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ORIGINAL ARTICLE

Beta 2-Microglobulin and the Severity of Coronary Stenosis in Patients With Acute Coronary Syndrome

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Background Previous studies have shown that beta 2-microglobulin (B2M) could predict all-cause mortality and cardiovascular mortality in various groups of people. However, the relationship between B2M and severity of coronary stenosis in patients with acute coronary syndrome has not been established.

Methods We enrolled 872 consecutive patients admitted with acute coronary syndrome in our study. All participants underwent coronary angiography examination or stent implantation after admission. The severity of coronary stenosis was assessed by Gensini score and the presentation of triple-vessel disease. B2M and other biochemical parameters were measured. All subjects were divided into quartiles of B2M. Multivariate linear regression and logistic regression were applied in the analysis.

Results Gensini score and the prevalence of triple-vessel disease were elevated in accordance with increasing B2M quartiles ($p = 0.002$ and $p < 0.001$, respectively). Multivariate regression showed diabetes ($p = 0.031$), high-sensitivity C-reactive protein (hs-CRP, $p = 0.043$) and B2M ($p = 0.006$) were positively correlated with Gensini score. Logistic regression analysis revealed that the crude and fully adjusted odds ratios of triple-vessel disease were 2.34 (95% CI: 1.58–3.46) and 1.97 (95% CI: 1.14–3.40) in the fourth quartile of B2M compared with the first quartile, respectively. However, no interactive relationships were found in subgroup analysis by estimated glomerular filtration rate or hs-CRP in the above associations, neither in the distribution of Gensini score (p for interaction>0.05 for both).

Conclusion Our data indicated that B2M was an independent risk factor of coronary stenosis in patients with acute coronary syndrome.

Keywords Beta 2-microglobulin • Acute coronary syndrome • Coronary angiography • Gensini score • Triple-vessel disease.

Introduction

Acute coronary syndrome (ACS), including unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI), appears as serious myocardial ischaemia or infarction. With better integration of early and correct diagnosis, optimal medication treatment, urgent reperfusion therapy and the utilisation of secondary prevention, the prognosis of the patients with ACS has improved significantly [1]. However, ACS is still one of the leading causes of death in the world [2].

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Beta 2-microglobulin (B2M), whose molecular weight is 11800 Da, is a non-glycosylated molecule and an important component of major histocompatibility complex-I (MHC-I), and it exists in almost all nucleated cells. B2M is able to freely pass through glomerulus and the production of B2M is constant under normal conditions which is 0.13 mg/h/kg [3], thus it could be used to reflect glomerular filtration rate (GFR) [4,5]. In addition, B2M is elevated in patients with immune or inflammatory diseases, such as acute lymphoblastic leukaemia [6], malignant lymphoma [7] and virus infection [8], hinting that B2M may be identified as a marker of inflammation [9].

Previous investigations indicated that B2M was a predictor of all-cause mortality and adverse cardiac events in different populations [10–14]. In addition, connections between B2M and peripheral artery disease (PAD) [15], carotid artery intima-media thickness (C-IMT) [16] and arterial stiffness [17] were also reported in recent years, which were all presentations of systemic atherosclerosis. Furthermore, a recent study suggested that B2M could be a biomarker for coronary artery disease (CAD) [18]. Nonetheless, studies concerning the relationship between B2M and coronary stenosis were rare and unavailable in patients with ACS. In this study, we assessed the relationship between B2M and severity of coronary stenosis which were reflected by Gensini score and the proportion of triple-vessel disease in patients with ACS.

Methods

Study Population

We recorded the medical information of 938 consecutive patients who received coronary angiography (including percutaneous coronary intervention, (PCI)) and subsequently diagnosed with ACS between January 2012 and December 2013 in Xiangya Hospital, Central South University. The diagnosis of ACS was based on the diagnostic criteria of ACS in published guidelines [19,20]. We excluded those patients with any missing information or those with severe renal dysfunction (defined as estimated glomerular filtration rate, eGFR <30 ml/min/1.73m^2), current infection, previous inflammatory disease and known malignancy. Finally, a total of 872 patients were enrolled in the current study. Our study was approved by the ethics committee of Xiangya Hospital.

