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Prognostic Value of Serum Uric Acid Level in Patients with ST Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

Mohamed Mahmoud Mohamed Abdellatif*, Ahmed Abdel-Galeel, Mohamad A. Alsherif, Salwa Demtry

Faculty of Medicine, Assiut University, Assiut, Egypt
Email: *dr.mohammed.abdellatif@gmail.com, Ahmed_gelil@yahoo.com, mohamedashraf2008@yahoo.com, salwademitry@yahoo.com

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Abstract

Background: Serum uric acid (SUA) has been correlated with cardiac morbidity and mortality. However, its prognostic value in acute ST-segment elevation myocardial infarction (STEMI) is still uncertain. The aim of this study was to evaluate the prognostic value of SUA on admission in patients with STEMI undergoing primary percutaneous coronary intervention (PPCI). **Methods:** We prospectively enrolled 150 STEMI patients underwent PPCI. The mean age of the studied population was 56.1 years, 78% were males while 22% were females. Patients were divided into tertiles based on the basal serum uric acid level. Patients with high SUA (n = 72) was defined as a value in the third tertile (>6.4 mg/dl), and a low SUA group (n = 78) was set as a value in the lower two tertiles (<6.4 mg/dl). Clinical characteristics, angiographic findings, echocardiographic data, in-hospital and three-month outcomes of PPCI were analyzed. **Results:** SUA level on admission carried prognostic value in patients with STEMI undergoing PPCI where the low uric acid group had better KILLIP class ($P = 0.001$), better TIMI flow ($P = 0.001$), higher ejection fraction (49.53 ± 8.75 versus 39.95 ± 7.06; $P = 0.001$), better survival and lower incidence of other major adverse cardiac events (MACE) ($P = 0.01$) during the hospital stay and three months follow up than the high uric acid group. Age, SUA > 6 mg/dl, TIMI flow, Killip class and EF < 40% were independent predictors for MACE in such patients. **Conclusions:** High SUA level on admission was associated with higher frequency of in-hospital and three months follow up MACE in patients with acute STEMI undergoing PPCI.

Keywords

Uric Acid, Primary Angioplasty, STEMI

1. Introduction

ST-elevation myocardial infarction (STEMI) is an acute medical emergency that requires care coordination to achieve myocardial reperfusion as early as possible. [1].

PPCI is defined as percutaneous catheter intervention in the setting of STEMI, without previous fibrinolysis. Primary PCI has replaced fibrinolysis to be the preferred reperfusion strategy in STEMI patients, if it can be done in time and in a high-volume PCI center [1] [2].

Several studies suggested a possible association between elevated serum uric acid level and prognosis in patients with acute coronary syndromes in spite of that the role of uric acid as a risk factor or a risk marker for cardiovascular disease is still an issue of debate [3].

The mechanism by which uric acid can cause cardiovascular disease is still uncertain but it has been explored using cell culture and animal models. It seems that uric acid has to enter the endothelial cells as well as the vascular smooth muscle cells through a specific organic anion exchanger, where it activates intracellular signaling molecules which in turn activate inflammation and proliferation. In the endothelial cells, uric acid decreases nitric oxide levels and it also inhibits endothelial proliferation, whereas in vascular smooth muscle cells, uric acid activates inflammatory and proliferative pathways [4] [5].

This work was designed to investigate the predictive role of serum uric acid level on admission and short term (in hospital and three months follow up) major adverse cardiovascular events as well as its relation to Killip classification, TIMI flow and LV function in patients with acute STEMI undergoing primary percutaneous coronary intervention (PPCI).

2. Methodology

This study was a prospective study, included 150 patients who had STEMI and underwent PPCI from the beginning of March 2017 till end of December 2017.

All the included patients presented STEMI and were eligible for primary PCI within the first 24 hours of chest pain at its maximum intensity but patients with Acute inflammatory states, Known malignancies, Kidney disease or Patients with previous PCI or CABG and Patients who are known to have RHD or congenital heart disease were excluded from the study.

2.1. All Patients Were Subjected to

1) Full history taking: including age, sex, history of DM, HTN, smoking, and dyslipidemia, also to assess the onset of chest pain and time to reperfusion.

2) Electrocardiogram (ECG): The diagnosis of STEMI is based on the presence of chest pain lasting ≥ 20 minutes associated with typical changes on surface electrocardiography (ST-segment elevation ≥ 0.1 mV in ≥2 limb leads or ≥0.2 mV in ≥2 contiguous precordial leads or complete left bundle branch block of new onset) **(Joint ESC/ACCF/AHA/WHF Task Force 2012)**.

