

Right ventricular diastolic function predicts clinical atrial fibrillation after coronary artery bypass graft

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Background: Patients with moderate-severe left ventricular systolic dysfunction undergoing coronary artery bypass graft (CABG) surgery are at high risk of mortality and morbidity. Our aim is to evaluate the right ventricular (RV) diastolic function in these patients, and monitor its effects on postoperation outcomes. **Materials and Methods:** In a cohort study, patients with moderate-severe left ventricular systolic dysfunction (ejection fraction $\leq 35\%$) who were candidate for CABG were included. Baseline transthoracic echocardiography (TTE) was performed, and RV diastolic function measures were obtained. After CABG, the length of intubation, inotrope dependency, hospital stay in intensive care unit and ward, in-hospital and after discharge mortality, postoperative atrial fibrillation (POAF) were evaluated in all patients. **Results:** Sixty-seven patients were prospectively included in the study. The mean \pm standard deviation age of our patients was 61.4 ± 9.3 . There was no difference between grades of RV diastolic function and postoperative outcomes. However, we found significant difference between grades of RV diastolic function and onset of in hospital, and total POAF (P -value = 0.017). Multivariate analysis demonstrated that preoperative tricuspid E_e/E'_t (ratio of peak early-diastolic flow rate across the tricuspid valve orifice to peak early-diastolic velocity at the lateral tricuspid annulus), left atrial volume and "high risk" Euroscore II were independent predictors for POAF during hospitalization and total POAF in patients with moderate to severely impaired left ventricular systolic function (P -values were 0.04, 0.003 and 0.001, respectively). **Conclusion:** We believe that patients with increased tricuspid E_e/E'_t are high risk for POAF; therefore, any risk score for POAF should include a comprehensive TTE including evaluation of RV diastolic function before surgery.

Key words: Atrial fibrillation, coronary artery bypass grafting, left ventricular dysfunction, right ventricular function

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BACKGROUND

Patients with severe left ventricular systolic dysfunction undergoing coronary bypass surgery are at high risk of mortality and morbidity.^[1,2] The risk of early death after coronary artery bypass graft (CABG) is more than doubled by reduced ejection fraction.^[3] Patients with reduced left ventricular ejection fraction (LVEF) are also at higher risk for postoperative complications such as stroke, infection, bleeding, respiratory failure,^[1] renal failure,^[1,4] and atrial fibrillation (AF)^[5] after CABG. Therefore, precise evaluation of these patients

before surgery plays a pivotal role in selecting the appropriate treatment for them.^[6] Although society of thoracic surgeons uses LVEF and significant valvular regurgitation/stenosis, and European system for cardiac operative risk evaluation II (EuroSCORE II) includes LVEF and pulmonary arterial pressure (PAP) for risk stratification before CABG,^[7] there is no recommendation for routine echocardiography before CABG. In addition, other echocardiographic criteria such as left ventricle (LV) diastolic function and right ventricular (RV) systolic and diastolic function as the predictor of postoperation outcomes have been evaluated in limited studies.^[8-10] LV diastolic function

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is shown to be associated with greater postoperative mortality and major adverse cardiac events, regardless of LVEF.^[9] In one retrospective study, RV diastolic dysfunction was shown to be an independent risk factor for early death after CABG surgery in patients with decreased left ventricular function,^[8] and in another study, the RV diastolic function was associated with difficult separation from cardiopulmonary bypass.^[11]

In this study, we decided to evaluate the RV diastolic function in patients with moderate-severe LV systolic dysfunction who was a candidate for CABG and monitor its effects on postoperative outcomes.

METHODS

In a cohort study, a total of 67 normal sinus rhythm patients with moderate-severe LV systolic dysfunction (LVEF \leq 35%) who underwent CABG at the Division of Cardiovascular Surgery of Imam Khomeini Complex from November 2014 to September 2018 were included. Exclusion criteria were patients with Pacemaker, significant valvular heart disease (moderate or more than moderate valvular regurgitation or stenosis), other heart surgery at the same time, and patient dissatisfaction. All of the patients had read and signed an informed consent form. The study was approved by our Institutional Research Ethics Board (IR.TUMS.IKHC.REC.1397.112).

