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Original article

Predictors of an adverse clinical outcome in patients with long-term right ventricular apical pacing

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ABSTRACT

Background: Right ventricular (RV) apical pacing can result in progressive left ventricular (LV) dysfunction and contribute to the development of heart failure (HF). This study aimed to predict the outcome after long-term RV apical pacing in patients with acquired atrioventricular (AV) block who required permanent pacing.

Methods: We included 247 patients who underwent long-term (>90% ventricular pacing with atrioventricular synchrony for more than 1 year) RV apical pacing for acquired AV block. We excluded patients with a reduced LV systolic function [ejection fraction (EF) <50%]. The paced QRS duration, degree of the axis, clinical characteristics, laboratory findings, and echocardiographic parameters were recorded. We evaluated the mortality and hospitalization due to HF.

Results: The mean follow-up duration was 6.9 years. Mortality and hospitalization due to HF occurred in 8.1% and 17%, respectively. In a multivariate analysis, a wider paced QRS duration and less superior paced QRS axis at the time of the implantation were independent risk factors for adverse events. The patients with a paced QRS duration of ≥163 ms and axis of ≥−65° had a 5.8 times higher risk for adverse events compared to those with a paced QRS duration of <163 ms and axis of <−65°.

Conclusions: The paced QRS duration and axis could help us predict adverse clinical outcomes after permanent RV apical pacing in patients with high-degree AV block.

Introduction

Cardiac pacing is the only effective treatment for symptomatic atrioventricular block (AVB). However, there have been several studies that have indicated that long-term right ventricular (RV) apical pacing is associated with left ventricular (LV) dilatation [1] or a decreased LV ejection fraction [2]. Large-scaled randomized studies also showed an increased hospitalization rate due to heart failure (HF) in patients with long-term RV apical pacing [3,4]. The decreased LV function may be due to abnormal electrical and mechanical activation patterns of the ventricles due to chronic RV pacing [5]. There have been studies that have suggested that the QRS duration and left-axis deviation could be related to the development of HF [6]. Nevertheless, there are no robust electrocardiographic (ECG) features that can predict cardiac outcomes. This study aimed to investigate the paced QRS features that could help predict the cardiac outcome after chronic RV apical pacing in patients with acquired AVB.

Materials and methods

Study population

This study comprised 247 consecutive patients who underwent long-term (>90% ventricular pacing with atrioventricular synchrony for more than a year) RV apical pacing for acquired high degree AVB from October 1995 to December 2012. We only included patients who were implanted with a DDD or VDD pacemaker to maintain atrioventricular sequential pacing. We excluded the patients with an LV ejection fraction of less than 50%, significant valvular disease, or any type of cardiomyopathy or atrial fibrillation before the pacemaker implantation. The demographic characteristics, laboratory findings, ECG findings, and echocardiographic

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findings were collected retrospectively. The current study was conducted in accordance with the declaration of Helsinki, and the Institutional Review Board of the Daegu Catholic University Medical Center approved the study protocol.

Electrocardiography

All ECGs were recorded at a speed of 25 mm/s. The ECG was sequentially obtained right after the implantation of a permanent pacemaker and repeated every year after the implantation. We collected data in terms of the paced QRS duration and axis. The paced QRS duration was assessed at the widest QRS duration at all paced QRS leads. The paced QRS axis was calculated from the voltage of lead I and lead aVF using trigonometry. All interrogated data from the pacemaker, which were obtained every 6 months, were reviewed to confirm the proportion of ventricular pacing.

Echocardiography

Echocardiography was done before the pacemaker implantation and followed up a year after. We also performed echocardiography in situations of cardiac events as well. The LV ejection fraction, LV end-diastolic and end-systolic dimensions, and left atrial diameter were obtained and recorded. The LV ejection fraction was measured by Simpson's method using apical 4 chamber view and apical 2 chamber view.

Pacemaker implantation

All patients were implanted with a pacemaker lead in right ventricular apex. Under fluoroscopic guidance, the pacing lead was inserted to right ventricle via superior vena cava and right atrium. After advancement of lead as far as possible toward the RV apex, we confirmed whether the tip of lead was stably lodged in RV apex in fluoroscopic imaging. ECG was also checked to find out negative QRS axis in lead II, III, and aVF. After the procedure, we checked chest X-ray daily to confirm the position of lead for 5 days. The cardiothoracic ratio in initial chest X-ray was calculated and recorded.

Clinical outcomes

As a primary outcome, the composite of the cardiac events including the all-cause mortality and hospitalization due to HF were evaluated. Further, each of the all-cause mortality and hospitalizations due to HF were analyzed separately as secondary outcomes.

