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Aortic knob width as a novel predictor of postoperative atrial fibrillation following off-pump coronary artery bypass grafting

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Abstract

The aim of this study was to determine whether aortic knob width (AKW) was related to the development of postoperative atrial fibrillation (AF) in patients undergoing off-pump coronary artery bypass grafting (CABG). Between July 2017 and June 2019, a total of 453 patients undergoing isolated off-pump CABG were enrolled to this retrospective observational cohort study. The patients were divided into two groups; as AF group (n=102) and non-AF group (n=351). The groups were compared with regard to preoperative demographics and clinical characteristics, intraoperative data, and postoperative outcomes, and then a multivariate logistic regression analysis was performed in order to determine the independent predictors of postoperative AF. The incidence of postoperative AF in our study population was found as 22.5% (n=102/453). The median age and AKW, and the frequencies of hypertension and chronic renal dysfunction were significantly higher in patients in AF group than in non-AF group. Multivariate logistic regression analysis revealed that age and AKW were the independent predictors of postoperative AF. The analysis yielded that the risk of POAF development increased by 5.2% with each one-year increase in patient age [OR 1.0520 with 95% CI= (1.0214, 1.0835), p<0.001], and by 3.36 times when AKW increased by 1 cm [OR 3.3614 with 95% CI= (2.6142, 4.3961), p<0.001]. ROC analysis revealed that AKW of 43.9 mm constituted the cut-off value for the development of AF with 68.6% sensitivity and 80.9% specificity. The present study demonstrated that AKW was a significant and independent predictor of AF following off-pump CABG.

Keywords: Aortic knob width, predictor, atrial fibrillation, off-pump coronary artery bypass grafting

Introduction

Atrial fibrillation (AF) is one of the most common complications following cardiac surgery. Previously, cardiac surgery associated postoperative atrial fibrillation (POAF) was considered a benign and harmless problem. However, recent studies demonstrated that POAF could significantly increase early and late mortality and morbidity. POAF is clinical associated with decreased left ventricular hemodynamic performance as well as increased frequency of heart failure and cerebrovascular events [1,2]. Moreover, there is a positive association between POAF and longer periods of intensive care and hospital stay duration. Thus, it poses a problem both for the patient and the health personnel and increases the burden of healthcare costs [3]. The etiology, predictors, prevention, and treatment of POAF associated with cardiac surgery are still controversial. Several studies have identified some basic predictors for POAF, but its pathophysiological mechanisms still have not been fully elucidated. Some studies suggested that existing electrophysiological abnormalities could be worsen throughout the surgery [4,5]. Advanced age has been reported to be the most strongest risk factor [5,6]. For instance, the risk of POAF was 80% in patients above 80 years of age. However, it was only 5% in patients, who were under the age of 50 [6]. In addition to the advanced age, there are other factors that could contribute the development of POAF, including male gender, decreased left ventricular ejection fraction, left atrial enlargement, heart valve surgery, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), rheumatic heart diseases, hypothyroidism, vitamin D deficiency, and cardiopulmonary bypass use during the surgery [5-11]. However, in recent years, an increase in the surgery rate performed on advance aged patients has increased the incidence of POAF.

Aortic knob width (AKW) is a radiologically determined configuration formed by a part of descending aorta and

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foreshortened aortic arch. It is a measured distance between the point of lateral edge of the trachea and the left lateral wall of the aortic knob on an anteroposterior chest radiograph. Several studies have reported that AKW could reveal significant predictive information associated with coronary artery diseases [12,13]. Furthermore, a recent study has suggested that an increase in AKW is positively associated with atherosclerotic process in the aorta and AKW is a novel indicator of the atherosclerosis [14].

To the best of our knowledge, the association between AKW and POAF in patients undergoing off-pump coronary artery bypass grafting (CABG) has never been investigated in the existing literature. Therefore, the aim of the present study was to investigate the existence of a potential association between AKW and POAF in patients undergoing off-pump CABG. Moreover, other possible predictors and postoperative outcomes of new-onset AF following off-pump CABG were also examined.

Materials and Methods

Ethics considerations

The present study was performed following the approval of local ethical committee (ethics number: 2019/321, decision date: 19.12.2019). The study was carried out in accordance with the principles of Helsinki Declaration. Detailed information about the operation were provided to all patients and their written surgical consents were obtained.

