Observational Study

Inflammation-based Glasgow Prognostic Score in patients with acute ST-segment elevation myocardial infarction
A prospective cohort study

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Abstract

The inflammation-based Glasgow Prognostic Score (GPS), which involves C-reactive protein and serum albumin levels, has been reported to be a strong independent predictor of mortality in many cancers. This study aimed to investigate whether the GPS is associated with mortality in patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI).

In this study, 406 consecutive patients with STEMI at our emergency department (ED) who were undergoing pPCI were prospectively enrolled and assigned a GPS of 0, 1, or 2. Kaplan–Meier survival and multivariable Cox regression analyses were used to evaluate the associations between the GPS and long-term mortality.

Twenty-three patients (5.7%) died at the hospital, and 37 (9.7%) died during follow-up (14.4 [9.3–17.6] months). Compared with patients with a lower GPS, those with a higher GPS had significantly higher in-hospital mortality (GPS = 0 vs GPS = 1 vs GPS = 2: 3.3% vs 6.3% vs 28.0%, $P < .001$), follow-up mortality (4.6% vs 14.3% vs 55.6%, $P < .001$), and cumulative mortality (9.6% vs 21.1% vs 71.1%, $P < .001$). Multivariable Cox regression analysis revealed that in patients with a GPS of 1 and 2 (versus 0), the multivariable adjusted hazard ratios (HR) for all-cause mortality were 2.068 (95% CI: 1.082–3.951, $P = .028$) and 8.305 (95% CI: 4.017–17.171, $P < .001$), respectively, after controlling for all of the confounding factors. Subgroup analysis showed that a higher GPS was associated with an increased risk of cumulative mortality in the different subgroups.

The GPS on admission may be useful for stratifying the risk of adverse outcomes in patients with STEMI undergoing pPCI in the ED.

Abbreviations: AF = atrial fibrillation, AMI = acute myocardial infarction, AUC = area under the curve, BUN = blood urea nitrogen, CI = confidence interval, CRP = C-reactive protein, cTnT = cardiac troponin T, ED = emergency department, GPS = Glasgow Prognostic Score, GRACE = Global Registry of Acute Coronary Events, HR = hazard ratios, LVEF = left ventricular ejection fraction, NT-proBNP = N-terminal pro-brain natriuretic peptide, PCI = percutaneous coronary intervention, PNI = prognostic nutritional index, pPCI = primary percutaneous coronary intervention, ROC = receiver operating characteristic, SA = serum albumin, STEMI = ST-segment elevation myocardial infarction, TC = total cholesterol, WBC = white blood cell count.

Keywords: acute myocardial infarction, biomarkers, Glasgow Prognostic Score, mortality

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1. Introduction

Ischemic cardiovascular disease is one of the most common causes of death and is accountable for up to 20% of all deaths.[1] Despite the progress in the techniques of percutaneous coronary intervention (PCI) and seasonable revascularization,[2] the in-hospital mortality rate is still 4% to 12%, and the first-year death rate is about 10% [1] in patients with acute ST-segment elevation myocardial infarction (STEMI). Although traditional risk factors, such as old age, female sex, and diabetes, can be used to predict adverse outcomes of patients with STEMI,[3–6] they are not capable of assessing full nature and severity of the STEMI. Hence, there is great interest in identifying simple and quick bedside biomarkers that could assist in predicting STEMI outcomes on admission so that appropriate treatment can be implemented. Coronary atherosclerosis is the main cause of STEMI, and one of the most important pathophysiological factors is inflammation.[7,8] Patients with more severe inflammation were found to have more vulnerable plaques than those with less severe inflammation.[9] Inflammation also consistently acts on the whole process of cancer, including its occurrence and development.[10,11] Previous studies have demonstrated that more severe inflammation is associated with more advanced cancer and a poorer prognosis.[12] Several common inflammatory

markers in acute myocardial infarction (AMI) and different cancers are associated with prognosis, suggesting that these diseases have a similar inflammation-mediated pathophysiological mechanisms.[13–19]

The inflammation-based Glasgow Prognostic Score (GPS), which is composed of C-reactive protein (CRP) and serum albumin (SA), has been reported as a strong independent predictor of long-term mortality in many tumor diseases.[20] CRP and SA can be used to predict the adverse outcome of AMI,[17,21] and examination of these parameters is sensitive, specific, and repeatable at a low cost. However, there is a paucity of relevant research showing that the combination of those 2 parameters or GPS alone has the same or a stronger predictive power in patients with STEMI than does CRP or SA alone. Hence, this study was conducted to confirm whether the GPS is also associated with mortality in patients with acute STEMI undergoing primary percutaneous coronary intervention (pPCI).

2. Methods

This single-center, prospective cohort study was designed to evaluate whether the GPS could predict in-hospital and long-term mortality in patients with STEMI. The study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the Human Ethical Committee of West China Hospital of Sichuan University. All study subjects provided written informed consent.

