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Total pulmonary vein diameter is a strong predictor of atrial fibrillation after coronary artery bypass graft surgery

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Abstract. – OBJECTIVE: Recent studies have shown that the pulmonary veins are important in atrial fibrillation (AF). This study evaluated the relationship between total pulmonary vein diameter and postoperative AF in on-pump coronary artery bypass graft (CABG) patients.

PATIENTS AND METHODS: Our study enrolled 149 patients undergoing on-pump CABG. The primary endpoint was defined as postoperative new-onset in-hospital AF. All patients underwent preoperative non-contrast tomography to measure pulmonary vein diameter.

RESULTS: The patients who developed AF had significantly greater total pulmonary vein diameters than those who remained in sinus rhythm. Logistic multivariate regression analysis revealed that only total pulmonary vein diameter was an independent predictor of the development of new-onset AF.

CONCLUSIONS: To our knowledge, this is the first report of an association between total pulmonary vein diameter and the development postoperative AF. The identification of high-risk patients using pulmonary vein diameters should facilitate preventive measures.

Key Words:
Total pulmonary vein diameter, Atrial fibrillation, On-pump coronary artery bypass grafting.

Introduction

Postoperative atrial fibrillation (AF) is an important predictor of cardiovascular mortality and morbidity, which affects 20-40% of patients after on-pump coronary artery bypass grafting (CABG)[1]. The frequency of AF increases with advanced age, impaired left ventricular function, male gender, right coronary artery bypass, elongated aortic cross-clamp and bypass times, and combined valve replacement/CABG procedures[2]. The early identification of patients at high risk of developing AF should facilitate the introduction of protective measures.

Although several mechanisms have been suggested for the initiation of AF, such as autonomic nervous system dysfunction and electrical remodeling of ion channels, the full mechanism has not been elucidated[3]. Recent studies[4] have shown that the pulmonary veins are an important factor in AF. Identifying the precise properties that predict AF will aid the development of pharmacological and interventional treatment strategies.

Recent studies[5] have identified close relationships between ischemia, oxidative stress, and autonomic dysregulation and AF in cardiopulmonary bypass surgery. Therefore, this study assessed the possible relationship between new-onset AF and total pulmonary vein diameter measured by computed tomography (CT) in a CABG cohort.

Patients and Methods

Patient Selection and Data Collection

The study reviewed 350 patients undergoing CABG in one or more vessels between December 2011 and May 2015. The 149 patients who underwent preoperative CT evaluation were enrolled as the study population. All patient demographics (age, gender, and body mass index (BMI)) and comorbidities were obtained from medical records. Perioperative factors such as aortic cross-clamp time, pump time, number of bypass grafts, length of stay in the intensive care unit (ICU), and cardiovascular surgery data were obtained from the surgical records. Patients were excluded if they

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had a history of persistent, paroxysmal AF, renal replacement therapy, systemic inflammatory disease, terminal illnesses, thyroid disorders, a pacemaker, or were taking corticosteroids. Also, this retrospective study was approved by the local Ethics Committee.

CT Imaging Protocol

All patients underwent preoperative non-contrast CT examination using a Somatom Sensation 64 (Siemens, Forchheim, Germany). The CT parameters were as follows: gantry rotation time 330 ms; tube voltage 120 kW and 250 mA; and detector collimation 0.6 mm. All CT measurements (right superior, right inferior, left superior, and left inferior pulmonary vein diameters, left atrial horizontal diameter, and left atrial volume) were made using Siemens Syngo (Siemens Medical Solutions, Forchheim, Germany) software. In the examination area, the threshold was set to 10 and 100 Hounsfield units to distinguish other structures from the pulmonary veins. The total pulmonary vein diameter was calculated by summing the diameters of each ostial pulmonary veins (Figure 1). All measurements were made by two experienced radiologists, who were unaware of the subject's clinical status. If measurements by the two investigators differed by >5% for any of the variables, the patient was not included; if the difference was <5%, the measurements were averaged.

Surgical Protocol and Postoperative Follow-up

All patients were anesthetized with midazolam, fentanyl, and isoflurane following a standard protocol. A standard sternotomy was performed for all patients in order to access the aortic fat pad. When the aortopulmonary window was explored, a cross-clamp was placed on the aorta. After starting cardiopulmonary bypass (CBP), the body temperature was maintained at 32–34 °C using ice slush and cold cardioplegia. The internal mammary artery was usually used to treat left anterior descending artery stenosis, and other grafts were used to treat stenosis of the right coronary artery, circumflex artery, and all branches. All proximal anastomoses were performed with aortic cross-clamping.

