Comparison of Glycated Albumin, Hemoglobin Alc and Admission Blood Glucoseforpredictionof in-hospital Major Adverse Cardiac Events: a Retrospective Study

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Original investigation

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Abstract

Background: Hyperglycemia is an independent predictor of major adverse cardiovascular events (MACEs) in patients with acute coronary syndrome (ACS) in 30 days.The purpose of this study is to evaluate the prognostic roles of different glycemic markers for in-hospital MACEs in acute myocardial infarction (AMI) patients undergoing percutaneous coronary intervention (PCI), including hemoglobin A1c (HbA1c) and glycated albumin (GA) and admission blood glucose (ABG).

Methods: We conducted a retrospective study with 200 MI patientswho undergone PCI during the hospitalization period. We collected the clinical data and divided all patients into groups based on MACEs.T test and Chi-Square (Fisher) test were conducted to examine the difference between the two groups. Univariate and Multivariate Logistic Analysis and receptor operating curve(ROC) were performed to investigate the prognostic role of each glycemic markers in AMI patients with PCI.Patients were regrouped based on ROC curve and cutoff levels. The Cox regression analysis, Kaplan Meier method and Log rank test was performed for MACEs cumulative events.

Results: Among the 200 patients, 18 patients developed MACE. Patients in MACE group had a higherdiastolic blood pressure (DBP) (p=0.019), high-sensitivity troponin T (HS-TnT) peak (p=0.011), CKMB peak (p=0.026),myoglobin (MYO) peak (p=0.006), estimated glomerular filtration rate (eGFR) (p=0.005), low-density lipoprotein cholesterol (LDL-c) (p=0.027),GA(p=0.001) and HbA1c (p=0.010). There were more smokers (p=0.017), diabetic patients (p<0.001) and patients with hypertension(p=0.009) in MACE group. Univariate and Multivariate logistic analysis showed GA (p=0.029) and HbA1c (p=0.048) were independent risk factors of MACEs. ROC curve showed GA had a larger area under the curve (AUC) as prognostic marker of in-hospital MACEs (0.743; 95%confidenceinterval[CI], 0.578-0.907; p=0.001) than HbA1c (0.689; 95%CI, 0.530-0.849; p=0.008) and ABG (0.593; 95%CI, 0.441-0.745; p=0.192).Kaplan Meier curves showed that patients with higher levels of GA (p=0.001), HbA1c (p<0.001) and ABG (p=0.008)had worse clinical events (p=0.001).Univariate and multivariate cox regression analysis presented GA has significant predictive role for MACEs.

Conclusion: Among ABG, GA and HbA1c, elevated GA were significant to predict the risk of in-hospital MACEs in AMI patients who undergone PCI during the hospitalization period.

Background

Hyperglycemia has been proved to be associated with inflammation of acute coronary syndrome [1]. There are many glycemic markers to evaluate blood glucose control, including ABG, HbA1c and non-traditional markers, such as GA. Admission blood glucose only reflects the blood control at the moment, which can be affected by diet and stress. HbA1c reflects blood control over the previous 8 to 12 weeks, while GA reflects blood control during the previous 1-3 weeks [2].Many studies have revealed the association between different glycemic markers and MACEs relatively, but few studies have compared the predictive roles in MACEs. Therefore, the aim of this study is to investigate the association between

ABG, GA, HbA1c and in-hospital MACEs in AMI patients with PCI and identify prognostic markers in MACEs.

Materials And Methods

1. Patients and groups

We retrospectively analyzed 200 patients who have been admitted in the Department of Cardiology of Shandong Provincial hospital from January 1, 2017 to December 31, 2019. All patients were diagnosed as acute ST segment elevated MI or acute non-ST segment elevated MI based on the American heart Association (AHA) guidelines [3], and undergone PCI. All patients with diabetes mellitus (DM) were well-diagnosed before this admission. The exclusion criteria were as follows: thyroid disease, hepatic or renal impairment, autoimmune disease and malignant tumor. Based on the in-hospital MACEs (general observation time is 7 days), patients were divided into non-MACE group and MACE group. The study protocol was proved by the medical ethic committee of Shandong Provincial Hospital.

