

Relationship between Perioperative Left Atrial Appendage Doppler Velocity Estimates and New-Onset Atrial Fibrillation in Patients Undergoing Coronary Artery Bypass Graft Surgery with Cardiopulmonary Bypass

Abstract

Background: Literature search reveals that postoperative atrial fibrillation (POAF) occurs in 15%–40% of coronary artery bypass graft (CABG) patients. Although several risk models exist for predicting the development of POAF, few have studied left atrial appendage (LAA) velocity. We hypothesize that an association between LAA velocity and development of POAF exists.

Design and Methods: Single institution university hospital prospective observational clinical study performed between May 2016 and November 2016 in 96 adult patients undergoing CABG surgery utilizing cardiopulmonary bypass (CPB). Transesophageal echocardiography was performed perioperatively to measure LAA velocity and left atrial (LA) size after anesthetic induction, post-CPB and during the postoperative period before extubation. Student's *t*-test was used for inter-group comparisons. Data are expressed as mean \pm (standard deviation). The value of $P < 0.05$ was considered statistically significant. **Results:** A total of 95 patients (69 males and 26 females) completed the study and were included in the final analysis. Of these, 21 (22%) (15 males and 5 females) developed POAF. The patient group which developed POAF was compared with the group that did not develop POAF. On comparing mean age of patients in each group (59 years in patients with no POAF and 63.71 years in patients with POAF, $P = 0.04$). LA volume indexed in POAF group (34.13 ml/m²) compared with that in group with no POAF (34.82 ml/m²) resulted in $P = 0.04$. Mean LAA velocities (pre-CPB, post-CPB, postoperative Intensive Care Unit) in group with no POAF were 41.06, 56.33, and 60.44 cm/s, respectively, whereas in the other group with POAF the values were 39.68, 55.04, and 58.09 cm/s, respectively. No statistical significance was noted ($P > 0.05$). Comparison of comorbidities also did not yield any significant results ($P > 0.05$).

Conclusions: Decreasing LAA velocity does not appear to independently predict the development of POAF in patients undergoing CABG surgery with the use of CPB. There is, however, a positive correlation of POAF with age and LA volume.

Keywords: Coronary artery bypass graft surgery, left atrial velocity, postoperative atrial fibrillation

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Introduction

Postoperative atrial fibrillation (POAF) is a common complication after cardiac surgery. It occurs in up to 15%–40% of patients undergoing coronary artery bypass graft (CABG).^[1-3] POAF occurs more frequently (more than 60%) in patients undergoing combined CABG and Valve surgery.^[1,4] The incidence of POAF is highest during the first 5 days after surgery, with most cases occurring on the postoperative day 2, 2, 3. In the event of development of POAF, the patient is subjected to a significant degree of morbidity in the form of hemodynamic instability and embolic phenomena such as

stroke. POAF may result in prolonged stays in both the Intensive Care Unit (ICU) and the hospital, and thus frequently leads to increased health-care costs.^[5-7]

Keeping in view of the above-mentioned issues, many risk models have been developed and validated for predicting the development of postoperative AF in cardiac surgical patients.^[2,8,9] Previous studies have attempted to identify perioperative risk factors that would predict a patient's likelihood of developing POAF.^[5,6,10] Transesophageal echocardiography (TEE) is being routinely performed at our center in patients before cardio-pulmonary

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Access this article online

Website: www.annals.in

DOI: 10.4103/aca.ACA_73_17

Quick Response Code:



How to cite this article: Sarin K, Chauhan S, Bisoi AK, Kapoor PM, Gharde P, Choudhury A. Relationship between perioperative left atrial appendage Doppler velocity estimates and new-onset atrial fibrillation in patients undergoing coronary artery bypass graft surgery with cardiopulmonary bypass. *Ann Card Anaesth* 2017;20:403-7.

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bypass (CPB) as a routine standard of care. Due to the immediate posterior location of the transducer, TEE provides excellent visualization of the left atrium and left atrial appendage (LAA) function can be easily assessed using Doppler techniques.^[11] The review of the literature suggests that development of POAF may be related in part to left atrial (LA) dysfunction before surgery. Hence, assessment of LAA function by TEE may be predictive of this complication.^[12,13]

After looking at the previous studies and understanding the pathophysiology of POAF, it appears that patients at high risk for developing postoperative AF likely have atria that contract less vigorously.^[12,13] Reduced atrial contraction would result in lower LAA velocity, we hypothesized that measurement of LAA velocity may have a predictive value for the development of POAF.