3) Physical examination:

- General examination including intra-procedural blood pressure and heart rate assessment.
- Cardiac examination to detect signs of heart failure.
- Chest examination: to define Killip score as following [6].

Killip I: No evidence of heart failure.

Killip II: Rales up to half of lung fields or S3 gallop.

Killip III: Frank pulmonary oedema and systolic blood pressure > 90 mmhg.

Killip IV: cardiogenic shock and pulmonary oedema.

4) Coronary angiography and primary PCI: were done by an interventional cardiologist.

- After the procedure TIMI flow of the culprit vessel after PCI was reported as following:

TIMI 0: complete occlusion.

TIMI 1: penetration of obstruction by contrast but no distal perfusion.

TIMI 2: perfusion of entire artery but with delayed flow.

TIMI 3: full perfusion and normal flow.

5) Collect baseline venous blood samples:

For assessment of haemoglobin (HB) level, serum creatinine and electrolytes. on admission SUA level was assessed using photometer 5010 device and SPINREACT kits.

6) Echocardiography:

All patients were examined by transthoracic 2D echocardiography within 24 hour of admission using GE VIVDE S5 ultrasound system device by a trained echocardiographer to assess left ventricular ejection fraction by the biplane method.

7) Follow up:

Follow up of the patient after three months from PPCI to assess morbidity and mortality due to major adverse cardiovascular events.

Follow-up data were obtained from hospital records or by interviewing (in person or by telephone) patients, family members, or primary care physician.

2.2. Ethical Considerations

Ethical approval:

An approval for the study is obtained from the ethical committee in our university.

Risk-benefit assessment:

There is no risk affecting the patient in this study.

Confidentiality:

Any data taken from the patient either from history, examination or investigations dealt with in a confidential manner.

Research statement:

Every patient was informed about the nature and steps of the study.

Informed consent:

Written consent was obtained from each patient participating in the study.

2.3. Statistical Analysis

Data was collected and analyzed those using SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York). Continuous data was expressed in form of mean ± SD or median (range) while nominal data was expressed in form of frequency (percentage).

Chi^2-test was used to compare the nominal data of different groups in the study while student t-test was used to compare mean of different two groups.

Multivariate regression analysis was used to determine the independent risk factors for prediction of MACE in patients with acute STEMI undergoing PPCI while Kaplan Meier curve was used for survival analysis. Optimal cutoff point of SUA for prediction of MACE was determined by ROC curve. *P* value was significant if <0.05.

The study included 150 patients underwent primary PCI. Patients were divided into tertiles based on the basal serum uric acid. Patients with high UA (n = 72) was defined as a value in the third tertile (>6.4 mg/dl), and a low UA group (n = 78) was set as a value in the lower two tertiles (6.4 mg/dl).

3. Results

3.1. Descriptive Data of the Study Population

Demographic Data of All Patients:

Our study included 150 patients, all presented STEMI and all underwent primary PCI. The mean age of the studied population was 56.1 years, 78% of them were males while 22% of them were females. Forty seven patients (31.3%) were smokers, 40 patients were known to have DM and 40 patients were known to have HTN and that represented 26.7% of the studied population for each.

Clinical Data and ECG Findings in Studied Patients:

The mean time delay for all patients from the onset of symptoms to the FMC was 5.75 hours.

Anterior STEMI was the most common presentation with 79 patients (52.7%) presented anterior STEMI and 43 patients (28.7%) presented inferior STEMI. Posterior STEMI came to the third with 25 patients (16.7%), while only 3 patients (2%) presented lateral STEMI.

The vast majority of our patients were Killip class I as 114 patients (76%) were Killip class I, 27 patents (18%) were Killip class II, while only 6 and 3 patients were Killip class III and IV respectively.

Angiographic Findings and Ejection Fraction in All Studied Group:

According to angiographic data, LAD was found to be the most affected artery as 87 patients (58%) had an LAD culprit lesion on coronary angiography. 44 patients (29.3%) had RCA culprit lesion while 19 patients (12.7%) had LCx culprit lesion.

