS and hypertension after PCI [8]. Furthermore, results regarding the consequences of hyperuricemia on morbidity and mortality after adjustment for traditional cardiovascular risk factors are conflicting [24]. Although the influence of renal function on SUA has been overlooked in some previous studies; these inconsistencies may be related to the fact that endogenous UA concentration is often influenced by renal clearance function. To overcome this confusing situation, researchers have considered the SUA/SCr, reflecting a net production of endogenous UA and as a standardized SUA index of kidney function and a newly defined biomarker for CVD [5]. Some literature data indicate that the SUA/SCr is significantly associated with unfavourable outcomes under a variety of clinical conditions known to increase the CVD risk, such as: hypertension, metabolic syndrome, type 2 diabetes and chronic kidney disease [5, 25–27]. A higher SUA/SCr has also been reported to be

associated with an increased risk of CVD as well as total and cause-specific mortality [5, 25, 28]. Recently, Çiçekçioğlu et al. [9] demonstrated the prognostic importance of the SUA/SCr in patients with severe aortic stenosis who underwent transcatheter aortic valve implantation [9]. In addition; Xi et al. [29] found that a higher SUA/SCr was associated with an increased risk of mortality in patients with heart failure compared to a lower SUA/SCr. This suggests that the SUA/SCr may be used as a preferred predictor of mortality risk in clinical practice [29]. Although several studies have demonstrated that SUA/SCr is associated with the CVD risk and CAD severity in patients with chronic CAD. To date, no study has evaluated the relationship between the SUA/SCr and MACCEs in patients with STEMI and MVCAD [9, 10]. According to available research, the present study is the first in this regard. Consistent with data from previous studies on various cardiovascular conditions such as hypertension, metabolic syndrome, heart failure and aortic valve stenosis treated with transcatheter aortic valve implantation, the current study demonstrated an association between a high SUA/SCr and poor prognosis in patients with STEMI and MVCAD [6, 9, 10, 29].

Although the relationship between the SUA/SCr and CVD has not yet been fully identified, The authors think that endothelial dysfunction, stimulation of apoptosis, decrease in endothelial nitric oxide production, activation of the renin–angiotensin–aldosterone system, and maladaptive immune system response may be the main primary mechanisms resulting from increased OS and inflammation. Indeed, increased OS associated with a high SUA/SCr has been found to lead to proliferative and pro-inflammatory responses in cultured vascular smooth muscle cells and results in senescence and apoptosis of human umbilical vein endothelial cells [5, 30]. Furthermore, the SUA/SCr has been associated with many cardiometabolic factors related to CAD, which partially explains the relationship between the SUA/SCr and CAD [29]. These abnormalities suggest that the SUA/SCr may play a crucial role in the promotion of atherosclerosis and genesis of acute vascular events. Based on literature data and the results of the present study; a high SUA/SCr indicates increased inflammation and OS; which may serve as biological mechanisms linking the SUA/SCr to an increase in MACCEs risk and poor outcomes among patients with ACS.

In line with literature data, the current study demonstrated that lower LVEF; smoking; postprocedural TIMI flow of < 3; and higher anatomical SxSI independently predicted MACCEs among the patients with STEMI [31–33].

Among patients presenting with ACS, those with MVCAD have a worse prognosis than those with single-vessel CAD [12]. Apart from that, it remains controversial whether NCLs should be routinely revascularized during the index pPCI or treated conservatively according to therapeutic guidelines. The treatment approach for ACS with MVCAD; except for infarct-related arteries; is complex because the appropriate timing of invasive interventions for NCLs is difficult to identify. Although many factors such as a patient's clinical findings; electrocardiographic changes, serum cardiac troponin level, heart rate, creatinine level, and heart failure symptoms are used in daily practice; a definitive consensus has not been reached on the treatment approach and timing for patients with ACS and MVCAD. Essentially, an integrated approach that considers clinical parameters; anatomical factors; and biomarkers associated with poor outcomes; such as the SUA/SCr; and that uses the fractional flow reserve or intravascular imaging may be key to identifying patients at a high risk of subsequent cardiovascular events and deciding on the treatment approach and timing for these patients is warranted.

Limitations

The current study has several limitations that should be noted. First, the study employed a retrospective design which can establish associations but not causality and represented the experience of a single center based only on data accessed through the hospital information system. Second, the sample size was relatively small, which may render the study underpowered in detecting the value of the SUA/SCr for predicting 30-day MACCEs. Third, the study focused only on preprocedural SUA and SCr levels on admission and ignored time-varying changes in the SUA/SCr; which may provide more valuable information than the baseline SUA/SCr to understand the underlying mechanisms. Fourth, there is an inability to interpret whether UA-reduction therapy could reduce the risk of MACCEs. Fifth, although several important covariates were adjusted for; other potential factors such as physical activities; drug use, and menstrual status may have introduced bias. Sixth, the current study could not evaluate whether the SUA/SCr contributed to the decision on PCI treatment and timing for NCLs among the patients with STEMI

and MVCAD due to the substantially small number of patients who underwent non-infarct artery interventions. Seventh, the CAD severity based on luminal stenosis was evaluated only using visual coronary angiograms. No additional information on quantitative assessments of coronary artery atherosclerosis was included, such as distribution, luminal area and plaque burden. Therefore, further prospective studies are needed to confirm and extend the results of the current study.

Conclusions

The findings herein suggest an independent role of the SUA/SCr ratio in predicting 30-day MACCEs in patients with STEMI and MVCAD undergoing pPCI. So, SUA/SCr may be easy-to-use, inexpensive and promising predictive oxidative biomarker that can be used as a part of cardiovascular examinations for identifying high-risk individuals with MVCAD and STEMI in clinical practice. Although the current study did not directly evaluate the role of SUA/SCr regarding PCI treatment and timing for NCLs in patients with STEMI and MVCAD; the findings can assist clinicians in making decisions regarding treatment, including the timing of invasive interventions; and in informing individual patients of their risk given the ability of the SUA/SCr to predict adverse outcomes in such patients.

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