

Comparison of SYNTAX Score I and SYNTAX Score II for Predicting Postoperative Atrial Fibrillation in Patients Undergoing Coronary Artery Bypass Graft Surgery

Semi Ozturk, MD,¹ Muhsin Kalyoncuoglu, MD,¹ Mazlum Sahin, MD,²

¹Department of Cardiology, Haseki Training and Research Hospital, Istanbul, Turkey; ²Department of Cardiovascular Surgery, Haseki Training and Research Hospital, Istanbul, Turkey

ABSTRACT

Background: Atrial fibrillation is a frequent cause of morbidity following coronary artery bypass grafting (CABG). SYNTAX score II (SSII) is associated with outcomes in patients undergoing coronary revascularization. We investigated the relationship between SSII and postoperative atrial fibrillation (POAF) in patients undergoing CABG.

Methods: Records of 461 consecutive patients who underwent elective isolated CABG were retrospectively reviewed. Characteristics of patients with and without POAF were compared.

Results: POAF developed in 51 (11.1%) patients. Patients with POAF were older (61.8 ± 7.8 versus 58.4 ± 7.7 ; $P = .003$). Chronic obstructive pulmonary disease (COPD) and history of coronary artery disease (CAD) were more frequent in patients with POAF whereas the frequency of hypertension (HT), diabetes mellitus (DM), and smoking did not differ. CRP was significantly higher in patients with POAF. Left atrial diameter (LAD), EuroSCORE II, SSI and SSII were greater in patients with POAF ($P < .001$ for all). Age, history of CAD, LAD, SSI, and SSII were independent predictors of POAF in multivariate regression analysis. In ROC analysis, SSII was more accurate than SSI for predicting POAF, albeit statistically insignificant [difference between AUC: 0.0483, 95% CI (-0.0411) - (0.138); z statistic: 1.059, $P = .29$]. In-hospital MACE (3.2% versus 9.8%, $P = .038$) and one-year mortality (4.6% versus 13.5%, $P = .008$) of patients with POAF were significantly higher.

Conclusion: POAF occurred in more than one-tenth of patients undergoing CABG, and it is associated with in-hospital MACE and one-year mortality. Age, history of CAD, LAD, SSI, and SSII are independent predictors of POAF. SSII seems to be more accurate than SSI for predicting POAF.

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Correspondence: Semi Ozturk, MD, Haseki Training and Research Hospital, Department of Cardiology, Millet Caddesi Aksaray/Fatih, Istanbul, Turkey, 34130; +90-212-529-4400, +90-5316676506; fax: +90-212-589-6229 (e-mail: semi_ozturk@yahoo.com).

INTRODUCTION

POAF is a significant cause of morbidity and mortality in patients undergoing coronary artery bypass grafting (CABG). Despite continuous efforts being made to overcome this issue, prevalence of POAF remains significant in the last decade [DiNicolantonio 2014; Romanov 2019]. Studies concluded that several clinical parameters such as age, left ventricular ejection fraction (EF), chronic obstructive pulmonary disease (COPD), left atrial diameter (LAD), and metabolic syndrome were associated with POAF [Ismail 2017; Özkan 2017; Manganas 2007]. Furthermore, risk scores, namely CHA2DS2-VASC, HATCH, EuroSCORE I were shown to predict POAF [Emren 2016; Kılıçgedik 2018; Luo 2017]. Recently, two studies concluded that SYNTAX score I (SSI) is an independent predictor of POAF [Cerit 2016; Geçmen 2016].

SSI solely takes into account angiographic properties, some of which significantly do not affect surgical outcomes (CTO, tortuosity, etc.). On the contrary, SSII was calculated by combining SSI and clinical parameters. In addition, parameters were differently weighted in SSII-CABG and SSII-PCI so that risk for two distinct treatment modalities can be accurately calculated. The superiority of SSII over SSI in deciding between PCI and CABG were demonstrated by previous studies [Seruys 2019]. We aimed to investigate the predictive accuracy of SSII-CABG in patients undergoing isolated CABG.

METHODS

Study population: Patients undergoing elective isolated CABG at Haseki Training and Research Hospital between January 2015 and August 2017 were included in the study. Only on-pump CABG procedures were included. The patients undergoing concomitant surgeries, such as valve repair/replacement, aneurysmectomy, and emergent procedures, were excluded. Patients with a history of atrial fibrillation (paroxysmal, persistent, permanent) and a history of arrhythmia, implying possible AF, were excluded. The same group of cardiovascular surgeons and anesthesiologists operated on the patients, using the same techniques and myocardial protection. The study population was retrospectively analyzed using the computerized hospital database. Demographic, laboratory, and clinical variables were recorded.