If any correlation exists between the LAA velocity and POAF, the same can be used for predicting the development of POAF in patients undergoing CABG surgery. This would result in benefit to the patients as prophylactic antiarrhythmic measures could be instituted for such patients to prevent the occurrence of the postoperative complication.

Materials and Methods

Patient population

After the Institutional Ethics Committee approval and obtaining written informed consent, we prospectively enrolled all adult patients more than 40 years of age scheduled for elective CABG surgery requiring CPB from May 2016 to November 2016 in our study. The patients with following existing preoperative criteria were made ineligible for the study: (a) Patient with associated valvular pathology; (b) Patient with any history of preexisting atrial fibrillation (AF); (c) Patient with contradiction to TEE examination such as esophageal stricture, diverticula or tumor, patient with esophageal varices or esophagitis; (d) Age <40 years; (e) Patients with permanent pacemakers; (f) Patients undergoing cardiac surgical procedures in addition to the planned CABG surgery; (g) Patients undergoing CABG surgery without the use of CPB, that is, off-pump surgery; (h) Patients on preoperative inotropes; (i) Patients on preoperative amiodarone or digoxin. All the patients were continuing beta-blocker therapy preoperatively. No other antiarrhythmics were being administered to the patients.

Study design

This was a prospective observational clinical study. All patients fulfilling the enrollment criteria were divided into two groups based on the occurrence or absence of POAF.

Anesthesia technique

All the patients included in the study were premedicated with 0.1 mg/kg morphine and 0.5 mg/kg promethazine

intramuscularly. Monitoring included pulse oximetry, noninvasive blood pressure and five-lead electrocardiogram (ECG). Venous access and radial artery cannulation were established after infiltration of 1% lignocaine. Induction of anesthesia was performed in all patients with thiopentone 3–4 mg/kg, fentanyl 3–5 µg/kg, Midazolam 0.1 mg/kg, and rocuronium 1 mg/kg followed by tracheal intubation. After intubation of trachea, the lungs were ventilated with 50% oxygen in air. Ventilation was controlled with tidal volume of 8–10 ml/kg and positive end-expiratory pressure of 0–5 mm Hg. Anesthesia was maintained by an intermittent dose of vecuronium, fentanyl, and midazolam as required. A X7-2t transesophageal probe was then inserted and connected to the TEE console (IE 33, Philips; Bothell WA, USA).

All surgeries were performed on CPB using a membrane oxygenator (Terumo) with mild hypothermia at 33°C, using CPB flows of 2.4 L/min/m². Hematocrit on CPB was maintained at 28%–30%, with packed red blood cell as needed. All patients were warmed to 35°C nasal temperature before weaning off CPB was attempted.

Data collection

Standard views of the heart were obtained using multiple imaging planes from 0° to 120° (multiplanar probes).^[14] LAA was visualized in the midesophageal 4-chamber view at 0° then multiplane to 30°, 60°, and 90° for optimization of the image to correctly measure the LAA velocity. The following measurements were obtained for each patient intraoperatively: (a) Average of three LAA velocity estimates uses pulsed wave two-dimensional Doppler measurements of the appendage before initiating CPB and at the termination of CPB [Figure 1]. The same was also measured during the postoperative period in ICU before extubation; (b) left atrial size was also measured during the same times.

The presence of an irregular heart rate (R wave to R wave interval) was used as an ECG criteria for POAF. The



Figure 1: Transesophageal echocardiogram pulsed-wave Doppler image of the left atrial appendage showing a peak left atrial appendage ejection velocity (32.4 cm/s)

absence of electrical P-wave activity or the presence of AF waves were also considered during making the diagnosis of POAF. The onset of an irregularly irregular heart rhythm (as recorded on the ECG) requiring treatment was considered as the primary outcome of new onset POAF. Patients were considered to have experienced an episode of POAF if they had any ECG documentation of POAF for at least 1 min, as noted on the medical record, or if they required medical therapy for the dysrhythmia.