Statistical analysis

The statistical evaluation was performed using SPSS software package version 18.0 for Windows (SPSS Inc., Chicago, IL, USA). A chi-square and t-test were used to compare the demographic characteristic, and laboratory, electrocardiographic and echocardiographic findings between the groups with events and those without events. A logistic regression analysis was used for the detection of the risk factors of cardiac events. A receiver-operating characteristic (ROC) curve was used to determine the cut-off values of the QRS duration and axis for the development of events. We used a Kaplan–Meier curve to describe the event-free survival rate in different risk groups determined by the paced QRS duration and axis deviation. All analyses required a p-value <0.05 for statistical significance.

Results

The follow-up duration was 6.7 ± 3.9 years. Among the patients, 51 (20.6%) developed events that were adjudicated as primary outcomes. Death from any cause occurred in 20 (8.1%) patients, and hospitalization due to HF occurred in 42 (17.0%) patients. The characteristics of the patients who developed events or not are described in Table 1. The age, gender, and presence of hypertension, diabetes, or coronary artery disease did not differ between the groups with events and those without events. There was no significant difference in the medications such as beta blockers, angiotensin-converting enzyme inhibitor, or angiotensin receptor blockers. Among the ECG parameters, the paced QRS duration was longer (167.3 ± 18.2 ms vs. 158.6 ± 17.9 ms, $p = 0.002$) and the degree of the paced QRS axis was less superior (−64.2 ± 7.2 vs. −68.4 ± 10.6, $p = 0.001$) in the patients who developed cardiac events. Among the conventional risk factors for poor cardiovascular outcomes, the LV ejection fraction was confirmed to be an independent risk factor for events. Also, a longer QRS duration and a lesser superior axis were independent risk factors of events (Table 2). The odds ratio of the QRS duration was 1.029 (CI 1.001–1.058, $p = 0.045$) for deaths and 1.047 (CI 1.010–1.053, $p = 0.004$) for hospitalizations due to HF, respectively. The odds ratio of the QRS axis was 1.031 (CI 1.002–1.093, $p = 0.038$) for deaths and 1.054 (CI 1.018–1.091, $p = 0.003$) for hospitalizations due to HF, respectively.

Fig. 1 describes the ROC curve showing the QRS duration and axis for the development of cardiac events. The best cut-off values of the QRS duration and axis for predicting cardiac events were 163 ms and −65°, respectively. Among the patients with a paced QRS duration of ≥163 ms, 29.3% developed cardiac events. In those with a paced QRS axis of ≥−65°, 28.4% developed cardiac events. The paced QRS duration and axis were also independent risk factors for composite cardiac events including all-cause mortality and hospitalizations due to HF. Using the best cut-off values of the QRS duration and axis for the development of cardiac events, we divided all patients into four different groups: group I, which included patients with a QRS duration of <163 ms and axis of <−65°, group II, which included patients with a QRS duration of <163 ms and axis of ≥−65°, group III, which included patients with a QRS duration of ≥163 ms and axis of <−65°, and group IV, which included patients with a QRS duration of ≥163 ms and axis of

Table 1
The characteristics of patients with cardiac events.

	Event(+) (n = 51)	Event(−) (n = 196)	p-value
Age at implantation, years	66.4 ± 12.2	65.5 ± 13.5	NS
Female, n (%)	31(60.8)	201(61.2)	NS
Hypertension, n (%)	22(43.1)	83(42.3)	NS
Diabetes, n (%)	11(21.6)	36(18.4)	NS
CAD, n (%)	5(9.8)	15(7.7)	NS
Medication, n (%)			
Beta blocker	7(13.7)	22(11.2)	NS
ACEi/ARB	16(31.4)	45(23.0)	NS
ECG after implantation			
Paced QRS duration, ms	167.3 ± 18.2	158.6 ± 17.9	0.002
Paced QRS axis,°	−64.2 ± 7.2	−68.4 ± 10.6	0.001
Initial cardio-thoracic ratio, %	53.0 ± 4.6	51.8 ± 5.8	NS
Initial echocardiography			
LVEF, %	60.0 ± 7.8	62.9 ± 7.0	0.012
LVEDD, mm	51.9 ± 7.4	50.5 ± 6.1	NS
LVESD, mm	34.7 ± 7.6	32.1 ± 5.6	0.008
LA dimension, mm	41.5 ± 7.7	39.1 ± 6.7	0.023
New onset AF, n (%)	15(28.3)	72(35.3)	NS
Follow-up echocardiography			
LVEF, %	49.9 ± 15.5	58.8 ± 8.9	<0.001
LVEDD, mm	53.6 ± 10.1	48.5 ± 10.0	0.003
LVESD, mm	38.7 ± 11.9	31.9 ± 7.9	<0.001
LA dimension, mm	43.7 ± 7.6	39.2 ± 8.3	<0.001

CAD, coronary artery disease; AF, atrial fibrillation; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; LVEF, left ventricular ejection fraction; LVEDD/LVESD, left ventricular end-diastolic/systolic dimension; LA, left atrium.

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