A Retrospective Study to Evaluate the Association Between the Glasgow Prognostic Score and Atrial Fibrillation, Stroke, and Mortality at 30 Days and at 1 Year After Coronary Artery Bypass Graft Surgery

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Data Collection B
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Background: The Glasgow prognostic score (GPS) consists of a combination of serum C-reactive protein and albumin levels as indicators of systematic inflammatory response and nutritional status, respectively. The present retrospective study aimed to evaluate the association between the GPS and atrial fibrillation, stroke, and mortality at 30 days and 1 year after coronary artery bypass graft (CABG) surgery.

Material/Methods: Patients with chronic coronary syndromes who underwent CABG surgery between 2012 and 2019 in a single center were included. Preoperative GPS was calculated. Then, patients were grouped according to postoperative atrial fibrillation (POAF) development. Further, groups were formed to evaluate the relationship between GPS and 30-day and 1-year cardiovascular mortality as well as stroke development.

Results: Patients who developed POAF had higher GPS, higher European System for Cardiac Operative Risk Evaluation (EuroSCORE II) score, advanced age, lower angiotensin converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB) use, lower left ventricular ejection fraction, and were more likely to be female and to have a history of carotid artery disease ($P<0.05$, for all). Additionally, GPS, EuroSCORE II, advanced age, and lower left ventricular ejection fraction were detected as independent risk factors for POAF development. When adverse outcomes were assessed, cardiovascular mortality at 30 days or 1 year, and stroke development at 1 year, were more frequent in patients with POAF. Moreover, POAF development was found to be an independent risk factor for adverse outcomes. Also, GPS was established as an independent risk factor both for 30-day and 1-year cardiovascular mortality ($P<0.0001$ and $P=0.001$, respectively).

Conclusions: GPS is an easy-to-calculate score that has reasonable diagnostic accuracy in determining the risk of POAF and stroke as well as 30-day and 1-year cardiovascular mortality.

Keywords: **Atrial Fibrillation • C-Reactive Protein (164-173) • Cardiovascular Diseases • Human Serum Albumin, Des-Leucyl(585)- • Prognosis**

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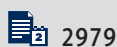
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Background

Postoperative atrial fibrillation (POAF) is among the most frequent complications of cardiac surgery. The incidence of POAF differs according to the type of surgery. It may develop in 15-40% of patients who undergo coronary artery bypass graft (CABG), while 33-49% of patients develop POAF after valvular surgery [1,2]. The 2 main arrhythmogenic mechanisms are re-entry and triggering activity, including perioperative inflammation, oxidative stress, pain, electrical remodeling, electrolyte disturbance, and ischemia [3-5]. Even though a number of episodes are asymptomatic and self-terminating, POAF is occasionally associated with myocardial infarction, stroke, and death [6]. Additionally, patients who develop POAF have a 4-5-fold increased risk of persistent atrial fibrillation (AF) in the 5 years following surgery [7].

The Glasgow prognostic score (GPS) is composed of C-reactive protein (CRP) and albumin levels, which are broadly used markers in clinical practice. CRP and albumin levels, as indicators of systematic inflammatory response and nutritional status, respectively, have been widely used for predicting oncological outcomes in various malignancies, for 2 decades [8]. In addition, studies have indicated that GPS can be used as a prognostic tool for determining survival after heart failure as well as predicting mortality in acute coronary syndromes [9,10]. Moreover, albumin has an antiplatelet effect by modulating arachidonic acid metabolism and a protective effect conferred by its antioxidant properties [11].

Although the pathophysiology of AF is well-defined, studies evaluating POAF are limited and not validated. Of note, POAF also poses a risk for AF development in the followup period [12]. POAF is thought to be triggered by perioperative inflammation, oxidative stress, pain, electrical remodeling, electrolyte disturbance, and ischemia [3-5]. These aforementioned factors facilitate myocardial vulnerability to AF development in the postoperative period. Arrhythmogenic remodeling due to comorbidities or transient triggering factors related to surgery may initiate POAF development involving pulmonary veins or 'non-pulmonary' vein regions. Thus, clinicians are seeking an easy way to calculate an accessible risk score based on everyday parameters for the purpose of predicting the development of POAF. To date, there have been several risk scoring systems like POAF, HATCH (hypertension, age, transient ischemic attack or stroke, chronic obstructive pulmonary disease, and heart failure), CHA2DS2-VASc [congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74, and female sex] and COM-AF (age, heart failure, female sex, hypertension, diabetes, previous stroke) to help predict POAF development [13-16]. However, more research is still needed. Since chronic coronary syndrome is associated with chronic inflammation, and CABG surgery causes acute inflammation, inflammatory biomarkers may provide the inflammatory status of the patient and help to identify patients at risk. Our aim was to evaluate whether preoperative GPS can be used to reveal the risk of POAF development in CABG patients and to evaluate the effect of POAF on long-term cardiovascular morbidity and mortality. Therefore, this retrospective study aimed to evaluate the association between the GPS and AF, stroke, and mortality at 30 days and at 1 year after CABG surgery.