Table 1. Demographic, clinical and laboratory characteristics of groups

	N = 410 POAF (-)	POAF (+) N = 51	P
Sex (Female), N (%)	85 (20.7)	5 (9.8)	.90
Age (years)	58.4 ± 7.7	61.8 ± 7.8	.003
Body mass index (kg/m ²)	27.4 ± 3.8	27.9 ± 4.2	.402
Smoking, N (%)	164 (40)	15 (29.4)	.171
DM, N (%)	138 (33.7)	20 (39.2)	.437
HT, N (%)	169 (41.2)	15 (29.4)	.129
COPD, N (%)	59 (14.4)	14 (27.5)	.024
PVD, N (%)	48 (11.7)	9 (17.6)	.257
CAD history, N (%)	46 (11.2)	21 (41.2)	<.001
MI at presentation, N (%)	137 (33.4)	23 (45.1)	.118
Stroke or TIA, N (%)	18 (4.4)	4 (7.8)	.288
Ejection Fraction (%)	50.6 ± 9.1	49.1 ± 9.5	.281
eGFR (mL/min/1.73m ²)	90.4 ± 19.2	92.6 ± 21.3	.469
Total Cholesterol (mg/dl)	268.1 ± 91.6	252.6 ± 77.7	.192
LDL-C (mg/dl)	134.6 ± 37.4	129.5 ± 35.3	.357
HDL-C (mg/dl)	45.6 ± 5.7	46.6 ± 6.3	.458
CRP (mg/dl)	6.9 ± 3.5	8.2 ± 3.6	.013
LAD (mm)	36.3 ± 2.1	37.7 ± 1.8	<.001
Aortic cross-clamp time (minute)	42.9 ± 16.4	45.3 ± 18.8	.329
CPB time (minute)	78.1 ± 28.3	82.1 ± 29.5	.341
Graft Count	2.8 ± 0.8	2.9 ± 0.7	.808
EUROSCORE II	2.9 ± 1.6	3.8 ± 1.9	<.001
SYNTAX I	19.7 ± 8.5	28.3 ± 10.4	<.001
SYNTAX II	25.4 ± 7.6	34.2 ± 8.7	<.001
In-hospital MACE, N (%)	13 (3.2)	5 (9.8)	.038
1-year mortality	19 (4.6)	7 (13.5)	.008

Values mean ± SD or n (%), DM, diabetes mellitus; HT, hypertension; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; CAD, coronary artery disease; MI, myocardia infarction; TIA, transient ischemic attack; eGFR, estimated glomerular filtration rate; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; CRP, C-reactive protein; LAD, left atrial diameter; CPB, cardiopulmonary bypass

Postoperative atrial fibrillation: Patients were routinely followed by a heart rhythm monitor, during their intensive care unit stay. Daily ECG was taken in the intensive care unit and also in the ward. Additional ECG was obtained in case the patient had any complaints, including pain, palpitation, lightheadedness, etc. POAF was defined as occurrence of any episode of AF lasted longer than 30 seconds captured on ECG or monitor.

Table 2. Univariate logistic regression analysis of POAF

	OR (95% CI)	P
Sex (Female)	2.406 (0.927-6.242)	.071
Age	1.065 (1.020-1.112)	.004
Body mass index	1.032 (0.959-1.111)	.401
Smoking	1.600 (0.849-3.016)	.146
DM	0.786 (0.432-1.430)	.431
HT	1.683 (0.893-3.171)	.107
COPD	2.251 (1.147-4.417)	.018
PAD	0.619 (0.284-1.350)	.228
CAD history	5.539 (2.931-10.467)	<.001
MI at presentation	0.611 (0.339-1.100)	.101
Stroke or TIA	0.540 (0.175-1.662)	.282
Ejection Fraction	0.983 (0.953-1.014)	.281
eGFR	1.006 (0.990-1.023)	.468
Total Cholesterol	0.998 (0.994-1.001)	.248
LDL-C	0.996 (0.988-1.004)	.357
HDL-C	1.029 (0.980-1.081)	.243
CRP	1.098 (1.019-1.184)	.015
LAD	1.321 (1.166-1.497)	<.001
Aortic cross-clamp time	1.009 (0.991-1.026)	.328
CPB time	1.005 (0.995-1.015)	.341
Graft Count	1.040 (0.759-1.425)	.807
EUROSCORE II	1.339 (1.136-1.578)	<.001
SYNTAX I	1.089 (1.058-1.121)	<.001
SYNTAX II	1.124 (1.085-1.164)	<.001