Regarding TIMI flow after PCI, the majority of the studied population precisely 108 patients (72%) had TIMI III flow after PCI versus 32 patients and 10 patients had TIMI II and TIMI I flow respectively. None of the studied population had TIMI 0 flow after PCI. Echocardiography was done to all studied patients after PCI. The mean EF of all patients was 44.49%

Baseline Laboratory Data in All Patients:

A blood sample was collected from the studied population on admission. The mean hemoglobin level was 13.01 gram/dl, the mean serum urea was6.9 mg/dl and the mean serum creatinine was 0.84 mg/dl.

The mean random blood sugar was 180 mg/dl and the mean serum CK and CKMB was 2187 U/L and 213 U/L respectively.

The mean serum uric acid level in all studied population was 6.49 mg/dl.

Short Term (in Hospital and Three Months) Follow Up:

Table 1 shows short term (in hospital and three months) follow up in the current study. 20 patients (13.3%) developed MACE.

Cardiovascular mortality was recorded in 8 patients (5.3%), 16 patients (10.7%) presented reinfarction and 2 patients (1.3%) reported CVS during the follow up period.

Also, other adverse events as advanced heart failure were noticed in 16 patients (10.6%) and GIT bleeding in 4 patients (2.7%).

3.2. Comparison between High SUA Group and Low SUA Group

The 150 Patients included in the study were divided into tertiles based on the basal serum uric acid level. Patients with high SUA (n = 72) was defined as a value in the third tertile (>6.4 mg/dl), and a low SUA group (n = 78) was set as a value in the lower two tertiles (<6.4 mg/dl).

Demographic Data of Studied Groups:

Table 2 shows the demographic data of studied groups. Mean age of those patients with high SUA was 58.28 ± 12.31 years and it was 54.09 ± 9.67 years for those with low SUA. Majority of patients (82.1% in low SUA group and 53 (73.6%) in high SUA group) were males.

Twenty five patients (32%) of those with low SUA and 22 patients (30.5%) of those with high UA were smoker. DM, HTN presented in 22 (28.2%) and 19 (24.4%) patients with low SUA respectively and in 18 (25%) and 21 (29.2%) patients with high SUA respectively.

In the other demographic data shown at Table 2, with exception of age (that was significantly high in those patients with high SUA), demographic data had no significant differences between both groups ($P > 0.05$).

Table 1. Descriptive data of the study population.

Variables	N = 150
Age (years)	56.10 ± 11.17
Sex	
Male	117 (78%)
Female	33 (22%)
Known risk factors	
DM	40 (26.7%)
HTN	40 (26.7%)
Smoking	47 (31.3%)
Duration of symptoms (hour)	5.75 (3.97)
ECG findings	
Anterior MI	79 (52.7%)
Inferior MI	43 (28.7%)
Posterior MI	25 (16.7%)
Lateral MI	3 (2%)
Killip class	
I	114 (76%)
II	27 (18%)
III	6 (4%)
IV	3 (2%)
Systolic blood pressure (mmHg)	123.93 ± 22.79
Diastolic blood pressure (mmHg)	77.22 ± 12.95
Angiographic findings	
Culprit lesion	
LAD	87 (58%)
RCA	44 (29.3%)
LCx	19 (12.7%)
TIMI flow	
0	0
1	10 (6.7%)
2	32 (21.3%)
3	108 (72%)
Ejection fraction (%)	44.94 ± 9.29
Laboratory data	
Hemoglobin level (g %)	13.01 ± 3.23
Creatinine (mg/dl)	0.84 ± 0.19
Urea (mg/dl)	6.90 ± 2.44
Random blood sugar	180.11 ± 40.23
CK (U/L)	2187.01 ± 603.33
CKMB	213.06 ± 66.03
Uric acid	6.49 ± 2.33
Short term follow up	
MACE	20 (13.3%)
Cardiovascular mortality	8 (5.3%)
Reinfarction	16 (10.7%)
Target vessels revascularization	13 (8.6%)
Stroke	2 (1.3%)
Advanced heart failure	16 (10.7%)
GIT bleeding	4 (2.7%)
Blood transfusion	2 (1.3%)

Data was expressed in form of frequency (percentage). *P* value was significant if <0.05. **LDA**, left anterior descending coronary artery; **RCA**, right coronary artery; **LCx**, left circumflex coronary artery **MACE**, major adverse cardiac events (cardiovascular mortality, reinfarction, target-vessel revascularization); **GIT**, gastrointestinal bleeding.

Table 2. Baseline demographic data of studied groups.