2.1. Patient selection

On the basis of our pre-experiment, the mortality of STEMI patients with a GPS of 0 was about 50% and that of those with a GPS of 2 was about 5%. To satisfy this difference with 80% power and 5% significance (2-tailed), 15 patients were required. Because STEMI patients with a GPS of 2 account for about 5% of our cohort, we planned to recruit 300 patients with STEMI in this study. The sample size was calculated using MedCalc Statistical Software version 15.2.2 (https://www.medcalc.org). From May 2016 to September 2017, 406 patients who were diagnosed as having spontaneous STEMI (type 1), according to the Third Universal Definition of Myocardial Infarction,[22] and were admitted to the Emergency Department of the West China Hospital were recruited. Inclusion criteria were onset of STEMI less than 12 hours before admission, first admission after the onset of STEMI symptoms, and patients who voluntarily signed the informed consent. Exclusion criteria were a history of neoplasm, cirrhosis, nephrotic syndrome, autoimmune disease, or systemic inflammatory disease; recent infectious disease, eating disorder, or surgery; patients who refused PCI or received coronary artery bypass grafting; and patients diagnosed as having non-spontaneous STEMI after PCI (Fig. 1).

2.2. Data collection

First, an electrocardiogram was promptly obtained on admission using an electrocardiograph (iMAC1200, Wuhan Zoncare Bio-Medical, Hubei Sheng, China). Second, we recorded patients' vital signs, medical history, and Killip class. Then, we collected data from laboratory examination, including the hemoglobin level, white blood cell count (WBC), neutrophil count, lymphocyte count, and platelet count, which were analyzed using an automated hematology analysis system (LH750, Beckman Coulter Inc., Brea, CA). The fibrinogen level was measured
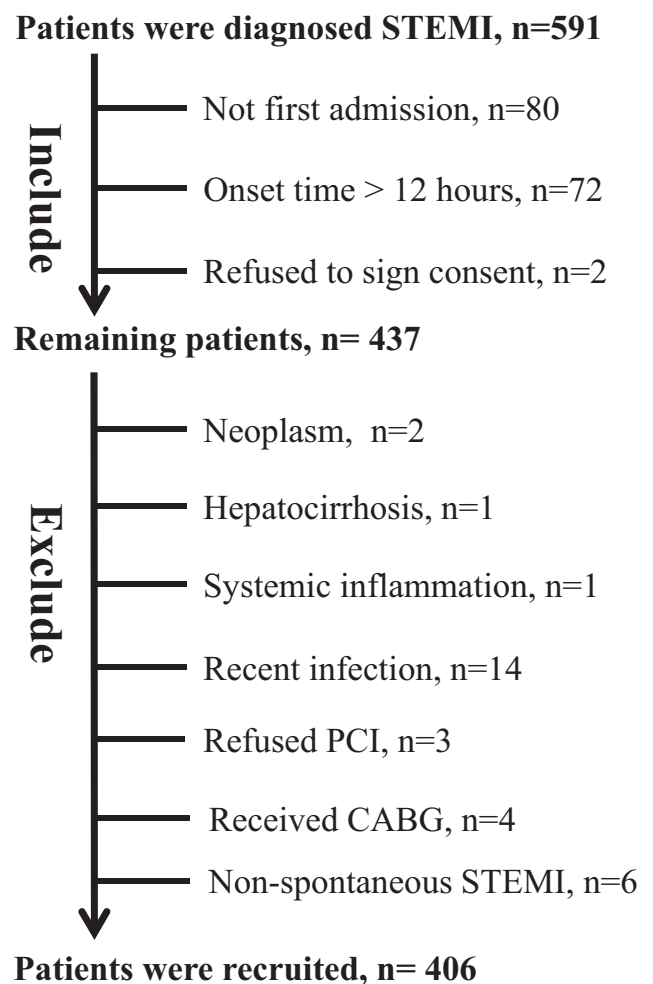
Patients were diagnosed STEMI, n=591

Include
- Not first admission, n=80
- Onset time > 12 hours, n=72
- Refused to sign consent, n=2

Remaining patients, n= 437

Exclude
- Neoplasm, n=2
- Hepatocirrhosis, n=1
- Systemic inflammation, n=1
- Recent infection, n=14
- Refused PCI, n=3
- Received CABG, n=4
- Non-spontaneous STEMI, n=6

Patients were recruited, n= 406

Figure 1. Flow diagram for recruitment of patients.

using a Sysmex CA-7000 analyzer (Siemens Healthcare Diagnostics, Eschborn, Germany); levels of creatinine kinase, albumin, blood urea nitrogen (BUN), creatinine, high-density lipoprotein, triglyceride, and total cholesterol (TC) were analyzed using an Architect c16000 analyzer (Abbott Diagnostics, Dallas, TX); the CRP level was determined using a Cobas S6000 Hitachi analyzer (Roche Diagnostics, Indianapolis, IN); the levels of creatine kinase-myocardial band isoenzyme, cardiac troponin T (cTnT), and N-terminal pro-brain natriuretic peptide (NT-proBNP) were analyzed using an immunology analyzer (Cobas E601, Roche Diagnostics) with the electrochemiluminescence method; and the urine protein level was analyzed using a UF1000 urinalysis analyzer (Sysmex Corporation, Kobe, Japan). The left ventricular ejection fraction (LVEF) was calculated using the biplane Simpson method with the Philips E33 echocardiography machine (Philips Medical Systems, Bothell, WA). Data on coronary artery involvement were obtained after PCI. Finally, The Global Registry of Acute Coronary Events (GRACE),[23] Gensini [24] scores, prognostic nutritional index (PNI),[25] and postoperative atrial fibrillation (AF) were calculated.