2. Clinical data collection

General admission clinical characteristics including sex, age, HR, systolic blood pressure (SBP), DBP, DM, hypertension, previous MI, previous stroke and laboratory data were recorded. Serum biochemical measurement were taken immediately at the admission, including HS-TnT, hemocyanin (HCY), blood glucose, creatinine, uric acid, triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), LDL-c, HbA1c and GA. The peak HS-TnT were the maximum value during hospitalization. MACEs were defined as cardiac death, malignant arrhythmia, unstable angina pectoris, acute heart failure and recurrent myocardial infarction [4]. The eGFR was calculated according to the CKD-EPI$_{SCr}$ formula [5].

3. Statistical analysis

All data analysis was conducted by SPSS version 21.0. Continuous variables were expressed as mean±SD and undergone independent-samples *t*-test. Categorical variables were expressed as number[percentage] and undergone chi-square test or Fisher exact test. Univariate and multivariate logistic regression analysis were performed to determine risk factors of MACEs. ROC curve was constructed to determine the prognostic role of ABG, HbA1c and GA. According tothe cutoff value of ABG, GA and HbA1c, patients were divided into two groups relatively, which are defined as follows: Group 1A, patients with ABG value<6.51, Group 1B, patients with ABG value≥6.51; Group 2A, patients with GA value<23.54, Group 2B, patients with GA value≥23.54;Group3A, patients with HbA1c value<7.46, Group 3B, patients with HbA1c value≥7.46.Kaplan Meier curve and Log Rank test were conducted for MACEs. A two-side $p<0.05$ was considered significant.

Results

1. Clinical characteristics of all patients

We collected clinical data of 200 AMI patients who undergone PCI, which were presented in Table 1. Compared with non-MACE group, patients with MACEs had higher percentage of female (p=0.019), HS-TnT (p=0.011), CKMB (p=0.026), MYO (p=0.006), GA (p=0.001), HbA1c (p=0.010)and lowerDBP (p=0.019), eGFR (p=0.005), LDL-c (p=0.027). There are more patients with history of smoking (p=0.017), diabetes (p<0.001) and hypertension (p=0.009) in MACE group than non-MACE group.There were no significant differences seen between the two groups in age, heart rate, systolic blood pressure, homocysteine, creatinine, uric acid, triglyceride, total cholesterol, high density lipoprotein cholesterol (HDL-c), history of previous MI, PCI, CABG and stroke.

2. Univariate and multivariate logistic regression analysis of all factors

Univariate and multivariate logistic regression analysis revealedthat there were significant differences between non-MACE group and MACE group in terms of sex, smoking, diabetes, hypertension, HR, DBP, Hs-TnT, CKMB, MYO, eGFR, HbA1c and GA. Multivariate logistic regression analysis showed HbA1c (p=0.048) and GA (p=0.029) were independent risk factors contributing to MACEs (Table 2).

3. Prognostic accuracy of GA for MACEs

Figure 1 presented that GA had a larger AUC (0.743; 95%CI, 0.578-0.907; p=0.001) than blood glucose(0.593; 95%CI, 0.441-0.745; p=0.192) and HbA1c (0.689; 95%CI, 0.530-0.849; p=0.008). The cutoff values of ABG, HbA1c and GA in ROC curve were6.51 (sensitivity, 33.3%; specificity, 65.9%), 7.46 (sensitivity, 61.1%; specificity, 85.7%) and 23.54 (sensitivity, 33.3%; specificity, 96.2%) relatively.

4. In-hospital outcomes

In the univariate cox regression analysis, sex, smoking, DM, HBP, HR, DBP, CKMB, HS-TnT, MYO, eGFR, GA and HbA1c were associated with MACEs. Multivariate cox analysis showed that GA (p<0.001) and MYO (p=0.027) were significant predictive markers for MACEs (Table 3).Kaplan Meier curves showed that patients with higher levels of GA had worse clinical events (p=0.001) (Figure 2-4).

