Original Article

New Onset Atrial Fibrillation after Coronary Artery Bypasses Grafting; an Evaluation of Mechanical Left Atrial Function

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Abstract

Background: This study attempted to identify the role of combined conventional and novel echocardiographic techniques in evaluation of left atrial (LA) function to predict the postoperative atrial fibrillation (POAF).

Methods: In this cross-sectional study, subjects with sinus rhythm who were candidates for CABG were enrolled. Preoperative LA function was evaluated by conventional echocardiography and 2-dimensional strain imaging based-velocity vector imaging (VVI). VVI-derived systolic peak positive, early and late diastolic strain rate were measured. Using tissue Doppler study, systolic peak velocities (Sm), early diastole (Em), atrial systole (Am) and AEMi were also measured. The patients were observed during their hospital stay. The primary endpoint of the study was postoperative AF lasting > 5minutes.

Results: POAF occurred in 12.7% of patients. Age, LA volume index (LAVI), LA area, LA empting fraction (LAeF) and cardiopulmonary bypass time were found to be the independent predictors of POAF. TDI-derived velocities were similar in study groups. LA systolic strain rate (SRs) and early diastolic strain rate were impaired in patients with no significant difference between those who developed POAF and those who did not.

Conclusions: Conventional echocardiography could be used as a feasible method for evaluating subclinical atrial dysfunction in patients undergoing CABG and the use of VVI- based 2-dimensional strain imaging may need further studies.

Keywords: Atrial fibrillation, atrial strain rate, coronary bypass grafting, vector velocity imaging

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Introduction

Postoperative atrial fibrillation (POAF) involves about 20% – 40% of patients treated by coronary artery bypass grafting (CABG)[1–3] which may result in different complications, including longer hospital stay, increased healthcare costs and mortality.[1,2,4–8] Despite the identification of possible mechanisms for the development of POAF, including advanced age, atrial fibrosis and remodeling, electrophysiological factors, perioperative atrial injury and ischemia, electrolyte imbalance, high sympathetic tone, inflammation, higher level of BNP and NT-proBNP and some biochemical factors in blood,[2,3,5,9,10,11] no consistent therapies have been found to be completely effective in preventing POAF. Atrial systolic dysfunction is also observed in patients with coronary artery disease.[2,5] Recent clinical studies have drawn more attention to the LA function, and demonstrated that conventional left atrial dimensions and TDI parameters are not the only independent predictors of POAF.

Left atrial longitudinal strain study, deriving from the analysis of myocardial deformation using 2-dimentional (2D) speckle tracking echocardiography allows the noninvasive assessment of atrial function as a reservoir, conduit and contractile element.[2,5,12]

Velocity vector imaging (VVI) is a novel 2-D speckle tracking algorithm. Previous studies have shown that this technique is a feasible and reliable method for quantifying regional myocardial function and identifying subclinical chamber dysfunctions.[5,13] However, the role of this technique in identification of subjects at risk of POAF has been assessed in limited studies.

In the current study, we attempted to evaluate the role of mechanical LA function in patients who develop POAF after CABG using conventional and novel echocardiographic techniques.

Methods

Study Population

From May to October 2012, 176 patients who underwent isolated CABG with stable sinus rhythm were enrolled. Twenty-six patients were excluded because of poor acoustic window and low quality for strain imaging. The other exclusion criteria were moderate or severe valvular heart disease, current or previous AF, other chronic atrial arrhythmias, emergency surgery, planned Cox's maze procedure, valve prosthesis, current use of anti-arrhythmic drugs for at least 1 week before the surgery (except for beta-blockers), and congenital cardiac abnormalities. Informed consent was obtained from all study subjects, and the protocol was approved by the review board of our institution.

Conventional Echocardiographic Study

On the day before CABG, a complete echocardiographic evaluation was performed by a trained operator, including standard api-

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cal four chamber and parasternal long axis views with the patient in the left lateral decubitus position, using a 2.5 MHz – 3.5 MHz phased array transducer (Mylab60, Esaote, Italy) in accordance with the guidelines of the American Society of Echocardiography. Machine settings were manually adjusted to optimize 2D endocardial and myocardial gray scale definition. All images were acquired at end expiratory apnea. Loops of 3 cardiac cycles were stored digitally and analyzed offline.

