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**Original Article**

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**ABSTRACT**

**Objective:** Postoperative atrial fibrillation (PoAF) is a common complication after coronary artery bypass grafting (CABG). The SYNTAX (synergy between percutaneous coronary intervention with taxus and cardiac surgery) score is an angiographic scoring tool for systematically quantifying the severity of each coronary lesion. The aim of this study was to evaluate the relationship between development of PoAF and SYNTAX score II in patient undergoing off-pump CABG.

**Design:** Retrospective study

**Setting:** Department of Cardiovascular Surgery, University of Health Sciences, Bursa Yüksek İhtisas Research and Training Hospital, Bursa, Turkey

**Subjects:** : A total of 68 consecutive patients who underwent off-pump CABG

**Intervention:** Predictive values of the variables were measured for the development of PoAF

**Main outcome measure(s):** The relationship between preoperative SYNTAX score II and PoAF in patients undergoing off-pump CABG.

**Results:** Twenty patients with PoAF and 48 patients without PoAF were enrolled. In univariate logistic regression analysis, the PoAF was significantly correlated with age (OR=1.083, 95% CI: 1.025-1.144, p=0.004), glomerular filtration rate (OR=0.963, 95% CI: 0.940-0.987, p=0.002), hematocrit (OR=0.848, 95% CI: 0.729-0.991, p=0.038) and Syntax score II (OR=1.079, 95% CI: 1.023-1.138, p=0.005). Only hematocrit levels were identified as an independent predictor of PoAF in multivariate analysis (OR=0.829, 95% CI: 0.694–0.990, p=0.039). It was determined that a cut-off level of 22.65 for SYNTAX score II predicts PoAF (AUC: 0.733, p=0.003)

**Conclusion:** SYNTAX score II was not an independent predictor for the development of PoAF . However, we observed that higher SYNTAX score II was correlated with the development of PoAF.

**Keywords:** aortocoronary bypass, cardiac arrhythmias, coronary angiography

**INTRODUCTION**

Postoperative atrial fibrillation (PoAF) is a common complication after coronary artery bypass grafting (CABG)<sup>[1]</sup>. PoAF has a high prevalence, affecting 20 to 45% of CABG patients<sup>[2]</sup>. This arrhythmia occurs most frequently in the first five days of the postoperative period, peaking between 24 and 72 hours, being uncommon after the first week<sup>[2]</sup>. PoAF has been associated with an increase in early and late mortality rates, hospital adverse events, particularly hemodynamic instability, thromboembolic events and heart failure progression<sup>[3]</sup>. Older age, obesity, hypertension, prior atrial fibrillation (AF) and congestive heart failure are associated with a higher risk of developing AF after cardiac surgery<sup>[4]</sup>.

The intraoperative factors can be consequent to cardiac ischemia and inflammation inherent to the complexity of the surgical technique<sup>[2]</sup>. The CABG with cardiopulmonary bypass appears to be associated with a higher incidence of PoAF compared to off-pump CABG<sup>[2]</sup>.

The SYNTAX (synergy between percutaneous coronary intervention with taxus and cardiac surgery) score is an angiographic scoring tool for systematically quantifying the severity

of each coronary lesion and assessing its individual characteristics<sup>[5]</sup>. This scoring tool is used worldwide to predict long-term outcomes in patients with coronary artery disease undergoing elective percutaneous transluminal angioplasty (PTCA) or CABG<sup>[5]</sup>. Recently, some authors have used SYNTAX scores to predict major adverse cardiac and cerebrovascular events following CABG<sup>[6,7]</sup>. The aim of this study was to determine the relationship between preoperative SYNTAX score II and PoAF in patients undergoing off-pump CABG.

## **SUBJECTS AND METHODS**

### **Patients**

This retrospective observational study included 86 consecutive patients who underwent off-pump CABG between 2014 and 2016 at Department of Cardiovascular Surgery, Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey. The study was approved by the local institutional Ethical Committee of University of Health Sciences.

