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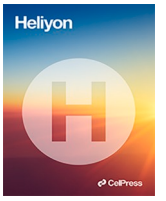

Research article

Prognostic value of Glasgow Prognostic Score and its modified scores on 5-year outcome in patients with coronary heart disease undergoing percutaneous coronary intervention

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ABSTRACT

Background: Glasgow Prognostic Score (GPS) and its modified counterparts, including the modified GPS (mGPS) and hsCRP-modified GPS (hs-mGPS), are widely used inflammatory indices in clinical settings. Inflammation has gained increased attention in the context of coronary heart disease (CHD); however, its long-term predictive value in patients with CHD remains uncertain.
Objective: This study aimed to assess the predictive values of GPS, mGPS, and hs-mGPS for long-term survival in patients following percutaneous coronary intervention (PCI).
Methods: Consecutive 10,724 PCI patients were enrolled in 2013. The primary endpoint was 5-year all-cause death.
Results: This study included 8,909 patients. Individuals with high GPS, mGPS, and hs-mGPS scores exhibited a significantly higher risk of all-cause death compared to those with low scores (all $P < 0.05$). All three indices (GPS, mGPS, and hs-mGPS) demonstrated predictive values for all-cause death, albeit with relatively low area under the curve values of 0.534, 0.522, and 0.545, respectively. Furthermore, we refined the hs-mGPS using cutoffs (hsCRP at 2 mg/L and albumin at 40 g/L) which are better suited for these patients, to establish the CHD-hs-mGPS. This modification significantly improved the prediction of all-cause death, outperformed the mGPS and demonstrated numerical superiority over both the GPS and hs-mGPS. Notably, only CHD-hs-mGPS exhibited a predictive value for both the ACS and non-ACS subgroups.
Conclusion: In patients with CHD who underwent PCI, GPS, mGPS, and hs-mGPS demonstrated significant long-term predictive values for all-cause death. Our parameter-adjusted score, the CHD-hs-mGPS, is applicable to a broad population and moderately enhances the predictive accuracy, facilitating the early identification of patients at high risk of long-term death.

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1. Introduction

Many patients with coronary heart disease (CHD) are still at a high risk of recurrent cardiovascular events despite receiving guideline-recommended comprehensive therapy [1]. In recent years, research on inflammation in CHD has progressed rapidly, and inflammation is considered an important residual risk factor for CHD, however, identifying patients at a high risk of inflammation is a significant challenge at present.

Glasgow Prognostic Score (GPS) is an inflammation-based prognostic scoring system that combines two readily accessible and cost-effective biomarkers: high-sensitivity C-reactive protein (hsCRP) and albumin. HsCRP serves as an indicator of systemic inflammation, and studies have indicated an association between elevated hsCRP levels in patients undergoing percutaneous coronary intervention (PCI) and an increased long-term risk of mortality [2]. Albumin is not only a nutritional indicator but is also closely related to the inflammatory response in patients [3]. During the inflammatory response, the synthesis of albumin may be inhibited, while its catabolism may increase, leading to a decrease in serum albumin levels. In the GPS scoring system, combining albumin with hsCRP, two indicators closely related to the inflammatory response, can more accurately assess a patient's systemic inflammatory status and predict the patient's prognosis. GPS was first proposed by Forrest et al. and was found to have a significant prognostic value in predicting the survival of patients with non-small-cell lung cancer [4]. Subsequently, its prognostic predictive value has been confirmed in patients with hepatocarcinoma [5], colorectal cancer [6], and gastric carcinoma [7]. Additionally, modified GPS (mGPS) [8] and hsCRP-modified GPS (hs-mGPS) [9] have been developed on the basis of GPS, placing greater emphasis on the inflammatory factor CRP, which can more accurately reflect the inflammatory status in patients with tumors. Similar to various cancers, inflammation plays a pivotal role in the progression of coronary artery atherosclerosis. Nevertheless, the prognostic value of the GPS and its modified scores (mGPS and hs-mGPS) remains unclear in patients with CHD.

With the emergence of large-scale clinical trials confirming the potential of anti-inflammatory treatments in reducing cardiovascular events [10,11], anti-inflammatory therapy has shown promise. However, the precise identification and treatment strategies for inflammatory states are lacking. This study aimed to assess the predictive value of the GPS and its derivative scores for long-term survival risk in patients with CHD who underwent PCI using a vast real-world dataset with extended follow-up. Our findings hold the potential to identify those at a high risk of inflammation among patients with CHD, providing valuable clinical data for future personalized anti-inflammatory interventions.

