Evaluation on prognostic ability of serum uric acid for very old acute coronary syndrome patients with diabetes mellitus

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Original investigation

Keywords: uric acid, very old, acute coronary syndrome, diabetes mellitus, prognosis

Posted Date: April 3rd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-18329/v1

Abstract

Background and aims This study sought to evaluate the prognostic power of serum uric acid (UA) in predicting adverse events of very old acute coronary syndrome (ACS) patients with diabetes mellitus (DM). Patients and methods This analysis involved 718 ACS patients >80 years old who were collected general clinical data and baseline blood biochemical indicators prospectively from January 2006 to December 2012, and these patients were classified into two groups based on DM, then followed up after discharge. Kaplan–Meier method was performed for major adverse cardiac events (MACE) rates and all-cause mortality. Multivariate Cox regression was performed to analyze the relationship between UA level and long-term clinical prognosis. Receiver operating characteristic (ROC) curve was analyzed to predict the cutoff value of UA of the very old ACS patients with DM. Results There were 242 and 476 patients in groups DM and non-DM(NDM) and the follow-up time after discharge was 40-120 months (median: 63 months; interquartile range: 51–74 months). The differences in all-cause mortality, cardiac mortality and MACE rates in DM and NDM patients between the control group were statistically significant (P=0.001). All-cause mortality, cardiac mortality and MACE incidence in DM patients with moderate and high UA level were significantly higher than those in control group (P=0.001). There were statistically significant differences in long-term survival rates among the ACS groups (P=0.001), and long-term survival rates decreased significantly with the increase of UA level. UA (OR=2.106, 95%CI=1.244-3.568, P=0.006) was found to be an independent risk factor for all-cause mortality and MACE in very old ACS patients with DM. The cutoff value of UA was 353.6μmol/L (sensitivity: 67.4%; specificity: 65.7%). The elevation of serum UA level play an important role in predicting the development of all-cause mortality in elderly ACS patients with DM. Conclusion Serum UA level is a strong independent predictor of long-term all-cause death and MACE in very old ACS patients with DM.

Background

With the aggravation of the population aging in China, cardiovascular diseases have become the leading killer threatening the life qualify and life safety of residents. According to China Cardiovascular Disease Report in 2018, the population with cardiovascular diseases in China has reached up to 290 million, with cardiovascular diseases as the leading causes of death in China, including 11 million patients with coronary heart disease (CHD). ACS is clinical subtype of CHD, which is a group of clinical syndromes caused by acute myocardial ischemia. The clinical classification includes unstable angina pectoris, acute ST-segment elevation myocardial infarction (STEMI), and acute non-ST-segment elevation myocardial infarction (NSTEMI) [1]. Microcirculation disorder, type of atherosclerotic plaque, function of vascular endothelium, decrease of coronary blood flow and inflammatory response are all important mechanisms for the occurrence of ACS [2]. Old age and DM are both independent risk factors for ACS. It is reported that about 75% of patients hospitalized for CHD are associated with abnormal glucose metabolism, and the degree of coronary artery lesions is relatively severe [3, 4]. Persistent hyperglycemia in patients results in disorders of platelet structure and function, enhances aggregation and adhesion of platelets, and increases the risk of thrombosis [5]. UA is the final product of purines oxidation metabolism in human body and is excreted with urine [6].Clinical studies illustrate that patients with CHD, hypertension, heart failure, DM, metabolic syndrome, chronic renal insufficiency and so on have high serum UA levels, and high UA in the body not only increases the risk of cardiovascular disease, but also is a risk factor for poor prognosis of these diseases [7–9]. One study shows that during a follow up of 2–3 years, with increase of serum UA level in CHD patients about 60 years old, the risk of all-cause mortality and cardiac death increases significantly [10]. Baseline serum UA level presents favorable values in evaluating and predicting the prognosis of patients with different subtypes of ACS [11–14]. In fact, hyperuricemia is closely related to DM. High UA level may lead to decreased hepatic insulin clearance rate, insulin sensitivity of target organs, and increased hepatic insulin resistance index, fasting and postprandial insulin levels [15–17]. Serum UA is an independent risk factor and an important predictor of DM [18–20]. However, among the clinical studies on the prognosis of ACS patients with DM, there are few studies on the predictive value of UA, especially among very old people, which have not been clearly reported, and the pathophysiological mechanism has not been clarified. Our study analyzed the baseline serum UA level

after admission and the incidence of main cardiovascular adverse events within 120 months after discharge of very old ACS patients, aiming to investigate whether serum UA level is an independent risk factor for the long-term prognosis of old-age ACS patients with DM.

