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Impact of Electrocardiographic Diastolic Parameters and Diastolic ECG Index in Predicting Postoperative Atrial Fibrillation

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Abstract

Background. Diastolic dysfunction (DD) is a significant predisposing factor for postoperative atrial fibrillation (POAF). Diastolic electrocardigraphy (ECG) parameters and ECG index (Tend-P / [PQ x Age]) provides a good diagnostic performance for the recognition of DD. In our study, we aimed to investigate the relation between diastolic ECG parameters, novel diastolic ECG index and POAF in patients undergoing elective coronary artery bypass grafting (CABG).
Methods. Patients who will undergo CABG electively were included in the study. Patients were monitored for the occurrence of POAF continuously. Preoperative 12-lead surface ECG were independently analyzed by two experienced cardiologists for the calculation of diastolic parameters and diastolic ECG index.
Results. A total number of 311 patients (age:60.1±8.7 years, 34,1% women) were included in our study, prospectively. 71 (22.8%) of them developed POAF(Group-1). PQ interval (161.4±32.6 vs 147.0±15.1 ms, $p<0.01$) and QTc (449.3±36.3 vs 426.9 vs 47.6) was significantly longer in Group-1. Tend-Q, Tend-P and QRS intervals were significantly shorter in Group-1. Diastolic ECG index was significantly different between two groups (0.040±0.017 vs 0.058±0.010, $p<0.01$). We calculated the cut-off value as 0,03 according to POAF occurrence. There was a statistically significant relationship between index lower than 0,03 and POAF occurrence ($p<0.01$).
Conclusion.Diastolic ECG parameters and novel diastolic index predict POAF after elective CABG operation. Diastolic ECG index lower than 0,03 was an independent and strong risk factor for POAF occurrence. From clinical point of view, preoperative assessment of these parameters could help identification of high risk patients who might benefit prophylactic treatment.

Keywords: Atrial Fibrillation, Coronary Artery Bypass Grafting, Electrocardiography

Introduction

Atrial arrhythmias, especially atrial fibrillation (AF) are significant complications after cardiac surgery with a reported incidence between 10 and 60% (1). Postoperative atrial fibrillation (POAF) is an important cause of morbidity and mortality. It is linked with higher risk of stroke and death and causes a substantial expenditure of community resources, including higher length of hospital stay and hospital costs (2). The identification of risk factors of developing POAF has produced inconsistent results, with the exception of increasing age (3).
Diastolic dysfunction (DD) shares many common risk factors with AF, including age, hypertension(4), obesity (5), and diabetes (6). DD has significant pathological effects on atrial structure and function, many of which are proarrhythmic. The pathophysiological mechanisms of POAF might be linked to preexisting, age

related, and degenerative, structural and functional changes in the atrial and ventricular myocardium. Therefore, it has been shown that diastolic dysfunction is a significant predisposing substrate for POAF after cardiac surgery.

Most noninvasive measurements of left ventricular relaxation, stiffness and filling pressures are indirect and not free of limitations, and are frequently based on simplified assumptions thereby limiting their general applicability. Moreover, their assessment is not infrequently highly variable in the same patient with changes in preload, afterload, and sympathetic tone, further complicating their measurement and interpretation (7). In contrast, electrocardiographic (ECG) parameters are generally less prone to acute hemodynamic changes, show a great reproducibility and are operator-independent(8).

In our study, we aimed to investigate the relation between novel diastolic ECG index and POAF in patients undergoing coronary artery bypass grafting (CABG).

Methods

The study was approved by the Institutional Ethical Committee, and all patients gave written informed consent for participation in the study. Between July 213 and February 2014, a total of 311 patients undergoing nonemergency CABG were included in the study. Patients with previous atrial arrhythmia, renal failure, antiarrhythmic drug user and undergoing concomitant valve surgery were excluded. In the postoperative period, heart rate and rhythm were continuously monitored for the first 48 – 72 hours and daily 12-lead electrocardiograms were performed from the preoperative day until discharge. Preoperative 12-lead surface ECG were independently analyzed by two readers for the calculation of diastolic parameters and diastolic ECG index. Measurements were taken manually from the tracings at 25mm/sec. The observers were blinded to the POAF status. The QTc interval was calculated using the Bazett formula(9), Tend-P and Tend-Q intervals of interest reflecting the mechanical diastole were also included in our analysis(10). These two intervals were both manually measured and calculated as: RR minus PQ minus QT for Tend-P and RR minus QT for Tend-Q.