Material and Methods

Study Population

This study was approved by the local Human Studies and Research Committee (Number: 2021-75) and patient consent was waived due to the study's retrospective nature. Patients diagnosed with chronic coronary syndromes who underwent CABG surgery at our institution between May 2012 and December 2019 were included in this retrospective study. Pre-, peri- and postoperative data were retrieved from the hospital database and patients' files. Demographic, clinical, and laboratory parameters were noted and European System for Cardiac Operative Risk Evaluation (EuroSCORE II) was calculated for each patient. Patients were excluded from the study if they had the following: preoperative AF rhythm or atrial/ventricular arrhythmia, valvular cardiac disease, congenital heart disease, preoperative renal impairment (serum creatinine >2 mg/dl), albuminuria and chronic liver disease, albumin replacement therapy in past 6 months, malignancy, endocrinologic disorders (hypothyroidism, hyperthyroidism), systemic inflammatory diseases, hematologic diseases, low hemoglobin (Hb) levels (≤10 g/dL), left atrial enlargement (>4.5 cm on echocardiography), or previous diagnosis of an autoimmune disease. In addition, those who had undergone emergency operations (eg acute myocardial infarction) were also excluded. Finally, those with unavailable serum CRP or albumin levels were also excluded.

Laboratory and Clinical Evaluation

Preoperative CRP and albumin levels were used for GPS calculation (https://www.mdcalc.com/glasgow-prognostic-score). Blood samples were obtained on admission. The albumin (3.5-5.4 g/dL) and CRP levels (0-5 mg/L) were measured using a Roche Diagnostics Cobas 8000 c502 analyzer (Indianapolis, USA).

An increased CRP level (>10 mg/L) or a low albumin level (<3.5 g/dL) were defined as 1 point each towards the GPS. The patient had a score of 0 if both parameters were normal, 1 if one parameter was abnormal, and 2 if both parameters were abnormal [17]. Patients with GPS=0 were accepted as 'low GPS' and those with GPS≥1 were accepted as 'high GPS'. During the hospital stay, all patients were evaluated with daily 12-lead electrocardiography
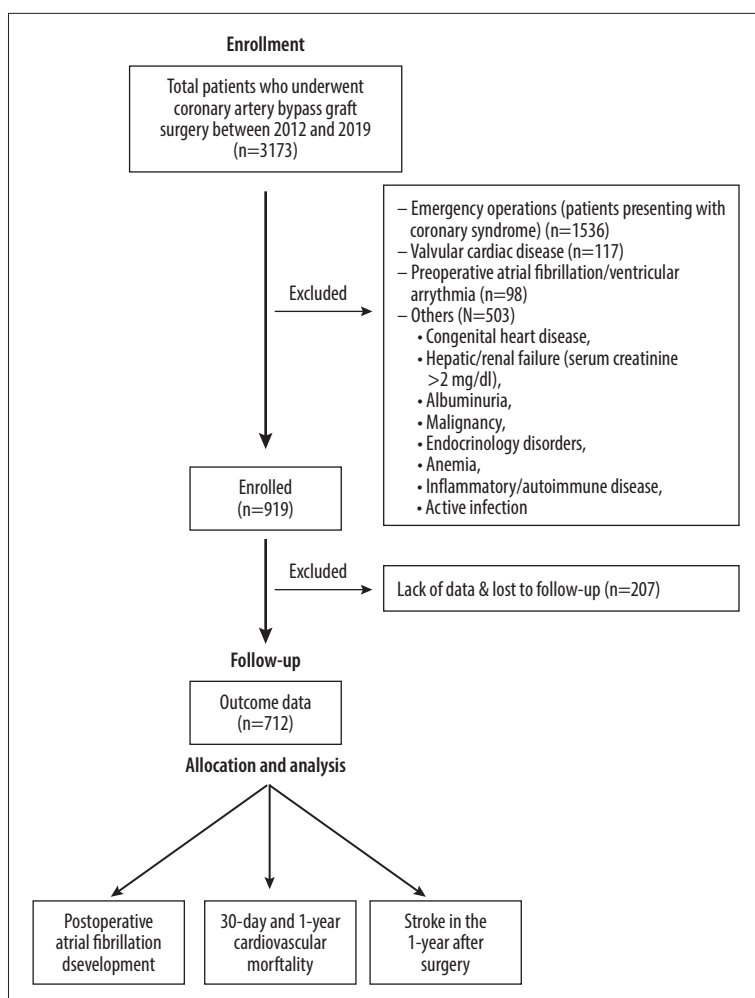
Figure 1. Flow chart of the study population indicating enrollment, followup, allocation, and analysis (designed in Microsoft Word and converted to tiff).

