Serum uric acid may modulate the inflammatory response after primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction

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Elevated serum uric acid (SUA) has been associated with impaired myocardial reperfusion and adverse outcomes in ST-segment elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (pPCI).[1–5] The mechanisms underlying these relationships are poorly investigated. Inflammation plays a central role in the pathogenesis of ischemia/reperfusion damage after pPCI.[6–8] Preclinical studies showed that SUA may induce the inflammasome, enhancing the synthesis of IL-1β.[8,9] The aim of our study was to explore the relationship between SUA and the inflammatory response in patients with STEMI undergoing pPCI.

Methods

Our study included consecutive patients presenting with STEMI within 12 h of symptom onset, treated with pPCI, between 2013 and 2014. SUA level was assessed on admission; high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) were measured before pPCI and after 6, 12, 24, and 36 h. Angiographical parameters of coronary and myocardial reperfusion were evaluated immediately after the PCI as previously described.[10] Angiographic microvascular obstruction was defined as TIMI flow grade 2 or less or TIMI flow grade 3 with myocardial blush grade less than 2. ST-resolution (STr) was assessed according to literature.[11]

Elevated (e)SUA was defined as more than 6.8 mg/dl in agreement with previous reports.[2,5,12] Categorical data were expressed as count (percentage), continuous data as mean ± SD or median (interquartile range); they were compared with the Fisher exact test and with *t*-test, respectively. Correlations between SUA, hs-CRP and IL-6 were adjusted for potential confounders using multiple linear regression model including age, sex, hypertension and myocardial infarct size as covariates. SUA, hs-CRP and IL-6 were log-normalized for statistical tests.

Results

We enrolled 44 STEMI patients. Overall age was 61 ± 13 years, 31 were man (70%), 7 had diabetes mellitus (16%). Twenty (45%) had an anterior myocardial infarction. Angiographic analyses are shown in Table 1. STr occurred less frequently in patients with eSUA as compared with patients with normal SUA ($P = 0.016$). Patients with eSUA had higher hs-CRP and IL-6 peak values (respectively, $P = 0.004$ and $P = 0.006$) (Table 1).

In the overall population, there was a significant linear correlation between SUA levels and both Lnhs-CRP and LnIL-6 peak values (respectively, $R = 0.366$, $P = 0.015$ and $R = 0.484$, $P = 0.001$; Fig. 1). The associations between SUA and hs-CRP peak ($\beta = 0.39$, $P = 0.019$) and between SUA and IL-6 peak ($\beta = 0.56$, $P = 0.001$) were maintained after adjusting for covariates.

Comment

Among patients with STEMI treated with pPCI we found that: eSUA was associated with a greater inflammatory response; in the overall population, there were significant correlations between baseline SUA levels and hs-CRP and IL-6 peak values. Previous findings suggested that SUA may induce the inflammasome[8,9] and this possible link may explain the association between eSUA and adverse outcomes after STEMI.[2–4]

eSUA has been linked with worse myocardial reperfusion and larger infarct size after pPCI.[4,5] We did not find any significant difference in angiographic parameters of reperfusion between the groups, maybe because of the good final

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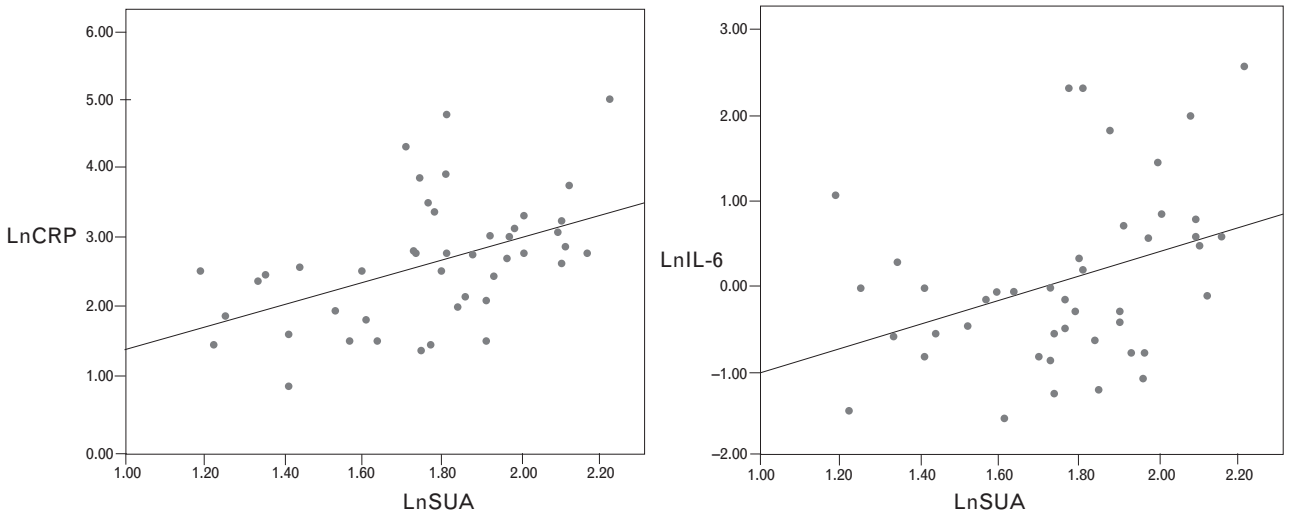
Table 1 Angiographic analyses