Complete medical histories including smoking status and past medical histories of hypertension and diabetes were collected by resident physicians from each patient right after admission to hospital. Heart rates (HR) were measured from at least 30 seconds' cardiac auscultation. Hypertension was defined as follows: 1) systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg on 2 different days; 2) use of antihypertensive medication; 3) previously diagnosed hypertension. Diabetes was defined as follows: 1) symptoms of diabetes plus casual plasma glucose concentration ≥11.1 mmol/L; 2) fasting plasma glucose (FPG) levels ≥7.0 mmol/L; 3) a 2-hour postload glucose ≥11.1 mmol/L during an oral glucose tolerance test (OGTT); 4) use of antidiabetic medication; 5) previously diagnosed diabetes.

Laboratory Examinations

Blood samples were taken from all patients on the next morning of admission after at least 12-hour overnight fasting. Fasting plasma glucose, total cholesterol (TC), triglycerides (TG), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), apolipoprotein A1 (ApoA1), apolipoprotein B (ApoB), creatinine, uric acid (UA), high-sensitivity C reactive protein (hs-CRP) and B2M were measured in the central laboratory of Xiangya Hospital using an automatic biochemical analyser (MODULAR PP, Roche Diagnostics GmbH, Manheim, Germany). Immunoturbidimetry was used to measure serum concentration of B2M. Renal function was determined by eGFR which was calculated according to the equation of the Modification Diet for Renal Disease modified by the Chinese coefficient [21]. Before analysis, all subjects were classified into quartiles of B2M. Patients were also divided into subgroups by eGFR and hs-CRP with a cut-off value of 90 ml/min/1.73m^2 and 10 mg/L, to explore the potential interplay relationship between B2M and renal function or inflammation parameter in relation to coronary atherosclerosis.

Assessment of Coronary Stenosis

All patients underwent coronary angiography examination and PCI, if severe stenosis was found. Standard transradial artery coronary angiography was performed for the majority of patients, and femoral artery approach was chosen for the rest. Two interventional cardiologists independently evaluated the angiographic findings and the results were further cross-checked. Coronary artery disease was defined if occlusion ≥50% of the lumen diameter was found in any of major epicardial coronary arteries, including left main coronary artery (LM), left anterior descending artery (LAD), left circumflex coronary artery (LCX) and right coronary artery (RCA). Stenosis in left main trunk was regarded as LAD and LCX diseases concurrently and stenosis in three vessels (LAD, LCX and RCA) was defined as triple-vessel disease. Gensini scoring system was chosen to evaluate coronary stenosis quantitatively by two interventional cardiologists [22] and the detailed computing method could be seen elsewhere in our previous study [23].

Statistical Analysis

Normal distributed variables were expressed as means (standard deviation, (SD)), and variables not confirmed to normal distribution were presented as medians (interquartile range, (IQR)) after examined by Kolmogorov-Smirnov test. Categorical variables were shown as numbers (percentages). One-way analysis of variance (ANOVA), Kruskal-Wallis rank test and the chi-squared test were used for comparison of continuous variables and categorical variables among quartiles of B2M appropriately. Log transformation was made for hs-CRP (skewed distribution data) when assessing the correlation with B2M. Univariate and

multivariate linear regressions were conducted for the correlations between baseline characteristics and Gensini score. Multivariate logistic regressions were carried out for exploring the relationships between quartiles of B2M and triple-vessel disease in different models. We also evaluated the interplay between B2M and hs-CRP, eGFR in relation to the severity of coronary stenosis in subgroups. All statistical analyses were conducted by the SPSS 19.0 software package (SPSS Inc., Chicago, IL, USA) for windows. A two-sided p value <0.05 was considered statistically significant.

Results

A total of 872 consecutive subjects were eligible for our final analysis (642 men and 230 women, average age 61.0 ± 10.0 years). All subjects were divided into four groups according to quartiles of B2M levels (<1.29 mg/L, 1.29–1.70 mg/L, 1.70–2.20 mg/L, ≥2.20 mg/L). The baseline characteristics of all subjects based on quartiles of B2M are summarised in Table 1. In general, subjects with higher levels of B2M were prone to be older, had elevated levels of UA, but had decreased levels of TC, ApoB and eGFR when compared with groups with lower levels of B2M. Patients in the highest quartile of B2M had highest levels of hs-CRP, but this difference was not statistically significant (p = 0.332). Overall, the mean ± SD of Gensini score and prevalence of triple-vessel disease was 96.0 ± 59.5 and 61.35%, respectively. As expected, Gensini score and the proportions of triple-vessel disease increased in accordance with B2M quartiles (p = 0.002 and p < 0.001, respectively). Besides, higher prevalence of stenosis in LCX and RCA was also found in patients with higher B2M.