2. Methods

2.1. Study design and patients

This was a post-hoc analysis of data from a real-world, prospective, single-center, observational cohort. From January 2013 to December 2013, 10,724 patients with CHD hospitalized for PCI at Fu Wai Hospital were consecutively and prospectively recruited into the cohort. Patients meeting the following exclusion criteria were excluded: (1) without baseline hsCRP or albumin data, (2) receiving

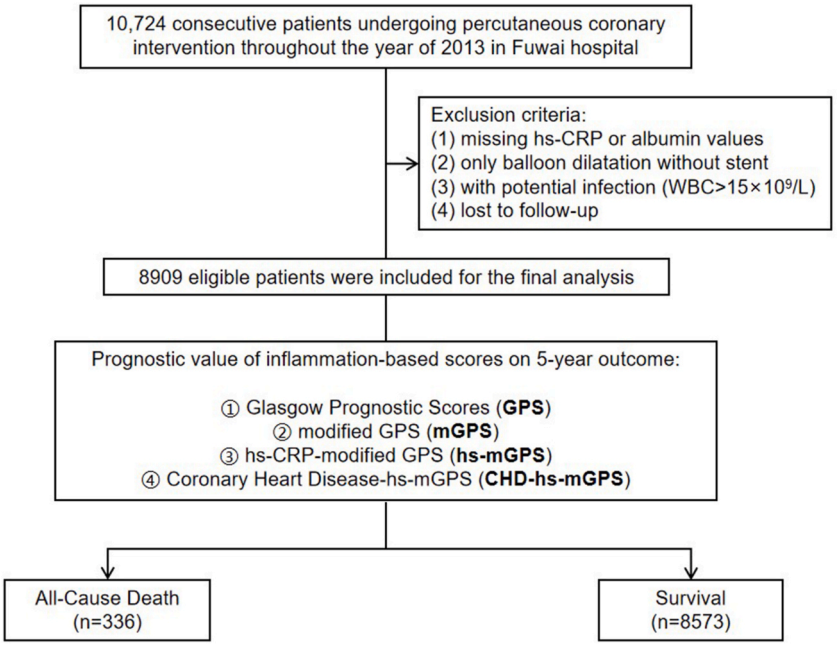

Fig. 1. Study flow chart.
PCI = percutaneous coronary intervention; hsCRP = high sensitivity-C reactive protein.

only balloon dilatation, (3) with potential infection (white blood cell count [WBC] $> 15 \times 10^9$/L), or (4) lost to follow-up. Finally, 8,909 participants were included in the current analysis (Fig. 1). This investigation followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies. In Compliance with the Helsinki Declaration, this study was approved by the ethics committee at Fu Wai Hospital (Beijing, China). Written informed consent was obtained from all participants.

Following PCI, all patients received DAPT for at least 12 months: aspirin 100 mg a day with clopidogrel 75 mg/day or ticagrelor 90 mg twice daily.

2.2. Parameters measurements

All patients underwent venous blood draws on admission following a longer-than-12-h fast. Serum albumin concentration was measured using an AU5400 automatic biochemical analyzer (Beckman Coulter, Brea, CA, USA), and serum hsCRP concentration was measured with an automated biochemical analyzer (LABOSPECT 008, Hitachi 7150, Tokyo, Japan) at the Clinical Chemistry Department of Fu Wai Hospital.

2.3. Details of PCI procedure

The surgeons were granted discretion in selecting the PCI strategy and stent type. Prior to the PCI procedure, patients not taking long-term aspirin or P2Y12 inhibitors were prescribed a one-time oral dose of aspirin (300 mg) and clopidogrel (loading dose of 300 mg). Similarly, patients with ACS (including ST-elevation myocardial infarction and NSTE-ACS) who were scheduled for PCI were given the same aspirin and clopidogrel doses (loading dose of 300 or 600 mg) as promptly as possible. During the procedure, all patients received an injection of unfractionated heparin (100 U/kg), and the decision to use glycoprotein IIb/IIIa inhibitors rested with the operator. If the PCI exceeded 1 h, an additional 1000 U of heparin sodium was administered. The coronary angiography results were interpreted by experienced cardiologists, who defined a stenosis greater than 50 % in the left main artery, left anterior descending artery, left circumflex artery, right coronary artery, or their main branches as coronary artery stenosis. A stenosis exceeding 70 % in these vessels indicated the need for coronary stent implantation. Post-procedure, patients were prescribed aspirin (100 mg daily indefinitely), and either clopidogrel (75 mg daily) or ticagrelor (90 mg twice daily) for at least one year following PCI.

2.4. Definition

All GPS, mGPS, and hs-mGPS values were calculated using baseline hsCRP and albumin levels, with minor variations (Fig. 2). Threshold values of hsCRP >10 mg/L and albumin <35 g/L were used to define the GPS and mGPS. Regarding the GPS, patients with both increased hsCRP levels and decreased albumin levels scored 2 points, those with either elevated hsCRP or reduced albumin levels received 1 point, and those with neither condition scored 0 points. Regarding the mGPS, all conditions were consistent with those of GPS, except for those with concurrent decreased hsCRP and albumin levels got 0 points, which emphasized the significance of elevated

A	GPS	Score
	hs-CRP≤ 10 mg/L & albumin ≥ 35 g/L	0
	hs-CRP≤ 10 mg/L & albumin < 35 g/L	1
	hs-CRP> 10 mg/L & albumin ≥ 35 g/L	1
	hs-CRP>10 mg/L & albumin < 35 g/L	2