Study population and design

This retrospective observational cohort study was performed on 453 patients with the presence of clinical data, who underwent isolated off-pump CABG surgery at the Department of Cardiovascular Surgery of our hospital between July 2017 and June 2019. The study population consisted of isolated off-pump CABG patients since routine CABG procedures have been performed with the "off-pump" technique for about 5 years in our hospital. Preoperative demographic and clinical information, operational data, and postoperative adverse events as well as clinical observations of these patients were withdrawn from the computerized medical database of the hospital. The patients were divided into two groups as new-onset atrial fibrillation (AF group, n=102) and non-developing patients (non-AF group, n=351) during the postoperative period. All patient data obtained from both groups were compared. Therefore, the predictors of atrial fibrillation developed during the postoperative period were determined.

POAF was defined as a new-onset AF that occurred during the postoperative period and requiring medical treatment (beta-blockers, calcium channel blockers, amiodarone, anticoagulants, etc.) until the patient was discharged.

The criteria that was used for exclusion was as follows: patients, who had atrial fibrillation before the surgery, underwent emergency coronary artery bypass surgery, had additional surgery together with coronary artery bypass surgery, underwent reoperations, performed on-pump CABG and planned with off-pump surgery but converted to on-pump surgery during the operation (conversion).

Surgical procedure

Isolated CABG operations, which are routinely performed with the off-pump beating-heart technique, have been performed in our department by the same surgical team for approximately five years. All patients were operated via median sternotomy. The internal thoracic artery (ITA), great saphenous vein, and radial artery were the most preferred bypass grafts. Pericardiotomy was performed following the median sternotomy, and then the aorta and coronary arteries were examined. "No-touch aorta" method was preferred in cases with severe calcific and porcelain aorta. Before the start of coronary anastomoses, the patients were intravenously administered with 200 IU / kg body weight of unfractionated heparin. The target activated clotting time (ACT) was > 300 seconds and anastomoses were started after ACT > 300 seconds was achieved. Without cardiopulmonary bypass on the beating heart, the heart was positioned with the help of the Octopus IV tissue stabilizer and primarily distal anastomoses were performed with 7/0 or 8/0 propylene sutures. After arteriotomy of the targeted coronary artery with distal anastomosis was achieved, bulldog clamps were used to create proximal occlusion. Air blowing was used to ensure optimal visualization during the anastomosis. After distal anastomoses were completed, proximal anastomoses were performed with 6/0 or 7/0 propylene sutures. Heparin protamine was used as a neutralizer. Then, bleeding control was performed and, afterwards, the tissues were closed in a standard way to terminate the surgery. Following the operation, all patients were transferred to the intensive care unit.

Postoperative monitoring

In our clinic, electrocardiogram (ECG), oxygen saturation, and invasive arterial and central venous pressures were monitored continuously for the first 48 hours in the postoperative early period in addition to the regular monitoring of arterial blood gases every 2-4 hours. Inotropic support needs were closely monitored, fulfilled as needed and recorded. During the following days, cardiac rhythm was examined through taking standard ECG at least twice a day (morning and evening). Additional cardiac rhythm was evaluated with additional ECG in case of the detection of irregular rhythm in the radial pulse; assessment was performed at least once every 4 hours until the patients were discharged. Similar evaluations were performed in the presence of tachycardia, palpitation complaints or any suspects of rhythm disorders.

The diagnosis of new-onset atrial fibrillation was performed in ECG with the loss of P wave and the presence of irregular RR intervals.

Measurement of the aortic knob width

In all cases, AKW was measured through evaluating the preoperative postero-anterior chest radiographs available in hospital records. AKW measurements were performed by an examiner, who was unaware whether the patient developed new-onset AF in the postoperative period. Using the postero-anterior chest X-ray, the examiner determined AKW through drawing a horizontal line from the left lateral edge of the trachea to the left lateral wall of the aortic knob and measuring its length on the computer (Figure 1).