Discussion

Many studies have confirmed that abnormal blood glucose control is associated with incidence of MACEs in ACS patients. Those findings showed admission blood glucose, HbA1c and non-traditional glycemic markers may be independent risk factors for MACEs within long-term and short-term follow-up [6-10]. MostafaAlavi et al. [11] demonstrated that abnormal ABG in ACS patients was an independent predictor of MACEs within 30 days. Chi Yuen Chan et al. [12] found that admission HbA1c levels were not associated with short-term MACEs in diabetic patients with ACS. Few studies have conducted to figure out the prognostic role of GA, ABG and HbA1c for in-hospital MACEs.

The aim of our study was to investigate the predictive ability of ABG, GA and HbA1c for MACEs in AMI patients who undergone PCI during hospitalization.Our study has showed that patients in MACE group had higher GA and HbA1c, compared with non-MACE group, while ABG showed no significant

difference.Logistic regression analysis showed that GA, as well as HbA1c were independent risk factors for MACEs. In order to compare predictive abilities of these glycemic markers, we performed ROC curve, identified the cutoff values and regrouped all patients. Kaplan Meier curve showed that patients with GA value≥23.54 had worse clinical outcomes than higher level of HbA1c and ABG. Cox regression analysis revealed that GA is the only predictive markers for in-hospital worse clinical events among these glycemic products.

Admission blood glucose can be affected by many factors, including diet, stress response and sympathetic activation [13]. Although ABG and heart rate has been proved to be associated stress response, which leads to vascular endothelial dysfunction and poor prognosis, stress hyperglycemia is a transient increase of blood glucose [14]. Blood glucose may not at the peak when blood sampleswere collected, which leading to weak correlation between ABG and MACEs.HbA1c is a reliable monitor for diabetic control during the previous 8-12weeks, which reflects general glucose metabolism. Therefore, the HbA1c level is not influenced by stress and acute inflammation. Thus, HbA1c may not be a marker for in-hospital poor clinical outcome.

Glycated albumin is a reflection of the preceding 8–12 weeks. Hepatic and renal dysfunction, inflammation and acute infection may affect GA [15]. In this study, we found that GA had predictive role for in-hospital MACEs in AMI patients who undergone PCI during hospitalization. We confirmed that GA may reflect the acute inflammation in AMI patients with PCI, which suggests that increase of GA may be driven by acute myocardial infarction.

There were also some limitations in this study. First, only patients with detection of HbA1c and GA during admission were enrolled, which may cause selective bias.Second, our study is a cross-sectional study and cannot determine the causal relationship between GA and AMI, which is worthy further study in the future.

Conclusion

We found that GA was significant independent risk factors for in-hospitals MACEs. HbA1c and admission blood glucose were not associated with poor in-hospital clinical outcomes in AMI patients undergone PCI. Our findings may provide anon-traditional marker for predicting MACEs during hospitalization.

Abbreviations

MACE: major adverse cardiovascular events; ACS: acute coronary syndrome; AMI: acute myocardial infarction; PCI: percutaneous coronary intervention; HbA1c: hemoglobin A1c; GA: glycated albumin; ABG: admission blood glucose; ROC: receptor operating curve; DBP: diastolic blood pressure; HS-TnT: high-sensitivity troponin T; MYO: myoglobin; eGFR: estimated glomerular filtration rate; LDL-c: low-density lipoprotein cholesterol; AUC: area under the curve; CI: confidence interval; AHA: American heart Association; DM: diabetes mellitus; SBP: systolic blood pressure; HCY: hemocyanin; triglyceride (TG), total

cholesterol (TC), high-density lipoprotein cholesterol (HDL-c); TG: triglyceride; TC: total cholesterol; HDL-c: high-density lipoprotein cholesterol;

Declaration

Ethics approval and consent to participate

The study was approved by the medical ethic committee of Shandong Provincial Hospital.

Consent for publication

Not applicable.

Availability of data and raw materials

The data analysed in this study are available from the corresponding author on reasonable request.

Competing interests

The authors declared no conflicts of interest.

Funding

None.

Authors' contribution

LS designed the study andanalysed the data. LS and HTY wrote the manuscript. All authors read and approved the final manuscript.

Acknowledgement

Not applicable.