2.3. Percutaneous coronary intervention and treatment

All patients with onset of STEMI <12 hours received a loading dose of aspirin (300 mg) and/or clopidogrel (300–600 mg) on

admission. All PCI procedures were performed by experienced interventional cardiologists who used a transradial approach and drug-eluting stents. Subsequently, all patients received a daily dose of aspirin (100 mg), clopidogrel (75 mg), and antilipoid (10–20 mg) if there were no contraindications. Other medications, such as a β-blocker, calcium-channel blocker, angiotensin-converting enzyme inhibitor, and angiotensin II receptor blocker, were given on the basis of each patient's condition. Finally, we administered corresponding medication for different diseases, such as diabetes, hypertension, cardiac insufficiency, arrhythmia, and postoperative infection.

2.4. Definition of the Glasgow Prognostic Score

Briefly, patients with an increased CRP level (>10 mg/L) and low SA level (<35 g/L, hypoalbuminemia) were assigned a GPS of 2. Patients with only one of these biochemical abnormalities were allocated a GPS of 1. Patients with neither of these abnormalities were assigned a GPS of 0.[20]

2.5. Follow-up and primary endpoint

The primary endpoint was all-cause death. Data on clinical characteristics and in-hospital outcomes were collected during patient revisits to the hospital. If patients were not readmitted or could not be contacted directly, their relatives were interviewed in person or over the telephone. Finally, we plan to complete a five-year follow-up.

2.6. Statistical analysis

Data were calculated as frequencies and percentages for categorical variables and as mean ± standard deviation or median with interquartile range (25th–75th percentile) for continuous variables. Patient characteristics were compared according to the GPS. Distribution of data was assessed by P–P (probability–probability or percent–percent) plot in SPSS research. If the mean accurately represented the center of distribution, the parametric test was considered. If the median suitably represented the center of distribution, the nonparametric test was considered. Parametric patient characteristics were compared using one-way analysis of variance, whereas non-parametric characteristics were compared using the Kruskal–Wallis test. Categorical data were compared using the chi-square (2) test. The receiver operating characteristic (ROC) curve contrast of the GPS, CRP level, SA level, cTnT level, NT-proBNP level, Gensini score, GRACE score, and PNI was evaluated according to the area under the curve (AUC). Stratified Kaplan–Meier curves were constructed on the basis of the GPS. Cox proportional hazard models were employed to determine whether the GPS was related to time to mortality during the study period. To construct the Cox model, univariate models for each predictive variable were used, with mortality as the outcome variable. Moreover, the variables that were significant (P < .05) in the univariate Cox models were entered into a multivariable Cox model. From the multivariable model, we identified variables that were significant (P < .05) predictors of mortality. In a different subgroup analysis, patients were grouped according to age, heart rate, Killip class, creatinine level, BUN level, LVEF, Gensini score, GRACE score, and cumulative survival of the GPS calculated by Kaplan–Meier survival analysis. Data analysis was performed using SPSS Statistics for Windows, version 22.0 (SPSS, Inc., Chicago, IL).

3. Results

3.1. Baseline patient characteristics

Overall, 406 consecutive patients with STEMI (mean age, 62.63 ± 12.98 years; 308 men) were included in the study. Of these patients, 23 (5.7%) died while hospitalized, and 37 (9.7%) died during the follow-up period (median follow-up time, 14.4 [9.3–17.6] months). Of these, 269 patients (66.2%) had a GPS of 0, 112 (27.6%) had a GPS of 1, and 25 (6.2%) had a GPS of 2 on admission.

Table 1 shows the baseline characteristics according to the GPS. Compared to patients with a lower GPS, those with a higher GPS were older (P < .001) and more likely to have a lower body mass index (P < .021), quicker heart rate (P < .001), higher frequency of a Killip class ≥2 (P < .001), higher WBC count (P < .001), higher neutrophil count (P = .001), lower lymphocyte count (P = .008), lower hemoglobin level (P < .001), higher fibrinogen level (P < .001), higher blood glucose level (P = .009), higher creatinine level (P = .017), higher BUN level (P < .001), higher triglyceride level (P = .002), higher TC level (P < .001), higher NT-proBNP level (P < .001), higher cTnT level (P < .001), lower LVEF (P < .001) on admission, less affected left anterior descending artery (P = .001), less affected left circumflex artery (P = .001), less affected right coronary artery (P < .003), and more affected left main coronary artery (P = .001). Other clinical characteristics did not vary significantly by the GPS (Table 1).