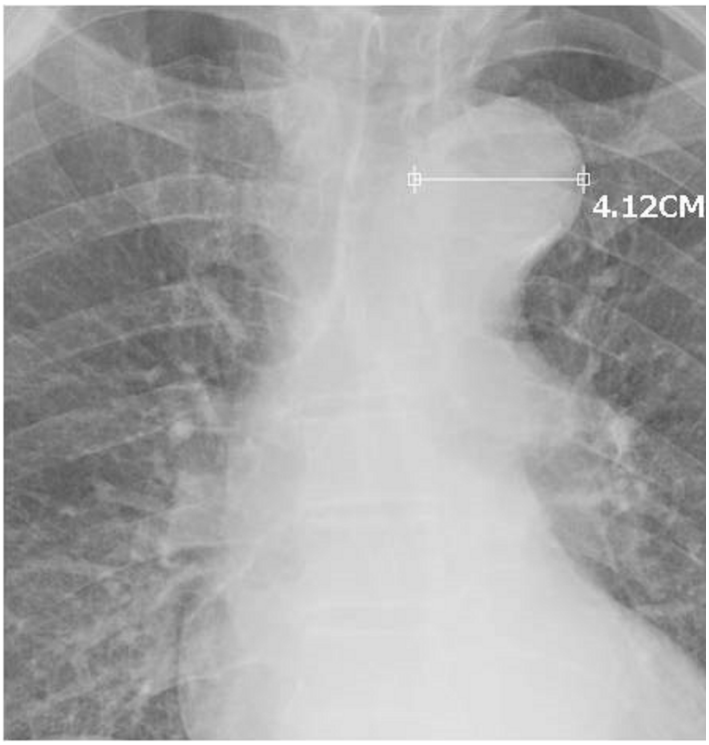

Figure 1. The view of aortic knob width (AKW) on chest X-ray

Statistical analysis

Normality of variables was evaluated using Anderson-Darling test. Descriptive statistics were obtained. Data were expressed as number (%) or median (min-max). Continuous variables were compared using Mann Whitney U test. Categorical data (two-way tables) were evaluated with Chi-square test. Receiver-operating characteristic (ROC) curve analysis was used to determine the cut-off values of AKW for POAF from the area under curve (AUC). ROC curve analysis was performed using "OptimalCutpoints" library by Lopez-Raton et al. for R software [15]. In the multiple explanatory variable logistic regression analysis, the initial model was fitted and all significant independent variables were included. Then, a backward-elimination approach in a multiple explanatory variable logistic regression model was conducted to evaluate the model for potential confounding effects. In this model, the factors/covariates were removed one at a time, starting with the factor/covariate that had the largest p value, until all remaining factors had a two-sided p value < 0.05. The goodness of fit was tested using the Hosmer–Lemeshow test. The single and multiple explanatory variable(s) logistic regression analysis methods were employed. In the single explanatory variable logistic regression analysis, we estimated the odds ratios with 95 % confidence intervals for each study variable, and the significance level of each factor/covariate was determined. The analyses were performed in R (R Core Team, 2014) [16].

Results

The current study included 102 patients with POAF (28 females and 74 males) and 351 patients without POAF (103 females and 248 males). The incidence of POAF in the study was 22.5% (102/453). The AF and non-AF groups were compared in terms of the preoperative demographic and clinical characteristics and intraoperative and postoperative data (Table 1 and Table 2).

Table 1. Preoperative demographic and clinical variables

Variables	Non-AF group (n=351)	AF group (n=102)	p value
Age (years)	63 (29-87)	69 (48-84)	<0.001
Male gender	248 (70.7%)	74 (72.5%)	0.805
Obesity	96 (27.4%)	32 (31.4%)	0.503
LMCA disease	73 (20.8%)	16 (15.7%)	0.316
Low LVEF	119 (33.9%)	36 (35.3%)	0.887
LVEF level (%)	55 (25-65)	52.5 (25-65)	0.811
LA diameter (cm)	3.70 (2.50-6.50)	4.00 (2.70-6.30)	0.121
Aortic knob width (cm)	3.50 (2.42-6.92)	4.70 (2.48-7.12)	<0.001
Beta blocker usage	141(40.1%)	42 (41.2%)	0.946
Hypertension	101 (28.8%)	43 (42.2%)	0.032
Diabetes mellitus	105 (29.9%)	27 (25.7%)	0.582
Hyperlipidemia	91 (25.9%)	22 (21.6%)	0.444
Myocardial infarction	161 (45.9%)	52 (51.0%)	0.425
Peripheral arterial disease	37 (10.5%)	10 (9.8%)	0.976
Chronic pulmonary disease	66 (18.8%)	23 (22.5%)	0.486
Chronic renal dysfunction	38 (10.8%)	19 (18.6%)	0.027
Chronic liver disease	3 (0.9%)	2 (1.9%)	0.687
Previous CVE	54 (15.4%)	16 (15.7%)	1.000
Previous PCI	65 (18.5%)	15 (14.7%)	0.459
Smoking	108 (30.8%)	37 (36.3%)	0.353