Methods

This was a prospective cohort study conducted in Chinese People's Liberation Army (PLA) General Hospital Cardiac Center from January 2006 to December 2012. We enrolled a total of 718 patients aged over 80 years who were hospitalized for coronary angiography due to chest tightness, chest pain and other suspicious symptoms of ACS, including 509 males and 209 females, 242 diabetic patients and 476 non-diabetic patients, with an average age of 81.57 ± 2.16 years. According to the results of coronary angiograms, the subjects were divided into the control group and the research group, and the control group had normal coronary angiograms with a total of 89 patients, while the research group included 629 patients diagnosed with ACS. The patients were followed up once every 12 months after discharge to record the occurrence of MACE, including nonfatal AMI, target vessel revascularization (percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]), cardiac death, and all-cause death. The main outcomes of this study were MACE and all-cause mortality (cardiovascular and non-cardiovascular cardiac or non-cardiac mortalities).

Inclusion criteria

All patients underwent coronary angiography in our hospital to confirm the diagnosis of CHD. All angiogram results were analyzed using the same image analysis software platform. The severity of coronary artery stenosis was recorded by Gensini score, and the recorders of experimental data were trained uniformly. According to the results of coronary angiogram, individualized treatment strategies were performed accordingly for all patients including intensive medicine treatment, PCI or CABG, and long-term follow-ups were performed after discharge. Our study was approved by Ethics Service Center of Chinese PLA General Hospital, and all patients signed the informed consents.

Exclusion criteria

Patients with severe valvular heart disease, pulmonary hypertension, severe liver insufficiency, rheumatism immunity diseases, malignant tumors, gout, infectious diseases, etc; taking UA lowering drugs within recent one month; or neuropsychiatric disorder prevented him from cooperating with the researcher were excluded.

Clinical data

General information (age, gender, body mass index [BMI], heart rate, blood pressure, left ventricular ejection fraction [LVEF] and Gensini score), cardiovascular risk factors (hypertension, hyperlipidemia, previous myocardial infarction [MI], previous stroke, chronic renal failure [CRF], smoking), blood biochemical index at admission (Total cholesterol [TC], triglycerides [TG], high density lipoprotein cholesterol [HDL-C], low density lipoprotein cholesterol [LDL-C], fasting blood glucose [FBG], UA, creatinine, HBA1C[glycosylated hemoglobin]), cardiovascular medication experience (aspirin, clopidogrel, beta-blocker, ACEI/ARB, statin) were recorded.

The estimated glomerular filtration rate (eGFR) was calculated by the Chinese modified Modification of Diet in Renal Disease equation:

eGFR (mL/min/1.73 m2) = 175 × standardized creatinine (mg/dL) − 1.234 × age (year) − 0.179 × 0.79 (if female).

Standardized creatinine (Scr) was calculated by the calibration equation:

Scr (mg/dL) = 0.795× (enzymatic method Scr [mg/dL]) + 0.29.

Chronic renal failure was defined as eGFR⩽60 mL/min/1.73 m2.

Statistical analysis

All data in this study were processed using a statistics software: Version 25.0 of SPSS software (IBM Corporation, Armonk, NY, USA). The measurement data of normal distribution were expressed as mean ± standard deviation, and if the variances were homogeneous, the t-test was used; if the variances were not homogeneous, the rank sum test was used. The measurement data of non-normal distribution were represented by medians with interquartile range (IQR). The enumeration data were expressed numerically and differences between groups were assessed using the chi-square test. Analysis of variance was used to compare data between groups. Multiple Cox proportional regression analysis (odds ratio [OR], 95% CI) was used to identify the factors associated with all-cause mortality and MACE. $P < 0.05$ means statistical significance of the difference.

Results

Baseline characteristics of the study subjects

Among the 718 subjects in this cohort study, a total of 629 patients diagnosed with ACS were assigned to the study group and divided into Group 1 (low UA level group) with UA level from 15.7 to 303 μmol/L including 205 patients, Group 2 (moderate UA level group) with UA level from 303.4 to 380.8 μmol/L including 209 patients and Group 3 (high UA level group) with UA level from 381.9 to 912.8 μmol/L including 215 patients according to the third equalization point of UA level. The UA level in the control group was normal, 344.2 ± 98.52 μ mol/L. All patients signed written informed consents to participate in the cohort study.