Subjects with triple-vessel disease had highest levels of B2M compared with those with one or two strictured vessels

Table 1 Baseline and angiographic characteristics of all subjects according to quartiles of B2M.

Variables	B2M (mg/L)				P-value
	Q1 (n = 217) <1.29	Q2 (n = 218) 1.29-1.70	Q3 (n = 218) 1.70-2.20	Q4 (n = 219) ≥2.20	
Clinical characteristics					
Male, n (%)	156 (71.9)	167 (76.6)	160 (73.4)	159 (72.6)	0.692
Age, years	57.0 (9.4)	60.5 (9.8)	61.9 (9.5)	64.69 (9.9)	<0.001
Hypertension, n (%)	126 (58.1)	122 (56.0)	137 (62.8)	138 (63.0)	0.336
Diabetes, n (%)	60 (27.7)	50 (22.9)	57 (26.2)	53 (24.2)	0.682
Smoking, n (%)	122 (56.2)	122 (56.0)	105 (48.2)	116 (53.0)	0.298
HR, beats per min	72.0 (65.0-78.0)	72.0 (65.0-79.0)	72.0 (65.0-80.0)	74.0 (65.0-83.0)	0.159
Laboratory examination					
FPG, mmol/L	5.20 (4.70-6.03)	5.10 (4.70-5.85)	5.30 (4.60-6.05)	5.20 (4.70-6.00)	0.698
TC, mmol/L	4.40 (3.84-5.22)	4.15 (3.51-4.98)	4.16 (3.51-5.09)	4.15 (3.53-4.94)	0.018
TG, mmol/L	1.41 (1.03-2.05)	1.36 (0.89-1.97)	1.54 (1.06-2.24)	1.44 (1.08-2.02)	0.126
HDL-C, mmol/L	1.10 (0.91-1.28)	1.10 (0.93-1.26)	1.06 (0.94-1.27)	1.04 (0.89-1.26)	0.567
LDL-C, mmol/L	2.70 (2.06-3.36)	2.43 (1.87-3.21)	2.58 (1.94-3.35)	2.52 (1.99-3.07)	0.099
ApoA1, g/L	1.19 (0.24)	1.20 (0.25)	1.19 (0.24)	1.13 (0.24)	0.057
ApoB, g/L	0.85 (0.71-1.04)	0.79 (0.65-0.96)	0.77 (0.65-0.92)	0.76 (0.60-0.90)	<0.001
UA, μmol/L	324.2 (270.9-379.9)	327.1 (274.2-390.4)	334.8 (284.8-387.5)	368.9 (304.9-446.9)	<0.001
hs-CRP, mg/L	4.21 (1.12-10.46)	4.06 (1.24- 8.35)	4.25 (1.35-10.49)	5.34 (1.52-14.30)	0.332
eGFR, ml/min/1.73 m^2	107.7 (21.4)	94.8 (57.4)	95.5 (19.5)	79.6 (22.2)	<0.001
Coronary angiographic characteristics					
Gensini score	74.0 (39.0-118.0)	86.0 (49.5-130.8)	92.0 (51.0-131.8)	103.0 (59.0-147.5)	0.002
Triple-vessel disease, n (%)	108 (49.8)	133 (61.0)	141 (64.7)	153 (69.9)	<0.001
LM stenosis, n (%)	18 (8.3)	19 (8.8)	20 (9.2)	29 (13.2)	0.278
LAD stenosis, n (%)	207 (95.4)	210 (96.3)	209 (95.9)	211 (96.3)	0.951
LCX stenosis, n (%)	148 (68.2)	161 (73.9)	180 (82.6)	177 (80.8)	0.001
RCA stenosis, n (%)	142 (65.4)	161 (73.9)	159 (72.9)	181 (82.6)	<0.001

Data are expressed as mean (standard deviation) or median (interquartile range) or n (%) as appropriate.

