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Preoperative Levels of Uric Acid and Its Association to Some Perioperative Parameters in the Patients with Unstable Angina or Myocardial Infarction

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Several studies have reported a relation between serum levels of uric acid and a wide variety of cardiovascular conditions. But, the relationship between serum levels of uric acid and coronary artery disease (CAD) is still controversial. The present study was retrospectively designed to investigate whether CAD can be stratified by the level of uric acid and there are the relationships between preoperative levels of uric acid and perioperative biochemical markers in fifty-adult patients that underwent coronary artery bypass grafting surgery (CABG) and twenty-normal subjects. They were divided into the control, the unstable angina (UA-group) and the myocardial infarction group (MI-group). In preoperative levels of uric acid, the MI-group was higher than control and the UA-group. The MI-group had significantly higher correlations than the UA-group between preoperative levels of uric acid and left ventricular ejection fraction, cardiac markers (creatine kinase, lactate dehydrogenase and brain natriuretic peptide), renal markers (blood urea nitrogen and creatinine) or total leukocyte levels. At postoperative periods, the MI-group had higher relationships of uric acid with aspartate aminotransferase, blood urea nitrogen or creatinine levels. Although there was not statistically significant, the UA-group tended to have higher correlation coefficients than the MI-group between preoperative levels of uric acid and intensive care unit-stay (ICU), or postoperative mechanical ventilation time. These results reflect that increased levels of serum uric acid may be a tool for the diagnosis of coronary heart disease and may be considered as a good predictor in assessing the cardiac and renal functions in patients with myocardial infarction or unstable angina at the preoperative period. However, further studies should be performed in a large patient population.

Key Words: Uric acid, CABG, Perioperative variables

INTRODUCTION

Uric acid is a heterocyclic compound of carbon, nitrogen, and hydrogen. It is produced by xanthine oxidase from xanthine and hypoxanthine, which in turn are produced from purine. Uric acid is released in hypoxic conditions (Baillie et al., 2007). With ischemia, ATP is degraded to adenine and xanthine, and there is also increased generation of xanthnine oxidase. The increased availability of xanthine and xanthine oxidase results in increased uric acid generation as well as oxidant formation (Many et al., 1996; Leyva et al., 1997; Johnson et al., 2003). Several studies have reported a relation between serum uric acid levels and a wide variety of cardiovascular conditions, including hypertension (Cannon et al., 1966), metabolic syndrome (Ford et al., 2007), coronary artery disease (CAD) (Tuttle et al., 2001), cerebrovascular disease (Lehto et al., 1998) and kidney disease (Siu et al., 2006; Talaat and el-Sheikh, 2007). However, most authorities do not consider hyper-

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uricemia to be an important risk factor for cardiovascular or renal disease. Most authorities have viewed elevated uric acid as a secondary phenomenon that is either innocuous or perhaps even beneficial, since uric acid can be an antioxidant. Although uric acid can act as an antioxidant, excess serum accumulation is often associated with CAD as well as a predictor of gout. It is not known whether this is causative or a protective reaction taking advantage of urate's antioxidant properties (Heinig and Johnson, 2006). The relationship between serum uric acid and CAD has been controversial (Baker et al., 2005; Feig et al., 2008). The relationship of serum uric acid with risk factors of coronary artery disease (CAD) or cardiac markers and severity of CAD patients has not been reported in Korea. The purpose of this study was to compare serum uric acid levels between normal subjects and the patients with CAD and to retrospectively investigate the association of preoperative levels of serum uric acid to some parameters and differences between the types of CAD (unstable angina vs. myocardial infarction) in CAD patients.

MATERIALS AND METHODS

Study population

Data for fifty patients that underwent coronary artery bypass grafting surgery (CABG) (from 2008, January to 2010, February) were divided into two groups: unstable angina (n=26, UA-group) and a myocardial infarction group (n=24, MI-group). Most of subjects in the control group was healthy and two subjects had slightly hypertension or hyperlipidemia, but were diagnosed as healthy condition by their physician (n=20, Control-group). They were retrospectively reviewed and analyzed; Blood or other samples were never collected from the patients and additional tests were not performed for the present study. All patients were discharged from the hospital. We only evaluated the recorded-data for this study. This study was accepted and exempted from the Institutional Review Board for Human Research Catholic University of Pusan.