Authorship information

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Tables

Table 1. Baseline Characteristics of Patients in non-MACE and MACE group.			
	Non-MACE group (n=182)	MACE group (n=18)	*p*
Age (years)	60.59±12.03	66.33±12.00	0.055
sex			0.019
Female [n (%)]	36(19.8%)	9(50.0%)	
Male [n (%)]	146(80.2%)	9(50.0%)	
DM [n (%)]	45(24.7%)	12(66.7%)	<0.001
HBP [n (%)]	121(66.5%)	6(33.3%)	0.009
Smoking [n (%)]	93(51.1%)	4(22.2%)	0.017
Heart rate (beats/min)	73.37±12.57	80.83±15.02	0.055
SBP (mmHg)	130.73±19.13	128.67±24.21	0.671
DBP (mmHg)	76.48±10.86	70.17±10.77	0.019
HS-TnT(pg/mL)	568.98±1227.35	1855.04±1888.31	0.011
CKMB (ng/mL)	14.01±38.77	53.00±67.36	0.026
MYO (ng/mL)	54.54±102.73	257.80±272.86	0.006
HCY(μmol/L)	15.49±7.78	12.35±2.73	0.091
Blood glucose (mmol/L)	6.59±2.30	7.20±2.10	0.273
Creatinine(μmol/L)	73.46±19.49	73.67±5.43	0.916
eGFR	94.06±18.08	81.33±17.58	0.005
Uric acid(μmol/L)	347.87±109.96	354.67±210.50	0.894
Triglyceride (mmol/L)	1.70±0.83	1.33±0.67	0.071
Total cholesterol (mmol/L)	4.38±1.12	3.93±0.85	0.096
HDL-c (mmol/L)	1.03±0.23	1.08±0.15	0.275
LDL-c (mmol/L)	2.79±0.94	2.47±0.49	0.027
GA (%)	15.93±4.05	23.71±8.53	0.001
HbA1c (%)	6.09±1.36	7.34±1.80	0.010
Disease history			
Previous MI [n (%)]	17(9.3%)	0(0.0%)	0.323

Previous PCI [n (%)]	7(3.8%)	0(0.0%)	1.000
Previous CABG [n (%)]	0(0.0%)	0(0.0%)	a*
Previous stroke [n (%)]	30(16.5%)	3(16.7%)	1.000
* a is a constant.			

Table 2. Univariate and Multivariate Logistic Regression Analyses for MACEs.

Variable	Univariate Analysis		Multivariate Analysis	
	OR (95%CI)	*p*	OR (95%CI)	*p*
Age (years)	1.045 (0.999, 1.093)	0.058	Not Selected	
sex	4.056 (1.502, 10.951)	0.006	6.452 (0.068, 60.836)	0.422
DM [n (%)]	6.089 (2.160, 17.162)	0.001	175.540 (0.000, 1103.892)	0.448
HBP [n (%)]	0.252 (0.090, 0.704)	0.009	5.542 (0.013, 22.995)	0.578
Smoking [n (%)]	0.273 (0.087, 0.862)	0.027	1.205 (0.002,7.072)	0.954
Heart rate (beats/min)	1.041 (1.006, 1.078)	0.023	0.998 (0.789, 1.263)	0.990
SBP (mmHg)	0.995 (0.970, 1.019)	0.669	Not Selected	
DBP (mmHg)	0.944 (0.898, 0.992)	0.022	0.736 (0.512, 1.059)	0.099
HS-TnT(pg/mL)	1.000 (1.000, 1.001)	0.002	1.001 (0.999, 1.004)	0.255
CKMB (ng/mL)	1.011 (1.004, 1.019)	0.003	1.020 (0.949, 1.097)	0.589
MYO (ng/mL)	1.005 (1.003, 1.008)	<0.001	1.016 (0.998, 1.034)	0.085
HCY(μmol/L)	0.869 (0.750, 1.006)	0.061	Not Selected	
Blood glucose (mmol/L)	1.113 (0.919, 1.348)	0.275	Not Selected	
Creatinine(μmol/L)	1.001 (0.975, 1.027)	0.965	Not Selected	
eGFR	0.962 (0.936, 0.989)	0.006	0.893 (0.754, 1.059)	0.193
Uric acid(μmol/L)	1.000 (0.997, 1.004)	0.821	Not Selected	
TG (mmol/L)	0.453 (0.192, 1.072)	0.072	Not Selected	
TC (mmol/L)	0.656 (0.397, 1.081)	0.098	Not Selected	
HDL-c (mmol/L)	2.353 (0.287, 19.303)	0.426	Not Selected	
LDL-c (mmol/L)	0.646 (0.349, 1.196)	0.164	Not Selected	
GA (%)	1.244 (1.141, 1.357)	<0.001	6.768 (1.216, 37.678)	0.029
HbA1c (%)	9.429 (3.351, 26.532)	<0.001	0.008 (0.001, 0.959)	0.048
Disease history				
Previous MI [n (%)]	a*	0.998	Not Selected	
Previous PCI [n (%)]	a*	0.099	Not Selected	
Previous CABG [n (%)]	b*		Not Selected	