(ECG) and additional ECGs, which were obtained when the patient reported a symptom or a rhythm abnormality was suspected during telemetry monitoring to identify rhythm abnormalities or AF development. Clinical AF was diagnosed when standard 12-lead ECG recording or a single-lead ECG tracing of ≥30 s showed heart rhythm with no discernible repeating P waves and irregular RR intervals (when atrioventricular conduction was not impaired) [2,18]. POAF was defined as an episode of AF requiring treatment after surgery that developed during hospitalization. Cardiovascular mortality was defined as death due to myocardial or cerebrovascular disease. The development of stroke requiring hospitalization after discharge and 1-year cardiovascular mortality data were obtained by using local hospital and national electronic databases. Patients were grouped according to POAF development, occurrence of 30-day and 1-year cardiovascular mortality, and stroke in the 1-year followup.

Statistical Analysis

All statistical tests were conducted using the Statistical Package for the Social Sciences 22.0 for Windows (SPSS Inc., Chicago,

IL, USA). The Kolmogorov-Smirnov test was used to analyze normality of the data. Continuous data are expressed as mean±standard deviation, and categorical data are expressed as percentages. Chi-square test was used to assess differences in categorical variables between groups. Either the *t* test or Mann Whitney U test was used to compare unpaired samples as needed. Univariate and multivariate regression analysis were used to identify independent predictors of POAF development, 30-day and 1-year cardiovascular mortality, and stroke development during followup. Significance was assumed at a 2-sided $P<0.05$.

Results

Demographic Findings

A total of 3173 patients who underwent CABG surgery between May 2012 and December 2019 were screened. After exclusion, 712 patients were included in this retrospective single-center study (**Figure 1**). The mean age of the cohort was 60.3±9.72 years

Table 1. Comparison of demographic and laboratory parameters and outcomes of groups with regard to postoperative atrial fibrillation development.