DM, diabetes mellitus; HT, hypertension; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; CAD, coronary artery disease; MI, myocardia infarction; TIA, transient ischemic attack; eGFR, estimated glomerular filtration rate; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; CRP, C-reactive protein; LAD, left atrial diameter; CPB, cardiopulmonary bypass

RISK SCORES

SYNTAX I-II score: Two experienced interventional cardiologists, who were unaware of the study, evaluated the angiograms. CAD was defined as a stenosis of more than 50% of the lumen diameter in any of the main coronary arteries. SYNTAX I-II scores were calculated by using the downloaded version from www.syntaxscore.com.

EuroSCORE II: Preoperative risk assessment was carried out for all patients by using the EuroSCORE II system using the downloaded version from www.euroscore.pil-media.com.

Major adverse cardiac event: MACE was defined as a composite of in-hospital mortality, postoperative non-fatal myocardial infarction (MI), cardiac arrest requiring

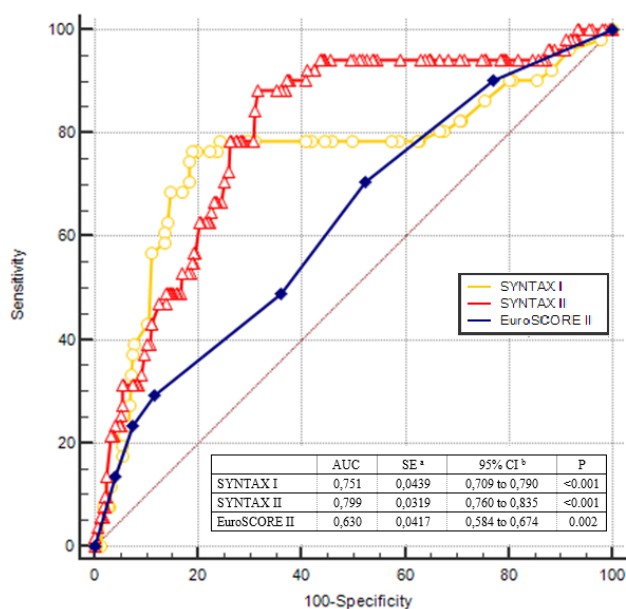


Figure 1. ROC curve analysis of EuroSCORE II, SYNTAX I and SYNTAX II for predicting POAF [a. Hanley & McNeil, 1983; b. binomial exact]

cardiopulmonary resuscitation, need for new mechanical circulatory support, and cerebrovascular event during intraoperative/postoperative hospitalization. One-year mortality was defined as death from all causes, during a one-year follow up after discharge from the hospital. The study was approved by the local ethics committee.

STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS version 22.0 (IBM Corp. Armonk, NY, USA) and MedCalc bvba version 16 (Seoul, Korea). Normality of the data was analyzed with the Kolmogorov-Smirnov test. Continuous data was expressed as mean \pm standard deviation (SD) and categorical data was expressed as percentages. Differences between patient subgroups were tested using Student's T-test. Categorical variables between groups were assessed with Chi-square test or Fisher's exact test, whichever was suitable. Logistic regression analysis was used to identify the independent predictors of POAF. Significant variables in univariate analysis were included in multivariate analysis. Two separate models were constructed. In the first model, variables other than SSII were included. In the second model, variables of SSII (COPD, age, SSI) were not included, due to possible multicollinearity. Receiver-operating characteristic (ROC) curve graphics were used to determine the cut-off values of predictors for POAF. ROC curves were compared, according to Hanley and McNeil [Hanley 1983]. A Kaplan-Meier estimate of survival was obtained to investigate the differences in mortality between the POAF and no-POAF groups. Differences were assessed by using the log-rank test. A P -value $< .05$ statistically was considered significant.

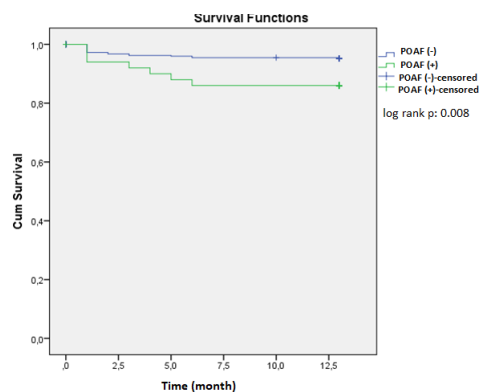


Figure 2. Kaplan-Meier cumulative survival curves for one-year mortality according to POAF.