B	mGPS	Score
	hs-CRP≤ 10 mg/L & albumin ≥ 35 g/L	0
	hs-CRP≤ 10 mg/L & albumin < 35 g/L	0
	hs-CRP> 10 mg/L & albumin ≥ 35 g/L	1
	hs-CRP>10 mg/L & albumin < 35 g/L	2

C	hs-mGPS	Score
	hs-CRP≤ 3 mg/L & albumin ≥ 35 g/L	0
	hs-CRP≤ 3 mg/L & albumin < 35 g/L	0
	hs-CRP> 3 mg/L & albumin ≥ 35 g/L	1
	hs-CRP> 3 mg/L & albumin < 35 g/L	2

D	CHD-hs-mGPS	Score
	hs-CRP≤ 2 mg/L & albumin ≥ 40 g/L	0
	hs-CRP≤ 2 mg/L & albumin < 40 g/L	0
	hs-CRP> 2 mg/L & albumin ≥ 40 g/L	1
	hs-CRP> 2 mg/L & albumin < 40 g/L	2

Fig. 2. Definitions of inflammation-based scores.
GPS = Glasgow Prognostic Scores; hsCRP = high sensitivity-C reactive protein; mGPS = modified GPS; hs-mGPS = hs-CRP-modified GPS.

hsCRP.

For the hs-mGPS, the threshold value of hsCRP was >3 mg/L and that of albumin was <35 g/L, which further highlighted the significance of elevated hsCRP. Patients with both increased hsCRP levels and decreased albumin levels were assigned a score of 2, those with only increased hsCRP levels were assigned a score of 1, and those without increased hsCRP levels were assigned a score of 0, regardless of albumin levels.

To further improved the predictive value of hs-mGPS, we established CHD-hs-mGPS with cut-off values that were more suitable for patients with CHD. The threshold value of hsCRP was >2 mg/L and that of albumin was <40 g/L (the normal reference value of albumin). Patients with both increased hsCRP levels and decreased albumin levels were assigned a score of 2, those with only increased hsCRP levels were assigned a score of 1, and those without increased hsCRP levels were assigned a score of 0, regardless of albumin levels.

2.5. Study outcomes

The endpoint of interest was all-cause death. After discharge, follow-ups were regularly conducted for all patients at 5-time nodes (1 month, 6 months, 1 year, 2 years, and 5 years). Follow-up included clinical visits and telephone visits. All endpoint events were centrally adjudicated by two independent cardiologists, and possible disagreements were resolved through consensus.

2.6. Statistical analysis

If the continuous variable follows a Gaussian distribution, expressed as mean ± standard deviation, if the continuous variable does not follow the Gaussian distribution, expressed as median [interquartile range, (IQR)]. The categorical variables were expressed as frequency (percentage). The continuous data were compared by Student's t-test or Mann–Whitney *U* test; the categorical data were compared by χ^2 test or Fisher's exact test. For survival analysis, the Kaplan–Meier approach (log-rank test) and Cox regression analyses (univariate and multivariate) were used to assess the associations of GPS, mGPS, hs-mGPS, and CHD-hs-mGPS with 5-year all-cause death. The variables entered into the multivariate Cox model for adjustment were diabetes mellitus, hypertension, previous myocardial infarction (MI), previous PCI, previous coronary artery bypass grafting (CABG), previous stroke, WBC count, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. Receiver operating characteristic curve analysis was performed to obtain the area under the curve (AUC), and the AUCs of the different scores were compared using the Delong test. All statistical analyses were performed at a significance level of two-sided 0.05. Statistical analyses were performed via SPSS 23.0 (IBM Corp., Armonk, New York, USA) and R Programming Language version 4.0.3 (R Core Team, 2014).

Table 1
Baseline characteristics.