Previous stroke [n (%)]	1.013 (0.276, 3.718)	0.984	Not Selected

* a is not applicable. b is a constant.

Table 3. Univariate and Multivariate Cox Regression Analyses for MACEs.				
Variable	Univariate Analysis		Multivariate Analysis	
	OR (95%CI)	*p*	OR (95%CI)	*p*
Age (years)	1.045 (1.000, 1.091)	0.050	Not Selected	
sex	3.737 (1.483, 9.418)	0.005	5.450 (0.609, 48.794)	0.130
DM [n (%)]	5.599 (2.100, 14.926)	0.001	0.059 (0.001, 4.386)	0.198
HBP [n (%)]	0.270 (0.101, 0.719)	0.009	0.804 (0.147, 4.409)	0.802
Smoking [n (%)]	0.290 (0.095, 0.881)	0.029	0.748 (0.161, 3.483)	0.712
Heart rate (beats/min)	1.039 (1.006, 1.073)	0.019	0.988 (0.924, 1.056)	0.717
SBP (mmHg)	0.995 (0.972, 1.019)	0.709	Not Selected	
DBP (mmHg)	0.947 (0.904, 0.991)	0.020	0.922 (0.838, 1.015)	0.096
HS-TnT(pg/mL)	1.000 (1.000, 1.000)	0.001	1.001 (1.000, 1.003)	0.064
CKMB (ng/mL)	1.008 (1.003, 1.014)	0.002	0.989 (0.952, 1.027)	0.567
MYO (ng/mL)	1.004 (1.003, 1.006)	<0.001	1.005 (1.001, 1.030)	0.027
HCY(μmol/L)	0.879 (0.767, 1.006)	0.061	Not Selected	
Blood glucose (mmol/L)	1.100 (0.920, 1.314)	0.295	Not Selected	
Creatinine(μmol/L)	1.001 (0.976, 1.025)	0.968	Not Selected	
eGFR	0.965 (0.942, 0.989)	0.005	0.981 (0.934, 1.030)	0.432
Uric acid(μmol/L)	1.000 (0.996, 1.004)	0.875	Not Selected	
TG (mmol/L)	0.456 (0.197, 1.054)	0.066	Not Selected	
TC (mmol/L)	0.672 (0.419, 1.076)	0.098	Not Selected	
HDL-c (mmol/L)	2.158 (0.299, 15.561)	0.445	Not Selected	
LDL-c (mmol/L)	0.666 (0.373, 1.188)	0.168	Not Selected	
GA (%)	1.243 (1.158, 1.335)	<0.001	1.773 (1.294, 2.430)	<0.001
HbA1c (%)	1.460 (1.181, 1.804)	<0.001	0.501 (0.211, 1.192)	0.118
Disease history				
Previous MI [n (%)]	0.043 (0.000, 55.112)	0.389	Not Selected	
Previous PCI [n (%)]	0.047 (0.000, 2691.184)	0.584	Not Selected	
Previous CABG [n (%)]	a*		Not Selected	

Previous stroke [n (%)]	0.933 (0.305, 3.644)	0.933	Not Selected
* a is a constant.			