Abbreviations: B2M, beta 2-microglobulin; HR, heart rate; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; UA, uric acid; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; LM, left main coronary artery; LAD, left anterior descending artery; LCX, left circumflex coronary artery; RCA, right coronary artery.

($p < 0.01$) (Figure 1A). In Figure 1B, no significant difference was detected for B2M concentrations between patients with unstable angina (n = 613) and acute myocardial infarction (n = 259) ($p = 0.440$). We investigated the correlations between B2M and hs-CRP (Log transformed), eGFR and Gensini score with Spearman correlation analysis. As shown in Figure 2, B2M was conversely correlated with eGFR ($r = -0.460$, $p < 0.001$) and positively correlated with Gensini score ($r = 0.125$, $p < 0.001$), while no significant association was found between B2M and hs-CRP in our study ($r = 0.046$, $p = 0.210$).

Univariate correlations between baseline characteristics and Gensini score using Spearman correlation analysis are presented in Table 2. We observed that male, diabetes, smoking, HR, LDL-C, ApoB, UA, hs-CRP and B2M were positively correlated with Gensini score, while HDL-C, ApoA1 and eGFR were negatively correlated with Gensini score. When including all the above correlated variables in the multivariate regression model, only diabetes (β=0.079, $p = 0.031$), hs-CRP (β=0.079, $p = 0.043$) and B2M (β=0.115, $p = 0.006$) remained independent influencing factors of Gensini score (Table 2).

For further investigating whether hs-CRP and eGFR had any interactive relationship with B2M for Gensini score, all subjects were stratified into subgroups by hs-CRP and eGFR, respectively. In Table 3, increasing trends for Gensini score across B2M quartiles were found both in lower hs-CRP subgroup (trend $p = 0.040$) and higher hs-CRP subgroup (trend $p = 0.029$), and no interaction was reached (interaction $p = 0.256$). As for eGFR, elevated Gensini scores were found in upper B2M quartiles in both subgroups though the trends were not statistically significant ($p = 0.076$ and $p = 0.109$) and no interactive relationship was obtained as well (interaction $p = 0.958$).

Finally, multivariate logistic regression analyses were conducted to calculate the odds ratios of triple-vessel disease in B2M quartiles in all subjects and in subgroups (Table 4). In Table 4, increasing odds ratios of triple-vessel disease were shown across B2M quartiles in all subjects in crude model [OR (95% CI): 1.00; 1.58 (1.08–2.31); 1.85 (1.26–2.72); 2.34 (1.58–3.46) in B2M quartiles, trend $p < 0.001$]. When adjusting for male, age, hypertension, diabetes, smoking and HR, the results in

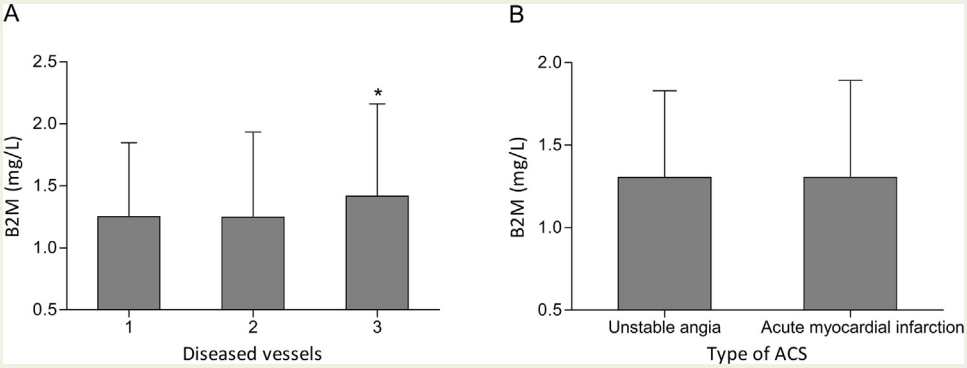

Figure 1 A: Beta 2-microglobulin levels according to diseased coronary vessels (1-3). B: Beta 2-microglobulin levels in patients with unstable angina and acute myocardial infarction. Bars in the box plot represent standard errors. * $p < 0.01$ the third group versus the other two groups.
Abbreviation: B2M, beta 2-microglobulin.

