The Prevalence of Apical Wall Motion Abnormalities in Patients with Long-Term Right Ventricular Apical Pacing

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Background: Long-term right ventricular apical pacing (RVAP) can lead to adverse clinical outcomes. Although left ventricular (LV) dyssynchrony is the major causative factor, other potential mechanisms are not fully understood. We sought to clarify whether RVAP elicits apical wall motion abnormalities that contribute to LV contractile dysfunction.

Methods: We studied annual echocardiographic data over a 5-year period after pacemaker implantation (PMI) for 74 patients who underwent RVAP. The patients were divided into two groups according to the percentage of ventricular pacing: right ventricular (RV) pacing <50% and RV pacing ≥50%. We assessed LV ejection fraction, LV end-diastolic volume, and left atrial dimension. To assess regional wall motion abnormalities, the wall motion score index was calculated.

Results: LV wall motion abnormality was observed in 64% of the subjects and was more pronounced in apical segments than in other segments. At 2 years after PMI, brain natriuretic peptide levels were significantly higher in the group with RV pacing ≥50% than in the group with RV pacing <50%. The subjects with RV pacing ≥50% had higher LV end-diastolic dimension and lower ejection fraction at 3 years after PMI.

Conclusion: Long-term RVAP elicits apical wall motion abnormalities that could in part contribute to LV contractile dysfunction. (J Am Soc Echocardiogr 2011;24:556-64.)

Keywords: Apical pacing, Left ventricular apical wall motion abnormality, Left ventricular contractile dysfunction, Pacemaker implantation, Regional myocardial damage

Cardiac pacing is a safe, effective therapy for patients with bradyarrhythmia. Right ventricular apical pacing (RVAP) is a standard, widespread procedure owing to the accessibility of the right ventricular (RV) apical site, which provides stability for the pacing device.[1] Recent clinical studies have reported that RVAP elicits abnormal left ventricular (LV) contractions and reduced pump function.[2,3] Pacing from the RV apex can alter the electrical LV activation sequence and lead to dyssynchrony in LV contraction, resulting in impaired hemodynamic function.[4-7] Many studies have examined the detrimental effects of RVAP,[8,9] and a number of investigators have focused on the relationship between the pacing site and intraventricular dyssynchrony. LV dyssynchrony is a critical factor in LV dysfunction; however, other potential mechanisms are not fully understood.

So far, little attention has been given to regional myocardial damage at the pacing site. Previously, Tl-201 scintigraphic studies in humans showed that long-term RVAP resulted in a high incidence of myocardial perfusion defects in the LV apical region.[10-12] In an experimental investigation using dogs, interstitial fibrosis and extracellular matrix remodeling, which are the cardinal features of tissue remodeling in heart failure, were obvious in apical pacing models.[13] These results led to the hypothesis that electrical stimulation delivered at the right apical site damages the regional LV apical myocytes and produces intraventricular dyssynchrony, resulting in wall motion abnormalities around the pacing site and global LV contractile dysfunction. However, it is difficult to conduct experimental animal studies involving long-term observations of the surrounding myocardium. The present investigation sought to clarify whether RVAP elicits abnormal LV apical wall motion leading to LV contractile dysfunction.

MATERIALS AND METHODS

Patients

This study retrospectively reviewed 86 consecutive patients who underwent pacing treatment between April 2000 and March 2002 at Akita University Hospital. The patients had sick sinus syndrome (SSS), complete atrioventricular block (AVB), or atrial fibrillation with bradycardia. All patients agreed to pacemaker implantation (PMI) and provided written informed consent to the study protocol, which was approved by the clinical research and ethics committee of the University of Akita.

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Abbreviations

AVB = Atrioventricular block

BNP = Brain natriuretic peptide

LV = Left ventricular

LVEDV = Left ventricular end-diastolic volume

LVEF = Left ventricular ejection fraction

PMI = Pacemaker implantation

RV = Right ventricular

RVAP = Right ventricular apical pacing

SPWMD = Septal-to-posterior wall motion delay

SSS = Sick sinus syndrome

WMSI = Wall motion score index

The enrolled patients were experiencing symptoms related to bradyarrhythmia and had preserved cardiac function with an LV ejection fraction (LVEF) of ≥50%. The patients excluded from this study were those with 1) ischemic heart disease (n = 7); 2) an LVEF <50%; 3) cardiomyopathies such as cardiac sarcoidosis (n = 2), cardiac amyloidosis (n = 1), hypertrophic cardiomyopathy, or dilated cardiomyopathy; 4) implantation of a resynchronization pacemaker or cardiac defibrillator (n = 2); 5) implantation of a non-apical pacemaker; or 6) a changing atrioventricular delay and pacing stimulation threshold. Seventy-seven of the 86 patients (89.5%) had confirmed coronary angiography to exclude ischemic heart disease. Because of chronic kidney disease, 9 patients could not undergo coronary angiography, but instead had thallium-201 exercise myocardial scintigraphy. Coronary artery disease was defined as ≥75% stenosis in at least one of the major coronary arteries. A total of 12 patients were excluded. Consequently, a total of 74 patients were included in the final analysis.