3.2. GPS and other risk factors

In the ROC curve analyses, the AUC of the GPS (0.846, 95% confidence interval [CI]: 0.759–0.925, P < .001) was similar to that of the GRACE score (0.849, 95% CI: 0.762–0.931, P < .001) but larger than that of the SA level (0.272, 95% CI: 0.201–0.346, P = .001), CRP level (0.811, 95% CI: 0.763–0.941, P < .001), NT-proBNP level (0.822, 95% CI: 0.765–0.931, P < .001), cTnT level (0.715, 95% CI: 0.603–0.814, P = .001), Gensini score (0.746, 95% CI: 0.667–0.826, P < .001), and PNI (0.775, 95% CI: 0.689–0.861, P < .001).

Compared with patients with a lower GPS, those with a higher GPS had higher GRACE and Gensini scores. For those with GPSs of 0, 1, and 2, the respective mean GRACE scores were 152.69 ± 38.89, 171.44 ± 44.06, and 209.48 ± 32.03 (P < .001), and the respective mean Gensini scores were 74.58 ± 51.25, 77.06 ± 52.29, and 124.29 ± 71.45 (P < .001) (Fig. 2A and B). In total, 26 patients (6.4%) developed postoperative AF. For those with GPSs of 0, 1, and 2, the number of patients with AF were 19 (7.1%), 11 (9.8%), and 8 (32.0%), respectively (P < .001) (Fig. 2C).

3.3. GPS and all-cause mortality

The in-hospital mortality (GPS = 0 vs GPS = 1 vs GPS = 2: 3.3% vs 6.3% vs 28.0%, P < .001) (Fig. 3A) and follow-up mortality (4.6% vs 14.3% vs 55.6%, P < .001) (Fig. 3B) of patients gradually increased with an increase in the GPS. The cumulative mortality was consistently more significant (9.6% vs 21.1% vs 71.1%, P < .001) in patients with a higher GPS than in those with a lower GPS (Fig. 4).

Univariate Cox models indicated that the GPS was positively associated with the hazard of all-cause mortality, and other variables were significant in the univariate Cox models. The multivariable Cox regression analysis revealed that in patients with a GPS of 1 and 2 (versus 0), the multivariable adjusted hazard ratios (HR) for all-cause mortality were 2.068 (95% CI:

Table 1

Relationships between clinical characteristics and the Glasgow Prognostic Score (GPS) in patients with ST-segment elevation myocardial infarction.

Variable	GPS=0 (n=269)	GPS=1 (n=112)	GPS=2 (n=25)	P
Age, years	62.38±13.06	66.31±14.59	71.88±9.23	<.001
Males, n (%)	210 (78.1%)	79 (70.5%)	19 (76.0%)	.294
BMI, kg/cm^2	24.00±2.97	23.61±4.53	21.81±3.20	.021
Smoking, n (%)	135 (50.2%)	54 (48.2%)	13 (52.0%)	.955
Drinking, n (%)	51 (19.0%)	16 (14.3%)	4 (16.0%)	.779
Hypertension, n (%)	158 (58.7%)	55 (49.5%)	12 (48.0%)	.192
Diabetes, n (%)	50 (18.6%)	22 (19.6%)	6 (24.0%)	.798
SBP, mm Hg	124.83±22.37	123.54±26.51	114.58±19.56	.122
DBP, mm Hg	78.95±16.15	77.45±16.77	74.33±13.25	.336
Heart rate, minutes	77.20±17.50	85.40±20.10	96.56±16.45	<.001
Killip class ≥ 2, n (%)	82 (30.5%)	49 (43.8%)	17 (68.0%)	<.001
Laboratory findings				
WBC, *10^9/L	10.35±3.37	10.93±3.78	13.70±5.86	<.001
Neutrophil count, *10^9/L	8.37±3.24	8.895±3.74	11.33±5.59	.001
Hemoglobin, g/L	138.56±19.87	133.12±20.81	107.98±47.40	<.001
Platelet count, *10^{12}/L	174.67±84.83	177.28±67.05	165.86±94.74	.849
Lymphocyte count, *10^{12}/L	1.68±0.73	1.39±0.65	1.12±0.84	.008
Fibrinogen, g/L	2.76±0.93	4.15±1.77	4.82±1.71	<.001
Blood glucose, mmol/L	8.91±3.36	9.86±4.66	12.67±5.32	.009
Creatinine, μmol/L	83.18±43.53	106.21±124.51	104.72±49.48	.017
Blood urea nitrogen, mmol/L	6.32±2.60	7.31±5.93	9.60±4.80	<.001
Triglycerides, mmol/L	2.16±2.26	1.55±0.99	1.11±0.38	.002
Total cholesterol, mmol/L	4.65±1.07	4.41±1.21	3.58±0.82	<.001
HDL, mmol/L	1.17±0.34	1.18±0.35	1.18±0.22	.943
NT-proBNP, pg/mL	1028 (820–1235)	3264 (2278–4249)	10289 (6016–14561)	<.001
Cardiac troponin T, pg/mL	1153 (904–1402)	1971 (1488–2454)	3235 (2040–4429)	<.001
Creatinine kinase, IU/L	690 (571–809)	804 (619–990)	649 (253–1044)	.550
CK-MB, U/L	55.96±81.20	56.74±80.73	28.84±48.55	.252
Proteinuria, (%)	66 (34.4%)	28 (36.8%)	6 (33.3%)	.651
Discharge medication				
Aspirin, n (%)	250 (92.9%)	106 (94.6%)	21 (84.0%)	.174
Clopidogrel, n (%)	232 (86.2%)	98 (87.5%)	22 (88.0%)	.929
β-blockers, n (%)	147 (54.6%)	59 (52.7%)	11 (54.0%)	.583
Antilipoid, n (%)	245 (93.5%)	104 (94.5%)	22 (88.0%)	.725
LVEF, (%)	54.10±10.27	49.30±12.05	39.95±12.24	<.001
Narrowed coronary artery				
Left main, n (%)	33 (13.1%)	13 (12.3%)	9 (36.0%)	.001
LAD, n (%)	218 (82.9%)	90 (84.9%)	11 (44.0%)	.001
Left circumflex, n (%)	172 (65.9%)	52 (52.8%)	6 (24.0%)	.001
Right coronary artery, n (%)	187 (72.1%)	78 (73.6%)	8 (32.0%)	.003