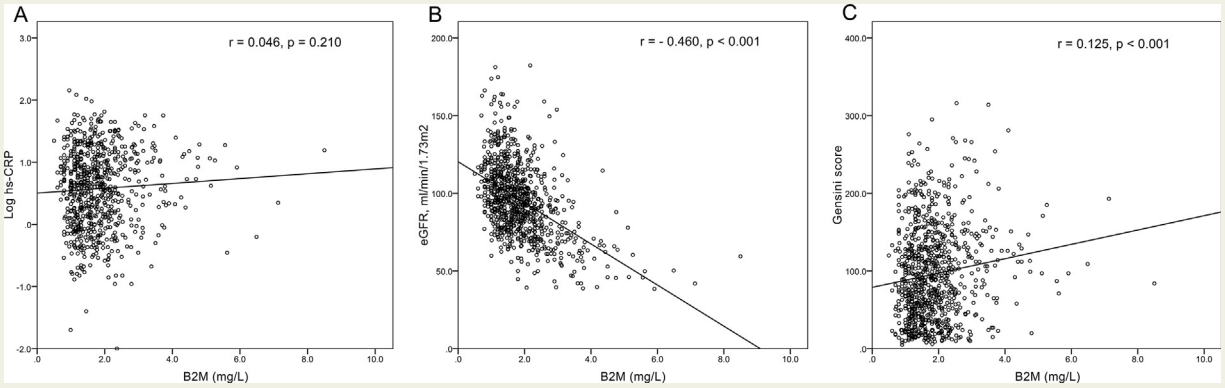

Figure 2 Correlations between B2M and hs-CRP (A), eGFR (B) and Gensini score (C). Spearman correlation analysis was performed to evaluate their associations. Hs-CRP was log transformed before analysis.
Abbreviations: B2M, beta 2-microglobulin; eGFR, estimated glomerular filtration rate; hs-CRP, high-sensitivity C-reactive protein.

model 1 were similar with the crude model [OR (95% CI): 1.00; 1.47 (0.99–2.18); 1.68 (1.12–2.50); 1.94 (1.28–2.94) in B2M quartiles, trend p = 0.001]. Further adjusting for all confounding baseline factors in model 2, the results were still solid [OR (95% CI): 1.00; 1.58 (0.99–2.52); 1.74 (1.08–2.81); 1.97 (1.14–3.40) in B2M quartiles, trend p = 0.012]. In the subgroup analysis, increased odds ratios of triple-vessel disease in increased quartiles of B2M in patients whose hs-CRP < 10 mg/L or those with an eGFR <90 ml/min/1.73 m^2 were detected after adjusting for confounding factors (trend p = 0.008 and 0.010, respectively). However, interaction analysis did not reach statistical significance (p > 0.05 for both).

Table 2 Univariate analysis and multivariate regression analysis of determinants of Gensini score.

Variables	Univariate analysis		Multivariate analysis		
	r	P-value	β	t	P-value
Male	0.103	0.002	0.060	1.340	0.181
Diabetes	0.099	0.004	0.079	2.156	0.031
Smoking	0.131	<0.001	0.060	1.368	0.172
HR	0.067	0.049	0.004	0.103	0.918
HDL-C	-0.132	<0.001	-0.020	-0.341	0.734
LDL-C	0.116	0.001	0.075	1.551	0.121
ApoA1	-0.182	<0.001	-0.077	-1.284	0.200
ApoB	0.131	<0.001	0.078	1.596	0.111
UA	0.069	0.040	0.000	-0.008	0.994
hs-CRP	0.164	<0.001	0.079	2.024	0.043
eGFR	-0.092	0.006	-0.076	-1.733	0.084
B2M	0.125	<0.001	0.115	2.767	0.006

Abbreviations: β, standardised regression coefficient; HR, heart rate; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; UA, uric acid; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; B2M, beta 2-microglobulin.

Discussion

To our knowledge, this is the first study evaluating the association between B2M and coronary stenosis in patients with ACS. Our results showed that B2M was independently and positively associated with Gensini score and triple-vessel disease after adjusting for confounding factors, even including parameters of renal function and inflammation.