RESULTS

A total of 461 patients were evaluated. POAF developed in 51 (11.1%) patients. Patients with POAF were older (61.8 ± 7.8 versus 58.4 ± 7.7 ; $P = .003$). Baseline characteristics of patients were presented in Table 1. COPD and history of CAD were more frequent in patients with POAF whereas the frequency of coronary artery risk factors, including hypertension (HT), diabetes mellitus (DM), and smoking, were similar between the two groups. CRP were significantly higher in patients with POAF. Left atrial diameter (LAD), EuroSCORE II, SSI and SSII were greater in patients with POAF, compared with those without ($P < .001$ for all). Age, LAD, COPD, history of CAD, CRP, EuroSCORE II, SSI and SSII were significantly associated with POAF in univariate regression analysis (Table 2). Age, LAD, history of CAD, and SSI were predictors of POAF in the first model of multivariate logistic regression analysis (Table 3). History of CAD, LAD, and SSII were predictors of POAF in the second model. In ROC curve analysis, all three scores statistically were significant predictors for POAF [SSI, AUC: 0.751, 95% CI (0.709–0.790), $P = .001$; SSII, AUC: 0.799, 95% CI (0.760–0.835), $P < .001$; EuroSCORE II, AUC: 0.630, 95% CI (0.584–0.674), $P = .002$]. When ROC curves were compared, SSII was more accurate than SSI for predicting POAF, albeit statistically insignificant [difference between AUC: 0.0483, 95% CI (-0.0411) - (0.138); z statistic: 1.059, $P = .29$] (Figure 1, Table 4). EuroSCORE II was significantly less accurate than both SSI and SSII. SSII greater than 26.7 had 88.2% sensitivity and 68.5% specificity to predict POAF [AUC: 0.799, 95% CI (0.760–0.835), $P = .04$]. In-hospital MACE [13 (3.2%) versus 5 (9.8%), $P = .038$] and one-year mortality [19 (4.6%) versus 7 (13.5%), $P = .008$] of patients with POAF significantly were higher (Figure 2).

DISCUSSION

The frequency of POAF was about 11% in our study population, which was reported between 10.4% to 38.5% in previous studies [Abdel-Salam 2017; Verdejo 2016]. Significant

Table 3. Multivariate analysis of POAF

	First Model		Second Model	
	OR (95% CI)	P	OR (95% CI)	P
CRP	1.081 (0.980-1.192)	.119	1.084 (0.989-1.189)	.086
COPD	2.199 (0.952-5.079)	.065	NI	
Age	1.084 (1.032-1.140)	.001	NI	
CAD history	2.800 (1.313-5.970)	.008	6.387 (2.975-13.712)	<.001
LAD	1.377 (1.196-1.586)	<.001	1.395 (1.197-1.625)	<.001
SYNTAX I	1.100 (1.060-1.142)	<.001	NI	
SYNTAX II	NI		1.137 (1.091-1.185)	<.001

CRP, C-reactive protein; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; LAD, left atrial diameter; NI, not included

Table 4. Pairwise comparison of ROC curves

	EuroSCORE II-SYNTAX I	EuroSCORE II-SYNTAX II	SYNTAX I-SYNTAX II
Difference between areas	0.121	0.170	0.0483
Standard Error*	0.0578	0.0512	0.0517
95% Confidence Interval	0.00813-0.235	0.0693-0.270	(-0.0530) - (0.50)
z statistic	2.101	3.313	0.934
Significance level (P)	.0357	.0009	.3503

*Hanley & McNeil, 1983

variation of frequency in previous reports may owe to the non-standardized definition of POAF in addition to inclusion of different types of surgeries such as off-pump CABG. Nevertheless, POAF is a significant cause of morbidity after CABG, despite significant efforts made to overcome it [Kaw 2011]. We showed that age, LAD, history of CAD, SSI and SSII were independent predictors for POAF. Our results were compatible with two previous studies, which demonstrated possible predictive value of SSI for POAF in patients undergoing on-pump CABG [Cerit 2016; Geçmen 2016]. Although SSI was shown to be associated with various cardiovascular outcomes, dependence solely to the angiographic data is the major limitation of SSI. Basically, SSI assesses the complexity of atherosclerosis and takes into account various features, such as calcification and tortuosity, which of these parameters are neither related to atherosclerosis severity nor surgical outcomes. In addition, although SSI was reported to be associated with surgical outcomes, it seems more suitable for assessing risk for percutaneous procedures rather than surgical [Bundhun 2017]. Regarding these limitations, separate SSII (CABG and PCI) scores were developed for addressing two disparate modalities. Therefore, SSII-CABG is made up of clinical parameters in addition to SSI. We investigated SSII for predicting POAF because variables included in SSII, such as EF, COPD, and peripheral vascular disease (PVD), were shown to be related to POAF in previous studies [Vlahou