BMI = body mass index, CK-MB = creatinine kinase-myocardial band isoenzyme, DBP = diastolic blood pressure, HDL = high-density lipoprotein, GPS = Glasgow Prognostic Score, SBP = systolic blood pressure, LAD = left anterior descending, LVEF = left ventricular ejection fraction, NT-proBNP = N-terminal pro-brain natriuretic peptide, WBC = white blood cell count.

1.082–3.951, P = .028) and 8.305 (95% CI: 4.017–17.171, P < .001), respectively, after controlling for all of the confounding factors (Table 2). Other predictors of all-cause mortality in the multivariable Cox model were age, the Killip class, BUN level, creatinine level, and LVEF (Table 2).

3.4. Subgroup analysis

Subgroup analysis of the cumulative survival rate was based on the age, heart rate, Killip class, creatinine level, BUN level, LVEF, Gensini score, and GRACE score of patients with STEMI by the GPS. The GPS remained an independent predictor of mortality on subgroup analysis, and all high-risk subgroups had a higher mortality (Table 3).

4. Discussion

Similar to other studies on cancers, our study showed that the GPS successfully predicted adverse outcomes in STEMI patients undergoing pPCI, and this was possibly based on the potential inflammatory mechanism in the whole course of AMI. In our study, patients with a higher GPS had higher in-hospital, follow-up, and cumulative mortalities. After adjusting for confounding factors, the increased GPS was a significant dominant factor of all-cause mortality. As we assumed, the GPS had a more convincing predictive capability than the SA, CRP, NT-proBNP, or cTnT level alone. Current research has revealed that PNI, as a nutritional marker combining SA and lymphocyte, is a prognostic predictor in patients with STEMI[25]; however, GPS seems to be stronger than PNI. Patients with a higher GPS had higher GRACE, Gensini scores, and incidence of postoperative AF, suggesting that the GPS could reflect the complex clinical baseline characteristics of patients, the severity of coronary atherosclerotic stenosis, and the inflammatory state which plays an important role in the myocardial remodeling process leading to AF.[26] In addition, the GPS had a stronger prognostic ability in the high-risk group than in the low-risk group; hence, we
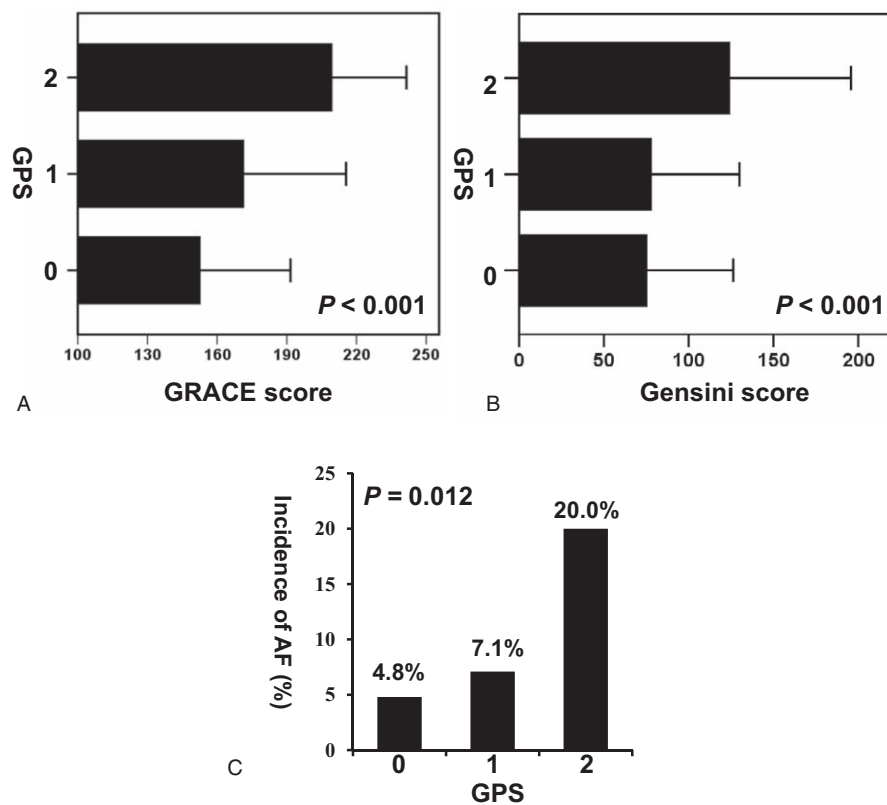
Figure 2. (A) The Global Registry of Acute Coronary Events (GRACE) score, (B) Gensini score, and (C) postoperative incidence of atrial fibrillation (AF) in different Glasgow Prognostic Score (GPS). AF = atrial fibrillation, GRACE = Global Registry of Acute Coronary Events, GPS = Glasgow Prognostic Score.

