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Left anterior descending coronary artery flow impaired by right ventricular apical pacing: The role of systolic dyssynchrony

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ABSTRACT

Introduction: Right ventricular (RV) pacing may affect myocardial perfusion and coronary blood flow; however, it remains unknown whether this is related to systolic dyssynchrony induced by RV pacing. This prospective study was aimed to assess the relationship between dyssynchrony and the changes of coronary blood flow.
Methods: Seventy patients with sinus node dysfunction were prospectively enrolled. Coronary flow was evaluated by measuring diastolic velocity time integral (VTI) and duration at the distal-portion of left anterior descending coronary artery (LAD) with transthoracic echocardiography at baseline and follow-up. Systolic dyssynchrony was assessed with tissue Doppler imaging by time standard deviation to peak systolic velocity of 12 left ventricular segments (Ts-SD, cutoff value ≥33 ms).
Results: Adequate data for analysis was available from 65 patients. At follow-up (mean follow up time: 127 ± 45 days), LAD velocity-time integral (LAD-VTI: 12.1 ± 4.2 vs. 10.7 ± 4.6 cm, $p < 0.001$) was decreased and there was deterioration of left ventricular systolic function (left ventricular ejection fraction: 65 ± 7% vs. 62 ± 7%). However, these changes were only detected in those with RV pacing induced systolic dyssynchrony. Significant reduction of LAD-VTI (defined as ≥5%) occurred in 34 (52%) patients which was more prevalent in those with pacing-induced systolic dyssynchrony than those without (85.3% versus 16.1%, $\chi^2 = 31.1$, $p < 0.001$). Though similar at baseline, LAD-VTI was significantly lower in the dyssynchrony group at follow up ($p < 0.001$). Cox-regression analysis showed that pacing-inducing systolic dyssynchrony [hazard ratio (HR): 3.62, $p = 0.009$] and higher accumulative pacing percentage (HR: 1.02, $p = 0.002$) were independently associated with reduction of LAD-VTI. ROC curve demonstrated that accumulative pacing percentage ≥35% was 97% sensitive and 84% specific in revealing significant reduction (area under the curve: 0.961, $p < 0.001$).
Conclusions: RV pacing induced dyssynchrony is associated with reduced coronary flow and this may account for, in part, the deleterious effect of RV pacing on ventricular function over time.

1. Introduction

It has become apparent that not only systolic function but also diastolic function could be impaired after long-term pacing even in patients with normal cardiac function, and this has been considered to be related to systolic dyssynchrony induced by the non-physiological conduction during right ventricular apical (RV) pacing [1,2]. Recent studies have shown that RV pacing can lead to regional perfusion defects, reduction of myocardial oxygen consumption as well as cardiac efficiency even in those without pre-existing coronary artery disease [3–5]. Coronary blood flow detected with transthoracic echocardiography that been shown to be disturbed in patients with LBBB; [6] whereas, data are inconclusive with regard to the coronary flow change after RV pacing despite the presence of an iatrogenic LBBB [6–9]. Furthermore, whether the impact of RV pacing on coronary blood flow is related to pacing-induced systolic dyssynchrony has not been elucidated. This is

Abbreviations: E′, peak myocardial early diastolic velocity of mitral annulus by pulse wave tissue Doppler imaging; LAD, left anterior descending coronary artery; LV, left ventricle/left ventricular; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; RV, right ventricular; TAPSE, tricuspid annular plane systolic excursion; TDI, tissue Doppler imaging; Te-SD, standard deviation of the time to early peak myocardial diastolic velocity among the 12 LV segments; Ts-SD, standard deviation of the time to peak myocardial systolic velocity among the 12 LV segments; VTI, velocity-time integral.

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particularly relevant to understanding the theoretical mechanisms of myocardial scintigraphic perfusion defects and the deterioration of left ventricular (LV) function after long-term RV pacing. Therefore, the aim of this prospective study was to explore the effect of RV pacing on coronary blood flow in left anterior descending artery (LAD) using non-invasive transthoracic echocardiography. In addition, the impact and relationship with systolic dyssynchrony were investigated in the current study.

2. Methods

2.1. Study population and study design

From April 2005 through July 2009, a total of 70 patients with sick sinus dysfunction were prospectively enrolled in the study. All patients were examined before pacemaker implantation and followed up. The mean follow-up period was 127 ± 45 days. They all had normal cardiac function with ejection fraction ≥50% at baseline. Patients were excluded if they had coronary artery disease, a history of coronary artery bypass surgery, atrial fibrillation, patients with life expectancy <6 months,and pregnant. Patients were also excluded for those with suboptimal acoustic window who cannot be detected with LAD Doppler. ECG data and New York Heart Association class were also recorded. All the pacemaker parameters were retrieved from the internal monitor record. The study was approved and conducted in compliance with the regulation of the institutional Ethics Committee.

2.2. Transthoracic echocardiography

Comprehensive transthoracic echocardiography (Vivid 7, General Electric) with tissue Doppler imaging (TDI) was performed to assess cardiac function and systolic dyssynchrony. Digital color TDI imaging was acquired with at least 3 cardiac consecutive beats on apical serial views (apical 4-chamber, 2-chamber, and long-axis views) after optimization of pulse repetition frequency, color saturation, sector size, and depth allowing the highest possible frame rate. Off-line analysis was performed with a dedicated software package (EchoPac 6.3.6, Vingmed, General Electric). Systolic dyssynchrony was calculated as the standard deviation of the time to peak myocardial systolic velocity in the ejection phase among the 12 left ventricular segments (Ts-SD) by using the QRS complex as the reference point. Systolic dyssynchrony was defined as Ts-SD ≥ 33 ms as reported previously. Tricuspid regurgitation was assessed by 2-dimensional color-flow and continuous-wave Doppler [10].