All data to be analyzed retrospectively retrieved from the hospital medical files. The exclusion criteria were preoperative AF or flutter, previous treatment with amiodarone, presence of valvular heart disease, chronic obstructive pulmonary disease (COPD), prolonged intensive care unit (ICU) stay, redo cardiac surgery, bleeding revision, and chronic renal failure. Eighty-six patients that underwent off-pump CABG were evaluated in this study. Five patients with COPD, 2 patients with chronic renal failure, 5 patients with moderate mitral valve disease, 2 patients with preoperative AF, 2 patients with previous cardiac surgery history, 1 patient with postoperative bleeding and 1 patient with prolonged ICU stay were excluded. Thus, the remaining 68 patients with off-pump CABG were included in the study.

All data were recorded, such as age, gender, history of hypertension, diabetes mellitus, preoperative drug use (beta-blockers, statins, ACE or ARB inhibitors), smoking, ejection fraction, left atrial diameter, body mass index, body surface area, Euroscore, number of anastomosis, extubation time, postoperative bleeding amount, duration of ICU stay, and discharge time from hospital. Laboratory parameters were also studied from venous blood sample before the surgery.

### **Diagnosis of PoAF**

The patients were monitored in ICU with continuous heart rhythm and invasive blood pressure monitoring. In addition, a 12-lead electrocardiography (ECG) were also obtained daily while in the ICU. Patients were monitored continuously by five-lead telemetry in the regular ward. When the patients complained of palpitation, dyspnea and angina, 12-lead ECG was taken. AF was verified using 12-lead ECG. AF was diagnosed according to the European Society of Cardiology guidelines<sup>[8]</sup>. Postoperative AF was described as irregular, fast oscillations, or fibrillatory waves instead of regular P waves at ECG. An AF episode lasting longer than 5 minutes was accepted as PoAF. Standard medical cardioversion treatment was conducted with amiodarone (5 mg/kg) for 30 minutes, followed by 900 mg/day.

## SYNTAX Score Analysis

SYNTAX score was performed by an experienced interventional cardiologist. For SYNTAX score II calculator, calculator version 2.28 (Cardialysis, Boston Scientific; available at: [www.syntaxscore.com](http://www.syntaxscore.com)) was used. The vessels with a diameter of  $\geq 1.5$  mm and the lesions with  $\geq 50\%$  stenosis were included in the SYNTAX score calculation. Scoring was performed for each patient according to the following parameters: coronary dominance, number of lesions, segments included per lesion, the presence of total occlusion, trifurcation, bifurcation, aorto-osteal lesion, calcification, severe tortuosity, thrombus, and diffuse/small vessel disease; and lesion length  $>20$  mm.

## Statistical Analysis

Statistical analysis data were analyzed with the Statistical Package for the Social Sciences (IBM SPSS Statistic Inc. version 21.0, Chicago, IL, USA). Continuous and ordinal variables were expressed as mean  $\pm$  standard deviation and nominal variables were expressed as frequency and percentage. Kolmogorov-Smirnov test and Shapiro-Wilk tests of normality were used to identify distribution of variables. Student's t test was used to compare two groups for continuous variables with normal distribution. Chi Square test was used to compare two groups for nominal variables. Mann-Whitney U test was used to compare two groups for continuous variables without normal distribution. The relationship between the preoperative independent variables and the development of postoperative AF was evaluated by a binary logistic regression analysis. For all tests, a p-value  $<0.05$  was considered statistically significant. Receiver-operating characteristic (ROC) curve was applied for the prediction of PoAF after off-pump CABG and the area under the curve was calculated for SYNTAX score II.

## RESULTS

A total number of 20 patients in the PoAF(+) group (70% male, mean age:  $66.4 \pm 8.1$  years) and 48 patients in the PoAF(-) group (75% male, mean age:  $57.02 \pm 11.8$  years) were recorded in the study. The demographic and clinical properties of the subjects are summarized in Table 1. Both PoAF(+) group and PoAF(-) group were similar to each other with regard to demographic properties. However, ACE-I/ARB therapy and SYNTAX score II were significant in the PoAF(+) group ( $p = 0.007$  and  $p = 0.02$ , respectively) (Table 1).

The comparison of laboratory and operative parameters are shown in Table 2. Significant differences were observed between two groups in terms of hematocrit, blood urea nitrogen, creatinin, glomerular filtration rate (GFR), free T3, time to extubation, ICU stay and hospital stay. There was a statistical difference between the two groups in terms of hematocrit, blood urea nitrogen, creatinin, GFR, time to extubation, ICU stay and hospital stay as a negative effect to PoAF(+) group ( $p = 0.029$ ,  $p = 0.017$ ,  $p = 0.015$ ,  $p = 0.002$ ,  $p = 0.024$ ,  $p = 0.000$  and  $p = 0.000$ , respectively) (Table 2). Also, ejection fraction and left atrium diameter were not significantly different between the groups ( $p = 0.692$  and  $p = 0.465$ , respectively) (Table 2).