Abbreviations: AF: Atrial fibrillation; CVE: Cerebrovascular event; LA: Left atrium; LMCA: Left main coronary artery; LVEF: Left ventricular ejection fraction; PCI: Percutaneous coronary intervention.
Data are presented as median (min.-max.) for continuous variables or number (%) for categorical variables

Table 2. Intraoperative and postoperative variables

Variables	Non-AF group (n=351)	AF group (n=102)	p value
LITA usage	334 (95.1%)	97 (95.1%)	1.000
Complete revascularization	322 (91.7%)	94 (92.1%)	0.801
Number of distal bypass	4 (1-6)	4 (1-6)	0.864
Extubation time (hour)	6 (2-22)	6 (3-24)	0.142
Length of ICU stay (hour)	48 (16-360)	48 (20-360)	0.999
Length of hospital stay (day)	5 (3-18)	6 (4- 21)	0.332
Transfused ES (unit)	0 (0-4)	0 (0-6)	0.072
Transfused FFP (unit)	1 (0-4)	1 (0-8)	0.082
Inotrope requirement	68 (19.4%)	22 (21.6%)	0.728
IABP requirement	25 (7.1%)	11 (10.8%)	0.319
Low cardiac output syndrome	18 (5.1%)	8 (7.8%)	0.426
Myocardial infarction	13 (3.7%)	5 (4.9%)	0.797
Cerebrovascular event	10 (2.8%)	5 (4.9%)	0.480
Reintubation	12 (3.4%)	3 (2.9%)	1.000
Pneumonia	10 (2.8%)	5 (4.9%)	0.480
Mediastinitis	13 (3.7%)	6 (5.9%)	0.493
Reexploration for bleeding	15 (4.3%)	6 (5.9%)	0.680
ARD requiring hemodialysis	9 (2.6%)	4 (3.9%)	0.700
Gastrointestinal bleeding	3 (0.9%)	1 (1.0%)	1.000
In-hospital mortality	8 (2.3%)	3 (2.9%)	0.987

Abbreviations: AF: Atrial fibrillation; ARD: Acute renal dysfunction; ES: Erythrocyte suspension; FFP: Fresh frozen plasma; IABP: Intraaortic balloon pump; ICU: Intensive care unit; LITA: Left internal thoracic artery.
Data are presented as median (min.-max.) for continuous variables or number (%) for categorical variables

The patients in AF group were significantly older compared to the patients in non-AF group (p<0.001). The median age of the patients in AF group was 69 years while the median age of the patients in non-AF group was 63 years. The median value of AKW was detected to be significantly higher in AF group compared to the non-AF group (4.70 vs 3.50 cm, respectively) (p<0.001). In addition, the incidences of both hypertension and chronic renal dysfunction were found to be significantly higher in AF group than the non-AF group (for hypertension 42.2% vs. 28.8%, p=0.032, and for chronic renal dysfunction 18.6% vs. 10.8%, p=0.027). In terms of other preoperative demographics and clinical parameters as well as all intraoperative and postoperative variables, it was detected that there were no significant differences between the groups.

After the determination of statistically significant variables, in order to assess the association between POAF development and its independent predictors by adjusting for the other significant parameters, the multiple explanatory variable logistic regression analysis was carried out. The analysis yielded that the risk of POAF development increased by 5.2% with each one-year increase in patient age [OR 1.0520 with 95% CI= (1.0214, 1.0835), p<0.001], and by 3.36 times when AKW increased by 1 cm [OR 3.3614 with 95% CI= (2.6142, 4.3961), p<0.001] (Table 3).