Variables	Low SUA group (n = 78)	High SUA group (n = 72)	*P* value
Age (years) mean ± SD	54.09 ± 9.67	58.28 ± 12.31	**0.02**
Sex			
Male	64 (82.1%)	53 (73.6%)	0.14
Female	14 (17.9%)	19 (26.4%)	
Known risk factors			
DM	22 (28.2%)	18 (25%)	0.39
HTN	19 (24.4%)	21 (29.2%)	0.31
Smoking	25 (32%)	22 (30.5%)	0.15

Data was expressed in form of mean (SD) and frequency (percentage). *P* value was significant if < 0.05. **DM**, diabetes mellitus; **HTN**, hypertension.

Clinical Data and ECG Findings in Studied Groups:

Clinical data and ECG findings in studied groups showed that the duration of symptoms was significantly prolonged in those who high SUA (6.5 (1.51) versus 5.06 (2.87) hour; $P = 0.02$) (Table 3).

Anterior MI was the major findings in all patients, where 55.1% of patients from those with high SUA and 50% of those with low SUA had anterior MI. Regarding the site of MI, there was no significant differences between both groups ($P = 0.26$).

We found that 93.6% of patients with low SUA were Killip class I and 6.4% of patients were Killip class II while 56.9%, 30.6%, 8.3% and 4.2% of patients with high SUA were Killip I, II, III and IV respectively ($P = 0.00$).

Baseline Laboratory Data in Both Studied Groups:

Table 4 shows the baseline laboratory data of studied patients. There were no significant differences between both groups regarding hemoglobin level, and random blood sugar ($P = 0.98$, and 0.91 respectively). Patients with high SUA had significantly higher creatinine, urea, CK and CKMB in comparison to those with low SUA ($P = 0.01$, 0.02, 0.03 and 0.01 respectively).

Angiographic Findings and Ejection Fraction in Both Studied Groups:

Table 5 shows the angiographic findings and ejection fraction in both studied groups. LAD was the most frequently affected artery (60.3% and 55.6% respectively) in both groups followed by RCA (30.8% and 27.8% respectively) and LCx (9% and 16.7% respectively).

TIMI flow was significantly better in those patients with low SUA where 93.6% of patients with low SUA had TIMI III flow versus 48.6% of patients with high SUA had TIMI III flow. Twenty seven percent of patients with high SUA had TIMI II flow versus only 6.4% of patients with low uric acid had TIMI II flow. Also, 13.9% of patients with high SUA had TIMI I flow while none of patients with low SUA had TIMI 1 flow. There were no patients in our study had final TIMI 0 flow after PCI.

Patients with low SUA had significantly higher ejection fraction in comparison to those with high SUA (49.53 ± 8.75 versus 39.95 ± 7.06; $P = 0.00$).

Table 3. Clinical data and ECG findings in studied groups.

Variables	Low SUA group (n = 78)	High SUA group (n = 72)	*P* value
Duration of symptoms (hour) **mean ± SD**	5.06 ± 2.87 SD	6.50 ± 1.51 SD	**0.02**
Killip class			
I	73 (93.6%)	41 (56.9%)	
II	5 (6.4%)	22 (30.6%)	**0.00**
III	0	6 (8.3%)	
IV	0	3 (4.2%)	
ECG findings			
Anterior MI	43 (55.1%)	36 (50%)	
Posterior MI	13 (16.7%)	18 (16.7%)	0.26
Inferior MI	19 (24.4%)	24 (33.3%)	
Lateral MI	3 (3.8%)	0	

Data was expressed in form of mean (SD) and frequency (percentage). *P* value was significant if <0.05.

Table 4. Baseline laboratory data in both studied groups.

Variables	Low SUA group (n = 78)	High SUA group (n = 72)	*P* value
Hemoglobin level (g %) mean ± SD	13.09 ± 2.76	12.99 ± 3.98	0.98
Creatinine (mg/dl) mean ± SD	0.78 ± 0.20	0.91 ± 0.15	**0.01**
Urea (mg/dl) mean ± SD	5.86 ± 2.98	8.34 ± 1.03	**0.02**
Random blood sugar mean ± SD	189.09 ± 32.43	176.12 ± 55.65	0.91
CK mean (unite/liter) ± SD	2041.34 ± 633.01	2344.94 ± 587.53	**0.03**
CKMB (unite/liter) mean ± SD	186.56 ± 54.89	242.26 ± 36.78	**0.01**

Data was expressed in form of mean (SD) and frequency (percentage). *P* value was significant if <0.05.