Statistical Analysis

All statistical analysis calculated by SPSS 20.0 (SPSS Inc., Chicago, USA). Continuous variables expressed as Mean±SD and percentages for categorical variables. Independent samples t-test for continuous variables and chi-square test for categorical variables were used to evaluate differences in both groups. Logistic regression analysis performed for determining predictors exhibiting a statistically significant relation with POAF and these variables taken for multivariate stepwise regression analysis. A p value ≤0.05 was considered statistically significant.

Results

311 patients (60.1±8.7 years and 34,1% women) who underwent elective CABG between July 2013 and February 2014 were included in our study. 71 (22.8%) of them developed POAF during their postoperative follow-up in the hospital. Patients were divided into two groups according to observation of AF in the postoperative period; Group-1 (POAF+) and Group-2 (POAF-). Group-1 patients were significantly older than Group-2 (62.0±10.1 vs 59.5±8.2, p=0.04), and they were significantly more hypertensive than

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Group-2. Diabetes mellitus was observed equally in these groups. Preoperative transthoracic echocardiography parameters were also similar in both groups in terms of left ventricular end diastolic and systolic diameters, left ventricular ejection fraction as well as left atrial diameter. Preoperative electrolyte levels were alike in both groups. QT intervals were similar in both groups, however PQ interval (161.4±32.6 vs. 147.0±15.1 ms, p<0.01) and QTc (449.3±36.3 vs. 426.9 vs 47.6) was significantly longer in Group-1. Mean heart rate was significantly higher in Group-1 and Tend-Q, Tend-P and QRS intervals were significantly shorter in Group-1. Diastolic ECG index was significantly different between two groups (0.040±0.017 vs 0.058±0.010, p<0.01). Diastolic ECG index was also significantly negatively correlated with POAF (r=-0.463, p<0.01) (Table-1).

Table 1: Evaluation of demographic variables according to postoperative atrial fibrillation

		Postoperative AF				**[a]p**
		Postop AF (+) (n=71)		**Postop AF (-) (n=240)**		
		Mean*(median)*	**SD *(range)***	**Mean*(median)***	**SD *(range)***	
Age		62,01	10,13	59,59	8,28	***0,041****
QTc		420,38	46,22	426,92	47,60	***0,300***
Diastolic ECG index		0,02 *(0,02)*	0,02*(0,08)*	0,04*(0,04)*	0,01*(0,06)*	***[c]0,001***
Qt		393,10	44,96	392,62	21,56	***0,902***
Tend Q		383,62	130,16	500,03	29,39	***0,001****
PQ		161,42	32,64	147,05	15,16	***0,001****
Tend P		222,23	130,07	348,24	33,83	***0,001****
Potassium		4,10	0,34	4,34	0,59	***0,001****
Calcium		8,88	0,44	9,16	0,42	***0,001****
Sodium		139,18	3,21	139,26	2,55	***0,838***
LA diameter		3,94	0,40	3,91	0,39	***0,653***
EF		54,93	8,34	55,04	8,33	***0,921***
Hemoglobin		13,35	1,48	13,70	7,88	***0,714***
		n	**%**	**n**	**%**	***[b]p***
Sex	**Female**	21	29,6	85	35,4	***0,362***
	Male	50	70,4	155	64,6	
Age>60		45	63,4	121	50,4	***0,054***
DM		29	40,8	76	31,7	***0,151***
HT		33	46,5	83	34,6	***0,069***

[a]Independent Samples Test *[b]Pearson's Chi Square Test* *[c]Mann whitney U test*
**p<0,05* ***p<0,01*

Logistic regression analysis revealed TendP and diastolic ECG index were independent risk factor for POAF occurrence. Odd's ratio for Tend-P was 0,988 (%95 CI:98-0,99) and Odd's ratio for diastolic ECG index was 6,209 (%95 CI:1,85-20,88). Logistic regression model was significant and explanatory coefficient of the model was very good (90%) (Table-2).

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Table 2: Diagnostic tests for Diastolic ECG Index

Diastolic ECG index	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Correction
≤ 0,028	60,56	97,08	86,00	89,27	88,75
≤ 0,029	61,97	96,25	83,01	89,53	88,42
≤ 0,030	**64,78**	**95,00**	**79,31**	**90,12**	**88,10**
≤ 0,031	67,60	93,75	76,19	90,73	87,78
≤ 0,032	69,01	92,08	72,05	90,95	86,82

Diastolic ECG parameters like PQ, Tend-P, Tend-Q and a combined novel ECG index consisting of Age, PQ – interval and Tend - P (Tend - P / [PQ x Age]) provides a substantial diagnostic performance (Figure-1), even after adjustment for possible confounders and when validated in an independent patient group.