Variables	All (n=712)	POAF (-) (n=591)	POAF (+) (n=121)	p
Demographic data and comorbidities				
Age (years)	60.3±9.7	59.6±9.8	63.3±8.7	**<0.0001**
Male, n (%)	539 (75.7)	457 (84.8)	82 (15.2)	**0.050**
Body Mass Index	27.9±4.4	27.8±4.4	27.9±4.5	0.735
Hypertension, n (%)	372 (52.2)	299 (50.6)	73 (60.3)	0.051
Chronic obstructive pulmonary disease, n (%)	135 (19)	105 (17.8)	30 (24.8)	0.074
Peripherial Artery Disease, n (%)	53 (7.4)	40 (6.8)	13 (10.7)	0.133
Carotid artery disease, n (%)	59 (8.3)	26 (4.4)	33 (27.3)	**<0.0001**
Coronary artery disease, n (%)	189 (26.5)	160 (27.2)	29 (24.2)	0.492
Diabetes mellitus, n (%)	295 (41.4)	238 (40.3)	57 (47.1)	0.169
Hyperlipidemia, n (%)	354 (49.7)	301 (50.9)	53 (43.8)	0.153
Cerebrovascular accident, n (%)	25 (3.5)	22 (3.7)	3 (2.5)	0.785
Smoking, n (%)	344 (48.3)	289 (48.9)	55 (45.5)	0.051
NYHA III-IV, n (%)	183 (25.7)	154 (26.3)	29 (23.9)	0.597
EuroSCORE-II	1.96±1.25	1.89±1.13	2.27±1.68	**0.02**
Preoperative treatment, n (%)				
Statins	367 (51.5)	313 (53)	52 (43)	0.07
β-blockers	226 (31.7)	184 (31.7)	42 (34.7)	0.492
ACEI/ARB	347 (48.7)	301 (51.2)	46 (38.6)	**0.048**
Laboratory parameters				
Creatinine, (mg/dl)	0.9±0.3	0.8±0.4	1.1±0.3	0.439
TSH, (mU/L)	2.5±1.8	2.8±1.6	1.7±1.0	0.069
HbA1c (%)	6.7±1.8	6.7±1.8	6.7±1.6	0.970
White blood cell, 10^3/μl)	7.9±1.7	8.1±0.8	7.7±1.5	0.805
Preoperative Hemoglobin (g/dl)	12.4±1.8	12.5±1.8	12.0±1.5	**0.012**
Preoperative Hematocrit (%)	39.1±4.8	39.4±4.8	37.8±4.7	**0.001**
Preoperative albumin (g/dl)	4.2±1.2	4.2±0.4	4.2±0.4	0.280
C-reactive protein (mg/L)	8.9±7.0	8.6±7.1	10.1±6.7	**0.036**
Glasgow prognostic score				
GPS=0	473 (66.4)	417 (70.6)	56 (46.3)	**<0.0001**
GPS≥1	239 (33.6)	174 (29.4)	65 (53.7)	
Intensive Care Unit stay (days)	3.7±2.8	3.62±2.80	3.76±3.05	0.628
In-hospital stay (days)	6.8±4.2	6.8±4.0	6.7±4.7	0.893

Table 1 continued. Comparison of demographic and laboratory parameters and outcomes of groups with regard to postoperative atrial fibrillation development.

Variables	All (n=712)	POAF (-) (n=591)	POAF (+) (n=121)	p
Ejection fraction, (%)	50.9±8.7	51.2±8.7	49.2±8.7	**0.018**
Left atrial diameter (mm)	35.8±4.1	36.6±4.8	35.6±3.9	0.12
Outcomes				
Mortality, n (%)				
30-day	40 (5.6)	25 (4.2)	15 (12.4)	**<0.0001**
1-year	76 (10.7)	42 (7.1)	34 (28.1)	**<0.0001**
Postoperative stroke, n (%)	26 (3.7)	3 (0.5)	23 (19)	**<0.0001**

POAF – post pperative atrial fibrillation; NYHA – New York Heart Association; EuroSCORE – European System for Cardiac Operative Risk Evaluation, ACEI/ARB – angiotensin converting enzyme/angiotensin receptor blocker, TSH – thyroid stimulating hormone; HbA1c – glycosylated albumin; GPS – Glasgow prognostic score.

and 75.9% of the patients were male. There were 473 (66.4%) patients in the low-GPS group (GPS=0) and 239 (33.6%) patients in the high-GPS group (GPS≥1). Forty (5.6%) patients died within 30 days and 76 (10.7%) patients died within 1 year after surgery. Stroke occurred in 26 (3.7%) patients during the 1-year follow-up, excluding early postoperative stroke cases. **Table 1** provides an overview of the demographic, laboratory, and clinical data.

Postoperative Atrial Fibrillation

POAF occurred in 121 (17%) patients at a median of 2 days after the operation. The patients with POAF were older (63.3±8.7 vs 59.6±9.8; *P*<0.0001) and 84.8% of the patients were female (*P*=0.05). Also, POAF developed in patients who had a significantly higher prevalence of carotid artery disease (27.3% vs 4.4%; *P*<0.0001). Furthermore, EuroSCORE II (2.27±1.68 vs 1.89±1.13; *P*=0.02) was significantly higher while Hb (12.0±1.5 vs 12.5±1.8; *P*=0.012), Htc (37.8±4.7 vs 39.4±4.8; *P*=0.001), and left ventricular ejection fraction (49.2±8.7 vs 51.2±8.7; *P*=0.018) were significantly lower in patients with POAF. In terms of preoperative medications, statins and β-blockers did not differ between groups. However, angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEI/ARB) use was less common in the POAF group (38.6% vs 51.2%; *P*=0.048). Ultimately, POAF developed more frequently in patients with higher GPS. Specifically, within the group of patients who developed POAF, GPS=0 was found in 56 patients (46.3%) and GPS≥1 in 65 patients (53.7%) (*P*<0.0001). **Table 1** provides data regarding the variables and their associations with POAF development.