Analysis of variables

The following variables were preoperatively or postoperatively analyzed and recorded.

Serum uric acid

A preoperative level of serum uric acid was measured by a Toshiba 200FR instrument (Toshiba Inc., Japan). Enzymatic method was applied for the determination of serum uric acid. Its normal value is 2.4~7.0 mg/dL.

Preoperative variables

In all patients, coronary artery stenotic findings, lipid profiles, fasting glucose, hemoglobin A1C, creatine kinase (CK), lactate dehydrogenase (LDH), brain natriuretic peptide (BNP), cardiac troponin I, C-reactive protein (CRP) and D-dimer were measured at the preoperative period (Pre-OP).

Perioperative variables

In all patients, total leukocyte counts, creatine kinase-MB (CK-MB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, blood urea nitrogen (BUN) and creatinine levels were analyzed at the Pre-OP, postoperative 0.5 hr (PO-0.5 hr), postoperative 24 hr (PO-24 hr) and postoperative 48 hr (PO-48 hr) period. However, in the control-group, above mentioned variables were postoperatively not measured because they were not patients.

Operative procedure

All of the patients received general anesthesia. After a median sternotomy, graft conduit (left internal mammary artery, left radial artery, and great saphenous vein) were harvested from all patients for CABG. Heparin was intravenously injected and the heart was exposed. Cardiac apex was lifted for fixing appointed sites of anastomoses using a cardiac holding apparatus (Octopus, Medtronic Inc., USA). After the anastomoses, the blood flow volume of graft conduit was measured by a HT 107 medical volume flow meter (Transonic systems Inc., USA) and 0.8~1.2 fold protamine of used heparins was administered.

The others variables

Operation time, postoperative mechanical ventilation time, intensive care unit stay length, hospital stay length

Table 1. Demographic characteristics of the three groups

Variable	Group		
	Control (n=20)	UA (n=26)	MI (n=24)
Gender ratio (Male : Female)	12:8	17:9	19:5
Age (year)	66.55±11.91	63.11±8.94	65.04±8.88
Height (cm)	166.21±5.05	161.12±8.13	165.16±6.90
Weight (kg)	63.12±8.63	62.33±11.00	64.26±11.91
BSA (m^2)	1.69±0.19	1.67±0.17	1.71±0.16
LVEF (%)	61.13±4.26	57.55±5.07$^{\dagger *}$	40.96±12.24$^{\ddagger **}$
SBP (mmHg)	120.20±11.03	124.30±18.46†	132.08±25.01††
DBP (mmHg)	72.00±7.51	73.88±9.73	77.75±12.36
Previous diagnosis (case)			
Hypertension	2 (10%)	14 (53.84%)††	16 (66.67%)‡
Diabetes mellitus	1 (5%)	11 (42.30%)‡	13 (54.17%)‡
Hyperlipidemia	2 (10%)	6 (23.07%)†	8 (33.34%)††

Data were expressed as mean ± standard deviation (SD).
†, $P<0.05$; ††, $P<0.01$; ‡, $P<0.001$ (compared with the control group); *, $P<0.05$; **, $P<0.01$ (compared with the UA group).
Abbreviation: BSA, body surface area; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure; DBP, diastolic blood pressure; UA, unstable angina; MI, myocardial infarction.

and mortality were recorded. However, in the control-group, above mentioned variables were postoperatively not measured because they were not patients.

Statistical analysis

Data were presented as mean ± SD (standard deviation). An ANOVA was utilized for comparison of the difference among the control-, UA- and MI-group. Pearson's correlation analysis was applied for the determination of association between preoperative levels of uric acid and preoperative and/or perioperative variables (SPSS program). Statistical significance was accepted with $P \leq 0.05$.