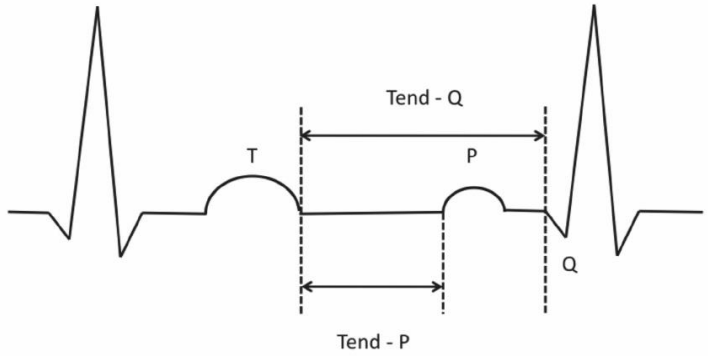

Figure-1: Schematic illustration of Tend-P and Tend-Q measurements.

Diastolic ECG index was a strong and independent risk factor for POAF occurrence. Because of that we wanted to calculate cut-off value of the diastolic ECG index. We used diagnostic test and ROC analysis for calculation of cut-off value. We calculated the cut-off value as 0,03 according to POAF occurrence (Table-3).

Table 3: Diagnostic test and ROC curve results for the cut-off value of Diastolic ECG Index

	Diagnostic Scan					ROC Curve		*p*
	Cut off	Sensitivite	Spesifisite	Positive Predictive Value	Negative Predictive Value	Area	95% Confidence Interval	
Diastolic ECG index	**0,03**	**64,78**	**95,00**	**79,31**	**90,12**	0,826	0,756-0,896	***0,001*****

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For this cut-off value sensitivity was 64,7%, specificity was 95%, positive predictive value was 79,3% and negative predictive value was 90,2%. Area under ROC curve was 82,6% (Table-4) (Figure-2). There was a statistically significant relationship between diastolic ECG index less than 0,03 and POAF occurrence ($p<0.01$).

Table 4: Logistic regression analysis of POAF risk factors

	p	ODDS	95,0% C.I. ODDS	
			Lower	Upper
TendP	0,001**	0,988	0,982	0,995
PQ	0,160	1,016	0,994	1,038
Age >60	0,351	0,676	0,297	1,538
DM (+)	0,638	1,198	0,565	2,540
HT (+)	0,975	0,988	0,464	2,101
Diastolic ECG index (<0,03)	0,003**	6,209	1,846	20,880

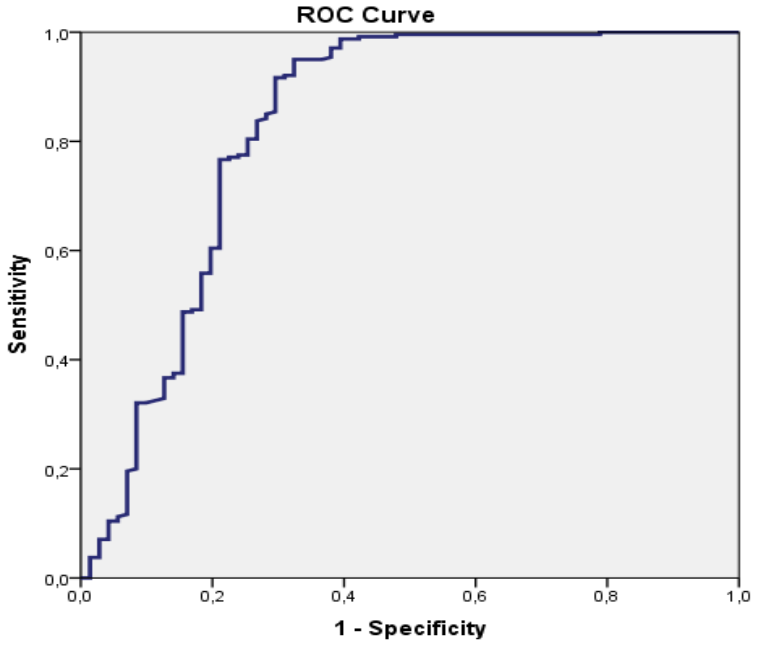

Figure-2: Receiver Operating Characteristic Curve of diastolic ECG index for predicting Postoperative Atrial Fibrillation

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Discussion

Our study is the first ever study investigating association between diastolic ECG parameters and diastolic ECG index with new onset POAF. Our main findings were; 1) electrocardiographic diastolic parameters significantly higher and diastolic index significantly lower in the POAF group, 2) Logistic regression analysis showed Tend-P and Diastolic ECG index were independent risk factors for POAF occurrence, 3)Diastolic ECG index lower than 0,03 value was a strong predictor of POAF.