The heart rate of Group 3 was higher than that of the control group. LVEF of patients with DM in Group 2 was significantly lower than that in Group 1 and in the control group ($P < 0.01$). TG of patients with DM in Group 3 was significantly higher than that of Group 2 ($P < 0.01$). In the study group, with the increase of UA level, eGFR showed a significant downward trend, and patients with DM had lower eGFR than that in patients without DM ($P < 0.01$), while TG ($P < 0.05$) and FBG ($P < 0.01$) levels of patients with DM were higher than those in patients without DM. There were no statistically significant differences in blood pressure, coronary artery stenosis score, combined diseases and medication status ($P > 0.05$) (Table 1).

Table 1

Study population: clinical characteristics in octogenarians

Characteristic, n(%)	Control group (n = 89)		Group 1 15.7–303 (n = 205)		Group 2 303.4-380.8 (n = 209)		Group 3 381.9-912.8 (n = 215)		P Value
	DM (n = 20)	Non DM (n = 69)	DM (n = 66)	Non DM (n = 139)	DM (n = 83)	Non DM (n = 126)	DM (n = 73)	Non DM (n = 142)	
General conditions									
Age (years)	82.1 ± 1.86	81.3 ± 1.73	81.3 ± 1.69	82.24 ± 2.38	81.36 ± 1.87	82.06 ± 2.28	81.98 ± 2.17	81.91 ± 2.02	0.325
Male	12	43	37	95	61	100	52	109	0.103
HR (bpm)	66.9 ± 11.5	71.88 ± 10.4	75.26 ± 13.8	74.19 ± 14.0	74.83 ± 13.3	72.07 ± 12.3	77.89 ± 14.5△△	76.20 ± 15.5	0.001
BMI (kg/m2)	24.38 ± 3.28	24.01 ± 3.96	24.38 ± 3.28	24.05 ± 3.52	25.60 ± 3.41	24.10 ± 3.06	24.30 ± 3.20	24.86 ± 3.29	0.501
SBP(mmHg)	142.5 ± 21.7	136.7 ± 17.7	141.8 ± 13.4	135.4 ± 22.6●	138.3 ± 21.9	136.5 ± 23.5	138.1 ± 24.1	135.1 ± 20.4	0.549
DBP (mmHg)	71.60 ± 14.6	72.86 ± 11.1	70.48 ± 11.6	71.06 ± 11.7	70.71 ± 12.7	72.59 ± 11.2	68.39 ± 12.1	72.39 ± 11.1●	0.006
EF (%)	60.1 ± 7.95	60.7 ± 6.58	58.1 ± 6.05	55.6 ± 13.71	54.1 ± 8.61△△##	56.6 ± 8.31	54.7 ± 11.01	53.6 ± 10.58	0.001
Gensini score	0	0	49.09 ± 39.6	50.83 ± 38.2	55.18 ± 40.8	45.84 ± 42.3	59.21 ± 42.4	60.63 ± 48.7	0.493
Risk factors									
Hypertension	17	55	55	97	75	90	63	109	0.641
Hyperlipoidemia	4	19	20	30	18	26	16	33	0.566
Previous MI	0	6	8	27	17	23	10	32	0.105
Previous stroke	5	7	10	27	21	27	18	32	0.441
CRF	2	3	7	9	14	12	15	20	0.367
Smoking	3	9	17	27	26	31	23	35	0.287
Baseline blood feature									
TC(mmol/L)	3.94 ± 1.03	3.78 ± 0.81	3.85 ± 1.03	4.05 ± 0.89	4.05 ± 1.02	4.11 ± 0.98	4.10 ± 0.88	4.24 ± 0.98	0.499
TG(mmol/L)	1.27 ± 0.56	1.17 ± 0.53	1.49 ± 0.90	1.24 ± 0.61●	1.37 ± 0.59	1.31 ± 0.67	1.72 ± 0.85▽▽	1.45 ± 0.80●	0.003
HDL-C(mmol/L)	1.26 ± 0.50	1.22 ± 0.34	1.17 ± 0.33	1.23 ± 0.37	1.08 ± 0.27	1.17 ± 0.37	1.08 ± 0.47	1.12 ± 0.29	0.297