Echocardiography and risk stratification

Baseline two-dimensional color Doppler transthoracic echocardiography (TTE) was performed with commercially available ultrasound system S5 (GE) by an expert cardiologist. All the patients were nothing by mouth (NPO), and none of them received diuretics at least for 12 h before echocardiography.

Echocardiographic parameters were collected following the recommendation of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI).^[12] The LVEF was measured using Simpson's method. In apical four-chamber view using pulsed-wave (PW) Doppler sample volume of 3 mm, at the level of mitral leaflet tips, with frame rate of 50-60 fps, depth of 100-110 mm, scale of 2.2 m/s, and sweep speed of 75 mm/s, the peak early and late diastolic flow velocities across the mitral valve orifice were measured (E_m and A_m). Then, the E_m/A_m values were calculated. Mitral annulus velocities were measured using a pulsed wave Tissue Doppler imaging (TDI) technique by placing a 3 mm sample volume at the level of the septal and lateral annulus with frame rate of 40-50 fps, depth of 100-110 mm, scale of 50 cm/s, and sweep speed of 100mm/s. Early diastolic (E'_m) and late diastolic (A'_m) velocities of the mitral annulus were

determined from the septal and lateral aspects, and the average was calculated. LV diastolic function grade was based on the latest ASE and the EACVI guideline.^[13] First peak early and late diastolic flow velocities were measured across the tricuspid valve (TV) orifices (E_t and A_t) with PW Doppler sample volume of 3 mm, frame rate of 40-50 fps, depth of 100-110 mm, scale of 2.2 m/s, and sweep speed of 75 mm/s in four-chamber apical view. Then, the E_t/A_t values were calculated. TDI was used to measure the peak early and late diastolic velocities at the lateral tricuspid annulus (E'_t , A'_t) by using PW Doppler sample volume of 3 mm, frame rate of 30 fps, depth of 100-110 mm and scale of 50 cm/s, and sweep speed of 100 mm/s. The E_t/E'_t ratios were calculated. Deceleration time of TV inflow was also measured. A tricuspid E_t/A_t ratio $<$ 0.8 suggests impaired relaxation. A tricuspid E_t/A_t ratio of 0.8 to 2.1 with an E_t/E'_t ratio $>$ 6 or diastolic flow predominance in the hepatic veins suggests pseudonormal filling. Tricuspid E_t/A_t ratio $>$ 2.1 with deceleration time $<$ 120 ms suggests restrictive filling.^[14] Tricuspid regurgitation peak gradient (TRG), RV fractional area change, left atrial (LA) volume, and right atrial (RA) volume were all measured in four chamber view. Inferior vena cava (IVC) size and its respiratory collapse were evaluated in subcostal view.

Risk stratification was done for all these patients by calculating EuroSCORE II.^[6] EuroSCORE II items are shown in Table 1.

Clinical data

All operations were performed by one surgery and anesthesiology team. After surgery, the length of being intubated, inotrope dependency duration, hospital stay in intensive care unit (ICU), hospital stay in ward, in-hospital mortality, mortality after discharge from the hospital, the incidence of AF during hospitalization and the incidence of AF after discharge were evaluated in all patients. All the patients were monitored in the ICU for 2 to 3 days after cardiac surgery. In this duration, patients were under electrocardiogram (ECG) monitoring, and then they were transferred to the ward, where an ECG was done once daily and heart rate and blood pressure were measured every 4 h. In cases of any disturbance of the heart rate, an ECG was done. As in this duration, patients were not under Holter-monitoring, the new episode of AF was defined as clinical AF (symptomatic or not) which means any episode of AF diagnosed by a physician during the hospital stay. Follow-up information at 1 month after operation was obtained at hospital clinic. Next follow-up was done by phone call to the patients or the patients' family.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 19 was used for statistical analysis. A two-tailed

Table 1: Euroscore II items

Patients related factors	Cardiac related factors	Operation related factors
Age	NYHA	Urgency
Gender	CCS class angina	Weight of the intervention
Renal impairment	LV function	Surgery on thoracic aorta
Extracardiac arteriopathy	Recent MI	
Poor mobility	Pulmonary hypertension	
Previous cardiac surgery		
Chronic lung disease		
Active endocarditis		