2016]. We concluded that SSII has an increased predictive accuracy for POAF compared with SSI. However, statistical insignificance of the result might be due to the fact that only age and COPD have a relationship with POAF and variables, such as creatinine clearance (CrCl), EF, and gender, showed no association with POAF in our study. Nevertheless, SSII seems more reliable than SSI owing to the inclusion of both angiographic and clinical parameters comprehensively.

The relationship between history of CAD and POAF independent of SSI score was another substantial finding of our study. This finding supported that exposure to chronic ischemia is one of the major factors causing susceptibility to POAF. Chronic ischemia causes atrial fibrosis and predisposition to reentry arrhythmia [Lieder 2018]. History of CAD not only results in greater SSI, but also might cause long-standing ischemia and complications. Anatolevna RO et al. showed that history of CAD longer than 36 months was associated with POAF [Anatolevna 2016]. Compatible with the previous research in-hospital, MACE and one-year mortality is increased in patients with POAF in our study. This finding is not a surprise since patients with POAF had higher clinical and angiographic risk scores, and we think increased mortality solely should not be attributed to cardioembolism related to AF.

Age was one of the most consistent predictors for POAF in several studies [Bhave 2012]. Impact of age on occurrence of POAF is multifactorial. Both age-related cardiac risk

factors and cardiac physio-anatomic changes seem to increase the tendency to AF. On the other hand, medications such as beta-blockers which were proven to be effective in preventing POAF might be less useful in elderly patients [Fuller 1989]. Even more, beta-blockers might induce AF manifesting tachycardia-bradycardia syndrome in elderly patients without overt clinical sinus node dysfunction given the altered pharmacokinetics [Lafarge 2018]. Compatible with previous studies age was an independent predictor in multivariate analysis in our study.

COPD was shown to be closely associated with PAF. Despite the fact that the exact mechanism by which COPD cause AF is unclear, hypoxemia and increased inflammation might trigger POAF. Previous two studies evaluating SSI and POAF found COPD as an independent predictor while some other studies did not [Cerit 2016; Geçmen 2016; Farouk 2018]. In our study, COPD was not an independent predictor of POAF, when adjusted for other factors in multivariate analysis. On the other hand, COPD is still significantly represented in SSII-CABG.

The strong association of POAF with LAD was reported in previous studies as well [Açil 2007]. LAD is an indicator of diastolic dysfunction, which was shown to be related to POAF [Ozben 2016]. Even in very young patients without any overt cardiac disease, LAD seems to predict AF [Boraita 2018]. History of CAD is more frequent in patients with POAF, which might cause a larger left atrium. Chronic ischemia not only causes atrial ischemia and remodeling, but also causes diastolic dysfunction and subsequently greater LAD before detectable ventricular structural and functional changes occur. Correlation of AF and systolic dysfunction is not linear, since LAD may be affected earlier before significant ventricular dilation and EF reduction. Therefore, LAD seems to be more accurate in predicting POAF than ventricular size and function.

Inflammation has a substantial role in atrial fibrillation as many studies obviously demonstrated the link [Harada 2015]. CRP as a marker of inflammation seems questionable due to controversial findings of different studies [Erдем 2014; Del Campo 2017]. CRP is not a reliable marker since affected by numerous factors. Whole inflammatory cascade, including IL-6, must be prompted to induce AF. Additionally, a recent study concluded that higher CRP levels might be associated with gene polymorphisms rather than increased inflammation [Del Campo 2017]. Since we included patients with recent acute coronary syndrome, CRP levels might be higher compared to other studies.

LIMITATIONS

Retrospective design of the study is the major limitation. We excluded patients undergoing emergent, off-pump CABG, and concomitant valve surgeries, which are daily routines of surgical practice. However, none of the risk scores are yet able to predict cardiovascular outcomes in these very high-risk patients. On the other hand, patients with low and high risk thoroughly were represented in our study.

CONCLUSION

POAF occurred in more than one-tenth of patients undergoing CABG, and it is associated with in-hospital MACE and one-year mortality. Age, history of CAD, LAD, SSI, and SSII are independent predictors of POAF. SSII seems to be more accurate than SSI for predicting POAF.

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