At the end of the operation, all patients underwent hemodynamic and rhythm monitoring in the cardiac surgery ICU. The electrolyte levels (potassium, calcium) were followed daily. Any hypocalcemia or hypopotassemia was treated with supplementation therapy immediately. Patients were monitored continuously in this period and monitoring was continued with a telemetric electrocardiograph (ECG) on the cardiovascular service. A 12-channel ECG was obtained when arrhythmia was suspected. Cardiovascular surgery nurses monitored the patient's blood pressure and pulse every 4 hours. Paroxysmal AF was defined as new-onset AF of at least 20 minutes duration that ended spontaneously or following medical or electrical cardioversion. Patients with established AF were treated with oral or intravenous amiodarone after administering the appropriate loading dose.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences, ver. 22 for Windows (SPSS, Chicago, IL, USA). The data are shown as the mean ± standard deviation for continuous variables, median (range) for ordinal variables, and frequency and percentage for categorical variables. A p-value of <0.05 was considered statistically significant. Continuous variables were analyzed using unpaired t-tests and the Mann-Whitney U-test and dichotomous data using the Pearson's χ^2 test or Fisher's exact test. Categorical variables were compared between groups by the χ^2 test. Multivariate logistic regression analysis was used to identify independent predictors of postoperative AF. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for independent parameters associated with AF. Receiver operator characteristic curve analysis was used to identify the optimal cut-off point of total pulmonary vein diameter (*i.e.*, the maximal sensitivity and specificity) for predicting postoperative AF.

Results

The study enrolled 149 patients undergoing CABG requiring CPB for the first times. The average patient age was 63.8 ± 9.4 (range 41-87) years; the average BMI was 28.3 ± 4.4 (range 17-48) kg/m^2. The study population included 35 (23.5%) women. The average duration of ICU follow-up was 2.2 ± 1.7 (range 1-17) days, the average total hospitalization was 9.8 ± 3.3 (range 5-24) days, and the average cross-clamp duration was 55.9 ± 16.8 (range 22-98) minutes.

In our study population, AF developed in 35 (23%) patients and the remaining 114 (77%) patients remained in sinus rhythm. Baseline characteristics, operative and radiological variables