Parameters	Overall	Survival	All cause-death	P value
	N = 8,909	N = 8,573	N= 336	
Age, years	58.42 ± 10.20	58.16 ± 10.10	65.11 ± 10.29	<0.001
Male Sex (%)	6,863 (77.03)	6,609 (77.09)	254 (75.60)	0.566
BMI, kg/m^2	25.93 ± 3.15	25.94 ± 3.15	25.65 ± 3.19	0.093
Hypertension (%)	5,736 (64.38)	5,487 (64.00)	249 (74.11)	<0.001
Hyperlipemia (%)	5,976 (67.08)	5,760 (67.19)	216 (64.29)	0.293
DM (%)	2,679 (30.07)	2,559 (29.85)	120 (35.71)	0.025
PAD (%)	232 (2.60)	218 (2.54)	15 (4.17)	0.097
Previous MI (%)	1,687 (18.94)	1,605 (18.72)	82 (24.40)	0.011
Previous Stroke (%)	926 (10.39)	879 (10.25)	47 (13.99)	0.035
Current/ever-Smoker (%)	5,192 (58.28)	4,988 (58.18)	204 (60.71)	0.386
ACS (%)	5,283 (59.30)	5,085 (59.31)	198 (58.93)	0.933
Previous PCI (%)	2,103 (23.61)	2,003 (23.36)	100 (29.76)	0.008
Previous CABG (%)	355 (3.98)	330 (3.85)	25 (7.44)	0.002
CK-MB, IU/L	12.66 ± 18.50	12.61 ± 18.47	13.99 ± 19.15	0.180
hsCRP, mg/L	1.59 [0.80, 3.55]	1.58 [0.79, 3.49]	2.06 [1.03, 4.87]	<0.001
Albumin, g/L	42.89 ± 4.06	42.93 ± 4.04	41.74 ± 4.49	<0.001
WBC Count, 10^9/L	6.79 ± 1.82	6.78 ± 1.82	7.01 ± 1.89	0.023
LDL-C, mmol/L	2.50 ± 0.90	2.51 ± 0.90	2.41 ± 0.89	0.051
HDL-C, mmol/L	1.04 ± 0.28	1.03 ± 0.28	1.07 ± 0.31	0.037
Aspirin (%)	8,802 (98.80)	8,471 (98.81)	331 (98.51)	0.813
Clopidogrel (%)	8,895 (99.84)	8,559 (99.84)	336 (100.00)	0.969
Calcium Channel Blocker (%)	4,361 (48.95)	4,174 (48.69)	187 (55.65)	0.014
Beta Blocker Inhibitor (%)	8,014 (89.95)	7,717 (90.02)	297 (88.39)	0.380
Statin (%)	8,553 (96.00)	8,229 (95.99)	324 (96.43)	0.793

BMI = body mass index; DM = diabetes mellitus; ACS = acute coronary syndrome; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; CK-MB: creatine kinase-MB isoenzyme; PAD = peripheral artery disease; MI = myocardial infarction; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; hsCRP = high-sensitivity C-reactive protein; WBC = white blood cell count.

3. Results

3.1. Baseline characteristics

Of 8,909 patients, the mean age of the participants was 58.4 ± 10.2 years, and 6,896 (77.1 %) were men. After a 5-year follow-up, 338 (3.8 %) all-cause deaths occurred. Table 1 presents the baseline characteristics of the total population, stratified by the occurrence of all-cause death. Individuals with all-cause death were older, had an extensive history of medical conditions (hypertension; diabetes mellitus; peripheral artery disease; previous MI, PCI, CABG, and stroke), had higher hsCRP and high-density lipoprotein cholesterol levels and lower albumin levels than those who survived.

3.2. Associations of GPS with 5-year all-cause death

Based on the GPS score, 7,946 (89.2 %), 889 (10.0 %), and 74 (0.8 %) patients were assigned to groups 0, 1, and 2, respectively. The incidence rates of all-cause death in patients with GPS scores of 0, 1, and 2 were 3.5 %, 5.7 %, and 9.5 %, respectively (Fig. 3A). The Kaplan–Meier survival curve revealed that patients with higher GPS had a significantly increased risk of all-cause death (log-rank P < 0.0001) (Fig. 3D), which is consistent with the results of the multivariate Cox analysis.

In the multivariable Cox model, patients with a GPS score of 1 had a 62.4 % higher adjusted risk of all-cause death than those with a GPS score of 0 (adjusted hazard ratio (HR): 1.624, 95 % confidence interval (CI): 1.187–2.224, P = 0.002), and the adjusted risk of all-cause death in patients with a GPS score of 2 was 2.792 times that in those with a GPS score of 0 (adjusted HR: 2.792, 95 % CI: 1.307–5.963, P = 0.008) (Table 2).

3.3. Associations of mGPS with 5-year all-cause death

For mGPS, 8,050 (90.4 %), 785 (8.8 %), and 74 (0.8 %) patients were assigned to groups 0, 1, and 2, respectively, and the incidences of all-cause death were 3.6 %, 5.0 %, and 9.5 %, respectively (Fig. 3B). The Kaplan–Meier survival curve revealed that patients with higher mGPS scores had a significantly increased risk of all-cause death (log-rank P = 0.0011) (Fig. 3E). In the multivariable Cox model, the results remained statistically significant: the adjusted risk of all-cause death in patients with a mGPS score of 2 was 2.662 times that in those with a mGPS score of 0 (adjusted HR: 2.662, 95 % CI: 1.247–5.682, P = 0.011) (Table 2).