Cardiovascular Mortality and Stroke

The patients' followup data were analyzed to define factors related to stroke and 30-day and 1-year cardiovascular

mortality. When patients were grouped according to 30-day cardiovascular mortality, the following were statistically higher in the 30-day cardiovascular mortality group: advanced age (63.5±11.1 vs 60.1±9.6; *P*=0.031), EuroSCORE II (3.3±1.3 vs 1.9±1.1; *P*<0.0001), high GPS (65% vs 31.7%; *P*<0.0001), history of chronic obstructive pulmonary disease (COPD) (37.5% vs 17.8%; *P*=0.042), history of carotid artery disease (22.5% vs 7.5%; *P*=0.004), and POAF (37.5% vs 15.8%; *P*<0.0001). The parameters that were significantly higher in the 1-year cardiovascular mortality group were similar to those in the 30-day cardiovascular mortality group: advanced age (62.4±10.5 vs 59.9±9.6; *P*=0.041), EuroSCORE II (3.7±1.5 vs 1.8±1.02; *P*<0.0001), history of carotid artery disease (26.3% vs 6.1%; *P*<0.0001), and high GPS (59.2% vs 30.5%; *P*<0.0001). In addition, stroke (22.4% vs 1.4%; *P*<0.0001) and POAF development (44.7% vs 13.7%; *P*<0.0001) were more common in the 1-year cardiovascular mortality group. **Tables 2 and 3** provide data regarding the association of the variables with 30-day and 1-year cardiovascular mortality, respectively.

The patients who developed stroke during the 1-year follow-up period had significantly higher values for the following: EuroSCORE II (3.6±2.2 vs 1.9±1.2; *P*<0.0001), GPS (76.9% vs 31.9%; *P*<0.0001), history of cerebrovascular accident (CVA) (42.3% vs 2.1%; *P*=0.004), and carotid artery disease (92.3% vs 5.2%; *P*<0.0001). Also, 1-year cardiovascular mortality (65.4% vs 8.6%; *P*<0.0001) and POAF development (88.5% vs 14.3%; *P*<0.0001) were higher in the patients who developed stroke (**Table 4**).

Logistic Regression Analysis

To further evaluate individual risk factors for POAF development, 30-day and 1-year cardiovascular mortality, and stroke

Table 2. Comparison of demographic, laboratory, and clinical parameters with respect to 30-day cardiovascular mortality.

Variables	Survivor n=671	Non-survivor n=40	p
Age	60.1±9.6	63.5±11.05	**0.031**
Body mass index (kg/m²)	27.8±4.5	28.8±4.2	0.209
EuroSCORE II	1.9±1.1	3.3±1.3	**<0.0001**
History of hypertension, n (%)	349 (51.9)	23 (57.5)	0.494
History of CVA, n (%)	23 (3.4)	2 (5)	0.416
History of COPD, n (%)	120 (17.8)	15 (37.5)	**0.042**
History of DM, n (%)	279 (41.5)	16 (40)	0.850
History of CAD, n (%)	175 (26.2)	14 (35.9)	0.181
History of carotid artery disease, n (%)	50 (7.5)	9 (22.5)	**0.004**
Preoperative treatment, n (%)			
Statins	347 (51.7)	20 (50)	0.502
β-blockers	216 (32.6)	10 (26.3)	0.058
ACEI/ARB	333 (49.9)	14 (35.9)	0.072
Preoperative hemoglobin (g/dl)	12.5±1.6	12.4±1.9	0.786
Preoperative hematocrit (%)	39.3±4.3	39.1±4.8	0.820
Ejection fraction, (%)	51.6±8.1	50.9±8.7	0.596
Glasgow prognostic score, n (%)			
GPS=0	459 (68.3)	14 (35)	**<0.0001**
GPS≥1	213 (31.7)	26 (65)	
POAF developed patients, n (%)	106 (15.8)	15 (37.5)	**<0.0001**
Intensive Care Unit stay (days)	3.3±1.4	3.7±2.9	0.136
In-hospital stay (days)	6.8±4.1	6.9±5.1	0.822