Characteristic, n(%)	Control group (n = 89)		Group 1 15.7–303 (n = 205)		Group 2 303.4-380.8 (n = 209)		Group 3 381.9-912.8 (n = 215)		P Value
LDL-C(mmol/L)	2.07 ± 0.73	2.12 ± 0.72	2.13 ± 0.88	2.52 ± 0.77●●	2.28 ± 0.87	2.39 ± 0.82	2.26 ± 0.74	2.51 ± 0.86●	0.003
FBG(mmol/L)	6.0 ± 1.75	5.73 ± 1.58	8.53 ± 3.07△△	6.26 ± 2.18●●	7.81 ± 2.61△△	6.31 ± 2.72●●	8.20 ± 3.03△△	6.48 ± 2.62●●	0.001
HbA1C(%)	7.89 ± 2.57	6.98 ± 2.76	8.21 ± 2.71	6.87 ± 2.33●●	8.05 ± 2.32	7.08 ± 2.56●●	8.42 ± 2.18	7.12 ± 2.38●●	0.001
e-GFR (ml/min/1.73 m2)	68.56 ± 17.6	78.21 ± 16.7●	79.39 ± 20.8	77.77 ± 30.1	69.03 ± 18.5##	71.46 ± 16.0△△#	62.15 ± 20.8**▽	68.49 ± 19.9●△△**	0.002
Cardiovascular medication									
Aspirin	19	64	66	137	81	122	71	136	0.483
Clopidogrel	15	58	66△△	138	80△△	120	67△*	133	0.001
Beta-blocker	14	36	42	83	53	67	56	98	0.336
ACEI/ARB	13	42	41	71	49	59	51	76	0.559
Statin	15	64	64△△	129	74	120	66	135	0.030

Pearson correlation analysis showed that UA level were negatively correlated with eGFR (r=-0.202, P = 0.002); EF (r=-0.139, P = 0.04) in ACS patients with DM (Fig. 1A and B).

Long-term prognosis of patients

We conducted long-term follow-up of all 718 enrolled subjects, with the follow-up time of 40–120 months (median: 63 months; IQR: 51–74 months). The all-cause mortalities of the four groups with DM were 10%(2/20), 10.6%(7/66), 39.75%(33/83) and 58.9%(43/73) (P□0.0001) respectively. Their cardiac mortalities were 5%(1/20), 3%(2/66), 18.1%(15/83) and 42.5%(31/73) (P□0.0001) separately. Their MACE rates were 15%(3/20), 21.2%(14/66), 54.2%(45/83) and 65.8%(48/73) (P□0.0001) respectively. The all-cause mortality of the four groups without DM patients were 13.0%(9/69), 15.1%(21/139), 19.0%(24/126) and 47.9%(68/142) (P□0.0001). Their cardiac mortality were 1.4%(1/69), 4.3%(6/139), 9.5%(12/126) and 32.4%(46/142) (P□0.0001). Their MACE rates were 1.4%(9/69), 25.2%(35/139), 31.0%(39/126) and 55.6%(79/142) (P□0.0001). The long-term prognosis of the four groups both with and without DM patients were significantly different.

The all-cause mortalities and MACE in Group 2 with DM were significantly higher than that in Group 2 without DM patients (P = 0.001), and there were no significant differences in the other three groups between DM and non-DM patients for long-term prognosis.

The all-cause mortality, cardiac mortality and MACE rates in group 3 with both DM and NDM were significantly higher than those in other three groups (control group, Group 1 and Group 2) (P□0.01)The all-cause mortality, cardiac mortality and MACE rates in group 2 with DM were significantly higher than those in other two groups (control group and Group 1) (P□0.01) (Table 2).

Table 2

Long term prognosis in ACS octogenarians according to UA tertiles

Characteristic, n(%)	Control group (n = 89)		Group 1 15.7-308.6(n = 205)		Group 2 308.8-388.8(n = 209)		Group 3 389-912.8(n = 215)		P Value
	DM (n = 20)	Non DM (n = 69)	DM (n = 66)	Non DM (n = 139)	DM (n = 83)	Non DM (n = 126)	DM (n = 73)	Non DM (n = 142)	
All cause death	2	9	7	21	33△##	24●●	43△△▽▽**	68△△▽▽**	0.000
Cardiac death	1	1	2	6	15##	12	31△△▽▽**	46△△▽▽**	0.000
AMI	1	0	2	5	2	4	0	0	0.433
Revascularization	0	0	5	9	10	11	5	11	0.308
MACE	3	9	14	35	45△△##	39●●	48△△**	79△△▽▽**	0.000

We analyzed the data by Kaplan–Meier survival curves, and the results showed a statistically significant difference in long-term survival in ACS patients with DM (P = 0.001). With the increase of UA level, the long-term survival rate decreased sharply, showing a significant difference (Fig. 2).