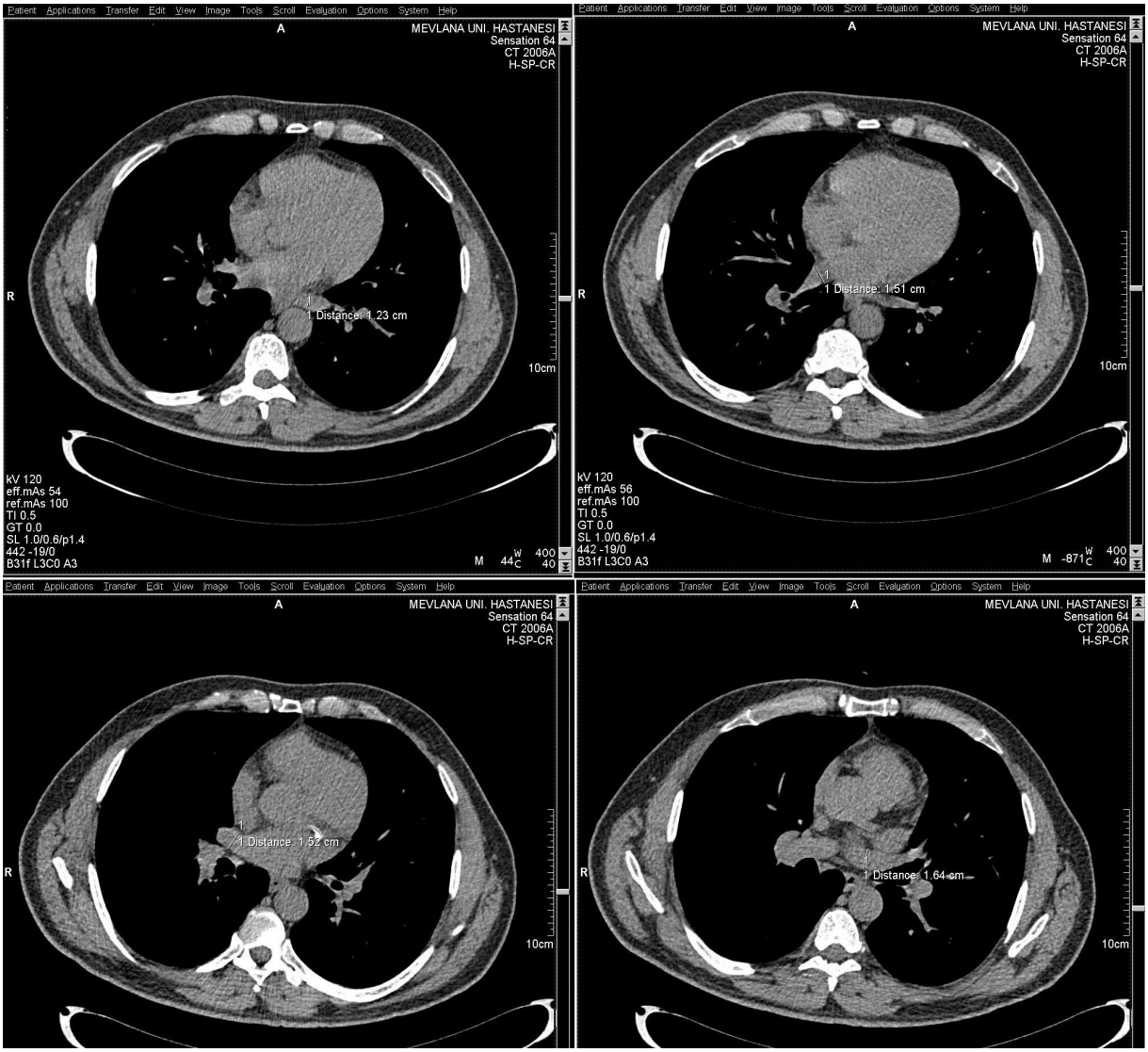

Figure 1. Tomographic measurement of the total pulmonary vein diameters. Images generated after the semiautomatic segmentation of the pulmonary veins.

stratified by the development of AF are summarized in Table I. The patients who developed AF had a significantly greater total pulmonary vein diameter (54.5 ± 6.5 *vs*. 49.9 ± 5.5 mm, $p = 0.0001$) and were older (69.2 ± 8.3 *vs*. 62.1 ± 9.1 years, $p = 0.0001$) than those who remained in sinus rhythm. Demographic variables such as diabetes and hypertension and procedural factors such as the cross-clamp time, pump time, number of bypass grafts, duration of hospitalization, and ICU stay were similar in both groups.

Receiver operator characteristic curve analysis revealed a cutoff of 51.15 mm (95% Confidence Interval 0.627-0.810, area under the curve 0.712, $p = 0.0001$) of the total pulmonary vein diameter for predicting the development of new-onset AF with 71% sensitivity and 61% specificity (Figure 2). A logistic multivariate regression analysis was performed on tomography variables, including the left atrial volume, left atrial horizontal diameter, and total pulmonary vein horizontal diameter. Only the total pulmonary vein diameter (OR 1.084, 95% CI 1.084-1.003; $p = 0.042$) was an independent predictor of the development of new-onset AF (Table II).

Discussion

Despite the implementation of new operative techniques, postoperative AF occurs in 20-40%

Table I. Baseline characteristic's, operative and radiologic variables stratified by development of new onset atrial fibrillation.

Variables	Atrial fibrillation	Sinus rhythm	*p*-value
Baseline characteristics			
N	35	114	
Age (years)	69.2 ± 8.3	62,1 ± 9.1	**0.0001**
Age >70 years old	17/42	18/107	
Male/female	26/19	30/16	0.46
Body mass index (kg/m^2)	28.4 ± 0.6	29.6 ± 0.9	0.46
Operative and postoperative variables			
Cross clamp time (minutes)	69.7 ± 37.3	59.3 ± 24.3	0,35
Pump time (minutes)	94.7 ± 47.4	84.5 ± 32	0.69
Stay in hospital (days)	11 ± 3.9	9.4 ± 3	**0.03**
Intensive Care Unit period (days)	3.3 ± 2.9	1.9 ± 0.8	**0.0001**
Number of bypass grafts			
1	7	10	
2	9	34	
3	11	41	
4	6	19	
5	2	10	
Radiologic parameters			
Total pulmonary vein diameter (mm)	54.5 ± 6.5	49.9 ± 5.5	**0.0001**
Left atrial diameter (mm)	47 ± 8.3	41 ± 6.2	**0.001**
Left atrial volume (mm^3)	72.9 ±27.2	56.8 ± 15.2	**0.003**

Bolded data are statistically significant.

Table II. Tomographic variables examined in the multivariate regression analysis.