RESULTS AND DISCUSSION

Clinical characteristics and perioperative outcomes

Table 1 shows clinical characteristics of the study population. Left ventricular ejection fraction (LVEF) was significantly higher, whereas systolic blood pressure (SBP) was lower in the control group than in the UA- and MI-group. Diastolic blood pressure was significantly lower in the control group than in the MI-group. On comparison between the two patient groups, LVEF was significantly lower in the MI-group than in the UA-group ($P<0.01$), but there were no differences in other variables between the two groups. Table 2 and 3 shows preoperative and post-operative results of the study population. Stenosis of left anterior descending artery, level of total cholesterol, cardiac troponin-I and C-reactive protein, and flow volume of right coronary artery graft conduit were significantly higher in the MI group than the UA group ($P<0.05$ or $P<0.01$). Patient mortality was only 2 cases in the MI group. Total cholesterol level was greater, whereas high density lipo-protein cholesterol (HDL-C) level was lower in the MI-group than in the control-group ($P<0.05$). Fasting glucose, hemoglobin A_1C, BNP, cTNI, CRP and D-dimer levels in the control-group were significantly higher compared those of the UA- and the MI-group ($P<0.05$, $P<0.01$ or $P<0.001$, respectively). Acute coronary syndrome (ACS) encompasses a spectrum of coronary artery disease, including unstable angina (UA), ST-segment elevation myocardial infarction (STEMI), and non-STEMI (Achar et al., 2005). The diagnosis of myocardial infarction (MI), which includes both STEMI and NSTEMI, requires at least two of the following: ischemic symptoms, diagnostic electrocardiogram changes, and serum cardiac marker elevation (Braunwald, 2000). NSTEMI is distinguished from unstable angina by ischemia sufficiently severe enough in intensity and duration to cause irreversible myocardial damage (myocardiocyte necrosis), recognized clinically by the detection of biomarkers of

Table 2. Comparison of biochemical and cardiac markers among the three groups at preoperative period

Variable	Group		
	Control	UA	MI
Total cholesterol (mg/dL)	174.30±31.62	165.84±33.19	189.20±49.63$^{\dagger *}$
Triglyceride (mg/dL)	110.20±79.08	140.50±74.84	123.57±84.29
LDL-C (mg/dL)	109.00±27.02	88.71±27.33	109.00±40.87
HDL-C (mg/dL)	47.85±8.20	43.52±11.23	40.88±11.55†
Fasting glucose (mg/dL)	95.30±13.83	153.65±68.20††	164.00±63.36††
HemoglobinA_1C (%)	5.71±0.31	6.84±1.58†	6.76±1.22†
Creatine kinase (U/L)	128.60±64.48	122.00±109.45	278.61±401.68
LDH (IU/L)	368.50±47.75	385.15±82.44	599.09±690.72
BNP (pg/mL)	53.59±20.30	268.91±664.92‡	677.12±819.30‡
cTNI (ng/mL)	0.01±0.01	0.04±0.08††	4.01±6.34$^{\ddagger **}$
CRP (mg/dL)	0.23±0.52	0.39±0.59†	2.72±4.78$^{\dagger *}$
D-dimer (μg/mL)	0.28±0.13	1.04±0.98††	1.30±0.95††

Data were expressed as mean ± SD.
†, $P<0.05$; ††, $P<0.01$; ‡, $P<0.000$ (compared with the control group); *, $P<0.05$; **, $P<0.01$ (compared with the UA group).
Abbreviation: LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; LDH, lactate dehydrogenase; BNP, brain natriuretic peptide; cTNI, cardiac troponin-I; CRP, C-reactive protein.