Independent risk factors affecting long-term prognosis

A Cox regression analysis was performed to determine the factors that were associated with all-cause mortality and MACE in the end of follow-up. After being adjusted for general conditions (sex, age, BMI, SBP and LVEF), risk factors (hypertension, hyperlipidemia, previous MI, stroke and CRF), and blood biochemistry indicators (TG, TC, HDL-C, LDL-C,), heart rate(OR = 1.04, 95%CI = 1.02–1.06, P = 0.001), eGFR (OR = 0.983, 95%CI = 0.965–0.998, P = 0.002), DBP (OR = 0.968, 95%CI = 0.945–0.990, P = 0.006), UA (OR = 2.106, 95%CI = 1.244–3.568, P = 0.006) were found to be independent risk factors for all-cause mortality in ACS patients with DM. Heart rate(OR = 1.03, 95%CI = 1.01–1.05, P = 0.001), UA (OR = 1.752, 95%CI = 1.068–2.876, P = 0.026) were found to be independent risk factors for MACE in ACS patients with DM.

Analyzing the all-cause mortality of the four groups, except that the all-cause mortality in the Group 2 was significantly higher than that in the NDM group (P < 0.001), the all-cause mortalities between DM patients and NDM patients in the other three groups was not significantly difference. The all-cause mortalities of DM and NDM patients in Group 3 were significantly higher than those in the other three groups (P < 0.001), and the data of DM patients in Group 2 were also significantly higher than those in the control group and Group 1 (Fig. 3).

Diagnostic powers of Uric acid for long-term all-cause death

We established respective ROC curves according to the survival and death conditions of the DM group and the NDM group (Fig. 4Aand B), and calculated the cutoff value of UA. The AUC (area under curves) of UA in DM group was 0.726 (95% CI = 0.658–0.794, P = 0.0001) and the cutoff value for all-cause mortality was 353.6 μmol/L (sensitivity: 67.4%; specificity: 65.7%). The AUC of UA in NDM group was 0.663 (95% CI = 0.601–0.726, P = 0.0001). According to the cutoff values of UA, DM patients in the study group were divided into two groups, Group A (UA≤353.6 μmol/L) and Group B (UA>353.6 μmol/L). The all-cause mortality rates of the two groups were 23.97%(29/121) in Group A and 53.47%(54/101) in Group B (P<0.001). The statistical results showed that elevated baseline of serum UA level was an independent risk factor for all-cause mortality in very old ACS patients with DM.

Discussion

ACS is a generic term for all kinds of clinical syndromes caused by acute or subacute myocardial ischemia. The main pathophysiological basis is thrombus formation secondary to coronary artery spasm or rupture of atherosclerotic plaque in coronary arteries [21–23]. Traditional risk factors of CHD include age, hypertension, DM, hyperlipidemia, and smoking [24], and as a major risk factor, DM has been widely concerned by many scholars. Studies have shown that long-term hyperglycemia leads to increased vascular endothelial permeability, abnormal expression of inflammatory factors, and thus causes the body to be in a state of high inflammatory response [25]. In addition, the hyperglycemia leads to excessive production of reactive oxygen species and decreases the activity of antioxidant enzymes, and thus causes the body to be in a state of oxidative stress [26]. All of these factors contribute to the development of coronary atherosclerosis, which ultimately leads to the occurrence of CHD. Studies illustrate that as an independent risk factor of CHD, DM has a high predictive value for the occurrence of CHD [27]. The most common type of DM is Type 2 DM. In this study, we selected elderly ACS patients with Type 2 DM as the research object, which has a good application prospect. We analyzed the general conditions and prognostic indicators of both DM and NDM patients. In the very old patients with ACS included in our study, the proportion of DM was more than one third, which was higher than 20% of the previously reported values [28].

Uric acid is the final metabolite of various purines in the body and the uric acid level of the body is affected by a variety of factors: excessive purine intake, reduced excretion, metabolic disorders, and gene mutations and so on may increase the uric acid level [29, 30]. Gertler et al firstly proposed the association between baseline serum uric acid level and CHD in 1951[31]. Since then, multiple epidemiological studies and meta-analyses shown that hyperuricemia is an independent risk factor for CHD and increases the risk of CHD. Baseline serum uric acid level is positively correlated with the incidence and severity of CHD, and for each 1 mg/dl increase in uric acid level, the patient's all-cause mortality increases by approximately 12% [32–34]. However, there is no clear report on the indicators of long-term prognosis in very old ACS patients with DM by uric acid as evaluation factor.