Factors related to the development of POAF were included in the univariate logistic regression analysis. In unadjusted univariate logistic regression analysis, the PoAF was significantly correlated with age (Odds Ratio [OR] = 1.083, 95% Confidence interval [CI]: 1.025-1.144,  $p = 0.004$ ), GFR (OR = 0.963, 95% CI: 0.940-0.987,  $p = 0.002$ ), hematocrit (OR = 0.848, 95% CI: 0.729-0.991,  $p = 0.038$ ) and Syntax score II (OR = 1.079, 95% CI: 1.023-1.138,  $p = 0.005$ ), but was not correlated with hypertension (OR = 5.600, 95% CI: 1.626-19.290,  $p = 0.171$ ), diabetes mellitus (OR = 556, 95% CI: 0.173-1.788,  $p = 0.324$ ), ejection fraction (OR = 0.997, 95% CI: 0.951-1.044,  $p = 0.883$ ), left atrium diameter (OR = 1.050, 95% CI: 0.923-1.191,  $p = 0.459$ ) (Table 3). Only hematocrit levels were identified as an independent predictor of development AF after off-pump CABG surgery in multivariate analysis (OR = 0.829, 95% CI: 0.694–0.990,  $p = 0.039$ ) (Table 3).

Additionally, in ROC curve analysis, it was determined that a cut-off level of 22.65 for Syntax score II was required for predicting PoAF with a sensitivity of 80% and a specificity of 66.7% (area under the curve: 0.733, 95% CI: 0.611-0.856,  $p = 0.003$ ) (Figure 1).

## DISCUSSION

In our study, we assessed the effect of the SYNTAX score II in the development of PoAF in patients that underwent off-pump CABG. In univariate logistic regression analysis, we found that age, lower GFR, lower hematocrit levels and higher SYNTAX score II were significantly correlated with the development of PoAF. In multivariate logistic regression analysis, only hematocrit levels were detected as an independent predictor for the development of PoAF. Also it was determined that a cut-off level of 22.65 of SYNTAX score II for predicting PoAF with a sensitivity of 80% and a specificity of 66.7% in ROC analysis (Fig 1). However, in our study, SYNTAX score II was not an independent predictor for the development of PoAF.

The incidence of PoAF following CABG surgery is seen in 25 - 40% of cases<sup>[1]</sup>. However, its frequency reaches 62% following combined CABG and valve surgery<sup>[9]</sup>. Atrial fibrillation is common in patients with rheumatic and non-rheumatic valvular heart disease<sup>[10]</sup>. A previous study demonstrated that patients with mitral regurgitation were more likely to experience recurrent AF post-ablation<sup>[11]</sup>. Mariscalco *et al*<sup>[12]</sup> identified the PoAF rates as 22.9%, 39.8%, and 45.2% for the isolated CABG, valve surgery, and combined surgery, respectively. Therefore, we excluded 5 patients with moderate mitral valve disease so that it does not affect the outcome of the study.

There have been an increased risk of new-onset AF in patients with COPD<sup>[13]</sup>. Mathew *et al*<sup>[14]</sup> have showed that COPD increased the incidence of both persistent and paroxysmal AF and the incidence of PoAF increased to 43% in the presence of COPD. Negative prognostic effect of atrial fibrillation has been demonstrated in COPD patients. For this reason, patients with COPD were excluded in order to make our results more accurate.

In their study, Kwon *et al*<sup>[15]</sup> found that the incidence of AF was significantly higher in patients with reduced renal function. In another study, Gursoy *et al*<sup>[16]</sup> investigated whether clinical Syntax scoring was a predictor of acute renal injury in patients on-pump and off-pump

CABG and showed that high clinical syntax scoring may be a predictor in the on-pump CABG group. Similar to these studies, in our study, high urea, high creatinine levels and low GFR were statistically significant in patients with PoAF. Also, SYNTAX score II levels were higher in these patients. We found that GFR significantly correlated with the development of PoAF in univariate logistic regression analysis.