Table 5. Angiographic findings in both studied groups.

Variables	Low SUA group (n = 78)	High SUA group (n = 72)	*P* value
Culprit lesion			0.22
LAD	47 (60.3%)	40 (55.6%)	
RCA	24 (30.8%)	20 (27.8%)	
LCx	7 (9%)	12 (16.7%)	
TIMI flow			**0.00**
0	0	0	
1	0	10 (13.9%)	
2	5 (6.4%)	27 (37.5%)	
3	73 (93.6%)	35 (48.6%)	
Ejection fraction (%) mean ± SD	49.53 ± 8.75	39.95 ± 7.06	**0.00**

Data was expressed in form of mean (SD) and frequency (percentage). *P* value was significant if < 0.05. **LDA**, left anterior descending coronary artery; **RCA**, right coronary artery; **LCx**, left circumflex coronary artery.

Short Term (in Hospital and Three Months) Follow Up:

Table 6 shows short term (in hospital and three months) follow up in the current study. MACE (cardiovascular mortality, reinfarction, target-vessel re-vascularization) was significantly higher in those patients with high UA (16.7%) in comparison to those with low UA ($P = 0.01$).

Table 6. Short term (in hospital and three months) follow up.

Variables	Low SUA group (n = 78)	High SUA group (n = 72)	*P* value
MACE	8 (10.2%)	12 (16.7%)	**0.01**
Cardiovascular mortality	3 (3.8%)	5 (6.9%)	**0.03**
Reinfarction	7 (8.9%)	9 (12.5%)	**0.00**
Staged PCI	5 (6.4%)	8 (11.1%)	**0.04**
Stroke	1 (1.25%)	1 (1.3%)	0.61
Advanced heart failure	5 (6.4%)	11 (15.2%)	**0.01**
GIT bleeding	1 (1.25%)	3 (4.2%)	0.11
Blood transfusion	1 (1.25%)	1 (1.3%)	0.61

Data was expressed in form of frequency (percentage). *P* value was significant if <0.05. **MACE**, major adverse cardiac events (cardiovascular mortality, reinfarction, target-vessel revascularization); **GIT**, gastrointestinal bleeding.

Also, other adverse events as advanced heart failure were significantly higher in those patients with high SUA. It was noticed that stroke, GIT bleeding and blood transfusion had no significant differences between both groups.

3.3. Diagnostic Accuracy of Serum UA in Prediction of MACE Patients with Acute STEMI Undergoing PPCI

For prediction of MACE in patients with acute STEMI undergoing PPCI, SUA at a cutoff point > 6 mg/dl had 71.4% sensitivity and 70.3% specificity with area under the curve was 0.73 as illustrated in Table 7 and Figure 1.

3.4. Survival Analysis in the Current Study (3 Months Follow Up)

Kaplan Meier survival analysis (Figure 2) showed that median and mean survival of patients with low SUA was 54 and 60 days respectively and this was significantly longer than median and mean of patients with high SUA (45 and 54 days respectively; $P = 0.02$).

3.5. Multivariate Regression Analysis for Prediction of MACE in Patients with Acute STEMI Undergoing PPCI

Table 8 shows the predictors for MACE in patients with acute STEMI undergoing PPCI where age, SUA > 6 mg/dl, TIMI flow, Killip class and EF < 40% are independent predictors for MACE in such patients.

4. Discussion

There are both clinical and experimental evidences supporting the presence of a relationship between high SUA levels and chronic kidney disease, hypertension, metabolic diseases as well as cardiovascular diseases [7].

The negative effects of increased SUA levels have been confirmed also in patients with preexisting cardiovascular diseases including coronary artery disease, heart failure and atrial fibrillation [8].

This study aimed to evaluate the prognostic value of SUA on admission and its relation to the outcome in patients with STEMI undergoing PPCI which is the standard treatment strategy in such conditions.

Table 7. Diagnostic accuracy of SUA in prediction of MACE patients with acute STEMI undergoing PPCI.

Indices	Values
Sensitivity	71.4%
Specificity	70.3%
Positive predictive value	54%
Negative predictive value	84%
Area under the curve	0.73
Cut off point	>6 mg/dl
***P* value**	<0.001

Table 8. Multivariate regression analysis for prediction of MACE in patients with acute STEMI undergoing PPCI.