	SUA≥6.8mg/dl ($n=14$)	SUA<6.8mg/dl ($n=30$)	*P* value
Age (years)	70 (8.9)	60 (15.3)	0.065
Male	13 (92.9)	24 (80)	0.27
Familiarity for CAD	3 (21.4)	8 (26.7)	0.51
Dyslipidemia	8 (57.1)	16 (53.3)	0.53
Hypertension	11 (78.6)	13 (43.3)	0.03
Active smokers	3 (21.4)	20 (66.7)	0.01
Diabetes	4 (28.6)	3 (10)	0.13
Previous myocardial infarction	2 (14.3)	6 (20)	0.49
Previous coronary intervention	1 (7.1)	6 (20)	0.27
Serum creatinine	0.90 (0.19)	0.77 (0.27)	0.2
Pain to balloon time (h)	4.17 (3.45)	3.75 (2.38)	0.17
Multivessels disease	10 (71.4)	19 (63.3)	0.43
Anterior MI	7 (50)	13 (44.8)	0.463
Culprit vessel			0.93
LAD	7 (50)	13 (44.8)	
CFX	2 (14.4)	4 (13.8)	
RCA	5 (32.6)	12 (41.4)	
Anti-GP IIb/IIIa	6 (42.9)	10 (33.3)	0.38
Aspirin at baseline	6 (42.9)	8 (28.6)	0.27
Statin at baseline	4 (28.6)	2 (6.7)	0.07
Anti-inflammatory therapy at baseline	0 (0)	0 (0)	1
SUA-lowering therapy at baseline	0 (0)	0 (0)	1
Basal TIMI flow grade			1
0	14 (100)	30 (100)	
Final TIMI flow grade			1
3	14 (100)	30 (100)	
TIMI frame count, frames	13.8 (5.6)	12.9 (8.9)	0.57
MBG			0.176
0/1	5 (45.5)	7 (24.1)	
2	6 (54.5)	22 (75.9)	
Angiographic MVO	5 (45.5)	7 (24.1)	0.176
ST-resolution 50%	5 (38.5)	8 (61.5)	0.016
LVEF	41 (11.2)	44.8 (7.8)	0.068
TNI peak (ng/ml)	48.7 (33.7–113.2)	49.1 (22.1–126.2)	0.614
hs-CRP peak (mg/dl)	1.6 (0.7–2.5)	0.67 (0.46–1.1)	0.0038
IL-6 peak (pg/ml)	23.4 (17.5–30.1)	13.6 (5.7–19)	0.006

Values are mean (± standard deviation) or *n* (%); TNI, hs-CRP and IL-6 peak values are median (IQR). CAD, coronary artery disease; CFX, circumflex artery; hs-CRP, high-sensitivity C-reactive protein; LAD, left anterior descendent artery; LVEF, left ventricular ejection fraction; MBG, myocardial blush grade; MI, myocardial infarction; MVO, microvascular obstruction; RCA, right coronary artery; SUA, serum uric acid; TIMI, thrombolysis in myocardial infarction; TNI, troponin I.

Fig. 1



Linear correlations between LnSUA–LnhsCRP and LnSUA–LnIL-6. CRP, C-reactive protein; IL-6, interleukin-6; SUA, serum uric acid. In the overall population, there was a significant linear correlation between LnSUA and LnhsCRP (R^2, 0.134, $P = 0.015$) and between LnSUA and LnIL-6 peak values ($R^2 = 0.235$, $P = 0.001$).

procedural result in the whole population and to the small sample size. Nevertheless, we found a significant difference in STr between the groups, suggesting a possible relationship between eSUA and myocardial reperfusion impairment after technically successful pPCI in STEMI.

The main limitation of our study is the limited sample size. However, we considered unselected STEMI patients and we performed seriate dosages of hs-CRP and IL-6 to accurately estimate the inflammatory response; additionally, we used multivariable analysis to adjust for possible confounders.

Our findings put the spotlight on a possible pathophysiological role of SUA in STEMI treated with pPCI and warrant further investigation. With anti-inflammatory agents potentially available, eSUA may represent an easily obtainable risk marker to identify good candidates for this novel therapeutic approach.

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Conflicts of interest

There are no conflicts of interest.

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