Figures

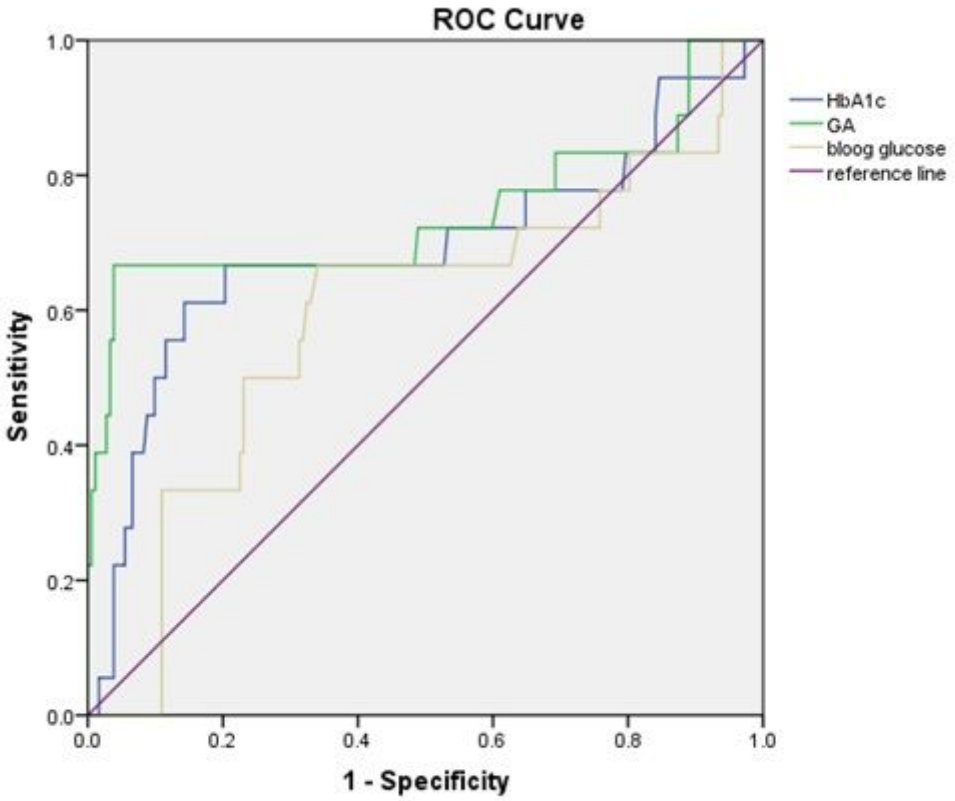

Figure 1.

Figure 1

ROC curves of HbA1c, GA and ABG. The AUC of GA is 0.743 (95%CI, 0.578-0.907; p=0.001).The AUC ofABG is 0.593 (95%CI, 0.441-0.745; p=0.192). The AUC of HbA1c is 0.689 (95%CI, 0.530-0.849; p=0.008). The cutoff value of GAis 23.54 (sensitivity, 33.3%; specificity, 96.2%). The cutoff valueof ABG is 6.51 (sensitivity, 33.3%; specificity, 65.9%). The cutoff value of HbA1c is 7.46 (sensitivity, 61.1%; specificity, 85.7%).