Variables	OR	95% CI		*p*-value
Baseline characteristics				
Total pulmonary vein diameter (mm)	1.084	1.084	1.003	**0.042**
Left atrium volume (mm^3)	1.013	0.984	1.043	0.391
Left atrium diameter (mm)	1.151	1.061	0.978	0.153

OD: Odds Ratio, CI: Confidence Interval. Bolded data are statistically significant.

of patients undergoing on-pump CABG[1,6]. In our series, the incidence of new-onset AF was similar. Recent reports have shown that the frequency of postoperative paroxysmal AF increases with patient age, prolonged pump time, obesity, hypertension, and valve replacement combined with CABG[2]. The development of postoperative AF increases the duration of hospital stay and prevalence of adverse cardiovascular events. Advanced age is another important risk factor for developing postoperative AF and is associated with increased morbidity[7]. In our study, the occurence of newly developed AF was higher in patients older than 70 years (17 of 42 (40%) elderly patients) and compatible with reported values[8].

Many studies[9-11] have examined the associations of the development of postoperative AF and structural features of the heart, including left atrial volume, serum uric acid level and horizontal and vertical diameters of the left atrium. The importance of the pulmonary veins in the development of AF has been described[4]. The electrical activity triggering AF is centered on the pulmonary vein ostia. In addition, the diameters of the pulmonary veins and association with the atrial myocardium are associated with the development of AF[12,13]. We found that the total pulmonary vein diameter was greater in patients with newly developed postoperative AF, and was a better predictor of AF than vari-

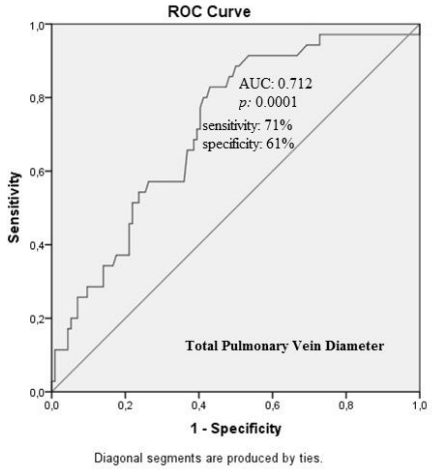

Figure 2. ROC curve illustrating sensitivity and specificity rates at all possible cut-off levels to assess the performance of total pulmonary vein diameter to predict postoperative CABG AF.

ous left atrial tomographic indexes according to the multivariate logistic analysis.

The plexus ganglia in the pulmonary veins ostia play a significant role in the triggering and continuation of AF[14]. The cardiac plexus ganglia are regulated by the central nervous system (CNS)[15]. Extreme activity (sympathetic hyperactivity) of the ganglionic plexus or weakened control of the CNS may trigger AF[16]. Excessive excitement as a result of sympathetic activity or temporary dysfunction of the CNS during the operation may result in dysfunction of the cardiac plexus ganglia.

The cause of stroke in bypass patients is usually unknown. Various factors are associated with perioperative strokes, including advanced age, prior cerebrovascular disease/stroke, prior carotid artery stenosis, prior peripheral vascular disease, prior unstable angina, prolonged cardiopulmonary bypass time, and postoperative AF[17]. Although most of these factors can be assessed easily, the identification of postoperative AF is possible only with close monitoring. Early prediction of postoperative AF should help prevent stroke. Some prophylactic measures for preventing AF, such as preoperative amiodarone treatment and atrial pacing, are not cost-effective[18,19]. The identification of predictors of AF, allowing preventive therapy to be targeted to high-risk patients, may lower overall cost.

There are some tomography studies of the relationships between peri-arterial fatty tissue, epicardial fatty tissue, and right superior pulmonary vein diameter and the development of postoperative AF[20,21]. Recently, Opolski et al[22] reported an association between cardiac tomography indexes and postoperative AF in 84% of off-pump surgery patients. However, this result cannot be extrapolated to patients undergoing on-pump CABG. To our knowledge, this is the first study of the relationship between AF and total pulmonary vein diameter in on-pump CABG patients.

The retrospective design and single-center experience are limitations of this study. Multicenter prospective studies are required to confirm our results. Other limitations are that we did not use contrast during CT, that heart rate was not controlled during CT, which may affect the evaluation of images, and that we did not examine the effects of statin use. Finally, since our work population comprised patients undergoing on-pump CABG, our conclusions might not be applicable to patients undergoing off-pump CABG.

Conclusions

To our knowledge, this is the first report of an association between total pulmonary vein diameter and the development postoperative AF in on-pump CABG. The identification of high-risk patients using pulmonary vein diameter might facilitate preventive measures and reduce cardiovascular morbidity and mortality.

Conflicts of interest

The authors declare no conflicts of interest.

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