This study prospectively collected the clinical information of 718 very old patients with suspected ACS who were admitted due to chest tightness and chest pain, and performed 10 years follow-up. Our objective was to analyze the relationship between baseline serum uric acid level and long-term prognosis including all-cause mortality, cardiovascular death, and MACE, and the emphasis was placed on the long-term prognosis of patients with DM. The main findings of our study are as follows: 1) uric acid is a predictor of all-cause mortality and MACE in very old ACS patients with DM. 2) The ability of uric acid to predict the prognosis of these patients increases with the uric acid level rise. 3) With the extension of follow-up time, the effect of uric acid on the prognosis of these patients becomes more significant. 4) the predict power of UA was stronger in DM patients than NDM patients. In addition, we also found that in the study group, with the increase of uric acid level, Gensini score of the patients did not present significant difference, which was inconsistent with the previous reports [35, 36]. It may be related to the significant increase in the scores of coronary artery lesions in all elderly patients enrolled in this study. By comparison and analysis of all-cause mortality and MACE rate in the study group, we found that only the results of DM and NDM patients in Group 2 were different, while there was no difference in Group 3 with high uric acid. However, the long-term prognosis indicators of both DM and NDM patients in Group 3 were significantly worse than that of the other three groups. These results suggest that the impact of elevated uric acid level on the long-term prognosis of elderly ACS patients may be higher than that of diabetes.

Our results also showed that the uric acid cutoff value of elderly ACS patients with DM was 353.6 μmol/L (sensitivity: 67.4%; specificity: 65.7%). Cox regression results showed that, after adjusting for other factors, uric acid was found to be an independent risk factor for all-cause mortality (OR = 2.106, P = 0.006) and MACE (OR = 1.752, P = 0.026) in elderly ACS patients with DM. Therefore, in clinical practice, we should not only pay attention to the traditional risk factors of CHD such as age, hypertension, hyperlipidemia, smoking, drinking, etc., but also to the uric acid level of patients, and physicians should consider the effect of drugs on uric acid metabolism of patients when prescribe.

Previous research indicated that the hyperuricemic state in the body mainly promotes the development of CHD via the following aspects: 1) Activates platelets, promotes thrombosis, and activates inflammatory mediators to reduce plaque stability [37–39]; 2) Stimulates NADPH oxidase, leading to the abnormal structure and function of vascular endotheliocytes and affects the production of ATP, resulting in the dysfunction of vascular endotheliocytes[40–43]; 3) leads to the precipitation of urate crystals and excessive generation of oxygen free radicals, reduces the stability of plaques [44–46]. Yuichi Saito [47] et al pointed out that elevated uric acid level was closely related to vascular endothelial dysfunction in ACS patients, which may further cause poor prognosis. In addition, uric acid reduces the ability of endotheliocytes utilizing NO, activates the oxidative stress response of mitochondria and renin-angiotensin-aldosterone system (RAAS), thus increasing the incidence of cardiovascular diseases[48]. In terms of the interaction between uric acid and DM, inflammation and oxidative stress induced by high UA may further reduce insulin sensitivity and affect the expression of insulin gene in patients [49]. Uric acid increases intracellular ectonucleotide pyrophosphatase/phosphodiesterase 1(ENPP1), thereby directly inhibiting the insulin signaling pathway at the receptor level [50]. In ACS patients with DM, uric acid causes insulin dysfunction and abnormal glucose metabolism, promoting oxidative stress, and ultimately aggravates the damage caused by the hyperglycemia itself to cardiovascular.

In summary, with the aggravation of global aging and the increasing incidence of CHD, the population with CHD complicated with DM is increasing year by year. With developing diagnostic techniques and treatment methods, it is necessary to find appropriate commonly used predictors to evaluate the prognosis of these patients. At present, there are relatively few studies on the predictor of prognosis for the very old ACS patients with DM. This study selected large samples, performed an up-to-10-year follow-up study, and finally confirmed that uric acid was an independent risk factor for evaluating the prognosis of such patients. What's more, the uric acid test process is simple and inexpensive. Therefore, it can be used as a clinical promotion of the detection index, having a good clinical application value.