Table 3. Comparison of preoperative and postoperative outcomes among the three groups

Variable	Group		
	Control	UA	MI
Coronary artery stenosis			
LAD (%)	0	87.38±12.94	89.16±12.99
RCA (%)	0	81.42±20.00‡	92.86±15.12$^{\ddagger **}$
LCA (%)	0	78.48±21.69‡	86.66±14.08‡
Operation time (min)	0	337.46±68.31‡	333.54±43.84‡
POMVT (hr)	0	16.28±6.79‡	18.52±27.47‡
ICU-stay length (hr)	0	76.67±21.38‡	74.04±33.84
Hospital stay length (day)	0	15.84±3.83‡	17.47±6.32‡
Mortality (number of case)	0	0	2 (8.3%)$^{\ddagger **}$
FVG (ml/min)			
LAD territory		39.61±15.09	49.04±30.61
RAD territory		31.40±18.22	49.04±28.40*
LCA territory		37.73±22.32	41.47±28.27

Data were expressed as mean ± SD.
‡, $P<0.001$ (compared with the control group); *, $P<0.05$ (compared with UA group).
Abbreviation: LAD, left anterior descending artery; RCA, right coronary artery; LCA, left circumflex artery; POMV, post-operative mechanical ventilation time; ICU, intensive care unit; FVG, flow volume of graft.

myocardial injury. In the remaining ~30% of patients with ACS, the intracoronary thrombus completely occludes the culprit vessel, resulting in STEMI (Morrow et al., 2007). Reduction of oxygen and energy supply by obstruction of coronary arteries can contribute to left ventricular wall stress and wall stiffness, resulting in myocardial injury or necrosis/dysfunction or heart failure. Classical cardiac markers which include CK-MB, cardiac troponin, and CRP, are usually considered as strong predictors among patients with coronary artery diseases (Alberto et al., 2006). Historically, CK-MB played an important role for years in aiding ACS diagnosis, detecting myocardial injury, and prognosis. CK-MB has been a predominant marker for identifying ACS patients with myocardial necrosis (Sim et al., 2006). Cardiac troponins are used to establish the diagnosis of MI and assess the prognosis of individuals presenting with acute coronary syndrome (Brown and Bittner, 2008). Cardiac troponin is currently the preferred biomarker for the diagnosis and prognosis of acute cardiac diseases (Sim et al., 2008). Also, CRP has been demonstrated to predict myocardial infarction, ischemic stroke, cardiovascular death, incident diabetes, and incident hypertension including individuals with and without cardiovascular disease and acute in those experiencing acute coronary syndrome (Ridker, 2007). Moreover, an angina pectoris study showed that elevated CRP levels highly correlate with low left ventricular ejection fraction (Haverkate et al., 1997).

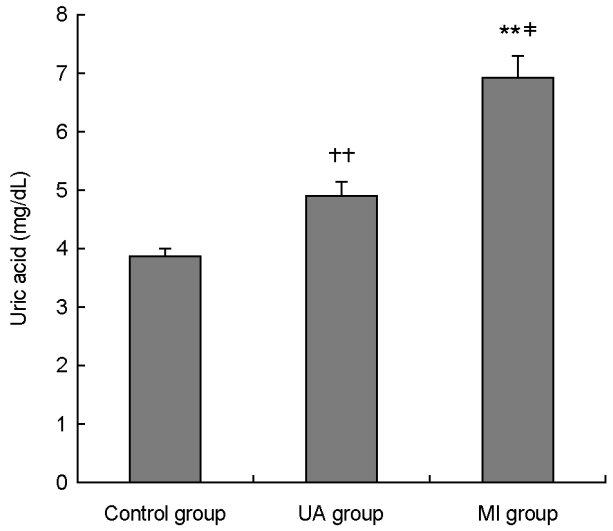

Fig. 1. Comparison of preoperative levels of serum uric acid among the control, unstable angina and myocardial infarction group. Preoperative level of serum uric acid in the control group was lower than those of the two patient groups (††, $P<0.01$ and ‡, $P<0.001$). Myocardial infarction group was significantly greater than unstable angina group (**, $P<0.01$). UA = unstable angina, MI = myocardial infarction.

Results of this study showed that stenosis degree of coronary arteries in the MI-group patients were more severe than that of the UA-group, while left ventricular function of heart was poor in the MI-group compared with the UA-group. Also, levels of cardiac troponin-I, CK-MB, and CRP in the MI-group were higher than those of UA-group (Table 1, 2, 3). According to ACC/AHA guidelines (Braunwald, 2000), in the present, it indicates that the UA-group was low/intermediate risk patients and the MI-group was intermediate/high risk patients.