Patients were monitored till second postoperative day using bedside electrocardiographic monitoring in the ICU and thereafter inward till their respective discharge from the hospital. The complete data were recorded in a separate worksheet for each patient and contained all the information about him. Each worksheet was kept confidential.

Statistical analysis

Normality was tested in this study using the Shapiro–Wilk test and Q-Q Plots. Student’s *t*-test was used for inter-group comparisons. Chi-square test for independence has been used to discover any relationship between two categorical variables. Data are expressed as mean ± standard deviation. A two-sided *P* < 0.05 was considered statistically significant. All analyses were performed with IBM SPSS Statistics 23 (Armonk, NY, IBM Corp). Logistic regression was performed to analyze the primary outcome defined by the occurrence of POAF.

Results

A total of 100 patients were identified who were scheduled to undergo CABG surgery with the use of CPB. Five patients were excluded from the final analysis. These patients were detected to have additional valve abnormalities during intraoperative transesophageal examination and were subjected to valve replacement surgery in addition to CABG procedure.

Out of the remaining 95 patients, 21 (22%) (16 males and 5 females) developed POAF. Table 1 summarizes the statistical comparison between the baseline characteristics of the two groups. On comparing the mean average age of patients in each group (59 years in patients with no POAF and 63.71 years in patients with POAF), *P* value was found to be 0.04 which is statistically significant. The gender ratio of patients in both groups (number of males and females developing POAF as compared to the other group), as well as comparison of height and weight in respective groups did not yield statistically significant results. The major comorbidities present in the study population under consideration were diabetes and hypertension. The percentage of patients developing POAF who had diabetes or hypertension was 29% and 64%, respectively. When compared with the percentage of people having similar conditions in the other group (diabetics - 37% and hypertensive - 51%), the results did not produce any significant data. Total number of smokers in the population

was 13. Of this 7 developed POAF and the rest did not. The comparison of both groups yielded a *P* = 0.04 which was considered statistically significant.

TEE findings in both the groups and their comparison are summarized in Table 2. Mean LAA velocities (pre-CPB, post-CPB, postoperative ICU) in group with no POAF were 41.06, 56.33, and 60.44, respectively, whereas in the other group with POAF the values were 39.68, 55.04, and 58.09, respectively. No statistical significance was noted (*P* > 0.05). LA volume index was found to be higher in the group which developed POAF, and statistically significant evidence to support the hypothesis could be brought out (*P* = 0.04).

Discussion

Technical advancements in the field of cardiac surgery have improved the surgical outcomes. Increasing number of cardiac surgeries are now being performed on older subset of patients due to increased life expectancy. This has resulted in an increasing trend of POAF which is a significant problem due to its substantial impact on hospital resources.^[15] Indirectly, there is an increase in the short- and long-term mortality risks. POAF is associated with increased patient’s hospital stay resulting in higher financial costs. Increased hospital stay directly increases the risk of iatrogenic complications and thus also decreases patient satisfaction.

Table 1: Baseline characteristics

	POAF absent (n=74)	POAF present (n=21)	<i>P</i>
Age (years)†	59 (8.0)	63.71 (8.2)	0.04
Males*	54 (73)	16 (76)	0.77
Females*	20 (27)	5 (24)	0.77
Height (cm)†	164.62 (6.8)	163.71 (6.4)	0.61
Weight (kg)†	68.64 (8.3)	67.47 (8.5)	0.6
Comorbidities (smoking)*	6/74 (8)	7/21 (35)	0.04
Comorbidities (diabetes mellitus)*	28/74 (37)	6/21 (29)	0.52
Comorbidities (hypertension)*	38/74 (51)	13/21 (64)	0.32

†Values are mean (SD), *Values are total *n* (%). POAF: Postoperative atrial fibrillation, SD: Standard deviation

Table 2: Transesophageal echocardiography findings and statistical difference between two groups

	POAF absent (n=74)	POAF present (n=17)	<i>P</i>
Pre-CPB LAA velocity (cm/s)†	41.06 (11.78)	39.68 (7.81)	0.65
Post-CPB LAA velocity (cm/s)†	56.33 (11.65)	55.04 (9.65)	0.67
Postoperative LAA velocity (cm/s)†	60.44 (11.17)	58.09 (9.46)	0.42
LAVI (ml/m ²)†	34.13 (1.22)	34.82 (1.24)	0.04