Limitations

This study had several following limitations: 1) Sample size - Although a total of 718 elderly ACS patients were included in this study, there were only 20 DM patients in the control group and 73 DM patients in the high uric acid group, which may require additional verification in these two groups; 2) this study was a single-center observational study, and the existence of selectivity bias may affect the results, which needs to be verified by multi-center studies; 3) the purpose of this study was to research the correlation between uric acid and the prognosis of elderly ACS patients with DM, but the experimental data lacked the mean data of blood glucose and uric acid during the process of following up the research subjects.

Conclusion

Baseline serum uric acid level is an independent predictor of long-term all-cause death, cardiac death, and MACE in elderly ACS patients with DM, and the accuracy of the prediction increased with the increase of uric acid level. Therefore, uric acid may become a new indicator to predict the long-term prognosis of elderly ACS patients with DM.

Abbreviations

UA: Uric acid; ACS: Acute coronary syndrome; DM: Diabetes mellitus; MACE: Major adverse cardiac events; ROC: Receiver operating characteristic; NDM: Non- diabetes mellitus; CHD: Coronary heart disease; STEMI: ST-segment elevation myocardial infarction; NSTEMI: Non-ST-segment elevation myocardial infarction; PLA: People's Liberation Army; PCI: Percutaneous coronary intervention; CABA: Coronary artery bypass grafting; BMI: Body mass index; LVEF: Left ventricular ejection fraction; MI: Myocardial infarction; CRF: Chronic renal failure; TC: Total cholesterol; TG: Triglycerides; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; FBG: Fasting blood glucose; HBA1C: Glycosylated hemoglobin; ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; eGFR:

Estimated glomerular filtration rate; IQR: Interquartile range; OR: Odds ratio; RAAS: Renin-angiotensin-aldosterone system; ENPP1: Ectonucleotide pyrophosphatase/phosphodiesterase 1

Declarations

Acknowledgements

We thanked patient advisers for the information they provided.

Authors' contributions

ZH F, YD C planned the study, MZ S, H X, Y J, JH W, J G conducted a survey, Y J analyzed the data and wrote the article. ZH F, Q X, X Y, W D contributed to the drafting. All authors read and approved the final manuscript.

Funding

This study was supported by National Natural Science Foundation of China (fund numbers 81500269, 81500202, and 81570383) and Open project of National Geriatrics Clinical Medicine Research Center (fund number NCRCG-PLAGH-2019002).

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study complied with the principles of the Declaration of Helsinki and was approved by Ethics Service Center of Chinese PLA General Hospital. Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors report no conflicts of interest in this work.

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Figures

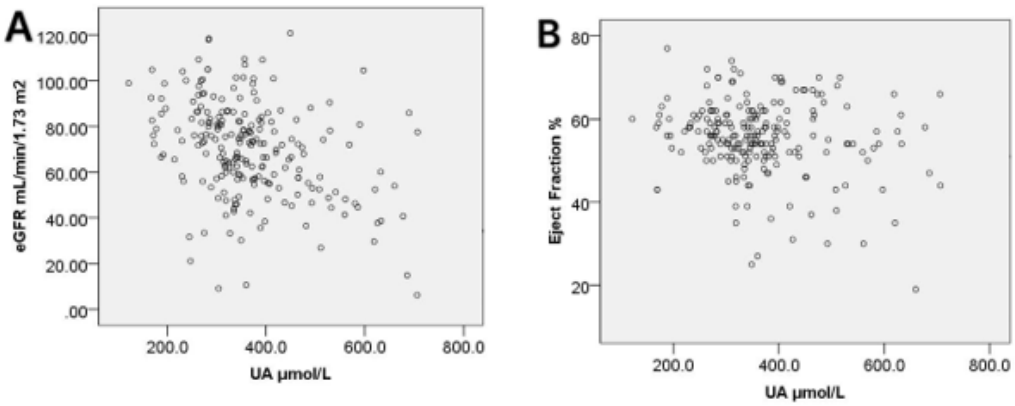

Figure 1

The correlation of UA between eGFR (A) and EF (B) in ACS patients with DM. Abbreviations: UA, uric acid; eGFR, estimated glomerular filtration rate; EF, eject fraction; DM, diabetes mellitus.