Table 3. Results of logistic regression analysis for the prediction of independent risk factors

Variables	p value	Odds ratio (95% CI)
Age	<0.001	1.0520 (1.0214, 1.0835)
LA diameter	0.403	1.2314 (0.8306, 1.8255)
Aortic knob width	<0.001	3.3614 (2.6142, 4.3961)
Hypertension	0.230	1.3457 (0.9647, 1.6432)
Chronic renal dysfunction	0.074	1.2502 (0.8646, 1.5487)
Extubation time	0.062	1.0890 (0.9966, 1.1900)
Transfused ES (unit)	0.127	1.2214 (0.9470, 1.5754)
Transfused FFP (unit)	0.093	1.1868 (0.9272, 1.4655)

Abbreviations: CI: Confidence interval; ES: Erythrocyte suspension; FFP Fresh frozen plasma; LA: Left atrium.
Variables with p value < 0.15 were put in the logistic regression model

ROC curve analysis revealed that the AKW of 43.9 mm constituted the cut-off value to predict POAF development with 68.6% sensitivity and 80.9% specificity [AUC= 0.81, 95% CI= (0.77-0.86), p<0.001] (Figure 2).

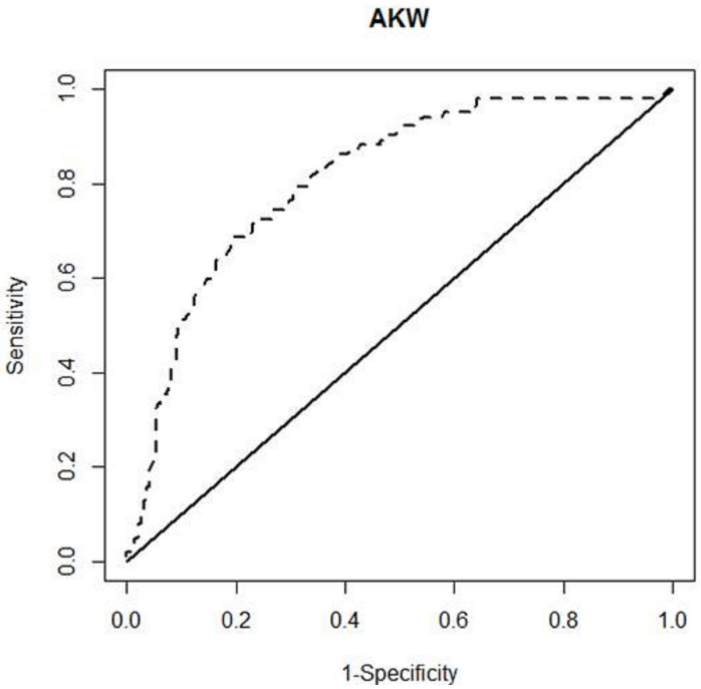

Figure 2. Receiver-operating characteristic (ROC) curve analysis of diagnostic accuracy of aortic knob width (AKW) in prediction of atrial fibrillation after off-pump coronary artery bypass grafting

Discussion

In the current study, the most considerable findings were advanced age and determination of AKW as independent predictors of POAF following off-pump CABG.

In the pathogenesis of AF, a rapid and chaotic rhythm occurs in the atrial tissues associated with multiple impulses rather than the normal regular electrical activity originating from the sinoatrial node. As a result of the loss of an adequate and synchronous contraction in the atria, the effective volume of blood passing from atria to the ventricles is reduced. Moreover, simultaneous start of multiple stimuli in the atrial tissues spreading irregularly into the atria causes a competition. This decreases the number of impulses from the AV node to the ventricles, but many impulses progress rapidly and chaotically towards the ventricles. As a result, the ventricles contract unevenly and rapidly in response to these irregular stimuli, resulting in an arrhythmic cardiac rhythm [17].

The frequency of postoperative atrial fibrillation (POAF) that was developed following cardiac surgery varied between 15 and 40%. Although it could be seen within the first week after surgery, it occurred most frequently on the postoperative 2nd and 3rd days [18-20]. It has been suggested that POAF could be triggered by various factors, including surgical trauma, excessive manipulation of the right atrium during surgery, use of cardioplegia, discontinuation of beta-blockers used during the preoperative period, postoperative hypoxia, hypovolemia and electrolyte imbalance [21]. However, less is known about the molecular mechanisms leading to the POAF electropathophysiology. Several studies suggested that different biochemical events or their combination could be responsible for the pathophysiological mechanisms of POAF. Some of these events include oxidative stress, inflammatory changes, ischemic status, excessive release of catecholamines into the systemic circulation, alterations in the autonomic tone, variations in the expression of connexins, and atrial fibrosis [22,23].