Several investigations have proposed B2M as a predictor of all-cause mortality, cardiovascular mortality and combined cardiovascular events in multiple groups of patients [10–14]. Moreover, accumulating data suggested that B2M was also linked with various cardiovascular disorders. B2M was found to be associated with cardiac valvular calcification [24], and the risk factors of valvular calcification and atherosclerosis are similar [25], referring that valvular calcification may be one cardiac presentation of systemic atherosclerosis. In addition, B2M was positively and independently correlated with disease severity in PAD, which could be regarded as a peripheral presentation of atherosclerosis [15,26]. Besides, B2M was correlated with C-IMT [16] and arterial stiffness reflected by brachial-ankle pulse wave velocity (baPWV) [17], which are both indices of subclinical target-organ damage of cardiovascular system. Therefore, patients with elevated B2M are more prone to have atherosclerosis.

Recently, an investigation revealed that B2M could discriminate CAD and was independently associated with the extent of coronary stenosis in patients suspected or documented with CAD and without renal dysfunction [18], however, inflammatory parameters were not adjusted in their analysis and the results in patients with renal dysfunction were unclear as well. Our study enrolled a group of patients with ACS, and those with severe renal dysfunction (eGFR <30 ml/min/1.73m^2) were excluded, besides, hs-CRP was also taken into our study as an inflammation marker. Our results further demonstrated that B2M was related to coronary stenosis severity in patients with ACS, which was in

Table 3 Gensini score across quartiles of B2M by subgroups of hs-CRP and eGFR.

Gensini score	n	B2M				P for trend	P for interaction
		Q1	Q2	Q3	Q4		
hs-CRP, mg/L							
<10	667	68.0 (36.0-114.5)	76.0 (43.0-128.0)	88.0 (44.0-131.5)	91.5 (49.5-135.5)	0.040	0.256
≥10	205	102.0 (61.5-125.8)	116.0 (85.0-135.0)	109.0 (70.0-131.5)	118.0 (94.5-155.0)	0.029	
eGFR, ml/min/1.73 m^2							
<90	358	70.0 (40.2-124.2)	82.0 (52.0-131.0)	91.0 (47.0-143.0)	105.5 (65.0-147.8)	0.076	0.958
≥90	514	75.0 (40.0-118.0)	89.0 (48.0-130.0)	93.0 (51.0-130.0)	94.0 (50.0-146.0)	0.109	

Gensini score are expressed as median (interquartile range).
Abbreviations: B2M, beta 2-microglobulin; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate.

Table 4 Odds ratios and 95% CI for triple-vessel disease according to quartiles of B2M in all subjects and in subgroups.

	n	B2M				P for trend	P for interaction
		Q1	Q2	Q3	Q4		
All Subjects							
Crude	872	1.00	1.58 (1.08, 2.31)	1.85 (1.26, 2.72)	2.34 (1.58, 3.46)	<0.001	
Model 1	872	1.00	1.47 (0.99, 2.18)	1.68 (1.12, 2.50)	1.94 (1.28, 2.94)	0.001	
Model 2	684	1.00	1.58 (0.99, 2.52)	1.74 (1.08, 2.81)	1.97 (1.14, 3.40)	0.012	
hs-CRP, mg/L							
<10	496	1.00	1.56 (0.92, 2.64)	1.71 (0.99, 2.95)	2.41 (1.26, 4.58)	0.008 [a]	0.150
≥10	193	1.00	2.20 (0.66, 7.40)	2.21 (0.66, 7.37)	0.82 (0.24, 2.86)	0.815 [a]	
eGFR, ml/min/1.73 m^2							
<90	276	1.00	1.71 (0.65, 4.54)	3.20 (1.24, 8.26)	3.12 (1.23, 7.91)	0.010 [a]	0.293
≥90	408	1.00	1.59 (0.91, 2.77)	1.28 (0.71, 2.30)	1.76 (0.83, 3.73)	0.174 [a]	

Abbreviations: CI, confidence interval; B2M, beta 2-microglobulin; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate.
Model 1 adjusted for male, age, hypertension, diabetes, smoking and heart rate;
Model 2 further adjusted for fasting plasma glucose, total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, apolipoprotein A1, apolipoprotein B, uric acid, hs-CRP and eGFR based on Model 1.
[a]adjusted variables were the same as in Model 2 if the variable was not classified into subgroups.

accordance with a previous study [18], and we further revealed that this association was independent of influencing factors even including eGFR and hs-CRP. However, we failed to identify difference on levels of B2M in patients divided by types of ACS (unstable angina and acute myocardial infarction), which need future study to verify.