CCS=Canadian cardiovascular society, NYHA=New York Heart Association, LV=Left ventricular, MI=Myocardial infarction

$P < 0.05$ was considered statistically significant. Continuous variables were described using mean and standard deviation (SD) or median and interquartile range and categorical variables using numbers and percentage. All continuous data were tested for normal distribution using the Shapiro–Wilk test. Comparisons between groups were made by independent samples *t*-test for normally distributed continuous variables, Wilcoxon rank-sum test for continuous variables with non-normal distribution, and Fisher's exact test for categorical univariate logistic variables. Correlation between continuous variables was assessed using Spearman correlation. Univariate binary logistic regression analysis was used to test risk factors for postoperative atrial fibrillation (POAF) after adjustment for sex and age. The odds ratios in the logistic models along with 95% confidence intervals (CIs) are reported. A multivariate logistic regression model of independent risk factors for POAF was pursued using variables from the univariate analysis with $P < 0.1$ as predictor variables. A diagnostic test performance of RV diastolic function (tricuspid E_r/E'_r) was assessed, including sensitivity, specificity, and area under the receiver operating curve. Receiver operating characteristic curve assessed the cutoff point of tricuspid E_r/E'_r for predicting POAF.

RESULTS

Sixty-seven patients were prospectively included in the study. The mean \pm SD age of our patients was 61.4 ± 9.3 (range: 43–80). Forty-nine patients were male (73.1%). Baseline TTE results are summarized in Table 2. Ten (14.9%) patients had normal RV diastolic function, but thirty-seven (55.2%), and twenty (29.9%) patients had mild and moderate RV diastolic dysfunction, respectively. There was not any patient with severe RV diastolic dysfunction. Seven patients were missed from follow-up after discharge. Therefore, we analyzed 58 patients for late outcomes. The overall rate of mortality was eight patients in 2 months (13.8%). Two patients died in hospital (3.0%), and six (10.3%) expired after discharge (four in the 1st month and two in the 2nd month after discharge due to cardiovascular diseases. From 67 patients, twelve (17.9%)

Table 2: Baseline risk score and transthoracic echocardiography characteristics of the patients

	Mean \pm SD	Range
Age (year)	61.4 \pm 9.3	43-80
Euro score II	4.1 \pm 3.2	1.1-21
E_r (cm/s)	42.4 \pm 10.7	21-75
A_r (cm/s)	95.8 \pm 360.4	27-100
Deceleration time of TV	218.9 \pm 76.6	102-545
E'_r (cm/s)	6.9 \pm 2.7	3-16
A'_r (cm/s)	11.9 \pm 3.7	3-20
LVEF (%)	23.6 \pm 5.1	15-35
RA volume (cc)	32.3 \pm 12.1	15-67
RV end diastolic area (cm ²)	14.38 \pm 3.1	8.6-26.3
RV end systolic area (cm ²)	9.5 \pm 11.8	3.4-100
FAC (%)	43.9 \pm 11.9	15-70.5
TRG (mmHg)	32.48 \pm 15.15	20-80
Systolic PAP (mmHg)	38.05 \pm 17.17	25-90
LV diastolic function, <i>n</i> (%)		
Normal	1 (1.5)	
Mild	8 (11.9)	
Moderate	51 (76.1)	
Severe	7 (10.4)	
RV diastolic function, <i>n</i> (%)		
Normal	10 (14.9)	
Mild	37 (55.2)	
Moderate	20 (29.9)	
Severe	0	

A_r =Peak late-diastolic flow rate across the tricuspid valve orifice; A'_r =Peak late-diastolic velocity at the lateral tricuspid annulus; E_r =Peak early diastolic flow rate across the tricuspid valve orifice; E'_r =Peak early diastolic velocity at the lateral tricuspid annulus; FAC=Fractional area change; LV=Left ventricle; LVEF=Left ventricular ejection fraction; PAP=Pulmonary artery pressure; RA=Right atrium; RV=Right ventricle; TRG=Tricuspid regurgitation gradient; TV=Tricuspid valve; SD=Standard deviation