EuroSCORE – European System for Cardiac Operative Risk Evaluation, CVA – cardiovascular accident; COPD – chronic obstructive pulmonary disease; DM – diabetes mellitus; CAD – coronary artery disease; ACEI/ARB – angiotensin converting enzyme/angiotensin receptor blocker; GPS – Glasgow prognostic score; POAF – post operative atrial fibrillation.

development, univariate logistic regression analyses were performed. The variables that were statistically significant in univariate logistic regression analyses were additionally evaluated by multivariate logistic regression analysis to define independent risk factors for outcomes. In multivariate logistic regression analyses, GPS [$P< 0.0001$, β: 0.401; OR (95% CI): 0.265-0.609], advanced age [$P=0.002$, β: 1.036; OR (95% CI): 1.013-1.060)], EuroSCORE II [$P=0.002$, β: 1.261; OR (95% CI): 1.087-1.462], and reduced left ventricular ejection fraction [$P=0.030$, β: 0.974; OR (95% CI): 0.952-0.997] were found to be independent risk factors for POAF development. In addition, high GPS [$P=0.001$, β: 0.267 OR (95% CI): 0.115-0.507] and EuroSCORE II [$P<0.0001$, β: 1.765 OR (95% CI): 1.429-2.181] were established as independent risk factors for 30-day cardiovascular mortality by multivariate logistic regression analysis.

Furthermore, high GPS [$P=0.001$, β: 0.329 OR (95% CI): 0.173-0.624], EuroSCORE II [$P<0.0001$, β: 2.691 OR (95% CI): 2.149-3.370], stroke [$P=0.028$, β: 0.220 OR (95% CI): 0.057-0.850] and POAF development [$P=0.017$, β: 0.410 OR (95% CI): 0.197-0.854] were found to be independent risk factors for 1-year cardiovascular mortality according to multivariate logistic regression analysis.

Last but not least, EuroSCORE II [$P<0.0001$, β: 1.704 OR (95% CI): 1.297-2.239] and POAF development [$P<0.0001$, β: 0.032 OR (95% CI): 0.008-0.123] were revealed as independent risk factors for stroke development during the 1-year followup.

Table 3. Comparison of demographic, laboratory, and clinical parameters with respect to 1-year cardiovascular mortality.

Variables	Survivor n=636	Non-survivor n=76	p
Age	59.9±9.6	62.4±10.5	**0.041**
Body mass index (kg/m²)	27.9±4.3	27.5±5.4	0.475
EuroSCORE II	1.8±1.02	3.7±1.5	**<0.0001**
History of hypertension, n (%)	331 (52.1)	41 (53.9)	0.754
History of CVA, n (%)	13 (2.1)	12 (15.8)	0.059
History of COPD, n (%)	117 (18.4)	18 (23.7)	0.266
History of DM, n (%)	265 (41.7)	30 (39.5)	0.714
History of CAD, n (%)	166 (26.2)	23 (30.7)	0.411
History of carotid artery disease, n (%)	39 (6.1)	20 (26.3)	**<0.0001**
Preoperative treatment, n (%)			
Statins	347 (51.7)	28	0.502
β-blockers	198 (31.7)	28 (37.8)	0.284
ACEI/ARB	306 (48.5)	41 (53.9)	0.312
Preoperative hemoglobin (g/dl)	12.4±1.9	12.3±1.6	0.427
Preoperative hematocrit (%)	39.2±4.8	38.5±4.6	0.475
Ejection fraction, (%)	50.9±8.7	50.8±8.9	0.940
Glasgow prognostic score, n (%)			
GPS=0	442 (69.4)	31 (40.8)	**<0.0001**
GPS≥1	194 (30.5)	45 (59.2)	
Postoperative stroke, n (%)	9 (1.4)	17 (22.4)	**<0.0001**
POAF developed patients, n (%)	87 (13.7)	34 (44.7)	**<0.0001**
Intensive Care Unit stay (days)	3.7±2.8	3.6±3.03	0.895
In-hospital stay (days)	6.7±4.1	7.3±5.1	0.225

EuroSCORE – European System for Cardiac Operative Risk Evaluation; CVA – cardiovascular accident; COPD – chronic obstructive pulmonary disease; DM – diabetes mellitus; CAD – coronary artery disease; ACEI/ARB – angiotensin converting enzyme/angiotensin receptor blocker; GPS – Glasgow prognostic score; POAF – post operative atrial fibrillation.