Serum uric acid

Fig. 1 reveals the comparison of serum uric acid levels in the two groups at preoperative period. The level of serum uric acid in the control-group (3.83±0.59 mg/dL) was significantly lower than those of UA- and MI-group ($P<0.05$ or $P<0.001$, respectively), suggesting that an increased level of serum uric acid may be associated with coronary heart disease. The level of serum uric acid was significantly higher in the MI-group (6.88±1.81 mg/dL) than in the UA-group (4.88±1.10 mg/dL) ($P<0.01$). Although the two patient groups had normal ranges of mean levels of uric acid, they were higher normal ranges. Serum uric acid may increase in failing circulation because of increased generation, decreased excretion, or a combination of the 2 factors (Hare and Johnson, 2003). As uric acid is excreted primarily by the kidney, decreased renal perfusion could lead to increased levels of uric acid. To the extent that heart failure leads to tissue ischemia and a rise in serum lactate, renal uric acid excretion can be further impaired as lactate competes with urate via an organic anion exchanger in the proximal tubule (Rock-Ramel et al., 1997). The relation between uric acid and cardiovascular disease is observed not only with frank hyperuricemia (defined as > 6.5 or 7 mg/dL in men and > 6.0 mg/dL in women) but also with uric acid levels considered to be in the normal to high range (> 5.2~5.5 mg/dL) (Johnson et al., 2003; Feig et al., 2008). In subjects with obesity, insulin resistance, dyslipidemia (the metabolic syndrome), and menopausal women, hyperuricemia frequently occurs because insulin stimulates sodium and urate reabsorption in the proximal tubule. Uric acid is increased in subjects with renal disease as the result of reduction in glomerula filtrate rate and renal urate excretion (Galvan et al., 1995). The increase in serum uric acid in hypertension may be due to the decrease in renal blood flow that accompanies the hypertensive state, since a low renal flow will stimulate urate reabsorption (Messerli et al., 1980). In addition, local tissue ischemia or oxidative stress also results in increased uric acid synthesis. The finding that ischemia results in an increase in uric acid levels may also account for why uric acid is increased in preeclampsia and congestive heart failure (Leyva et al., 1997). The MI-group's patients of the present study population were obvious hyperuricemia. Expired patients occurred in the MI-group (Table 2). These patients had severe hyperuricemia but didn't have gout symptoms. Serum concentration of uric acid in one patient was 7.4 mg/dL, but the others were 10.9 mg/dL. Mortality causes were left heart failure and multi-organ failure. Previous epidemiologic follow-up study of the First National Health and Nutrition Examination Survey showed that increased levels of serum uric acid were independently and significantly associated with risk of cardiovascular mortality (Fang and Alderman, 2000). Anker et al. (2003) found a strong correlation between elevated levels of serum uric acid and all cause

Table 4. Comparison of total WBC count, CK-MB, hepatic, and renal markers levels among the three groups at perioperative periods