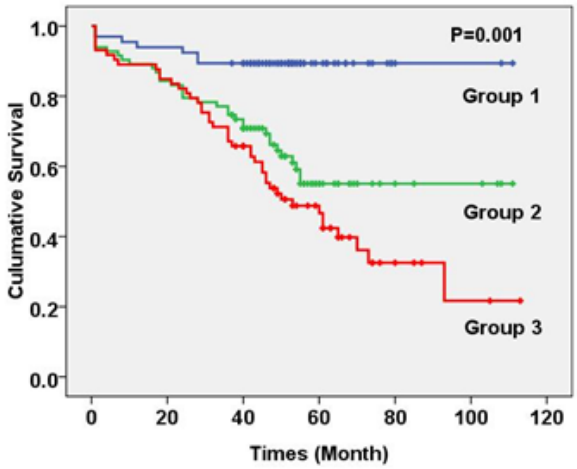

Figure 2

Kaplan–Meier survival curves of long-term survival rates of study group of diabetic patients

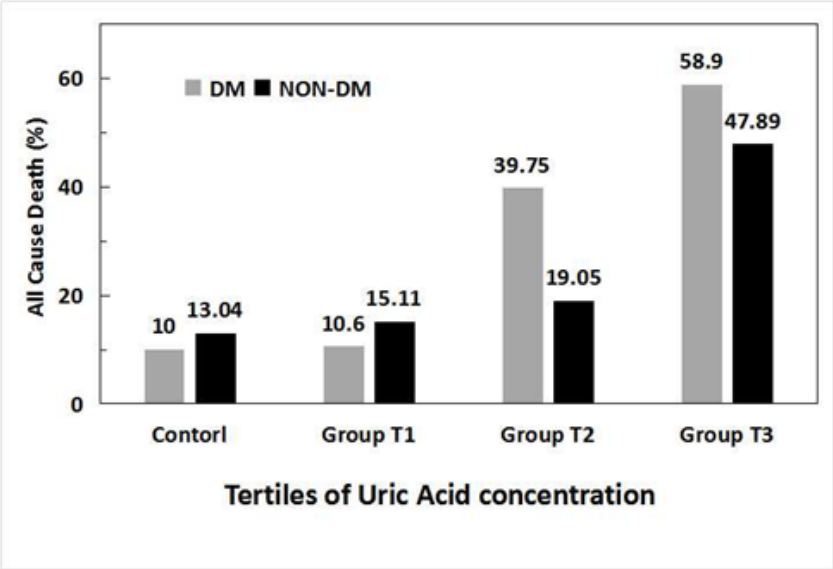

Figure 3

All-cause mortalities in four groups according to the triplicate of uric acid concentration both of DM and NON-DM patients. Notes: Con: DM 366.88±114.44, NDM 332.55±86.24(range: 105-488.8) μmol/L, group T1: NDM 252.41±51.18, DM 253.47±44.66 (range: 15.7-303) μmol/L, group T2: NDM 348.57±23.38, DM 346.80±22.22 (range: 303.4-380.8) μmol/L, group T3: NDM 486.47± 91.08 DM 499.66±100.73(range: 381.9-912.8) μmol/L. Abbreviations: DM, diabetes mellitus; NON-DM, non-diabetes mellitus; T, tertile.

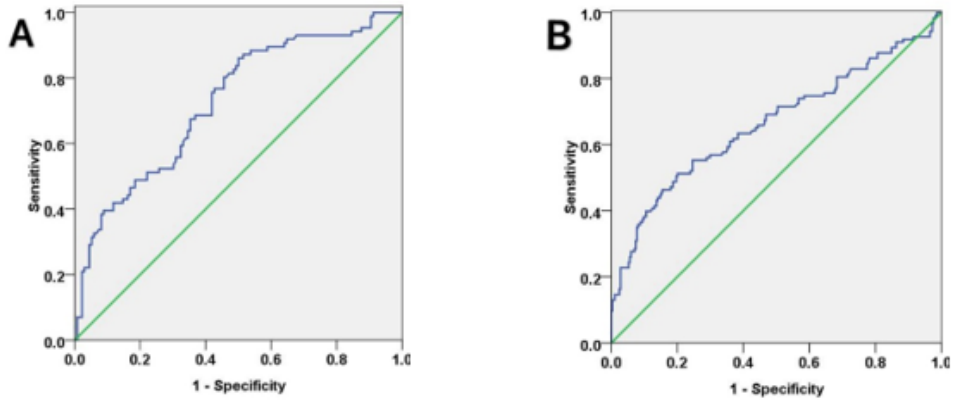

Figure 4

ROC curves of UA for discrimination between surviving and dead patients in ACS patients with DM (A) and Non-DM (B). Abbreviations: ROC, receiver operating characteristic; UA, uric acid; ACS, acute coronary syndrome; DM, diabetes mellitus; NON-DM, non-diabetes mellitus.