conclude that the GPS may be more predictive in critical patients. Despite timely reperfusion treatment, it is difficult for patients with a GPS of 2 to have a good prognosis (their median survival time was 3 months), indicating that traditional treatment is ineffective for such patients.

The formation of many cancers and coronary heart disease is accompanied by inflammation ;[10] subsequently, inflammation contributes to the whole disease progression.[7,11] Expectedly, destruction of the surrounding tissue by the growing tumor and

ruptured atherosclerotic plaques lead to microcirculatory disturbance, followed by aggravated systemic inflammation.[7,27] In AMI, the inflammatory response can directly affect the transfer of lipoprotein within the vessel wall, increase the binding of lipoprotein to the endothelium and smooth muscle cells, induce deposition of lipid-laden foam cells in the subendothelial space, and accelerate atherosclerotic formation.[7,8] Inflammation plays a critical role in the instability of atherosclerotic plaque and the adhesion of thrombus to the surface of damaged plaques.[9]
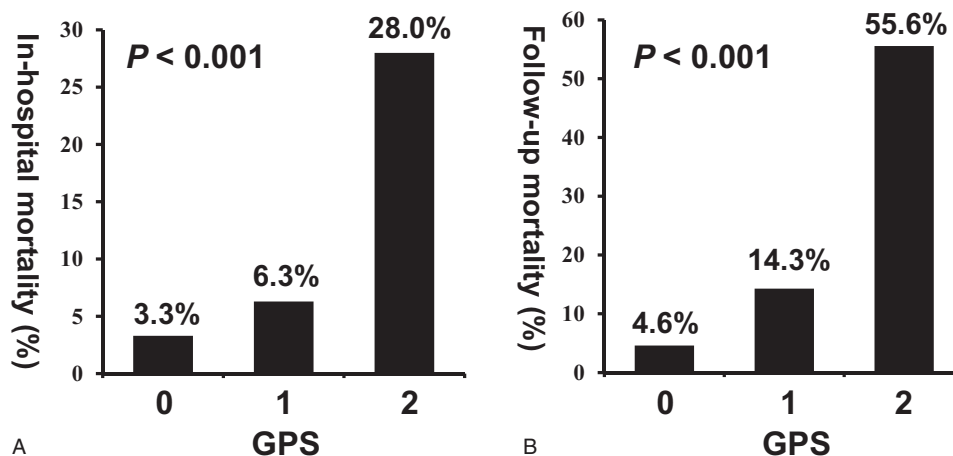

Figure 3. (A) In-hospital and (B) follow-up mortality in different Glasgow Prognostic Score (GPS) patients with ST-segment elevation myocardial infarction. GPS = Glasgow Prognostic Score.
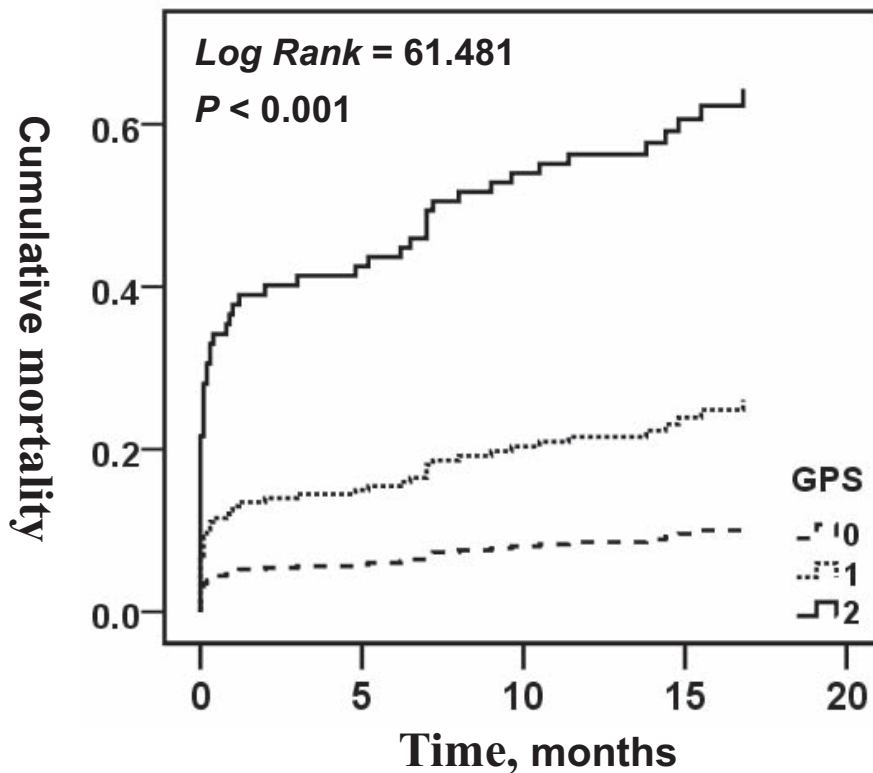
Figure 4. Kaplan–Meier analysis survival curve according to different Glasgow Prognostic Score (GPS) in patients with ST-segment elevation myocardial infarction. GPS = Glasgow Prognostic Score.