VA	Group	Sampling point			
	Control				
	UA	Pre-OP	PO-0.5 hr	PO-24 hr	PO-48 hr
	MI				
T-WBC ($\times 10^3/\mu L$)		6.16±1.63	not measured	not measured	not measured
		6.52±1.75	8.85±2.86	11.28±2.90	11.47±3.14
		7.75±3.23†	10.35±4.34*	11.19±3.41	12.03±3.75
CK-MB (U/L)		1.63±0.95	not measured	not measured	not measured
		8.62±4.01†	23.58±23.23	36.08±44.44	14.44±7.63
		29.90±41.18$^{\ddagger **}$	49.95±65.62	40.50±29.35	15.00±5.76
AST (IU/L)		22.15±5.01	not measured	not measured	not measured
		28.61±26.36	34.84±19.99	54.73±34.98	58.66±39.43
		48.95±44.94$^{\dagger **}$	61.50±54.74*	82.66±51.33*	60.04±29.60
ALT (IU/L)		19.15±8.19	not measured	not measured	not measured
		29.15±29.60†	21.15±8.54	26.46±9.45	28.87±11.93
		34.29±24.53†	29.12±22.16	36.66±24.25*	36.08±17.20
T-bilirubin (mg/dL)		0.67±0.20	not measured	not measured	not measured
		0.64±0.31	1.03±0.39	1.07±0.52	0.97±0.49
		0.85±0.26$^{\dagger **}$	1.03±0.41	1.00±0.55	0.91±0.40
BUN (mg/dL)		15.96±3.70	not measured	not measured	not measured
		15.19±5.15	11.38±3.23	15.15±4.50	15.88±5.81
		20.20±12.78†	17.12±10.98*	22.37±12.92**	27.91±16.80**
Creatinine (mg/dL)		0.91±0.12	not measured	not measured	not measured
		0.97±0.19	0.76±0.19	0.98±0.24	0.90±0.36
		1.19±0.36$^{\dagger **}$	1.05±0.35**	1.29±0.50**	1.33±0.69**

Data were expressed as mean ± SD.
†, $P<0.05$; ‡, $P<0.001$ (compared with the control group); *, $P<0.05$; **, $P<0.01$ (compared with the UA group).
Abbreviation: VA, variable; T, total; WBC, white blood cell; CK-MB, creatine kinase-MB isoenzyme; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen.

mortality in patients with chronic heart failure. Niskanen et al. (2004) insisted that serum levels of uric acid are a strong predictor of cardiovascular disease mortality in healthy middle-aged men, independent of variables commonly associated with gout or metabolic syndrome. These studies suggested that serum uric acid level was as useful a prognostic indicator as clinical status and other established parameters.

Total leukocyte counts and biochemical markers

Changes of total leukocyte counts and biochemical marker levels in the two groups were summarized in Table 4. In total leukocyte counts, the MI-group was higher than the control-group ($P<0.05$), while there were no significant differences between the two patient groups at any sampling period ($P>0.05$). Preoperative levels of CK-MB and ALT were higher in the UA- and MI-group ($P<0.05$ or $P<0.001$, respectively) than in the control-group, while preoperative levels of AST, total bilirubin, BUN and creatinine were significantly greater in the two patient groups than in the control-group ($P<0.05$). On comparison between the two patient groups, preoperative levels of CK-MB and total bilirubin in the MI-group were higher than the UA-group ($P<0.05$). AST levels at Pre-OP, PO-0.5 hr and PO-24 hr were higher in the MI-group than those in the UA-group ($P<0.05$). ALT levels were higher in the MI-group than in the UA-group at PO-24 hr period ($P<0.05$). Blood urea nitrogen (BUN) levels at PO-0.5 hr, PO-24 hr and PO-48 hr were higher in the MI-group than in the UA-group ($P<0.05$ or $P<0.01$). Creatinine levels were higher in the MI-group than the UA-group at all sampling periods ($P<0.05$ or $P<0.01$). Even mild deterioration of renal function is an

important risk factor for poor outcome in patients with congestive heart failure, myocardial infarction, and cardiovascular surgery. Kidney function deterioration may be a consequence of cardiac and baroreceptor dysfunction or may be primarily caused by intrinsic kidney disease (Schrier, 2006). Anderson et al. (1999) and Ryckwaert et al. (2002) show that small increases in serum creatinine level after cardiac surgery or CABG are associated with increased non-renal complications and poor prognosis. One explanation for this relationship is that small increase in serum creatinine concentration after cardiothoracic surgery may be a sensitive marker of diffuse hypoperfusion throughout the body. Results of this study showed that BUN and creatinine concentrations were higher in the MI- group than in the UA-group at all sampling periods. Moreover, as times goes, BUN and creatinine concentrations in the MI-group were increasing, suggesting that these patients must be more carefully monitored. This present may be a consequence of cardiac dysfunction.