In previous studies, hypertension, diabetes mellitus, left atrium diameter and low ejection fraction have been shown to play a role in the development of PoAF<sup>[17,18]</sup>. In our study, in terms of these parameters they were not significantly different between the groups. However, these factors which are effective in AF development, are included in the logistic regression analysis. None of these variables were significantly associated with the development of PoAF.

In our study, in univariate logistic regression analysis, we found that age significantly correlated with the development of PoAF. However, in multivariate logistic regression analysis, it was not detected as an independent predictor of the development of PoAF. Age-related changes, including atrial fibrosis and accumulation of amyloid, can cause intra-atrial reentry, which leads to the development of AF<sup>[19]</sup>. Age has been repeatedly shown to be the major risk factor for AF after cardiac surgery<sup>[20,21]</sup>. Cerit *et al*<sup>[22]</sup> found that age was significantly associated with development of POAF following CABG in univariate logistic regression analysis. In another study, Geçmen *et al*<sup>[23]</sup> showed that age was an independent variable predicting the development of PoAF in both univariate and multivariate logistic regression analysis. Although it was not detected as an independent predictor of the development AF in our study, when the age is considered as a risk factor, it is known that elder patients have a high risk for developing AF.

The SYNTAX score shows the complexity of coronary artery disease and is able to predict the rate of major advanced cardiovascular events after revascularization<sup>[24]</sup>. However, there are few studies about the relationship between the SYNTAX score II and PoAF. In a previous study, Geçmen *et al*<sup>[23]</sup> reported that advanced age, COPD, and SYNTAX score II were independent predictors of PoAF in patients undergoing isolated on-pump CABG surgery. Another study by Cerit *et al*<sup>[22]</sup> on patients with on-pump CABG showed that the SYNTAX score II was an independent predictor of the development of PoAF. However, a study on patients undergoing off-pump CABG reported that there was no significant difference between a higher SYNTAX score II and development of POAF<sup>[25]</sup>. In our study, we observed that higher SYNTAX score II was correlated with the development of PoAF. However, SYNTAX score II was not an independent predictor for the development of PoAF. On the other hand, our study had homogeneity because we excluded risk factors for development atrial fibrillation as COPD and valvular heart diseases. In our study, in terms of factors related to the development of PoAF such as hypertension, diabetes mellitus, left atrium diameter and low ejection fraction, there were no significant differences between the groups. In ROC curve analysis, we found that a cut-off level of 22.65 for SYNTAX score II was required for predicting PoAF with a sensitivity of 80% and a specificity of 66.7%. Therefore, the results of our study may take into consideration the relationship between high syntax score and postoperative AF.

## CONCLUSION

Several factors contribute to the development of AF after coronary bypass surgery. Many studies have been done on PoAF development. SYNTAX score II is a marker of the severity of preoperative coronary artery disease and may be a predictor of postoperative complications such as AF. As a result of this study, we thought that high SYNTAX score II could be a factor of the development of PoAF. High Syntax score may be one of the reasons for PoAF development. We think that this factor should be taken into account before surgery.

## Limitations

Our study has some limitations. The main limitation of this study is a retrospective study and it was done in a single center. The number of patients included in the study is small and there is no record of long-term outcomes. In addition, off-pump CABG operations were not performed by a single surgeon. Further prospective studies with a larger number of patients are required.

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**Ethical statement:** The material has not been published anywhere. Authors of the manuscript have no financial ties to disclose and have met the ethical adherence.

**Disclosure of interest:** The authors declare that they have no competing interests.

**Declaration of authorship:** All authors have directly participated in the planning, execution, analysis or reporting of this research paper. All authors have read and approved the final version of the manuscript.