patients developed AF during hospitalization and from 58 patients after discharge, seven patients (12.1%) developed clinical AF. Postoperation outcome of patients based on grade of RV diastolic function are listed in Table 3. Early postoperative outcomes (Intubation duration, days admitted to ward or ICU, Inotrope dependency) did not significantly differ between grades of RV diastolic function. However, we found significant differences in onset of in hospital and total POAF between grades of RV diastolic function [Table 3]. In addition, there was not any significant difference of mortality (In hospital, after the

discharge and total mortality) between different groups of RV diastolic function (P -value > 0.05). Univariate binary logistic regression analysis after adjustment for age and sex showed moderate RV systolic dysfunction, Tricuspid E_r/E'_t , LA volume, and high risk Euroscore II significantly predict total POAF in patients with moderate to severely impaired LV systolic function [Table 4]. Multivariate analysis demonstrated that preoperative E_r/E'_t value, LA volume and "high risk" Euroscore II are independent predictors for POAF during hospitalization and total POAF in patients with moderate to severely impaired LV systolic function. Tricuspid E_r/E'_t larger than 6.3 had 69% sensitivity and 57% specificity for prediction of total POAF (AUC 0.734, 95%CI [0.603,0.865]) [Figure 1]. In spite of this, there was no correlation between preoperative E_r/E'_t value and mortality during hospitalization, after the discharge, and total mortality (P -values were 0.25, 0.13, and 0.49, respectively).

None of the echocardiographic parameters [which is shown in Table 2] had correlation with in hospital mortality, but the EuroSCORE II had the correlation with both total mortality and after the discharge mortality ($P = 0.003$ and 0.018 , respectively). Furthermore,

Table 3: Comparison of the right ventricle diastolic function and postoperative outcomes

	RV diastolic function grades		P
	Normal or mild	Moderate	
Intubation duration (h)	13.0±3.9	17.3±20.8	0.51
Admitted to ward (days)	5.0±3.3	5.2±2.8	0.84
Admitted to ICU (days)	6.6±13.7	4.2±1.8	0.20
Inotrope dependency (h)	107.0±283.3	47.1±38.6	0.12
POAF, n (%)			
In-hospital	4 (33.3)	8 (66.7)	0.017
After-discharge	3 (8.1)	3 (14.2)	0.65
Total	7 (19)	11 (52.3)	0.017

ICU=Intensive care unit; POAF=Postoperative atrial fibrillation; RV=Right ventricular

Table 4: Association between predictor parameters and atrial fibrillation in univariate binary logistic regression model after adjustment for age and sex

	OR (95% CI)	P
RV diastolic dysfunction		
No	1	
Yes	4.71 (1.44-15.46)	0.010
E_r/E'_t	1.20 (1.01-1.43)	0.043
LA volume	1.04 (1.01-1.07)	0.003
PAP	1.03 (1.00-1.07)	0.080
Euroscore II		
Low	1	
Moderate	2.45 (0.44-13.59)	0.31
High	10.50 (1.72-63.91)	0.010

AF=Atrial fibrillation; CI=Confidence interval; E_r =Peak early diastolic flow rate across the tricuspid valve orifice; E'_t =Peak early diastolic velocity at the lateral tricuspid annulus; LA=Left atrial; OR=Odds ratio; PAP=Pulmonary artery pressure; RV=Right ventricle

increase in PAP and LA volume, raised the risk of total mortality in the patients (P -value = 0.040 and 0.033, respectively).

DISCUSSION

The results of this study showed that in patients with moderate-severe LV systolic dysfunction, increase in E_r/E'_t value (an index of RV diastolic dysfunction) was associated with increased risk of POAF onset. However, we did not find any correlation between E_r/E'_t and postoperation mortality in hospital and during first 2 months after surgery. LA volume and Euroscore II were the other two independent variables that could predict the POAF.