RV long-axis function was evaluated using tricuspid annular plane systolic excursion (TAPSE), which was acquired by placing the M-mode cursor at the tricuspid annulus of the RV free wall from the apical 4-chamber view.

Doppler study of distal LAD was done by placing the transducer in the 4th to 5th intercostal spaces on the modified apical 2-chamber view under the coronary examination item which can detect flow with low velocity. Under this specific blood flow guidance, the probe was adjusted to get the optimized long-axis flow view of the distal LAD after the detection long-axis color signal of LAD. The images were then zoomed and pulsed Doppler with sample volume (5 × 2.5 mm) on the distal portion of coronary artery was adopted to obtain the velocity. If there was Doppler angle between ultrasound beam and color signal, an angle correction was performed without exceeding 30°. Peak diastolic velocity, diastolic duration and velocity-time integral (VTI) were calculated [11–13].

2.3. Statistical analysis

Data were analyzed with the statistical software of SPSS version 17 (SPSS Inc, Chicago, Illinois, USA). All continuous variables were expressed as mean ± SD and Kolmogorov–Smirnov test was applied to test the normality. Paired *t*-test and independent *t*-test were used to compare the mean value of the parametric values as appropriate. Categorical variables were expressed as frequency and compared by Pearson Chi-square test or Fisher Exact test as appropriate. Pearson's correlation was performed to test the correlations between parameters. Cox regression analysis was used to identify the predictors of the reduction of LAD VTI. Receiver Operating Characteristic (ROC) curve was performed to determine the cut-off value of the potential parameter predicting LAD reduction. A significant difference was defined as $p < 0.05$ (2-tailed).

3. Results

3.1. Patients' characteristics

Although 70 patients were enrolled 5 patients were excluded due to suboptimal LAD Doppler recording during on-line scanning. Therefore, the results from 65 patients were analyzed. The mean age was 57 ± 7 years and there were 45 (69%) males. Diabetes mellitus was found in 11 (17%) patients and hypertension in 26 (40%). The medical therapy included angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) in 15 (23%), calcium channel antagonists in 12 (19%) and statin in 16 (25%) as well as aspirin in 8 (12%) patients.

3.2. Clinical and echocardiographic changes before and after right ventricular apical pacing

After pacing, QRS width was prolonged (100 ± 29 versus 129 ± 31 ms, $p < 0.001$) but New York Heart Association class remained unchanged (0.03 ± 0.17 versus 0.08 ± 0.17, $p = 0.83$). The changes of echocardiographic parameters after RV pacing are presented in Table 1. At follow-up, LV systolic function was reduced with an increase in LV end-systolic volume. Moreover, LV diastolic function was also decreased as evident by reduction of septal E′ and increase of E/E′ (both $p < 0.05$). Regarding LAD Doppler variables, peak velocity, VTI and diastolic duration were significantly reduced after pacing (all $p < 0.01$).

Table 1
Comparison of echocardiographic parameters between baseline and follow-up.

	Baseline	During follow-up	p Value
Cardiac function			
LVEDV, ml	57 ± 16	62 ± 15	0.024
LVESV, ml	20 ± 7	24 ± 8	0.001
LVEF, %	65 ± 7	62 ± 7	0.014
Mitral E/A ratio	0.91 ± 0.33	0.95 ± 0.36	0.203
LV septal E′	7.4 ± 2.6	7.1 ± 3.0	0.027
LV septal E/E′	10.3 ± 3.9	11.7 ± 5.2	0.002
TAPSE, cm	2.0 ± 0.4	1.7 ± 0.3	<0.001
Tricuspid regurgitation pressure gradient, mm Hg	36 ± 9	41 ± 13	0.011
LAD Doppler Variables			
Peak diastolic velocities, cm/s	0.33 ± 0.12	0.26 ± 0.14	<0.001
LAD diastolic duration, ms	520 ± 97	508 ± 95	0.007
LAD-VTI, cm	12.1 ± 4.2	10.7 ± 4.6	<0.001
TDI variables			
Ts-SD, ms	23 ± 7	39 ± 16	<0.001
With systolic dyssynchrony, n (%)	4 (6)	38 (59)	$\chi^2 = 40.03$, $p < 0.001$
Te-SD, ms	27 ± 13	31 ± 15	0.097
With diastolic dyssynchrony, n (%)	17 (26%)	22 (34%)	$\chi^2 = 0.916$, $p = 0.222$
Mean systolic septal velocity, cm/s	3.9 ± 0.8	3.5 ± 0.8	<0.001
Mean early diastolic septal velocity, cm/s	3.5 ± 1.1	2.9 ± 0.9	0.003

E′ = peak myocardial early diastolic velocity of mitral annulus by pulse wave tissue Doppler imaging; LAD = left anterior descending artery; LV = left ventricular; LVEDV = left ventricular diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; TAPSE = tricuspid annular plane systolic excursion; VTI = velocity time integral; Te-SD = standard deviation of the time to early peak myocardial diastolic velocity among the 12 LV segments; Ts-SD = standard deviation of the time to systolic myocardial diastolic velocity among the 12 LV segments.