3.4. Associations of hs-mGPS with 5-year all-cause death

Regarding hs-mGPS, there were 6,298 (70.4 %), 2,489 (28.2 %), and 122 (1.4 %) patients in groups 0, 1, and 2, respectively. The incidences of all-cause death in patients with hs-mGPS scores of 0, 1, and 2 were 3.3 %, 4.6 %, and 9.0 %, respectively (Fig. 3C). The Kaplan–Meier survival curve revealed that patients with higher hs-mGPS scores had a significantly increased risk of all-cause death (log-rank P < 0.0001) (Fig. 3F). The results remained significant in the multivariable Cox model: patients with an hs-mGPS score of 1 had a 43.9 % higher adjusted risk of all-cause death than those with an hs-mGPS of 0 (adjusted HR: 1.439, 95 % CI: 1.130–1.832, P =

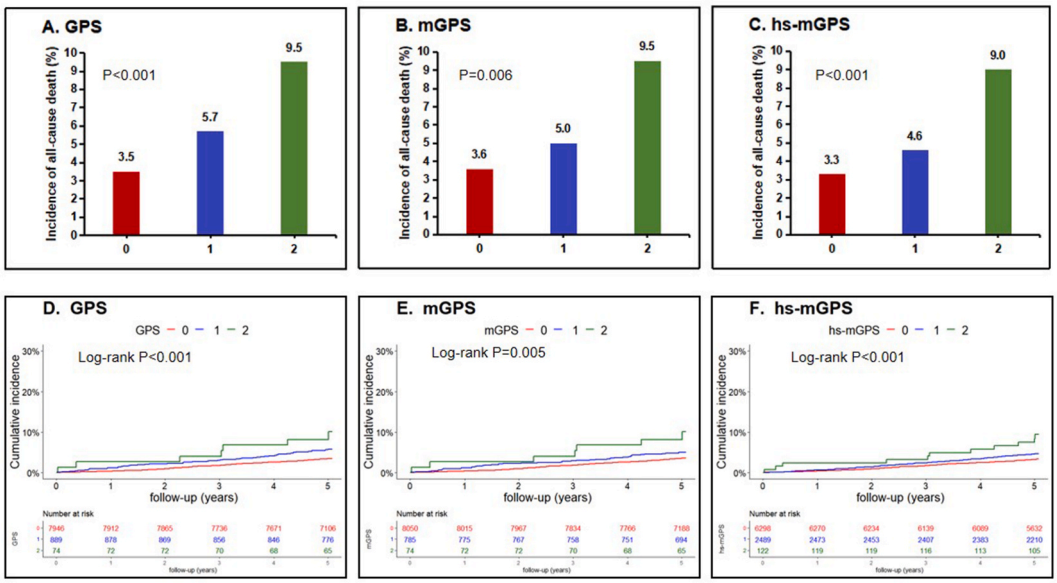

Fig. 3. Incidence of all-cause death according to different inflammation-based scores.
GPS = Glasgow Prognostic Scores; mGPS = modified GPS; hs-mGPS = hs-CRP-modified GPS.

Table 2
Univariate and multivariate Cox analysis of inflammatory scores and long-term all-cause death.

Inflammatory scores	Points	Crude HR	95 % CI	P value	Adjusted HR	95 % CI	P value
GPS							
	0	Reference	–	–	Reference	–	–
	1	1.661	1.232–2.239	0.001	1.624	1.187–2.224	0.002
	2	2.807	1.326–5.943	0.007	2.792	1.307–5.963	0.008
mGPS							
	0	Reference	–	–	Reference	–	–
	1	1.392	0.996–1.944	0.053	1.344	0.946–1.909	0.099
	2	2.725	1.287–5.766	0.009	2.662	1.247–5.682	0.011
hs-mGPS							
	0	Reference	–	–	Reference	–	–
	1	1.395	1.112–1.752	0.004	1.439	1.130–1.832	0.003
	2	2.789	1.521–5.113	0.001	2.784	1.503–5.157	0.001
CHD-hs-mGPS							
	0	Reference	–	–	Reference	–	–
	1	1.225	0.957–1.567	0.107	1.246	0.961–1.614	0.096
	2	1.868	1.407–2.480	<0.001	1.973	1.465–2.659	<0.001

The multivariate Cox model was adjusted for the following covariates: diabetes mellitus, hypertension, previous MI, previous PCI, previous CABG, previous stroke, WBC count, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol.

0.003), and the adjusted risk of all-cause death in patients with an hs-mGPS score of 2 was 2.784 times that in those with an hs-mGPS score of 0 (adjusted HR: 2.784, 95 % CI: 1.503–5.157, P = 0.001) (Table 2).

3.5. Performance of GPS, mGPS, and hs-mGPS predicting 5-year all-cause death

GPS, mGPS, and hs-mGPS demonstrated predictive values for all-cause death, with AUCs of 0.534 (95 % CI: 0.513–0.555), 0.522 (95 % CI: 0.503–0.540), and 0.545 (95 % CI: 0.518–0.572), respectively (Table 3). Although the AUC of the hs-mGPS was numerically larger than that of the GPS, the difference was not statistically significant (P = 0.382). The AUC of both GPS (P = 0.014) and hs-mGPS (P = 0.048) were significantly larger than that of mGPS.