Discussion

POAF is considered an important complication following CABG, and it is crucial to predict its occurrence as it has both short- and long-term consequences. The results of our study indicated that high GPS, high EuroSCORE II, advanced age, female gender, history of carotid artery disease, lower ACEI/ARB use, and lower left ventricular ejection fraction were seen in patients who developed POAF. In addition, high GPS, EuroSCORE II, advanced age, and lower left ventricular ejection fraction were shown to be independent risk factors associated with POAF development. With regard to adverse events, cardiovascular mortality either within 30 days or 1 year, and stroke development within 1 year following the surgery were more frequent in patients who developed POAF. Moreover, POAF development

was found to be an independent risk factor for adverse outcomes, and GPS was established as an independent risk factor both for 30-day and 1-year cardiovascular mortality, even in patients with chronic coronary syndromes.

The most common type of arrhythmia after CABG is POAF, which may be observed in up to 40% of patients [19]. A history of AF, older age, obesity, presence of valvular and rheumatic heart disease, impaired left ventricular systolic function, left atrial enlargement, previous myocardial infarction, hypertension (HT), diabetes mellitus (DM), COPD, presence of metabolic syndrome, coronary ischemia, and hypoxemia are known risk factors for POAF [20]. Preoperative conditions such as clinical presentation and comorbidities, related surgery, and perioperative complications are the facilitator factors that make the myocardium vulnerable

Table 4. Comparison of demographic, laboratory, and clinical parameters with respect to stroke development in the 1-year followup period.

Variables	Stroke (-) n=686	Stroke (+) n=26	p
Age	60.1±9.7	63.1±9.4	0.131
Body mass index (kg/m²)	27.9±4.5	27.6±3.9	0.713
EuroSCORE II	1.9±1.2	3.6±2.2	**<0.0001**
History of HT, n(%)	357 (52.2)	14 (53.8)	0.862
History of CVA, n(%)	14 (2.1)	11 (42.3)	**0.004**
History of COPD, n(%)	128 (18.7)	7 (26.9)	0.208
History of DM, n (%)	282 (41.2)	13 (50)	0.370
History of CAD, n(%)	181 (26.6)	8 (30.8)	0.636
History of carotid artery disease, n (%)	45 (5.2)	24 (92.3)	**<0.0001**
Preoperative treatment, n (%)			
Statins	352 (51.4)	15 (57.7)	0.482
β-blockers	216 (32.1)	10 (4)	0.407
ACEI/ARB	331 (48.7)	16 (64)	0.132
Preoperative hemoglobin (g/dl)	12.4±1.8	12.1±1.6	0.360
Preoperative hematocrit (%)	39.2±4.8	37.5±5.7	0.082
Ejection fraction, (%)	50.9±8.7	49.5±9.5	0.423
Glasgow prognostic score, n (%)			
GPS=0	466 (68.1)	6 (23.1)	**<0.0001**
GPS≥1	219 (31.9)	20 (76.9)	
1-year cardiovascular mortality, n (%)	59 (8.6)	17 (65.4)	**<0.0001**
POAF developed patients, n (%)	98 (14.3)	23 (88.5)	**<0.0001**
Intensive Care Unit stay (days)	3.6±2.6	6.3±5.3	**0.002**
In-hospital stay (days)	6.7±4.1	8.2±4.9	0.073

EuroSCORE – European System for Cardiac Operative Risk Evaluation; CVA – cardiovascular accident; COPD – chronic obstructive pulmonary disease; DM – diabetes mellitus; CAD – coronary artery disease; ACEI/ARB – angiotensin converting enzyme/angiotensin receptor blocker; GPS – Glasgow prognostic scale; POAF – post operative atrial fibrillation.

to AF development in the postoperative period. Re-entery and triggered activity are known to be the 2 main arrhythmogenic mechanisms. Arrhythmogenic remodeling due to comorbidities or transient triggering factors related to the surgery may initiate POAF development involving pulmonary veins or 'non-pulmonary' vein regions. Including all these parameters to obtain a risk score to predict the development of POAF would be extremely time consuming. On the other hand, the role of inflammation and related biomarkers have already been studied and inflammation has been established as a pathological mechanism for AF development [21,22]. Our study's analysis of serum CRP, a marker of acute inflammation, showed that increased age, female sex, reduced ejection fraction, and lower preoperative hemoglobin and hematocrit levels were associated with POAF development in concordance with previously stated risk factors.