Inflammation plays a vital role in the development and progression of atherosclerosis. Hs-CRP is a well-studied inflammation marker which could assess inflammation in a quantitative manner, besides it is also an indicator of CVD events [27]. As B2M was associated with a range of inflammatory disorders [6–8], some researchers proposed that B2M may be an inflammation marker [9]. In both acute and chronic inflammation response, a large amount of B2M was shed from the surface of lymphocytes during the generation and migration of lymphocytes, leading to an increased level of B2M. High levels of B2M could be modified by advanced glycation end products (AGEs) [28], and glycosylated B2M could release a range of inflammatory agents, such as interleukin-1, interleukin-6, interleukin-8, interleukin-10 and tumour necrosis factor-α (TNF-α) [29–31]. Besides, B2M could induce apoptosis and necrocytosis in fibroblast and vascular endothelial cells. Apoptotic or necrotic cells could release intracellular enzyme and cytokine to recruit inflammatory cells which cause inflammatory reaction, indicating that B2M may initiate inflammation in this pathway [32]. Taken together, B2M may participate in the process of inflammation.

One clinical follow-up study indicated the addition of B2M and hs-CRP to baseline risk factors could improve the risk stratification for major cardiovascular events in patients with asymptomatic carotid atherosclerosis [14]. In the current study, we found that hs-CRP was highest in the fourth quartile of B2M, but no statistical significance was obtained among quartiles (p = 0.332). Hs-CRP was not correlated with B2M as well (p = 0.210). The negative finding between B2M and hs-CRP was inconsistent with previous studies [15,33], which may be explained by the difference in the enrolled participants as we noticed that hs-CRP were dramatically elevated in patients with ACS compared with patients with stable angina or without CAD [34]. Besides, in subgroup analysis by hs-CRP, interaction effect was not detected in B2M quartiles either with Gensini score or triple-vessel disease (interaction p = 0.256 and 0.150). But we found hs-CRP appeared as an independent risk factor of both Gensini score (β=0.079, p = 0.043) and triple-vessel disease (Odds ratios: 1.035, 95% CI: 1.015–1.055, data not shown in the results) after adjustment, which was in line with a previous study [34]. Therefore, whether inflammation plays a role in the connection between B2M and coronary atherosclerosis could not be answered in our study and we inferred that their association may be beyond inflammation itself.

Beta 2-microglobulin is a sensitive marker of renal function and has been used in estimating GFR in selected populations [4,5]. Cardiovascular disease is one of the main causes of death in chronic kidney disease patients, and even mild renal dysfunction may increase cardiovascular mortality and morbidity [35,36]. A previous study has shown that impaired renal function was independently correlated with Gensini score in CAD patients [37]. In our study, eGFR was negatively and closely correlated with B2M and Gensini score, but eGFR was not an independent risk factor of Gensini score. Patients with abnormal eGFR who also lay in the fourth B2M quartile had highest Gensini score, though the interaction analysis was not significant (interaction p = 0.958). As for triple-vessel disease, patients with abnormal eGFR had higher odds ratios in increasing B2M quartiles (trend p = 0.010), but the interactive analysis was not significant

as well (interaction p = 0.293). Besides, one previous study revealed the independent association in B2M with Gensini score and Syntax score in patients without renal dysfunction [18]. Therefore, it seems that renal dysfunction may not account for the association between B2M and severity of coronary stenosis.

There are some limitations in our study. First, we could not draw a causal conclusion between B2M and coronary severity because of the cross-sectional design of our study. Second, the subjects enrolled in our study were patients with ACS, whose coronary strictures were more serious (for example, 96.0% of patients had LAD stenosis in our study), so generalisation of our conclusion should be cautious. Third, the predicting ability of B2M for long-term prognosis and progression of coronary stenosis was not examined, so future follow-up investigations may be needed.

Conclusion

In the present study, we found that B2M was independently associated with Gensini score and prevalence of triple-vessel disease in patients of ACS, indicating that B2M may be an eligible index to estimate the severity of coronary stenosis.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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