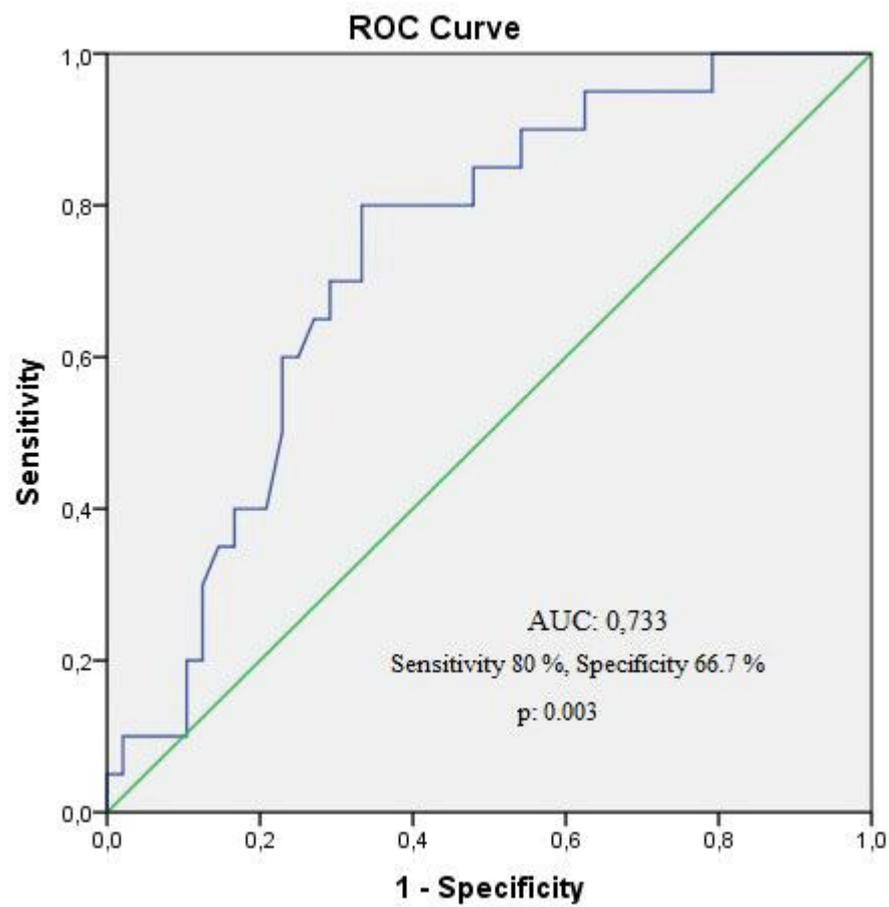
**Conflict of interest:** None

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**Figure 1:** ROC (Receiver Operation Characteristic) curve and area under the curve (AUC) for Syntax score II for predicting PoAF

**Table 1:** Demographic features of the patients

Characteristics	PoAF(-) group n = 48	PoAF (+) group N = 20	p-value*
Age (years)	57.02 ± 11.8	66.4 ± 8.1	0.272
Male gender, n (%)	36 (75)	14 (70)	0.670
Hypertension, n (%)	20 (41.7)	16 (80)	0.168
Diabetes mellitus, n (%)	18 (37.5)	5 (25)	0.321
CAD, n (%)	6 (12.5)	6 (30)	0.085
PAD, n (%)	2 (4.2)	3 (15)	0.119
Preoperatif MI, n (%)	13 (27.1)	3 (15)	0.284
Beta-blocker therapy, n (%)	48 (100)	20 (100)	-
Statin therapy, n (%)	34 (70.8)	15 (75)	0.727
ACE-I/ARB therapy, n (%)	27 (56.3)	18 (90)	<b>0.007</b>
SYNTAX score I	14.44 ± 5.7	15.05 ± 6.49	0.882
SYNTAX score II	19.32 ± 11.5	28.57 ± 9.3	<b>0.020</b>
EuroSCORE II	2.6 ± 1.89	3.65 ± 2.1	0.071
Number of anastomosis	1.6 ± 0.82(1-3)	1.33 ± 0.59(1-3)	0.096
BSA	1.86 ± 0.17	1.85 ± 0.13	0.793
BMI	27.36 ± 4.61	27.93 ± 3.54	0.353

\*Student's *t* test; Mann-Whitney U test; Pearson Chi- Square

PoAF: Postoperative atrial fibrillation; CAD: Carotid artery disease; PAD: Peripheral artery disease; ACE-I: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin-receptor blocker; SYNTAX: synergy between percutaneous coronary intervention with taxus and cardiac surgery; BSA: Body surface area; BMI: Body mass index.