LV end-diastolic and end systolic diameters and anteroposterior LA dimension were measured on the parasternal long- axis view. End-diastolic and end-systolic volumes of LV cavity and LVEF were calculated on the apical 4-chamber view using modified Simpson's method. Additionally, maximal (max) and minimal (min) LA area and volumes (LAV) were determined by the single-plane area – length method. LA total emptying fraction (LAeF) was defined as (max LAV - min LAV) / max LAV. The maximum LA volume was also indexed for body surface area and reported as LA volume index (LAVi). Diastolic function was evaluated by mitral inflow velocities assessed by standard pulsed-wave Doppler at the tips of the mitral valve leaflets in an apical four-chamber view (E and A waves, E/A and deceleration time as DT).

Tissue Doppler was recorded using a standard pulsed-wave technique with the sample volume placed at the medial side of mitral annulus on the 4-chamber view. The systolic and diastolic peak velocities (Sm, Em and Am) and the atrial electromechanical interval (AEMi in milliseconds) were measured (Figure 1). AEMi is the time interval from the onset of the P-wave to the beginning of the atrial systole (Am).

Vector velocity imaging (VVI) Two-dimensional Strain Echocardiography

The VVI-derived technique using Xstraine licence software (frame rate of 45 to 60 frames per second) was performed to calculate regional LA myocardial velocities and average strain rates. First, on a standard 4-chamber view, a line was manually drawn along the LA endocardium when the LA was at its minimum volume after contraction (Figure 2A). Before processing, a cine loop preview feature visually confirmed that the internal line follows the LA endocardium throughout the cardiac cycle (Figure 2B). If tracking of the LA endocardial border is unsatisfactory, manual adjustments or changing software parameters can be made. The software divided the LA wall into six segments; the global systolic strain rate (LAsSR), early diastolic strain rate (LAeSR) and late diastolic strain rate (LAaSR) were calculated by averaging the data revealed from all segments (Figure 2C).These data were also obtained separately from the basal and mid segments of septal and lateral walls. All measurements were performed in two different times.

All operations were performed according to the standard technique by two surgeons with or without cardiopulmonary bypass. All the patients received total revascularization. The time of cardiopulmonary bypass was recorded.

Electrocardiographic analysis and monitoring

In order to evaluate POAF, the patients were continuously monitored for arrhythmias during their stay in the intensive care unit (ICU). Standard 12-lead electrocardiographic recordings were obtained for all patients on a daily basis until discharged. Additional electrocardiography recordings were taken if the patients developed new symptoms or signs, such as palpitation, tachycardia or irregular pulse rhythm. The end point of the study was the occurrence of the new-onset AF during the first 5 days after CABG surgery. AF was defined as an absent P wave before the QRS complex together with irregular ventricular rhythm on the rhythm strips. Only AF episodes lasting longer than 5 minutes were counted.

Statistical Analysis

Data were presented as mean ± SD for interval and count (percent) for categorical variables. One-Sample Kolmogorov-Smirnov test was used to assess the fitness of interval variables to Gaussian distribution. To investigate the associations between AF and other variables, Student's t-test for normally distributed variables, Mann Whitney U for non-normally distributed variables and Pearson's chi square or Fisher's exact tests for nominal variables were applied. Logistic regression model was used to determine the adjusted associations between AF and other factors. P-values ≤ 0.05 were considered as statistically significant.

To examine intra observer variability, a sample of 10 VVI measurements were randomly selected and studied by the same observer on 2 different days. Bland–Altman analysis demonstrated good intra- and inter-observer agreements, with a small bias not significantly different from 0. Mean differences ± 2 SDs were 0.2 ± 2.2% and 0.3 ± 2.3% for intra- and inter-observer agreements, respectively.

Data were analyzed using Statistical Package for the Social Sciences (SPSS) 16.0 for Windows (SPSS Inc. Chicago, Illinois).