Furthermore, inflammation can attenuate myocardial ischemia-reperfusion injury, indicating that very severe inflammation possibly causes a larger infarction area.[28] In previous reports, many inflammation-related markers, such as the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, interleukin-6 level, CRP level, and SA level, were related to AMI [13–17] and certain cancers.[18,19] In our study, similar to those inflammatory markers, GPS, which includes the CRP and SA levels, could also reflect the inflammatory state and

predict the survival time in STEMI on the basis of the inflammatory pathophysiological mechanism.

As one of the components of the GPS, SA is the main material that maintains plasma oncotic pressure and carries other massive materials and components in acute and chronic inflammatory reactions.[29,30] Furthermore, SA has antioxidant and anti-inflammatory properties; thus, hypoalbuminemia may result in deteriorating oxidative damage and inflammation.[31–34] SA stabilizes the completeness of the microvasculature and coactions

Table 2

Cox regression of all-cause mortality for patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention.

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
GPS	–	–	<.001	–	–	.002
GPS (1 vs 0)	2.684	1.476–4.882	.001	2.068	1.082–3.951	.028
GPS (2 vs 0)	13.148	6.894–25.075	<.001	8.305	4.017–14.171	<.001
Age	1.057	1.034–1.080	<.001	1.048	1.024–1.072	<.001
Heart rate	1.026	1.014–1.039	<.001	1.007	0.516–2.405	.353
Killip class	3.552	2.089–6.040	<.001	1.478	1.080–2.021	.015
Hemoglobin	0.981	0.974–0.988	<.001	1.001	0.991–1.011	.896
Neutrophil count	1.114	1.052–1.178	<.001	1.024	0.940–1.114	.588
Creatinine	1.003	1.002–1.004	<.001	1.003	1.001–1.005	.020
Blood urea nitrogen	1.072	1.047–1.098	<.001	1.083	1.037–1.131	<.001
BNP (per 100/pg/mL)	1.008	1.006–1.011	<.001	0.996	0.987–1.005	.392
CTnT (per 100/pg/mL)	1.015	1.007–1.023	<.001	1.008	0.996–1.020	.192
LVEF	0.905	0.882–0.929	<.001	0.950	0.909–0.993	<.001
Left main	2.048	1.093–3.837	.025	1.724	0.852–3.486	.130

cTnT = cardiac troponin T, GPS = Glasgow Prognostic Score, LVEF = left ventricular ejection fraction, NT-proBNP = N-terminal pro-brain natriuretic peptide.

Table 3

Subgroup analysis of cumulative survival in patients with ST-segment elevation myocardial infarction by Glasgow Prognostic Score (GPS).

Variable	Cumulative survival, (%)			Log rank	P
	GPS=0	GPS=1	GPS=2		
Age ≤ 60 years old	96.4	92.5	75.0	5.996	.014
Age > 60 years old	85.8	72.5	19.6	69.408	<.001
Heart rate ≤ 78*, minutes	94.3	80.4	40.0	26.672	<.001
Heart rate > 78*, minutes	86.3	77.5	25.0	58.331	<.001
Killip class = 1	93.7	86.5	31.3	26.911	<.001
Killip class > 1	83.1	69.0	26.5	63.206	<.001
Creatinine ≤ 78*, μmol/L	91.3	86.2	25.0	18.863	<.001
Creatinine > 78*, μmol/L	89.1	72.2	32.3	38.868	<.001
BUN ≤ 5.8*, mmol/L	92.7	86.9	40.0	23.562	<.001
BUN > 5.8*, mmol/L	87.9	70.4	24.6	54.611	<.001
LVEF ≤ 0.44*	92.5	86.8	50.0	19.414	<.001
LVEF > 0.44*	77.6	60.5	19.0	22.313	<.001
Gensini score ≤ 67*	93.6	88.5	71.4	12.313	.002
Gensini score > 67*	86.5	68.8	25.0	21.840	<.001
GRACE score ≤ 156*	95.0	92.1	50.0	6.872	.009
GRACE score > 156*	83.5	70.0	27.3	42.856	<.001