	Odd's ratio	95% Confidence interval	*P* value
Age	1.21	1.13- 1.24	**<0.001**
No comorbidities	0.98	0.34 - 3.98	0.09
Diabetes mellitus	1.12	0.78 - 2.12	0.65
Hypertension	1.56	0.45 - 1.23	0.11
TIMI flow< 3	0.95	0.90 - 0.98	**<0.001**
Killip Class > I	2.3	2.11 - 3.99	**<0.001**
Uric acid > 6 mg/dl	1.89	1.78 - 2.34	**<0.001**
Ejection fraction < 40%	1.58	1.20 - 3.45	**<0.001**
Raised creatinine	1.09	0.45 - 1.11	0.98

P value was significant if <0.05.

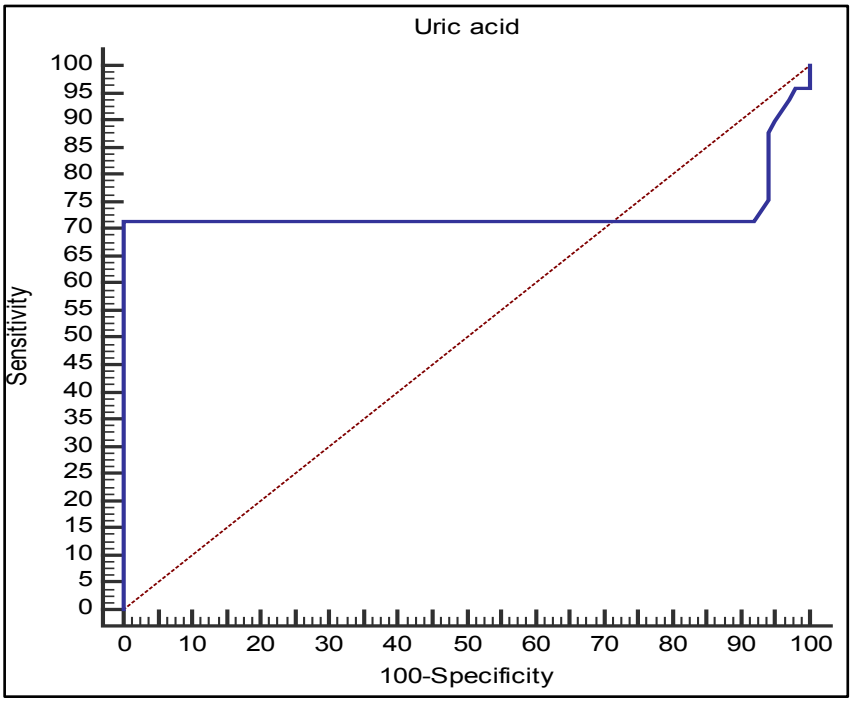

Figure 1. Diagnostic accuracy of SUA in prediction of MACE patients with acute STEMI undergoing PPCI.

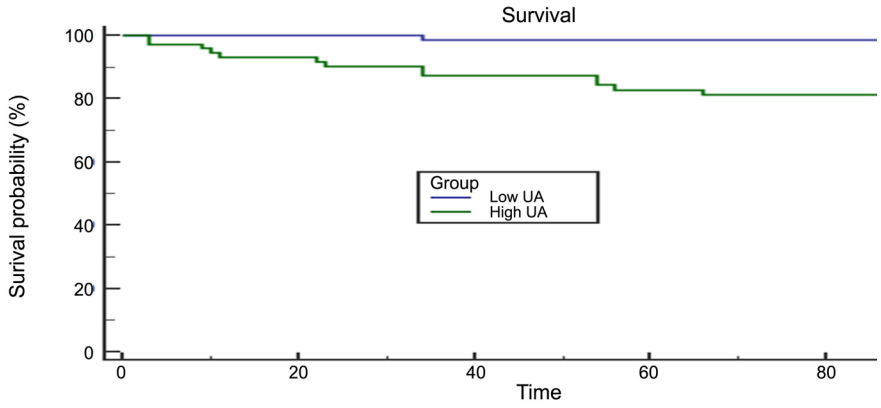

Figure 2. Survival analysis in the current study (3 months follow up).

We found that on admission SUA level carries a significant predictive value regarding the prognosis in patients with STEMI undergoing primary PCI as the low uric acid group had a better KILLIP class (*P* value = 0.00), better TIMI flow after stenting (*P* value = 0.00), higher ejection fraction (*P* value = 0.00) and a lower incidence of MACE during the hospital stay and three months follow up (*P* value = 0.01) in comparison to the high uric acid group.