Results

The majority of patients were male (113 patients, 75.3%) with a mean age of 60.19 ± 9.02 years. Twenty-eight patients (18.7%) underwent off-pump CABG. One hundred twenty two patients (81.3%) were operated on pump with a mean cardiopulmonary bypass time of 91.32 ± 30.09 minutes. Patients were not receiving antiarrhythmic before surgery, but all patients were receiving beta-blockers, statins, and aspirin before surgery; these drugs were restarted within the first 24 hours after operation. All patients in this study were discharged alive except one who died due to brain stroke. Nineteen patients (12.7%) developed POAF during the hospital stay. AF was observed 3.8 ± 2.6 days after the CABG. Sinus rhythm was restored in eighteen patients with medical therapy (duration of the AF was 11.3 ± 9.6 hours). Those who developed POAF were treated with amiodarone 150 mg IV bolus followed by continuous infusion of 0.5 – 1 mg/Kg/24 h until sinus rhythm was restored). AF rhythm did not respond to therapy in only one patient and became permanent. Patients with POAF were older ($P < 0.001$). The mean hospital and ICU stays were longer in patients with POAF (3.74 ± 1.82 and 13.63 ± 9.97 days vs. 2.52 ± 0.83 and 8.55 ± 3.33 days, respectively; $P < 0.001$) as expected. The cardiopulmonary bypass time was significantly longer in the AF group (109.67 ± 39.02 minutes vs. 88.75 ± 27.90 minutes; $P = 0.010$). Clinical and baseline echocardiographic features of our patients are summarized in Table 1.

The gender and coronary risk factors (DM, HTN and cigarette smoking) were similar in both groups. PR-interval was more prolonged in the AF group ($P = 0.037$), but the duration of P wave did not show any significant difference. Patients with POAF had higher LVESV, LA area and LAVi (P = 0.033, 0.015 and 0.006 respectively). There was no statistical difference between the 2

Table 1. Clinical and echocardiographic characteristics

Variable	Total	No AF (n =131)	AF (n = 19)	P-value
Age (years)	60.19 ± 9.02	59.19 ± 8.59	67.11 ± 9.049	< 0.001
Gender; male (%)	75.3	75.6	73.7	0.858
Hypertension (%)	50.7	51.9	42.1	0.424
Diabetes Mellitus (%)	50	54.2	21.1	0.070
Active smoking (%)	28.7	29.8	21.1	0.432
Body Mass Index (Kg/m^2)	26.92 ± 4.25	26.66 ± 4.78	27.63 ± 4.02	0.401
Body Surface Area (m^2)	1.82 ± 0.18	1.83 ± 0.18	1.74 ± 0.17	0.040
P wave duration (ms)	71.87 ± 17.40	71.50 ± 17.66	74.21 ± 15.74	0.528
PR-interval	153.86 ± 26.75	152.12 ± 25.72	165.79 ± 31.14	0.037
LVEF (%)	42.63 ± 9.7	42.78 ± 9.59	41.63 ± 10.87	0.633
LVEDD (cm)	5.15 ± 0.63	5.11 ± 0.59	5.40 ± 0.81	0.062
LVESV (cm)	3.53 ± 0.79	3.47 ± 0.76	3.89 ± 0.92	0.033
LVEDV (mL)	100.79 ± 36.99	100.45 ± 36.30	103.11± 42.46	0.771
LA dimension (mm)	3.22 ± 0.54	3.19 ± 0.52	3.45 ± 0.60	0.051
LA area (cm^2)	14.71 ± 3.18	14.47 ± 2.96	16.37 ± 4.16	0.015
LAVi (mL/m^2)	31.72 ± 11.11	40.29 ± 13.445	30.48 ±10.20	0.006
LAeF (%)	58.80 ±15.31	59.19 ± 15.40	56.12 ± 14.82	0.030
Mitral inflow DT(ms)	182.28 ± 42.69	181.77 ± 43.00	185.79 ± 41.43	0.703
E/A	0.84 ± 0.44	0.83 ± 0.39	0.94 ± 0.71	0.033
Cardiopulmonary bypass time (min)	91.32 ± 30.09	88.75 ± 27.90	109.67 ± 39.02	0.010
ICU stay (days)	2.68 ±1.09	2.52 ± 0.83	3.74 ±1.82	< 0.001
Hospital stay (days)	9.23 ± 5.05	8.55 ± 3.39	13.63 ± 9.97	< 0.001