3.6. Associations of CHD-hs-mGPS with 5-year all-cause death

Given the limited predictive value of these three inflammatory scores (GPS, mGPS, and hs-mGPS), we further improved hs-mGPS by setting hsCRP at 2 mg/L and albumin at 40 g/L and then established a new score called CHD-hs-mGPS (Fig. 2D). According to the CHD-hs-mGPS score, 5,184 (58.2 %), 2,595 (29.1 %), and 1,130 (12.7 %) patients were categorized into groups 0, 1, and 2, respectively. The incidences of all-cause death in patients with CHD-hs-mGPS scores of 0, 1, and 2 were 3.2 %, 3.9 %, and 5.9 %, respectively (Fig. 4A). The Kaplan–Meier survival curve revealed that patients with higher CHD-hs-mGPS scores had a significantly increased risk of all-cause death (log-rank P < 0.001) (Fig. 4B). In the multivariable Cox model, the adjusted risk of all-cause death in patients with a CHD-hs-mGPS score of 2 was 1.973 times that in those with a CHD-hs-mGPS score of 0 (adjusted HR: 1.973, 95 % CI: 1.465–2.659, P < 0.001) (Table 2).

3.7. Performance of CHD-hs-mGPS predicting 5-year all-cause death

CHD-hs-mGPS showed a predictive value for all-cause death with an AUC of 0.554, which was significantly higher than that of

Table 3
The predictive value of inflammatory scores on long-term all-cause death.

Inflammatory scores	All population (n = 8,909)		ACS (n = 5,283)		non-ACS (n = 3,626)	
	AUC (95 % CI)	P for comparison	AUC (95 % CI)	P for comparison	AUC (95 % CI)	P for comparison
CHD-hs-mGPS	0.555 (0.525–0.584)[a]	Reference	0.541 (0.502–0.580)[a]	Reference	0.575 (0.529–0.620)[a]	Reference
GPS	0.534 (0.513–0.555)[a]	0.156	0.544 (0.514–0.573)[a]	0.874	0.520 (0.494–0.546)	0.017
mGPS	0.522 (0.503–0.540)[a]	0.017	0.531 (0.503–0.558)[a]	0.561	0.509 (0.486–0.531)	0.003
hs-mGPS	0.545 (0.518–0.572)[a]	0.329	0.532 (0.496–0.567)	0.462	0.565 (0.524–0.606)[a]	0.515

AUC = area under curve.
The AUCs were compared using the Delong's test.
[a] P < 0.05.

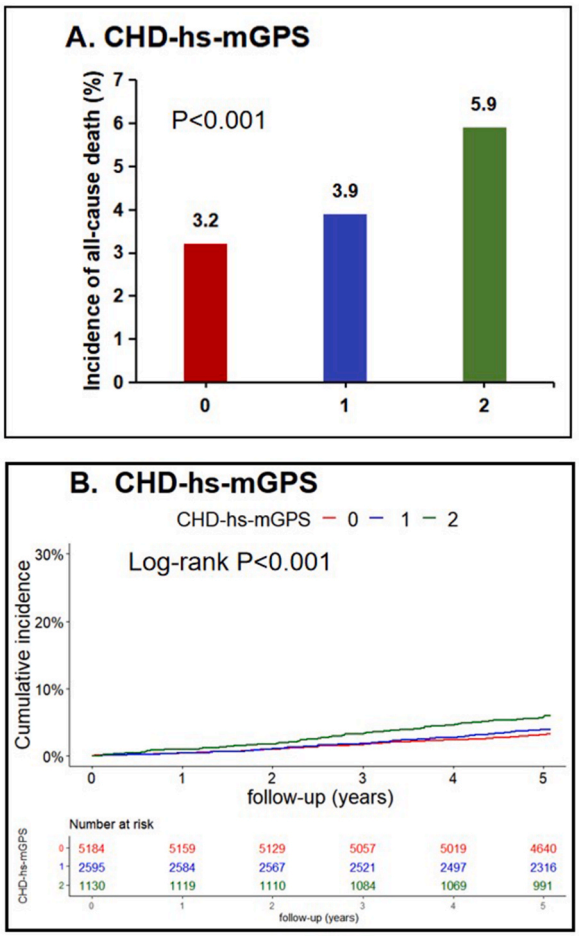

Fig. 4. Kaplan–Meier curves of GPS, mGPS, and hs-mGPS on long-term all-cause death.
GPS = Glasgow Prognostic Scores; mGPS = modified GPS; hs-mGPS = hs-CRP-modified GPS.

mGPS (P = 0.017) and numerically higher than that of GPS and hs-mGPS in the total population (Table 3). Moreover, compared to several established prognostic factors (including hsCRP >2 mg/L, male sex, diabetes mellitus, hypertension, previous stroke, current/ever-smoker, peripheral artery disease, previous PCI, previous CABG, and previous MI), CHD-hs-mGPS showed a significantly higher predictive value than hs-CRP >2 mg/L, male sex, previous stroke, current/ever-smoker, peripheral artery disease, and previous CABG (Table 4).

Table 4
Comparison of CHD-hs-mGPS and other established prognostic factors in CHD.