After PMI, all patients were examined at Akita University Hospital during outpatient visits and observed every 2 months for 5 years. Adverse events were defined as death from any cause and a first occurrence of hospitalization for congestive heart failure. The diagnosis of congestive heart failure was validated using Framingham criteria.[14,15]

Pacing

PMI followed standard procedures using a transvenous approach via the left infraclavicular route. The RV leads were positioned at the RV apex, and the right atrial leads were placed at the right atrial appendage. The stimulation threshold in the RV leads was <1.5 V, with a pulse width of 0.4 ms; the intracardiac R wave was >5 mV. The parameters for right atrial lead positioning were threshold <1.5 V, pulse width 0.4 ms, and P wave >3 mV. VDD mode pacemakers were implanted in patients with AVB, DDDR mode pacemakers were implanted in patients experiencing SSS and AVB, and VVIR mode pacemakers were implanted in patients with long-lasting atrial fibrillation, as defined previously.[16] All pacemakers were programmed at a lower rate of 60 bpm, an upper rate of 120 bpm, and a paced atrioventricular delay of 180 msec. The atrial and ventricular pacing stimulation voltage was three times the threshold stimulation voltage, and these settings were not changed during follow-up.

Echocardiographic Techniques

Two-dimensional echocardiography was performed using a SEQUOIA 512 (Siemens, Erlangen, Germany). Echocardiographic images were obtained in the standard parasternal long and short axes with apical four-, two-, and three-chamber views. For wall motion assessment, at least four cardiac cycles were acquired at the LV base, mid-papillary muscle level, and apex. The presence of an apical wall motion abnormality was recognized if it was observed in both the parasternal short-axis view and apical four-, two-, or three-chamber view. Regional wall motion was assessed according to the standard 16-segment model recommended by the American Society of Echocardiography.[17] The wall motion score index (WMSI) was calculated for regional wall motion analysis. In this scoring system, a higher score indicates a more severe wall motion abnormality (1, normal; 2, hypokinesis; 3, akinesis; 4, dyskinesis; and 5, aneurismal). The WMSI was calculated by dividing the sum of the wall motion scores by the number of segments visualized:

$$\text{WMSI} = \frac{\text{Sum of wall motion scores}}{\text{Number of visualized segments}}$$

The LVEF and LV end-diastolic volume (LVEDV) were measured using Simpson's biplane method. All echocardiographic measurements were performed with full pacing of the ventricle. Echocardiographic analyses were performed before PMI, immediately after surgery (before discharge from the hospital), and at 1, 2, 3, and 5 years after PMI. Experienced sonographers analyzed the echocardiographic images, which were stored on Super-VHS. Two independent echocardiologists who were blind to the clinical data reviewed all images off-site. LV dyssynchrony was assessed at baseline and at 5 years after PMI. In addition to the paced QRS duration obtained from 12-lead electrocardiograms, the septal-to-posterior wall motion delay (SPWMD) was measured using M-mode recordings from the parasternal short-axis view. Specifically, the interval between the maximal posterior displacement of the septum and maximal displacement of the LV posterior wall was measured.

The interobserver variability for all measurements and regional wall motion scores was analyzed by finding the difference between two measurements made by two observers. The intraobserver variability was analyzed using two measurements by one observer. Inter- and intraobserver agreements for these measurements were evaluated using intraclass correlation coefficients. The following values for intraclass correlation coefficients (±95% CI) were obtained, suggesting good reproducibility of the echocardiographic parameters. Interobserver variability was as follows: LVEF 0.949 (0.878–0.979), LVEDV 0.906 (0.782–0.961), left atrial dimension 0.874 (0.714–0.948), and WMSI 0.973 (0.933–0.989). Intraobserver variability was as follows: LVEF 0.974 (0.936–0.989), LVEDV 0.933 (0.833–0.973), left atrial dimension 0.974 (0.955–0.986), and WMSI 0.987 (0.967–0.995).

Statistical Analysis

Continuous variables are expressed as the mean ± SD. For continuous and normally distributed data, Student t test was used to compare groups. For non-normally distributed data, the Mann–Whitney U test was used. A multiple linear regression analysis was performed to estimate factors influencing the LVEF at 5 years after PMI. All parameters with a significance value less than .1 by univariate analysis were entered into the multivariate model. Cumulative event rates were calculated using the Kaplan–Meier method. Comparisons among groups were made using log-rank tests. A P value < .05 was considered statistically significant. All statistical analyses were performed with SPSS for Windows Ver. 13.0 (SPSS, Chicago, IL).