LVEF: left ventricular Ejection Fraction; LVEDD: left ventricular end diastolic diameter, LVESD: left ventricular end systolic diameter; LVEDV: left ventricular end diastolic volume; LA: left atrium; LAVi: left atrial volume index; LAeF: left atrial total empting fraction; DT: deceleration time; E: peak early diastolic velocity; A: peak atrial diastolic velocity; ICU: intensive care unit

Table 2. Preoperative assessment of regional longitudinal atrial functions by tissue doppler and velocity vector imaging (VVI)

	Total (n=150)	No AF (n=131)	AF (n=19)	P-value
TDI-derived atrial function				
Sm (cm/s)	0.08 ± 0.01	0.086 ± 0.016	0.081 ± 0.018	0.629
Em (cm/s)	0.08 ± 0.05	0.085 ± 0.057	0.074 ± 0.017	0.474
Am (cm/s)	0.11 ± 0.09	0.11 ± 0.099	0.11 ± 0.022	0.718
E/Em	6.85 ± 2.83	6.71 ± 2.44	7.71 ± 4.71	0.068
AEMi (ms)	99.53 ± 21.7	98.85 ± 21.71	104.26 ± 22.25	0.313
VVI-derived global left atrial deformation				
LAsysSR (1/s)	1.33 ± 0.63	1.32 ± 0.62	1.36 ± 0.70	0.803
LAe SR (1/s)	-0.97 ± 0.67	-1.61 ± 0.62	-0.76 ± 0.58	0.595
LAa SR (1/s)	-1.52 ± 0.91	-1.51 ± 0.92	-1.55 ± 0.87	0.878

Sm: tissue Doppler imaging (TDI) derived peak systolic velocity; Em: TDI derived E wave velocity; Am: TDI derived A wave velocity; AEMi: atrial electromechanical interval; LAsysSR: peak left atrial systolic strain rate; LAeSR: left atrial early diastolic strain rate; LAaSR: left atrial late diastolic strain rate

Table 3. Preoperative assessment of regional longitudinal left atrial functions by velocity vector imaging

	Total (n = 150)	No AF (n = 131)	AF (n = 19)	P-value
Base of interatrial septum				
LA sys SR (1/s)	1.80 ± 1.01	1.87 ± 1.04	1.30 ± 0.59	0.022
LA e SR (1/s)	-1.65 ± 1.5	-1.76 ± 1.80	-0.94 ± 0.80	0.354
LA a SR (1/s)	-1.77 ± 1.14	-1.79 ± 1.14	-1.61 ± 1.12	0.518
Mid of interatrial septum				
LA sys SR (1/s)	1.62 ± 0.85	1.65 ± 0.86	1.46 ± 0.73	0.364
LA e SR (1/s)	-1.03 ± 0.80	-1.06 ± 0.83	-0.83 ± 0.60	0.237
LA a SR (1/s)	-1.74 ± 0.93	-1.74 ± 0.94	-1.74 ± 0.86	0.990
Base of LA lateral wall				
LA sys SR (1/s)	1.53 ± 1.02	1.53 ± 1.01	1.57 ± 1.13	0.878
LA e SR (1/s)	-1.16 ± 0.85	-1.18 ± 0.86	-1.02 ± 0.83	0.728
LA a SR (1/s)	-1.51 ± 0.94	-2.39 ± 1.13	-1.58 ± 0.93	0.427
Mid of LA lateral wall				
LA sys SR (1/s)	1.67 ± 1.05	1.63 ± 1.04	1.93 ± 1.11	0.253
LA e SR (1/s)	-1.19 ± 0.94	-1.21 ± 0.96	-1.04 ± 0.81	0.455
LA a SR (1/s)	-1.75 ± 1.14	-1.75 ± 1.13	-1.71±1.17	0.871

LAsysSR: peak left atrial systolic strain rate; LAeSR: left atrial early diastolic strain rate; LAaSR: left atrial late diastolic strain rate

groups in terms of the LVEF, LVEDV, LAEDD, and DT. LAeF was significantly lower in the POAF patients (56.12 ± 14.82% vs. 59.19 ± 15.40%; P = 0.006). LV diastolic dysfunction was obtained in both groups by conventional echocardiography, and no statistical differences between E velocities, A velocities, peak Sm velocity, Em, Am velocities, E/Em and AEMi was detected (Table 2). However, the E to A ratio was significantly higher in the POAF group (P = 0.033). Despite statistically insignificant difference (P = 0.09), more advanced diastolic dysfunctions were seen in the POAF group.