Established prognostic factors in CHD	AUC (95 % CI)	P for comparison
CHD-hs-mGPS	0.555 (0.525–0.584)	Reference
hsCRP >2 mg/L	0.545 (0.517–0.572)	0.011
Male Sex	0.508 (0.485–0.532)	0.010
DM	0.530 (0.504–0.556)	0.187
Hypertension	0.551 (0.528–0.575)	0.859
Previous Stroke	0.520 (0.501–0.539)	0.046
Current/ever-Smoker	0.512 (0.486–0.539)	0.033
PAD	0.510 (0.498–0.521)	0.005
Previous PCI	0.532 (0.507–0.557)	0.225
Previous CABG	0.518 (0.504–0.532)	0.031
Previous MI	0.528 (0.505–0.551)	0.161

AUC = area under curve; DM = diabetes mellitus; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; PAD = peripheral artery disease; MI = myocardial infarction; hsCRP = high-sensitivity C-reactive protein.
The AUCs were compared using the Delong's test.

3.8. ACS and non-ACS subgroups

Further studies were conducted in both the ACS and non-ACS subgroups. The GPS and mGPS exhibited predictive values in the ACS subgroup, while the hs-mGPS demonstrated predictive values in the non-ACS subgroup. The CHD-hs-mGPS exhibited a predictive value in both the ACS and non-ACS subgroups (Table 3).

4. Discussion

This real-world study aimed to assess the predictive value of three inflammation-based scores (GPS, mGPS, and hs-mGPS) for all-cause death in patients who underwent PCI. The results revealed that patients with high GPS, mGPS, and hs-mGPS scores (1 or 2) had an increased risk of 5-year all-cause death compared to those with a score of 0. Recognizing the limited predictive value of GPS, mGPS, and hs-mGPS, we established a novel inflammation-based score, CHD-hs-mGPS, specifically tailored for patients with CHD. This new score was significantly associated with a higher risk of all-cause death. CHD-hs-mGPS had the broadest applicability (covering all patients who underwent PCI, ACS, and non-ACS subgroups) and showed significant potential for prediction.

GPS, mGPS, and hs-mGPS are inflammation-based prognostic scoring systems that incorporate hsCRP and serum albumin levels and are commonly used for patients with cancer. hsCRP and albumin are biomarkers of inflammation, both of which have significant predictive value for cardiovascular outcomes in patients with CHD. Inflammation plays a crucial role not only in the initiation and progression of cancer but also in the development of atherosclerosis and the occurrence of cardiovascular events. However, the predictive value of these inflammation scores in the prognosis of patients with CHD remains unclear. Our results demonstrated a significantly higher risk of long-term all-cause death in patients with GPS and hs-mGPS scores of 1–2 and in patients with an mGPS score of 2 compared to 0 in patients undergoing PCI.

In the field of CHD, previous studies have primarily relied on small sample sizes and relatively short follow-up periods, with most focusing solely on the predictive value of the GPS. The results of these earlier investigations are largely consistent with our findings. Jia et al. [12] conducted a study involving 406 patient with STEMI who underwent emergency PCI, and the results revealed a higher risk of in-hospital and long-term all-cause death (average follow-up of 14.4 months) in patients with high GPS scores than in those with a score of 0. Similarly, Wang et al. [13] and Xu et al. [14] ($n = 175$) concentrated on the in-hospital prognosis of GPS in patients with AMI, finding significantly higher risks of all-cause death or major adverse cardiovascular and cerebrovascular events in patients with high GPS scores compared to those with a score of 0. Lee et al.'s [15] study including 593 patients with ACS who underwent PCI revealed that a GPS score of ≥ 1 was associated with nearly six times higher all-cause death within 1 month compared to a GPS score of 0. Overall, the results of these studies are consistent with our findings. Zhu et al. [16] conducted a study of 188 patients with AMI who underwent PCI or traditional drug therapy. Their study revealed that although patients with GPS scores of 1 and 2 had a seven-fold and eighteen-fold higher risk of major adverse cardiovascular events, respectively, than those with a GPS score of 0, mGPS and hs-mGPS were not independent influencing factors for major adverse cardiovascular events. Furthermore, the GPS, mGPS, and hs-mGPS were not independent factors influencing all-cause death. We believe that these results may be related to the small sample size and low incidence rate of in-hospital events in the study by Zhu et al. which could have led to insufficient statistical power. Therefore, our study possessed several strengths. First, this observational study has the largest sample size to date, enrolling 8,949 patients receiving PCI. Second, our median follow-up time was 5.1 years, which is the longest duration thus far. Third, our study simultaneously evaluated the predictive value of three inflammation scores (GPS, mGPS and hs-mGPS) for all-cause death.