†Values are mean (SD). POAF: Postoperative atrial fibrillation, SD: Standard deviation, LAA: Left atrial appendage, LAVI: Left atrial volume indexed, CPB: Cardiopulmonary bypass

The prophylactic strategies for management of POAF namely beta-blockers, sotalol, or amiodarone are themselves expensive.^[6-9] Moreover, the side effects of these medications, namely bradycardia, QT prolongation, and hypotension, are not well tolerated by all cardiac patients. Therefore, pre-operative risk stratification is essential to identify high-risk groups. This would make it possible for the physicians to prescribe and recommend the necessary interventions and medications for such subset of high-risk patients. By doing so, the practice would not only be more cost effective but also decrease the chances of the side effects and the associated health-care costs in the individuals who did not meet the criteria for high risk and were thus not provided with any intervention.

Many factors are involved in causing POAF. The exact nature and the extent to which each are involved or is responsible for causing POAF has still not been agreed upon. Both structural and electrophysiologic abnormalities are found in the high-risk individuals which predispose them to increased risk of developing POAF. One of the common findings associated with AF is myocardial atrial fibrosis.^[16] Pulmonary veins due to their unique histologic, anatomic, and electrophysiologic properties have been identified as the area contributing toward the development of POAF. Other nonpulmonary foci such as coronary sinus, ligament of Marshall, posterior wall of the left atrium and septum, vena cava, and appendages have also been described as sites for development of POAF. The sympathetic nervous system plays an important role in the pathogenesis of new onset POAF. Surgical stress leading to increased circulating catecholamine levels after cardiac surgery as well as the inotropic infusions started per operatively all contribute significantly toward development of POAF.^[17]

We had hypothesized that measurement of LAA velocity may have predictive value for development of POAF. After reviewing previous literature, we had predicted that decreased LAA velocities would be associated with increased risk and incidence of POAF. The same has not been confirmed by the results of the study. Previous studies had mainly concentrated efforts on the pre-CPB measurement of the LAA velocity to validate its predictive nature for the development of POAF. We had given equal importance to the post-CPB and postoperative TEE measurements, to eliminate any chance of bias while selecting the timing of TEE measurements. We had also sought to look for any relationship between the LA size and development of POAF. However, we could find only weak evidence to support relationship of the LA size in patients with coronary artery disease who develop POAF.^[16,18] POAF can be caused by many pathologic mechanisms, and may include surgery induced pericardial injury, CPB-induced systemic inflammatory state or elevated sympathetic tone.^[19]

Ngai *et al.*,^[20] conducted a single institution retrospective study on 562 patients between January 2013 and December 2013 to determine if there is an association between the single measurement of pre-operative LAA velocity and the development of POAF. The authors found that there was a higher risk of POAF in patients with a lower LAA velocity. They further concluded that decreasing LAA velocity is an independent predictor of risk for the development of POAF following cardiac surgery with CPB. In this study, no such correlation has been found. Leibowitz *et al.*,^[21] in their retrospective analysis of 36 patients who had undergone cardiac surgery with the use of CPB 12 months prior found no association of LAA velocity and size with the development of new-onset POAF. While the findings in our study amount to same, we have collected data in a prospective manner on a much larger group of patients.

When compared with the previous studies, this study had the main advantage of being prospective in nature. While extensive data are available based on the retrospective analysis, the same is exposed to potential selection bias. Moreover, such retrospectively collected data are also subjected to the possibility that all the potentially confounding variables on the relationship between LAA velocity and POAF have not been identified. Another advantage of our study was the elimination of potential variability in the collection of data. This was achieved by performance of TEE examination by only one physician in all the cases, instead of multiple physician anesthesiologists performing the same as in retrospectively collected data leading to increased chances of data collection variability in such studies. The major limitation of our study is its relatively small size.

Conclusion

TEE measurement of LAA velocity before the initiation of CPB as well as post-CPB and finally postoperatively does not appear to predict the development of POAF. No consistent relationship could be shown between the LAA velocity and development of POAF by our data and thus, the same cannot be a marker for AF. A positive correlation was however found with the increased LA size, increased age, and smoking with the development of POAF.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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