BUN = blood urea nitrogen, GPS = Glasgow Prognostic Score, GRACE = the Global Registry of Acute Coronary Events, LVEF = left ventricular ejection fraction.
* Median.

on the endothelium and myocardium by its oncotic nature.[35,36] In addition, SA is the most sensitive indicator of one's nutritional status, which has a significant impact on the prognosis of cancer [37] and AMI.[25] Hypoproteinemia stimulates the synthesis of lipid and coagulation factors, leading to hyperlipidemia and hypercoagulability, which results in the formation of atherosclerotic plaques and thrombosis.[38] Moreover, hypoproteinemia may affect the outcome of reperfusion treatment [39] and anticancer therapy.[35]

As a sensitive and nonspecific biomarker of inflammation, CRP is a very important risk factor for AMI,[21] and an increased CRP level is negatively correlated with survival time, as reported in various cancers.[12] CRP induces peripheral blood monocytes to aggregate neutrophil and product tissue factor, activates the coagulation system, mediates enhanced expression of adhesion molecules, reduces nitric oxide production, and participates in

the oxidative stress process, resulting in endothelial dysfunction and thrombus formation.[40,41] Additionally, CRP directly promotes the proliferation and tissue factor expression of endothelial cells and smooth muscle cells and induces the pro-atherothrombotic phenotype of the vascular wall cells.[42] Researchers have shown that adipokines, such as leptin, induce the production of CRP by coronary endothelial cells, increasing the local concentration of CRP, which directly promotes the expression of adhesion molecules and tissue factors and accelerates atherothrombosis in the coronary arteries.[43–45]

These concepts may be the potential common mechanisms of SA and CRP in patients with STEMI that lead to adverse survival (Fig. 5). Although the GPS effectively predicted the prognosis of AMI, it is based on only 2 markers. Recent studies reported that urotensin II and Pentraxin-3 are independent prognostic factors of AMI[46,47]; the pathophysiological mechanism associated with
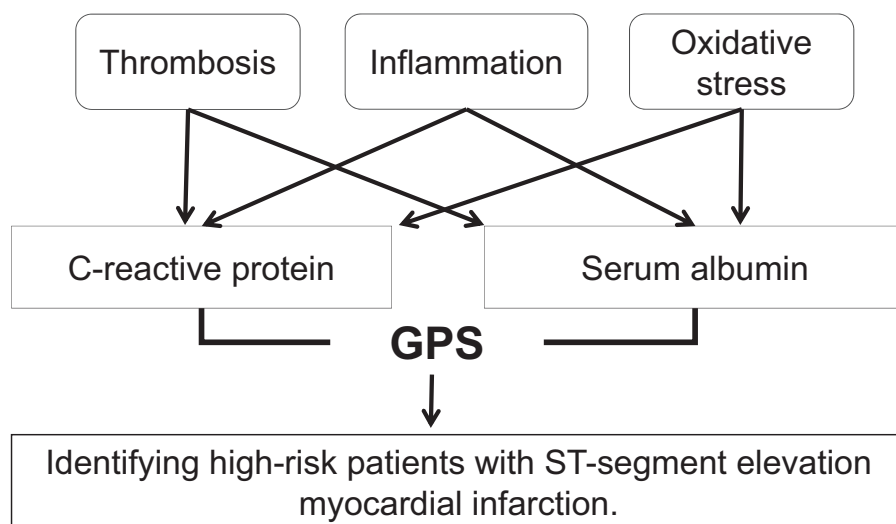
Figure 5. Potential pathophysiological mechanism of Glasgow Prognostic Score (GPS) in patients with ST-segment elevation myocardial infarction. GPS = Glasgow Prognostic Score.

urotensin II is known to induce tissue factor expression and promote atherothrombosis, and to modulate vascular inflammation,[48,49] whereas the mechanism involving Pentraxin-3 may include inflammation and thrombosis.[47] Therefore, urotensin II and Pentraxin-3 combined with the GPS may improve the predictive power to STEMI. Further studies with large samples are needed to prove this theory.

4.1. Study limitations

Some limitations should be noted. First, this was a single-center study with a small sample size. Second, we only measured baseline SA and CRP levels, and the changes in these levels may provide an additional prognostic value. Third, we did not evaluate the complications and cardiovascular death of patients with STEMI. Fourth, the cut-off values of the SA and CRP levels were based on those for cancer; thus, they may not be optimal values for STEMI. Finally, future prospective studies are warranted to clarify whether the GPS is only a biomarker or whether it plays a pathophysiologic role in the course of STEMI.

5. Conclusions

The GPS is useful in reflecting patient's inflammatory status, and it is a powerful predictor of all-cause mortality of patients with STEMI undergoing pPCI. Therefore, the GPS may be used to risk stratify patients with STEMI in the emergency room by short-term and long-term outcomes at an early stage.

Author contributions

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