In addition, it remains unclear which scoring system (GPS, mGPS, or hs-mGPS) provides superior predictive value for all-cause death. As an inflammation-based scoring system, hs-mGPS places greater emphasis on the significance of elevated hsCRP levels than GPS and mGPS. Furthermore, hs-mGPS refines the hsCRP cutoff point from 10 mg/L in GPS and mGPS to 3 mg/L. Our study demonstrated that hs-mGPS significantly outperformed mGPS and numerically surpassed GPS in predicting five-year all-cause death. Patients with CHD typically have a low-grade inflammatory status; thus, using a 3 mg/L cutoff for hsCRP in hs-mGPS may be more suitable for this population compared to the 10 mg/L cutoff used in GPS and mGPS. However, it is essential to acknowledge that the predictive value of hs-mGPS remains relatively limited. Furthermore, our subgroup analysis revealed that hs-mGPS only exhibited a predictive value in non-ACS populations and did not effectively predict the long-term prognosis of patients with ACS.

Therefore, we aimed to establish an inflammation-modified scoring system tailored for the PCI population with CHD, surpassing the predictive capabilities of GPS, mGPS, and hs-mGPS. Considering that these scoring systems were originally developed for patients with cancer and that hs-mGPS exhibited the highest AUC in our study, we sought to further enhance hs-mGPS by employing cutoff points better suited for patients with CHD. We made adjustments based on the following considerations: (1) hsCRP cutoff: given that these patients typically exhibit a low-grade inflammatory status, we adjusted the hsCRP cutoff value from 3 mg/L to 2 mg/L, a modification inspired by the Canakinumab Anti-inflammatory Thrombosis Outcome Study [17]. (2) Albumin cutoff: in contrast to patients with cancer, the nutritional status of those with CHD is typically less compromised. Therefore, we raised the albumin level cutoff value from 35 to 40 g/L (considered an abnormal threshold). This newly developed inflammation-modified scoring system, CHD-hs-mGPS, clearly outperformed mGPS and demonstrated a numerical advantage over GPS and hs-mGPS in predicting all-cause death. Our study encompassed a large-scale PCI cohort that including both patients with and wthout ACS. Subgroup analyses further indicated that the newly established CHD-hs-mGPS is particularly valuable in predicting adverse prognoses and is applicable to the overall population, as well as both to non-ACS and ACS subgroups. Hence, CHD-hs-mGPS may prove to be a more suitable option than GPS, mGPS, or hs-mGPS alone for the CHD population.

The GPS, mGPS, hs-mGPS, and CHD-hs-mGPS reflect the inflammatory status of patients. Consequently, higher GPS, mGPS, and hs-mGPS values are associated with worse clinical outcomes in patients with PCI. This may be associated with increased inflammation

leading to higher platelet reactivity, enhanced platelet aggregation, smooth muscle cell proliferation, and increased thromboxane activity [18–20]. Based on our research findings, CHD-hs-mGPS represents an improvement compared to previous scoring systems. It lowers the hsCRP cutoff value and elevates the albumin cutoff point, rendering it more user-friendly and potentially better suited for early inflammatory risk stratification in patients with CHD. This modification holds significant clinical implications. Recent advancements, such as the use of interleukin-1β and low-dose colchicine as anti-inflammatory agents, have shown promise in further reducing event risk in patients with CHD. In the future, CHD-hs-mGPS may serve as a valuable tool for identifying patients at higher risk of inflammation. Early identification can guide healthcare professionals in providing timely anti-inflammatory treatments to this subset of patients, potentially leading to a further reduction in the risk of long-term cardiovascular events.

This study had several limitations. First, as this was a single-center observational study, further research is necessary to validate the generalization of the conclusions. Second, while we accounted for significant confounding factors, unmeasured confounding factors may still be linked to the risk of all-cause death. Third, although four indices (GPS, mGPS, hs-mGPS, and CHD-hs-mGPS) demonstrated significant predictive values for all-cause death, they showed relatively low AUC values, indicating a limited clinical predictive value. Therefore, a more valuable inflammatory model for risk stratification should be developed. In addition to hsCRP and albumin, novel inflammatory markers could potentially enhance the development of more refined inflammatory scoring systems.

5. Conclusion

Our extensive real-world dataset indicated that GPS, mGPS, and hs-mGPS possess significant predictive values for 5-year all-cause death in patients undergoing PCI. Moreover, our refined scoring system, CHD-hs-mGPS, may be more suitable for patients with CHD. This discovery expanded the scope of application of GPS, mGPS, and hs-mGPS such that these scores were no longer restricted to patients with tumors, providing valuable data for the precise anti-inflammatory treatment of patients with CHD in the future.

Data availability statement

Data will be made available on request.

Ethics approval and consent to participate

The study was approved by the ethics committee of Fuwai Hospital (approval number 2021-1501), and was conducted in accordance with the Declaration of Helsinki.

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CRediT authorship contribution statement

Jiawen Li: Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Kailun Yan:** Data curation. **Pei Zhu:** Data curation. **Xiaofang Tang:** Data curation. **Yuejin Yang:** Supervision, Resources, Data curation. **Runlin Gao:** Supervision, Resources, Project administration. **Jinqing Yuan:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition. **Xueyan Zhao:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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