Identification of the predictors and risk factors of AF associated with cardiac surgery is of great importance, as it allows the application of preventative methods and quick management. Several different risk factors of POAF that can develop following cardiac surgery have been reported in the literature. However, among these risk factors, 'advanced age' is the most important risk factor that has been reported in almost all research in the literature [1-11,18-21,23]. The impact of the advanced age on the development of POAF could be associated with age-induced atrial dilation, muscle atrophy, decrease in the conducting tissues, and fibrosis. Age-associated pathologies in atrial tissues could lead to multiple re-entry pathways that cause atrial dysrhthmias [24]. Similar to the previously published data in the literature, the present study demonstrated that advanced age is a significant and independent risk factor of POAF. Moreover, each one-year increase in patient age was associated with a 5.2% increase in the risk of POAF development. In addition, the current study also suggested that the AKW was another independent predictor of POAF following off-pump CABG. Furthermore, it was also observed that the risk of POAF development increased by 3.36 times for every 1 cm AKW increase.

Advanced age is related to essential hypertension, aneurysmal alterations on the aortic tissue and subsequent aortic dilatation. Therefore, the aorta is frequently more dilated and tortuous at the advanced age [12]. In a large autopsy study by Sawabe et al. [25], the authors concluded that aortic circumference served as a major age-related pathobiological determinant. Yun et al. [12] studied the clinical significance of AKW and aortic knob calcification on 178 patients with coronary artery disease (CAD) and demonstrated that the AKW that was easily measured on a simple chest radiograph was considerably related to the severity of CAD. Higaki et al. [13] examined the utility of AKW for the prediction of central hemodynamics in patients with CAD and revealed that larger AKW was an independent predictor of increased systolic blood pressure. Erkan et al. [26] showed a significant relationship between carotid intima media thickness and AKW in patients with essential hypertension and suggested that the AKW could ensure significant predictive data for subclinical atherosclerosis in hypertensive patients. Apart from these, in a prospective observational multicenter large-scale study on 4657 patients at 70 centers from 17 countries, Mathew et al. [6] reported that the aortic atherosclerosis was an important predictor of POAF in patients undergoing CABG.

Studies investigating the relationship between AKW and POAF following cardiac surgery are very limited, and to the best of our knowledge, only one study examining the relationship between AKW and AF development following CABG is present in the existing literature. For the first time in the literature, Erdem et al. [27] assessed the AKW as a possible predictor of POAF after on-pump CABG and demonstrated that an AKW of 36.5 mm constituted the cut-off value to predict POAF development

with 84.4% sensitivity and 64.6% specificity. Our study also assessed the AKW as a possible predictor of POAF after CABG. Nonetheless, our study population consisted of a larger sample size (453 patients in our study vs. 135 patients in study of Erdem et al.) as well as off-pump CABG patients instead of on-pump CABG patients. Therefore, our study is the first to assess the AKW as a possible predictor of POAF following off-pump CABG and also the first to report that an AKW of 43.9 mm constitutes the cut-off value to predict POAF development with 68.6% sensitivity and 80.9% specificity. We suggest that determination of the AKW in preoperative period might be a beneficial method for the prediction of POAF in patients undergoing off-pump CABG.

The present study had some major limitations. The major limitations of the study were retrospective design and reflection of experience of a single institution. Another major limitation was the absence of mid-term and long-term results of study population and, hence, the inability to establish an association between POAF and mid- and long-term survival. Additionally, the postoperative monitoring of the cardiac rhythm was not done continuously in the ward after the ICU stay. It could be possible to miss the short and silent episodes of asymptomatic POAF, even though the ward ensured that the cardiac rhythm was followed with the standard ECGs routinely at least 2 times in a day and in all of the cases where any rhythm disorder was suspected.

Conclusion

In conclusion, the current study showed that the age and AKW were independent predictors of new-onset AF after off-pump CABG surgery. Nevertheless, to support our study and acquire stronger scientific evidence, further large-scale randomized studies with prospective design are required.

Conflict of interests
The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Financial Disclosure
The authors received no financial support for the research and/or authorship of this article.

Ethical approval
The present study was performed following the approval of local ethical committee (ethics number: 2019/321, decision date: 19.12.2019).

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