A total of 600 basal and mid LA segments were used to identify regional longitudinal function on the apical 4-chamber view. Preoperative longitudinal peak global systolic, early diastolic and late diastolic strain rates of the LA were not significantly different between patients who developed POAF and those who did not (Table 3). In addition, there were no statistical differences be-

Table 4. The Results of Multivariate Logistic Regression Analysis for POAF

Variable	Coefficient (β)	OR	CI	P-value
Age	0.144	1.16	1.05- 1.27	0.003
Cardiopulmonary bypass time	0.032	1.03	1.01-1.06	0.011
PR-interval	0.011	1.01	0.99- 1.03	0.329
LA area	0.042	1.04	0.81- 1.35	0.750
AEMi	0.015	1.02	0.98- 1.05	0.384
LAVI (mL/m^2)	0.061	1.06	0.99- 1.15	0.108
LAeF	-0.014	0.99	0.93- 1.04	0.609

POAF: postoperative atrial fibrillation; OR: odds ratio; CI: confidence interval; LVEF: left ventricular ejection fraction; E/A: E to A waves ratio; LAVi: left atrial (LA) volume index; AEMi: atrial electromechanical interval

tween the strain rates of each segment in the LA except for significant decrease of LAsSR in base of interatrial septum of the POAF patients (1.30 ± 0.59 s^{-1} Vs 1.87 ± 1.04s^{-1}; P = 0.022). On multiple analysis, only age (OR = 1.66, 95% CI: 1.052 – 1.29), cardiopulmonary bypass time (OR = 1.034, 95% CI: 1.008 – 1.061) and LAVi (OR = 1.078, 95% CI: 1.009 – 1.165) were significant independent predictors of postoperative AF (Table 4).

Discussion

Many previous studies have reported an increased incidence of thromboembolic complications, cardiac and non-cardiac mortality in patients developing post-operative AF.[2, 9] These reasons are sufficient to emphasize the importance of tools for identification of patients at risk of developing this arrhythmia after CABG.[5]

Our finding that 12.7% of patients had postoperative AF is smaller than that reported by previous studies.[2,3,12,14] The different findings may be partly explained by the restricted inclusion criteria of respective study populations and could be explained by our approach to AF detection, because after the transferring of patients from ICU to the ward, we detected the AF rhythm based on daily 12-lead ECG recording and reported symptoms by patient, but not on continuous monitoring.

In contrast to some studies, our study along with others did not confirm the finding that gender is a risk factor of postoperative AF.[7,8,11,12,14] Whether sex is a surrogate of other predictors of postoperative AF remains to be determined.

In contrast to studies by Tayyareci and Nakai[5,12] and consistent with the study by Rostagno,[8] the cardiopulmonary bypass time is significantly more prolonged in POAF patients.

Similar to Nakai's study, P-wave analysis with standard 12-lead ECG did not provide predictive information on AF after CABG in our study.[12] This finding is inconsistent with the results of Chang, et al.[15] however, PR-interval was longer in the AF group, more detailed analysis such as signal-averaged P-wave duration will be of more predictive value[7].

Our results agree with previous studies demonstrating that advanced age and LA enlargement were independent predictors of postoperative AF.[7,12,16,17] Structural LA wall abnormality and stiffness induced by enlargement might lead to the development of multiple reentrant wavefronts starting and possibly perpetuating AF.[7]

Similar to previous studies, left ventricular systolic function and dimensions were not related to postoperative AF.[10,12,16,18,19] However, inconsistent with Acil's study[16] we found LV diastolic function may be associated with postoperative AF and statistically insignificant difference between the two groups may be related to the small sample size. Also, the relation between diastolic dysfunction and POAF has been shown in many previous studies.[12,20,21]