CRP is an acute-phase reactant and a well-known marker of systemic inflammation. Not only surgery, but also most of the coronary artery disease risk factors, as well as coronary artery disease itself, may cause increased CRP levels. The association between higher baseline CRP level and POAF was revealed in a meta-analysis which considered high CRP as a positive predictor [22]. Similarly, in our study, CRP levels were higher in the patients who developed POAF.

Serum albumin levels represent nutritional status, but they are also known as a negative acute-phase reactant (decreasing levels with increasing inflammation). Moreover, as stated before, albumin exerts antiplatelet effects through modulation of arachidonic acid metabolism and a protective effect through antioxidant properties [11]. The relationship between

hypoalbuminemia and acute coronary syndromes, cardiovascular ischemic disease, and stroke was reported previously [23,24]. In contrast to the consensus in the literature, there were no significant differences in albumin levels between groups in our study. However, it should be noted that the exclusion of patients with acute or chronic inflammatory conditions and those with disorders related to the loss of or impaired production of albumin may be the reasons for similar albumin levels in our study.

GPS consists of CRP and albumin concentrations and is among the validated inflammatory risk scores for cancer patients [8]. Moreover, it has been studied in different cardiac disorders and shown to be a prognostic tool for determining survival after heart failure as well as cardiovascular mortality in acute coronary syndromes [9,10]. Concerning the influence of CRP and albumin on POAF development, higher GPS values were found to be associated with POAF development. Our results emphasize the importance and utility of this scoring system (GPS), rather than biomarkers individually (CRP and albumin), for the anticipation of POAF development in patients who have undergone CABG surgery with a diagnosis of chronic coronary syndrome. High GPS was displayed as an independent risk factor for POAF development; moreover, it was an independent predictor of 30-day and 1-year cardiovascular mortality. Furthermore, high GPS was significantly related to stroke development in the POAF group during the 1-year followup period, although it was not found to be an independent predictor.

POAF is an important phenomenon related to myocardial infarction, stroke, and even death [6]. Besides, patients with POAF have increased risk of persistent AF in the first 5 years after CABG [7]; thus, it is crucial to define patients who are at high risk. We demonstrated the relation between POAF and 30-day and 1-year cardiovascular mortality, as well as stroke development in the 1-year followup period. POAF was also found to be an independent risk factor for cardiovascular mortality and stroke development within 1 year after surgery. Since high GPS was found to be an independent predictor of POAF development and 30-day and 1-year mortality, effective responses to preoperative conditions, including inflammation and nutritional status of the patient, may improve outcomes by decreasing POAF development.

There are several limitations of our study. Firstly, although the cohort was large, the study population remained low, mostly due to strict exclusion criteria (patients with disease that might have altered serum CRP and/or albumin levels). Moreover, all pitfalls of retrospective studies are relevant to our study. Further, information on preoperative medications (β-blockers, statins, ACEI/ARB), such as doses and length of treatment, might have influenced the results. Baseline CRP and albumin levels were used in the study whereas monitoring the changes in serum levels throughout the course of hospitalization may reveal additive knowledge. Also, our data is limited to in-hospital detection of POAF, whereas a longer duration would give better diagnostic ability. The patients were revascularized with arterial (mostly left internal mammalian artery) and venous (saphenous vein) conduits in our center. Thus, a comparison could not be made in terms of the graft effect on POAF development. Future studies comparing complete arterial revascularization CABG with CABG including venous conduits may give additional valuable information. Last but not least, this study was not designed to evaluate short- or long-term treatment of POAF. However, the guideline-directed anti-arrhythmic and anticoagulant therapy, either for short- or long-term periods, is essential to reduce mortality and morbidity.

Conclusions

GPS is an easy-to-use and rapidly measured score with widely available tools for calculation. In addition, it has reasonable diagnostic accuracy in determining POAF and stroke development as well as 30-day and 1-year cardiovascular mortality. Since POAF is related to mortality and stroke, GPS may help to predict patients who are at risk with minimal effort. Further prospective studies with larger patient cohorts and longer followup periods are needed to improve the clinical utility of GPS.

Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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