Association between uric acid and other perioperative variables

Table 5 shows association between the preoperative level of uric acid and perioperative outcomes. In the control-group, the preoperative level of uric acid was significantly associated with total cholesterol, low density lipoprotein cholesterol (LDL-C), CK or BNP ($P<0.05$ or $P<0.001$). In the UA-group, uric acid had a negative correlation with LVEF, HDL-C, or blood flow volume of right coronary artery graft ($P<0.05$). There was a positive relationship between uric acid and triglyceride level ($P<0.05$). These findings in the UA-group indicate that increased uric acid may contribute to dyslipidemia and a paired coronary blood flow. In the MI-group, uric acid had a negative correlation with LVEF. However, there were each positive correlation with HDL-C, CK, LDH or BNP ($P<0.05$ or $P<0.01$). Operation time, postoperative mechanical ventilation time, and hospital stay length did not show significant correlation with uric acid. On the comparison between two groups in the association, most correlation coefficients, including hospital stay length tended to be greater in MI-group than in those of the UA-group, suggesting that as uric acid level

Table 5. Each correlation of preoperative and postoperative outcomes with preoperative levels of serum uric acid in the three groups

Variable	Uric acid Group		
	Control	UA	MI
SBP	0.09	-0.34	-0.09
DBP	-0.23	0.13	-0.07
LVEF	0.36	-0.36*	-0.49*
Total cholesterol	0.73‡	0.04	0.07
Triglyceride	-0.29	0.36*	-0.16
LDL-C	0.72‡	0.27	-0.028
HDL-C	0.22	-0.44*	0.41*
Fasting glucose	-0.15	-0.11	-0.20
Hemoglobin A_1C	0.31	-0.129	-0.306
Percent of CAS			
LAD	not calculated	0.02	0.03
RCA	not calculated	-0.18	0.14
LCA	not calculated	-0.02	-0.03
Creatine kinase	0.47*	-0.15	0.47*
Lactate dehydrogenase	-0.18	-0.39	0.49**
BNP	0.37*	-0.25	0.37*
cTNI	-0.13	0.05	0.22
CRP	0.01	0.19	0.14
D-dimer	-0.00	-0.03	0.11
Operation time	not measured	0.15	0.18
POMVT	not measured	0.30	0.11
ICU-stay length	not measured	0.31	0.25
Hospital stay length	not measured	0.19	0.23

Data were correlation coefficient (r).
*, $P<0.05$; **, $P<0.01$; ‡, $P<0.001$ (significant correlation).
Abbreviation: LVEF, left ventricular ejection fraction; SBP, systolic blood pressure; DBP, diastolic blood pressure; CK-MB, creatine kinase-MB isoenzyme; CAS, coronary artery stenosis; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipootein cholesterol; LDH, lactate dehydrogenase; BNP, brain natriuretic peptide; cTNI, cardiac troponin-I; CRP, C-reactive protein.

respectively is increasing, risk of CAD also is elevated. However, the present data that correlation coefficients between uric acid and postoperative mechanical ventilation time or ICU length tended to be greater in the UA-group than in the MI-group suggest that preoperative levels of uric acid may have more effects on low/intermediate risk patients. This will lead to us need further studies.

Association of uric acid with perioperative variables

Associations between uric acid and total leukocyte counts,

Table 6. Each correlation of total WBC count, CK-MB, hepatic, and renal markers levels with preoperative levels of serum uric acid in the three groups

VA	Group	Sampling point			
	Control				
	UA	Pre-OP	PO-0.5 hr	PO-24 hr	PO-48 hr
	MI				
T-WBC ($\times 10^3/\mu L$)		0.25	not measured	not measured	not measured
		0.25	0.17	0.06	0.10
		0.45*	0.24	0.10	0.11
CK-MB (U/L)		0.20	not measured	not measured	not measured
		-0.48**	-0.14	-0.31	-0.06
		0.42*	0.11	0.32	0.04
AST (IU/L)		-0.48**	not measured	not measured	not measured
		-0.266	-0.10	-0.23	-0.12
		0.19	0.22	0.25	0.25
ALT (IU/L)		-0.48**	not measured	not measured	not measured
		-0.13	0.00	-0.15	-0.20
		0.21	-0.03	-0.01	0.12
T-bilirubin (mg/dL)		-0.15	not measured	not measured	not measured
		0.38*	0.02	0.24	0.22
		0.03	0.19	0.28	-0.20
BUN (mg/dL)		0.36	not measured	not measured	not measured
		0.09	0.10	0.03	0.24
		0.52**	0.49**	0.47*	0.47*
Creatinine (mg/dL)		0.06	not measured	not measured	not measured
		0.28	0.30	0.20	0.15
		0.51**	0.37*	0.43*	0.58**