As was first described by Riggs *et al.* the RV diastolic function has a pivotal role in evaluation of patients with heart failure.^[15] Many factors are known to affect the RV diastolic function such as coronary reserve flow, ventricular interdependence, and ventriculoarterial coupling.^[16] Therefore, in patients with LVEF $< 35\%$, who are candidate for CABG, right coronary artery stenosis, LV systolic and diastolic dysfunction and pulmonary artery hypertension, all are leading factors to RV diastolic dysfunction, and it would not be surprising that more than 85% of our patients had some degree of RV diastolic dysfunction. The prognostic value of RV diastolic dysfunction has been evaluated in limited studies. In 2006, Denault *et al.* evaluated both LV and RV diastolic function in patients who were candidate for CABG and showed that moderate and severe LV and RV diastolic

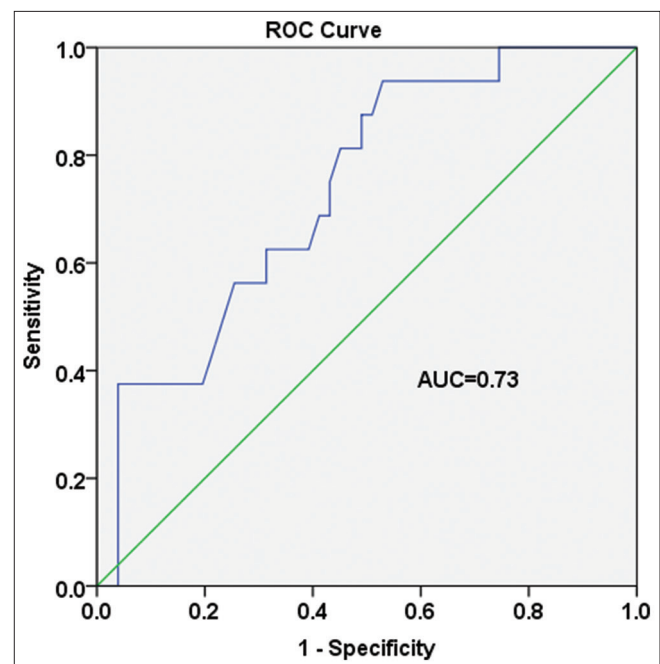


Figure 1: Receiver operating characteristics curve of the tricuspid E_r/E'_t for the predicting postoperative atrial fibrillation. AUC=Area under curve

dysfunction were associated with difficult separation from cardiopulmonary bypass. In another retrospective study Jin *et al.* showed that RV diastolic dysfunction (tricuspid $E/E' \geq 10$) is significantly associated with early death after CABG in patients with severe impaired LV systolic dysfunction.^[17]

Our results showed that the higher value of E_t/E'_t is related to POAF onset in hospital and total POAF. We speculate that increased RV diastolic pressure causes RA overdistention and atrial wall stretch, which could consequently trigger POAF. There are some evidences in favor of predictive value of heart failure for POAF, but almost all of them focused on clinical risk factors and systolic function of LV and RV.^[18-21] To the best of our knowledge, this is the first comprehensive study, which evaluated the RV diastolic function and its predictive value for postoperative outcomes. In this study, two other independent predictors of POAF were LA volume and EuroSCORE II. Similarly, some other studies showed that enlarged LA volume^[20,22,23] and EuroSCORE are risk factors for POAF.^[24-27]

In our study, the tricuspid E_t/E'_t cutoff value of 6.2 is in agreement with previous studies for predicting poor outcomes,^[28] but lower than the cutoff reported by Jin *et al.*^[17]

The results of this study show that in candidate for CABG specifically those with LVEF <35% a comprehensive evaluation of RV may predict the POAF, which is a potential risk factor for mortality and morbidity.

This study had some limitations that should be mentioned. First, the lack of long-term follow-up restricted analysis of overall longer mortality rate in our patients. Second, we did not utilize right heart catheterization for evaluation of increased diastolic RV pressure; instead, we used the echocardiography guideline. Third, the subjects in our study were not under 24-Holter monitoring after they were discharged from ICU that is why we used the clinical AF that means any episode of AF diagnosed by a physician during the hospital stay or after that. It is needed that other larger prospective studies evaluate the role of RV diastolic function in outcomes of patients with moderate-severe LV systolic dysfunction.

CONCLUSION

We believe that patients with increased tricuspid E_t/E'_t are high risk for POAF; therefore any risk score for POAF should include a comprehensive TTE including evaluation of RV diastolic function before surgery. This would help to identify patients who might be candidates

for prophylactic therapy or close electrocardiographic monitoring.

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Conflicts of interest

There are no conflicts of interest.

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