In our study 93.6% of patients with low SUA were Killip class I and 6.4% of patients were Killip class II. there were no patients in the low uric acid group had KILLIP class III or IV while in the other hand, in the high uric acid group, only 56.9% of patients had KILLIP class I but 30.6% had KILLIP class II besides 8.3% and 4.2% of patients with high SUA had Killip III and IV respectively (*P* = 0.00).

These results were compatible with the findings that were reported by Akgul *et al.* In that study, 434 consecutive STEMI patients who underwent primary PCI were enrolled. Compared to the low SUA group, Killip class > 1 at admission was more prevalent in the high SUA group (3.4% vs. 17.5%, $P < 0.001$, respectively). Higher in-hospital cardiovascular mortality and six-month all-cause mortality rates were also observed in the high SUA group than in the lower group [9].

Liu *et al.* also reported an association between SUA and Killip class in STEMI patients undergoing primary PCI. This study also confirmed that hyperuricemia is a risk factor for increased 30-day and 1-year mortality in STEMI even in patients with Killip class I [10].

According to the TIMI flow after PCI, TIMI flow was significantly better in patients with low SUA where 93.6% of patients with low SUA had TIMI III flow versus 48.6% of patients with high SUA had TIMI III flow. Twenty seven percent of patients with high SUA had TIMI II flow versus only 6.4% of patients with low uric acid had TIMI II flow. Also, 13.9% of patients with high SUA had TIMI 1 flow while none of patients with low SUA had TIMI I flow. There were no patients in our study had final TIMI 0 flow after PCI (*P* value = 0.00).

These findings were concordant with the data published by Akpek *et al.* when

289 patients with STEMI who was treated with primary PCI were enrolled to the study. Patients were divided into two groups based upon the TIMI flow grade. No-reflow was defined as TIMI Grade 0, 1 and 2 flows (group 1). Angiographic success was defined as TIMI 3 flow (group 2). A uric acid level ≥ 5.4 mg/dl measured on admission had a 77% sensitivity and 70% specificity in predicting no-reflow at ROC curve analysis, and they concluded that Plasma uric acid level on admission is a strong and independent predictor of poor coronary blood flow following primary PCI (*P* value = 0.006) [11].

In our study, it was clear that patients in the low uric acid group had better LV ejection fraction after PCI (49.53 ± 8.75) in comparison to those with high uric acid (39.95 ± 7.06) (*P* value = 0.00) and that explains the higher incidence of readmission with heart failure in the high uric acid group during the follow up period.

Data reported by Lazzeri *et al.* strongly suggest that in the acute phase of STEMI patients submitted to primary PCI, uric acid had a prognostic role for in-hospital mortality as well as expected LV ejection fraction. The patients with increased SUA on admission had a lower LV ejection fraction as the mean LV ejection fraction in those patients were 40% versus 45% in the low SUA group and that was statistically significant ($P < 0.001$) [12].

Akgul *et al.* reported that incidence of heart failure with reduced ejection fraction (HFREF) (LVEF < 40%) was significantlly higher in the high uric acid group as 30% of the patients with high uric acid versus 15% of patients with low uric acid had LVEF < 40% (*P* value = 0.001) and this is similar to our results [9].

These results are also compatible with another meta-analysis published by Huang *et al.* which supports an association between SUA and incident HF, as well as adverse outcome even in patients with established diagnosis of HF [13].

In the current study, we found a strong association between SUA levels on admission and short-term outcomes in patients with STEMI undergoing primary PCI. It was noticed that the incidences of reinfarction, heart failure, and the total all cause cardiovascular mortality were significantly higher in the high SUA group than in the low SUA group (*P* value = 0.01).

Other adverse events as advanced heart failure and inotropic agent usage were significantly higher in those patients with high SUA. It was noticed that stroke, GIT bleeding and blood transfusion had no significant differences between both groups.

Kojima *et al.* studied 1124 consecutive patients who were admitted with acute STEMI; he reported that mortality in patients whose SUA levels were in the highest quartile was significantly higher than in those whose SUA levels were in the lowest quartile [14]

Lazzeri *et al.* demonstrated that a high UA level was an independent predictor of in hospital mortality in patients with STEMI who underwent primary PCI, contrary to this study [15].

In another study with a larger patient population with STEMI published also by Lazzeri *et al.* showed that the SUA level predicted the occurrence of compli-

cations in the intensive care unit, but not early mortality [16].