**Table 2:** Laboratory and operative variables

Parameters	PoAF (-) group n = 48	PoAF (+) group n = 20	p-value*
Hematocrit (%)	40.91 ± 3.57	38.83 ± 3.29	<b>0.029</b>
White blood Cell (10 <sup>3</sup> /μL)	9.08 ± 2.25	9.19 ± 2.5	0.865
Platelet (10 <sup>3</sup> /μL)	255.58 ± 76.89	248 ± 94.14	0.518
Red cell distribution width (%)	13.67 ± 1.24	14.19 ± 0.88	0.018
Mean platelet volume (fL)	8.75 ± 0.86	8.63 ± 0.8	0.756
BUN (mg/dL)	17.83 ± 7.57	22.45 ± 8.33	<b>0.017</b>
Creatinine (mg/dL)	0.85 ± 0.21	1 ± 0.21	<b>0.015</b>
GFR (ml/min/m <sup>2</sup> )	103.16 ± 24.82	80.66 ± 22.22	<b>0.002</b>
Na (mEq/L)	139.15 ± 2.67	138.8 ± 2.39	0.683
K (mEq/L)	4.04 ± 0.61	4.09 ± 0.37	0.745
Ca (mg/dl)	9.25 ± 0.5	9.04 ± 0.54	0.113
Mg (mg/dl)	1.93 ± 0.23	1.89 ± 0.17	0.489
Free T <sub>3</sub> (pg/mL)	3.11 ± 0.4	2.86 ± 0.3	<b>0.017</b>
Free T <sub>4</sub> (ng/dL)	1.16 ± 0.2	1.07 ± 0.18	0.086
TSH (IU/mL)	3.02 ± 4.77	2.56 ± 1.33	0.443
C Reactive protein (mg/dL)	10.02 ± 17.88	13.96 ± 23.64	0.182
Total Cholesterol(mg/dl)	198.42 ± 30.03	194.4 ± 30.31	0.618
LDL-C (mg/dl)	125.39 ± 26.56	121.66 ± 25.73	0.596
HDL-C (mg/dl)	40.37 ± 5.11	40.38 ± 6.31	0.997
TG (mg/dl)	164.4 ± 67.79	151.6 ± 52.16	0.453
Ejection fraction (%)	48.44 ± 12.03	48 ± 9.37	0.692
Left atrium diameter (mm)	37.19 ± 3.85	38 ± 4.81	0.465
Time to extubation (minute)	597.92 ± 277.38	754.25 ± 302.77	<b>0.024</b>
Postoperative bleeding (ml)	607.29 ± 268.76	622.5 ± 233.66	0.826
ICU stay (day)	2.1 ± 0.37	2.85 ± 0.81	<b>0.000</b>
Hospital stay (day)	6.02 ± 1	7.3 ± 1.34	<b>0.000</b>

\*Student's-t test; Mann-Whitney test PoAF: Postoperative atrial fibrillation; ICU: Intensive care unit; GFR: Glomerular Filtration Rate (According to Cockcroft-Gault Equation)

**Table 3:** Binary logistic regression analysis to identify predictors of PoAF

Variables	Univariate analysis			Multivariate analysis		
	p-value	Exp(B) Odds Ratio	95% C.I. Lower Upper	p-value	Exp(B) Odds Ratio	95% C.I. Lower Upper
<b>Age</b>	<b>0.004</b>	1.083	1.025 – 1.144	0.629	1.029	0.917 - 1.154
<b>HT</b>	0.171	5.600	1.626 - 19.290			
<b>DM</b>	0.324	556	0.173 - 1.788			
<b>EF</b>	0.883	0.997	0.951 - 1.044			
<b>LAD</b>	0.459	1.050	0.923 - 1.191			
<b>Syntax score II</b>	<b>0.005</b>	1.079	1.023 - 1.138	0.748	1.019	0.910 - 1.141
<b>GFR</b>	<b>0.002</b>	0.963	0.940 - 0.987	0.076	0.972	0.943 - 1.003
<b>Hct</b>	<b>0.038</b>	0.848	0.729 - 0.991	<b>0.039</b>	0.829	0.694 - 0.990

PoAF: Postoperative atrial fibrillation; SYNTAX: synergy between percutaneous coronary intervention with taxus and cardiac surgery; GFR: Glomerul filtrate rate; HT: Hypertension; DM: diabetes mellitus; EF: ejection fraction; LAD: Left atrium diameter; Hct: Hematocrit