The time of POAF in this study is in line with the 2011 ACC/AHA Guideline for Coronary Artery Bypass Graft Surgery that reported postoperative AF almost always occurs within 5 days postoperatively, with a peak incidence on the second postoperative day.[14]

We could not show any association between POAF and coronary risk factors (DM, HTN, smoking), or some conventional and tissue Doppler echocardiographic parameters (DT, E/A, Sm, Em, Am, E/Em and AEMi). AEMi, a new proposed method for identifying patients vulnerable to post operative AF in some studies with cutoff point 120 milliseconds[4,22,23] was not significantly different in those with and without POAF. However, Uijl's study in 2011 showed the total atrial conduction time assessed by measuring the time interval between the onset of the P-wave in lead II of the surface ECG and the peak A-wave on the tissue Doppler tracing and Left atrial maximum volume index were independent predictors of AF recurrence after radiofrequency catheter ablation.[24]

In the current study, LA area, LAVi, LAeF, and E/A alone showed a trend toward being a univariate predictors of POAF and were even better predictors than tissue Doppler and strain studies. On multiple logistic regression analyses, only age, cardiopulmonary bypass time and LAVi were significant independent predictors of postoperative AF. A study by Osranek and Tayyareci identified the LAVi as a useful predictor of postoperative AF[5,20]- a finding that was not reproduced in Gibson' study.[10] On the other hand, it should be noted many recent studies have demonstrated that increased LA volume index is related to increased morbidity and mortality in patients with cardiovascular disease,[1,25,26] thus the importance of this index should not be minimized. Tayyareci and Hafajee considered 32 mL/m^2 as the cut-off point for LAVi to predict the development of POAF,[5,3] the mean ± SD in our study was 30.48 ± 10.20 mL/m^2. In addition, LAeF in patients with POAF was significantly lower -consistent with previous studies;[3, 27] however, the mean ± SD in our patients (56.12 ± 14.82%) is a little more than cut-off point in Hafajee study.[3]

Longitudinal LA strain rate analysis by two-dimensional (2D) speckle tracking has emerged as a novel feasible and reproducible method for the assessment of LA function and deformation dynamics.[1,28–34] In 2011, Liu demonstrated that although conventional echocardigraphic parameters are abnormal in CAD patients with enlarged LA, there are no significant differences between CAD with normal-size left atrium and control groups; therefore, his group suggested that LAs SR is the most accurate index in identifying patients with CAD[35] and many other studies showed LA dysfunction, evaluated by strain and strain rate is an independent predictor of POAF and contributes to classic risk factors like age and atrial volume.[2,36,37] In the present study, we used VVI-derived systolic and diastolic indices to evaluate subclinical preoperative atrial dysfunction. We did not find statistically significant impairment in LA systolic and diastolic SRs in patients with POAF compared to those who maintained sinus rhythm after CABG operation. In Tayyareci's study, the optimal cut-off point of LA sSR and LA eSR were 1.7 s^{-1} (88% sensitivity and 86.2% specificity, AUC: 0.79, CI: 0.69 – 0.87; P = 0.0001) and 1.95 s^{-1} (72% sensitivity, 70.4% specificity, AUC: 0.77, CI: 0.68 – 0.86; P = 0.0001), respectively. Comparably, our findings indicate 1.36 ± 0.70 s^{-1} and 1.55 ± 0.87 s^{-1}, respectively, which show lower cutoff points that Tayyareci's study. Nevertheless, we did not compare our results with a golden standard method for LA function and this could be a limitation for the present study.

Inconsistencies between our results and results of previous studies with regard to LA deformation indices, such as LASRs, might have resulted from differences in sample size and echocardiographic techniques, because almost all studies have performed 2D speckle tracking method as method of choice and only a few studies used vector velocity imaging.[5,37] Although our results failed to show any significant difference in LASRs between two groups, regarding to the importance of LA deformation analysis and comparable results between 2-D speckle-based strain and velocity vector imaging in previous studies,[38] we emphasize the use of this technique in the prediction of postoperative AF after isolated CABG may need further future studies.

LA dysfunction assessed by preoperative transthoracic echocardiography, including both conventional and advanced techniques, may play an important role in prediction of postoperative AF.

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