Akpek *et al.* reported that there was not only a significant relationship between baseline SUA levels and impaired coronary flow but also with in-hospital MACE [11].

Kowalczyk *et al.* reported that elevated SUA levels predicted the short-term and long-term mortality in patients with acute myocardial infarction and impaired renal function treated with PCI regardless of the degree of renal dysfunction. In our study, the high SUA group showed a significantly higher creatinine values in spite of being within normal ranges in both studied groups (*P* value = 0.01) [17].

Recently, Li *et al.* found rather similar results when they investigated 673 patients with acute STEMI treated by primary PCI. Patients were divided into high SUA level group (N = 168) and low SUA level group (N = 505) according to the SUA levels on admission where SUA more than 6 mg/dl was considered high in all subjects. They concluded that the incidences of postoperative angina pectoris, heart failure, and the total adverse cardiovascular events were significantly higher in the high SUA than in the low SUA group [18].

But in contrast to our study the incidence of death was similar between the two groups, and that may be due to the relatively lower cut off point for hyperurecimia which was 6 mg/dl in their study while we compared the two groups according to a SUA of 6.4 mg/dl (the value in the third tertile).

A second important explanation is that their study focused only on the elderly population, as they included only the patients who were 60 years old or older and that might lead to a relatively higher mortality in both groups.

It is worth to be mentioned in that context that we found that the high uric acid group was generally older than the low uric acid group as the mean age of the high uric acid group was 58.28 years versus 54.09 years for the low uric acid group and that was statistically significant (*P* value = 0.02).

Although all the previous studies have shown SUA could be a marker of adverse prognosis in patients with STEMI, this issue has some controversy about it.

Homayounfar *et al.* concluded that SUA was not an independent prognostic marker for in hospital mortality after AMI. In fact this study was a case-control study included only 59 patients who died during hospital admission and 104 patients randomly selected from the discharged patients to be the control group. They found no evidence of statistically significant relation between hyperuricemia and in hospital mortality. In this study, the type of AMI was neglected (weather it is STEMI or NSTEMI) and it also didn't consider the management protocol as not all patients underwent primary PCI as a management protocol. They also didn't follow up the control group after discharge for mortality and other MACE [19].

Hajizadeh *et al.* also concluded that In spite of that high SUA level was associated with lower LVEF, higher Killip class and AF, elevated cTnI, creatinine, and triglyceride level, the high SUA level in patients with acute MI was not asso-

ciated with higher in-hospital or midterm mortality rate. In this study the High SUA level was defined as more than 8 mg/dL in men and more than 7.5 mg/dL in women which is much more than the cutoff point for hyperuricemia in most literatures. It also included a generally older population than our population as the mean age for all population in the study, in years, was 62.6 ± 13.4 SD versus 56.10 ± 11.17 in our study, and that is expected to increase the mortality in all groups without discrimination [20].

Another important thing is that we noticed that the time delay from the onset of symptoms to PCI was significantly longer in the high uric acid group mean time delay was 6.5 hrs versus only 5.06 hrs for the low uric acid group (*P* value = 0.02) in contrast to all the previous studies as Li *et al.* [18] where the time delay was 4.93 hrs and 4.79 hrs for the high and low uric acid groups respectively, and this carried no significant statistical difference between the two groups.

This may be due to lack of general knowledge concerning acute coronary syndromes and the differentiation of typical chest pain and seeking urgent medical advice in such situations in our local community, and this should draws our attention to the urgent need to increase the public awareness about acute coronary syndromes and to improve the public health education programs to minimize the patient delay as much as possible.

5. Conclusion

We found that on admission SUA level carries a significant predictive value regarding the prognosis in patients with STEMI undergoing primary PCI as the low uric acid group had a better KILLIP class, better TIMI flow after stenting, higher ejection fraction and better survival besides lower incidence of other MACE during the hospital stay and three months follow up in comparison to the high uric acid group.

Limitations

Some limitations of our study should be declared. This study was a single-center study. A larger study with more female patients may be more informative.

We did not evaluate the B-type natriuretic peptide, the high-sensitivity C-reactive protein, other pro-inflammatory cytokines, or markers of oxidative stress. In spite of that we adjusted multiple risk factors, residual conditions or medications may have been present so another confirmatory sample in the follow up could be more informative.

Because of the limited number of patients receiving antihyperuricemic therapy, we didn't evaluate the effect of antihyperuricemic treatment on the prognosis and based on our results, this could be a subject for future research.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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