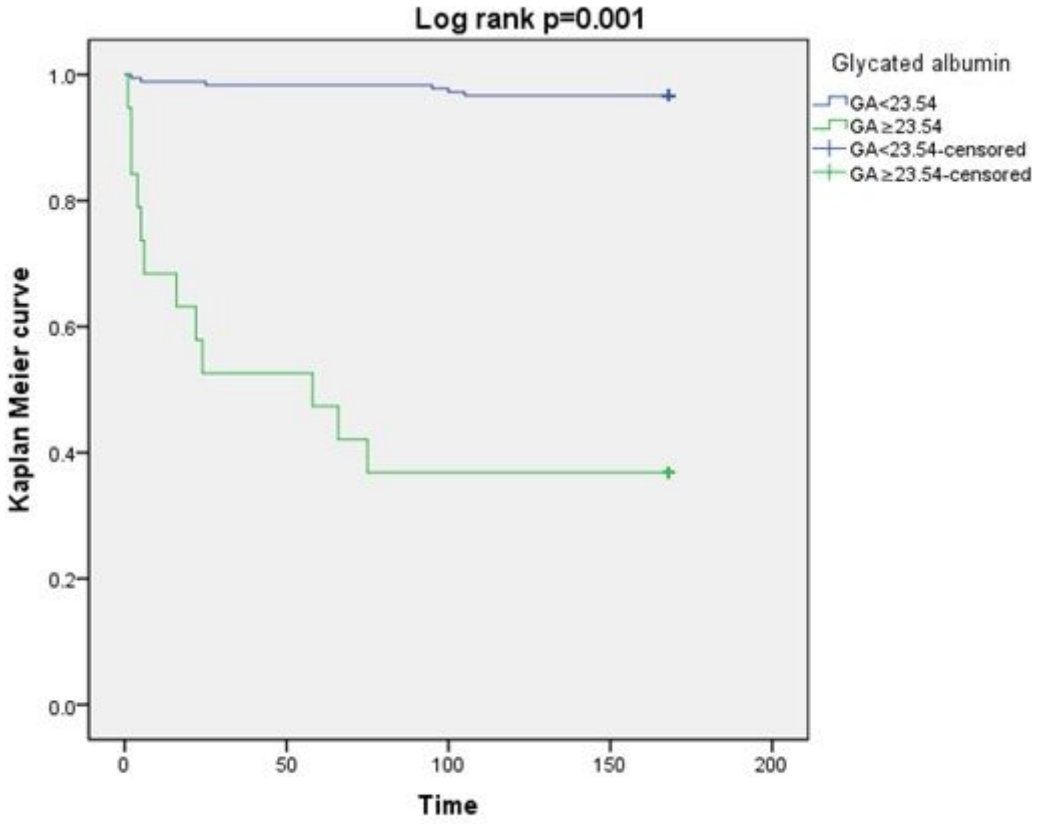

Figure 2

Figure 2

Kaplan Meier curve of GA. We conducted K-M curveand log rank test for cumulative incidence of in-hospital MACEs of GA (p=0.001). General observation time is 7 days (168 hours).