Data were expressed coefficient rate (*r*).
*, $P<0.05$; **, $P<0.01$.
Abbreviation: T, total; WBC, white blood cell; CK-MB, creatine kinase-MB isoenzyme; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen.

biochemical markers and other variables at perioperative period are summarized in Table 6. In the control-group, the preoperative level of uric acid was significantly associated with AST or ALT ($P<0.05$). In the UA-group, uric acid had a positive correlation with total bilirubin, but a negative correlation with CK-MB at preoperative period ($P<0.05$). In the MI group, uric acid had a positive correlation with CK-MB, BUN, or creatinine at pre or postoperative period ($P<0.05$ or $P<0.01$). Even though postoperative AST, ALT, or total leukocyte counts had no significant relationships with uric acid, correlation coefficients in AST and total leukocyte counts tended to be higher in the MI-group than in the UA-group, suggesting that preoperative levels of uric acid have more effect on the development and prognosis of CAD. Previous studies showed that the association between increasing uric acid concentrations and development of endothelial dysfunction, and allopurinol improves endothelial dysfunction in subjects with congestive heart failure or diabetes (Butler, 2000; Doehner et al., 2002; Farquharson et al., 2002; Dawson and Walters, 2006). Uric acid also stimulates the production of cytokines from vascular smooth muscle cells. This suggests a potential role for uric acid for xanthine oxidase in mediating the systemic inflammatory response that is linked to cardiovascular events (Johnson et al., 2003). Serum markers such as AST, LDH and total CK no longer are used because they lack cardiac specificity and their delayed elevation precludes early diagnosis (Braunwald, 2008). However, their markers may be used as a screening test to determine the need for more specific testing (Achar et al., 2005). LDH is a

ubiquitous tetrameric enzyme that catalyzes the reversible reduction of pyruvate to lactate in the last step of glycolysis. Each of its subunits are type M (for muscle) or H (for heart), and the resulting five isoenzymes are named in the order of their rates of migration in an electrophoretic field (Lee and Goldman, 1986). Elevated LDH levels can be caused by a number of several conditions, including heart failure, myocardial infarction, hypothyroidism, anemia, and lung or liver disease. CK is a dimeric enzyme that catalyzes the transfer of high-energy phosphate groups and is found predominantly in tissues that consume large amounts of energy. It has two subunits, each can be type M (for muscle) or B (for brain) (Lee and Goldman, 1986). Total CK is assayed in blood tests as a marker of myocardial infarction, rabdomyolysis, muscular dystrophy, the autoimmune myositis and in renal failure. CK-MB band has been a predominant marker for identifying ACS patients with myocardial necrosis. The CK-MB level has been the gold standard for acute myocardial infarction (Storrow and Gibler, 2000). Incorporation of BNP measurement into the clinical evaluation facilitates the diagnosis of heart failure due to either left ventricular systolic or diastolic dysfunction. BNP levels are correlated intracardiac filling pressures, left ventricular mass and ejection fraction, renal function and symptoms (de Lemos and Morrow, 2002). In patients with heart failure, higher concentrations of BNP are associated with increased cardiovascular and all-cause mortality (de Lemos et al., 2003).

In summary, the present study results showed that increased levels of serum uric acid may be a tool for the diagnosis of coronary heart disease and may be considered as a good predictor in assessing the cardiac and renal functions in patients with myocardial infarction or unstable angina at the preoperative period.

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