The exact pathophysiological mechanisms responsible for the onset and continuation of POAF are incompletely understood. Factors facilitating POAF can be classified in acute factors directly related to surgery (e.g. adrenergic stimulation) and factors that are reflecting a chronic process of remodeling or aging of the heart (e.g. DD)(11). Advanced age has been the only consistent, independent predictor of POAF(12). In our study, age was also a significant clinical predictor for POAF. This finding is due to the age related structural changes such as degeneration of large-vessel elastin, increase in afterload, altered filling dynamics, atrial dilation and fibrosis(13). This increase in atrial fibrosis corresponds to an increase in conduction heterogeneity and AF vulnerability(14). As previously reported by Chang et al.(15), the stretch-induced increase in the arrhythmogenic activity of the pulmonary veins due to impaired diastolic distensibility. DD was likely a predisposing common factor underlying these events. Studies in patients with myocardial infarction(16), or diabetes mellitus(17) have detected an increase in the risk of incident AF in patients with DD. Vasan et al.(18), examined data from the Framingham Heart Study and found a trend toward increased incident AF in patients with transmitral peak E/A greater than median. DD is associated with an increasing stretch in pulmonary veins due to increased left atrial pressure(19). Through these studies, it has been shown that atrial fibrosis and impaired LV compliance, especially when superimposed by the acute stress of surgical intervention(20), create a proarrhythmic environment that is manifested clinically as POAF.

Namdar et al.(21) has shown that diastolic ECG parameters and diastolic ECG index demonstrates a high diagnostic accuracy for the diagnosis of DD. It has been shown that the PQ - interval is an exact determinant to define the timing of atrial contraction and thus atrial contribution to late diastolic left ventricular filling(22). To that effect, as the PQ - interval lengthens, atrial contraction occurs earlier in diastole resulting in a shorter mid-diastolic slow ventricular filling and a shorter total diastole in patients with normal ventricular function(23). PQ - interval was significantly longer in the DD group. Also, in our study, PQ interval was significantly longer in the POAF group.

Namdar et al.(21) also showed that diastolic ECG index (Tend - P / [PQ x Age]) has the highest specificity and sensitivity in the recognition of DD. Index was significantly lower in DD patients in their study. Also in our POAF group, index was significantly lower and index lower than 0,03 was an independent and strong predictor of POAF occurrence ($p<0.01$).

Tend-P and Tend–Q intervals were reflecting the timing of the electrical as well as mechanical diastole. So, these intervals were calculated shorter in the DD group. So, POAF patients has statistically

significant shorter Tend-P and Tend-Q intervals.

Wilcox et al.(24) showed a correlation between Doppler-derived parameters of DD and QTc duration. They have shown that QTc intervals were longer in the DD group. In our study, POAF group also had longer QTc intervals.

Tekkesin et al.(25) showed both the PQ interval and the diastolic ECG index have an acceptable diagnostic accuracy, as well as a high specificity to predict atrial high rate episodes (AHRE). Since AHREs are associated with paroxysmal AF, a prolonged PQ interval or shortened diastolic index should be further evaluated for the presence of paroxysmal AF. Our study investigated only in hospital POAF occurrence. Other POAF cases could be missed if they occurred after discharge. So we might underestimate POAF occurrence rate and prolonged PQ interval or shortened diastolic index should be considered for prophylactic treatment to prevent postoperative atrial fibrillation.

In conclusion, diastolic dysfunction is a powerful predisposing substrate for the initiation of POAF after cardiac surgery. Diastolic ECG parameters and novel diastolic index predicts POAF after elective CABG operation. Diastolic ECG index lower than 0,03 was an independent and strong risk factor for POAF occurrence. From clinical point of view, preoperative assessment of these parameters could allow identification of high risk patients who might benefit prophylactic treatment.

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