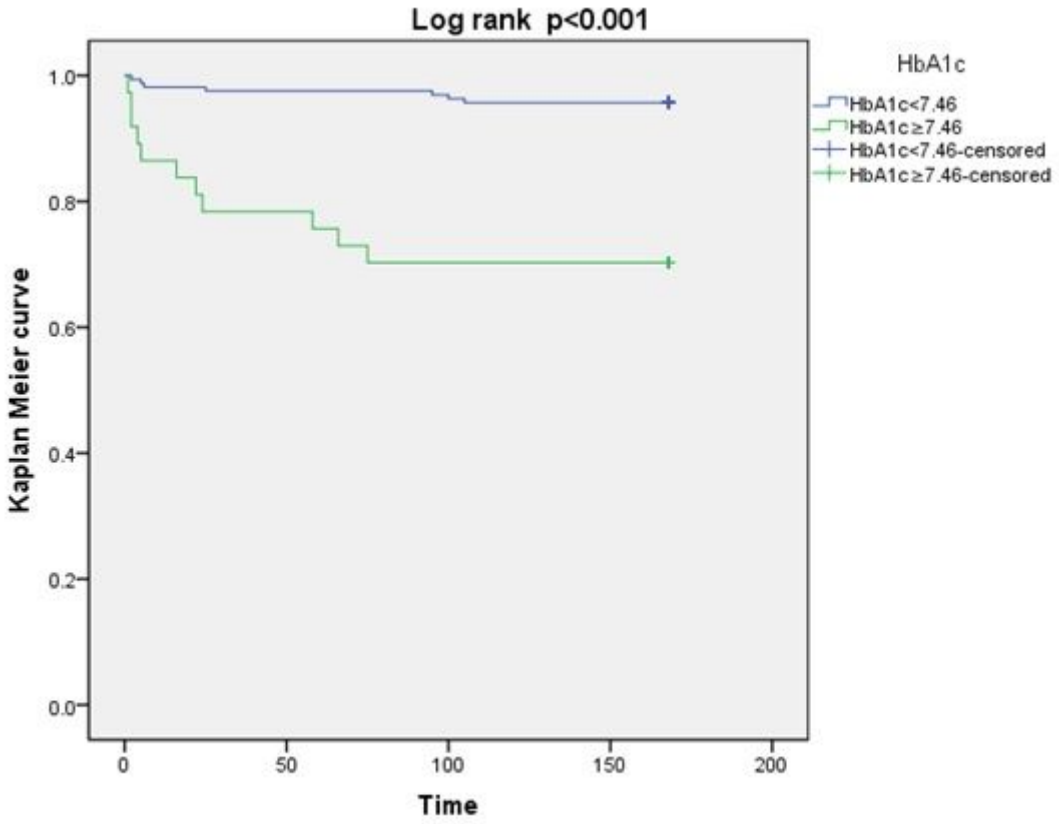

Figure 3.

Figure 3

Kaplan Meier curve of HbA1c. We conducted K-M curve and log rank test for cumulative incidence of in-hospital MACEs of HbA1c (p<0.001). General observation time is 7 days (168 hours).

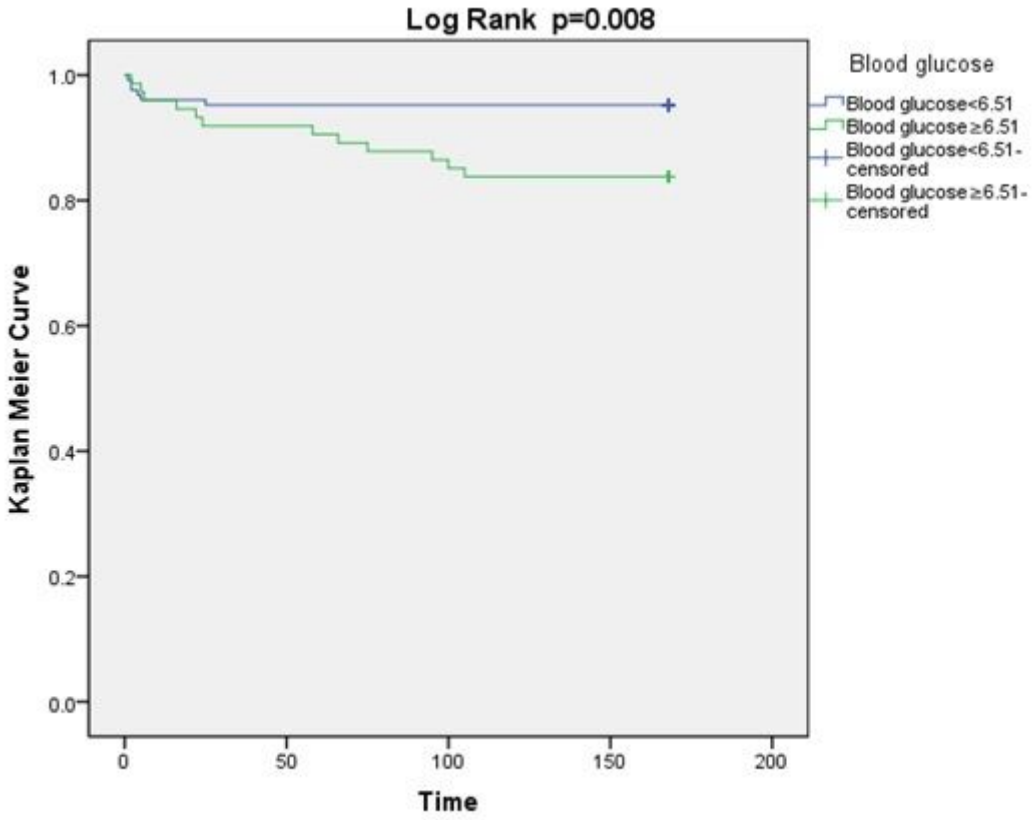

Figure 4.

Figure 4

Kaplan Meier curve of ABG. We conducted K-M curve and log rank test for cumulative incidence of in-hospital MACEs of ABG (p=0.008). General observation time is 7 days (168 hours).