Optimal Right Ventricular Pacing Site from the Perspective of QRS Duration, Heart Function and the Configuration of 12-lead Electrocardiogram

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Introduction: It has become clear that the onset of heart failure is closely linked to right apex pacing, which lengthens the QRS duration and evokes discoordinate contraction of the left ventricle (LV). Currently, it is thought that the site inducing the shortest QRS duration is optimal for pacing.

Objectives: The purpose of this study was to ascertain the pacing site inducing the shortest QRS duration and to examine the configuration of the 12-lead electrocardiogram and heart function while pacing at this site.

Methods: Nine patients with normal heart function were enrolled. Pacing at right ventricular outflow, mid-interventricular septum (MS), and right ventricular apex was performed. QRS duration was measured and the configuration of the 12-lead electrocardiogram changed by pacing was studied. Output and LV dp/dt were calculated at each pacing site.

Results: QRS duration became shorter with MS pacing and the pacing lead situated at the periphery of the coronary sinus and turned in a posterior direction. The configuration of the 12-lead electrocardiogram showed an Rs or rS pattern with II, III, and aVF leads. Output and LV dp/dt showed a tendency to increase with MS pacing.

Conclusion: It is thought that mid-interventricular septum pacing shortens the QRS duration.

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Key words: Septal pacing, Narrow QRS

Background

In large-scale trials on pacemakers before 2002, the subjects were patients with bradyarrhythmia who required pacemaker therapy, and the purposes of the trials were to study the complications or long-term prognosis of pacemaker therapy, which pacemaker was superior, and how differences in major compli-
cations were related to pacemaker mode. For this reason, in large-scale trials, such as Danish,\textsuperscript{1)} PACE,\textsuperscript{2)} CTOPP,\textsuperscript{3)} and MOST,\textsuperscript{4)} the endpoints were overall mortality, cardiovascular mortality, stroke, and onset of atrial fibrillation (AF) compared in AAI, DDD, and VVI modes. As a result, the rate of onset of atrial fibrillation was significantly low and overall mortality, cardiovascular mortality, and stroke in DDD mode compared to VVI mode tended to be lower, but not significantly. DDI mode was therefore thought to be the more physiological pacemaker mode. From about 2002, the most widely-used implantable cardioverter defibrillator (IDC) changed from sensing only bradyarrhythmia to a device that responded to low heart function. The DAVID trial\textsuperscript{5)} showed that in the group with low heart function, overall mortality and the onset of heart failure were significantly lower in patients with VVI-mode than those with DDD mode IDCs. Thereafter, large-scale trials, such as CTOPP,\textsuperscript{6)} Most sub,\textsuperscript{7)} Danish II,\textsuperscript{8)} MADIT II,\textsuperscript{9)} and DAVIT sub,\textsuperscript{10)} clarified that the endpoints were related to pacemaker mode. For this reason, in large-scale trials, such as Danish,\textsuperscript{1)} PACE,\textsuperscript{2)} CTOPP,\textsuperscript{3)} and MOST,\textsuperscript{4)} the endpoints were overall mortality, cardiovascular mortality, stroke, and onset of atrial fibrillation (AF) compared in AAI, DDD, and VVI modes. As a result, the rate of onset of atrial fibrillation was significantly low and overall mortality, cardiovascular mortality, and stroke in DDD mode compared to VVI mode tended to be lower, but not significantly. DDI mode was therefore thought to be the more physiological pacemaker mode. From about 2002, the most widely-used implantable cardioverter defibrillator (IDC) changed from sensing only bradyarrhythmia to a device that responded to low heart function. The DAVID trial\textsuperscript{5)} showed that in the group with low heart function, overall mortality and the onset of heart failure were significantly lower in patients with VVI-mode than those with DDD mode IDCs. Thereafter, large-scale trials, such as CTOPP,\textsuperscript{6)} Most sub,\textsuperscript{7)} Danish II,\textsuperscript{8)} MADIT II,\textsuperscript{9)} and DAVIT sub,\textsuperscript{10)} clarified that the course of the onset of heart failure or atrial fibrillation was closely linked to right ventricular apex pacing (AP), the increasing frequency of which induced the onset of heart failure or atrial fibrillation because it prolonged the QRS duration, which induced discordant contraction of the left ventricle. This caused a P-V relation rightward shift, neuro-humoral activation, regional mechanical difference, asymmetric hypertrophy of left the ventricle, molecular/cellular change, etc. and, in consequence, heart failure or atrial fibrillation developed.\textsuperscript{11)} Recently, from the results of large-scale trials, alternative pacing sites for right pacing, such as the right ventricular outflow tract (RVOT) or right interventricular septum\textsuperscript{12–15)} have been studied. Currently, it is thought that the pacing site with the shortest QRS duration is optimal, and no report has stated that pacing from the pacing site with the shortest QRS duration made heart function worse.

The purpose of this study was to identify the optimal pacing site with the shortest QRS duration in the right ventricle and to examine the configuration of the 12-lead electrocardiogram and heart function with pacing from this site.

Patients

Nine patients with normal heart function who had undergone catheter ablation for tachyarrhythmia were enrolled (men: 5, women: 4, average age: 45 ± 17 years old). All patients showed a short QRS duration (QRS duration <100 ms) without bundle branch block and the ejection fraction measured by cardiac ultrasonography before catheter ablation was >55%.

Methods

After ablation or EPS, pacing with ablation or an EPS catheter at the right ventricular outflow, mid-interventricular septum (MS), and right ventricular apex was performed at each site in descending order. There is no commonly-accepted definition for RVOT location, as to whether it is high-, mid- or low-septum. In this study, as a matter of convenience, RVOT was defined as being located above the His bundle, MS as below the His bundle and above half of the right ventricular height in a horizontal direction. As a control, AAI mode pacing at 80 beats per minute (bpm), 100 bpm, and 120 bpm was performed and then the pacing mode was changed to DDD and the pacing rate was changed at 80 bpm, 100 bpm and 120 bpm at each site. The reason why DDD and not VVI mode was selected was that consistent VVI mode pacing was impossible in the presence of normal atrioventricular (AV) conduction. AV delay was set at 10 ms shorter than the AV interval in sinus rhythm in order to avoid the fusion of ventricular pacing and spontaneous ventricular beats. If fusion beats appeared with the AV interval shortened by 10 ms, the AV delay was made another 10 ms shorter. As the purpose of this study was to identify the optimal site for ventricular pacing on the assumption of pacemaker implantation, pacing was performed within 1 mV, and if this could not be achieved, another pacing site was selected. Pacing was performed for 1 second and QRS duration was measured during the subsequent second. QRS duration was measured in all 12 electrocardiogram leads and the QRS duration at lead II was adopted. The configuration of the 12-lead electrocardiogram changed by pacing at each site was studied. At the same time, output and LV dp/dt were calculated at each pacing site at each pacing rate using the TASK Force Monitor (Nihon Kohden), which allows non-invasive assessment of cardiac output (CO) by measuring changes in the transthoracic electric impedance of a low amplitude (1 mA), high frequency (100 kHz) current constantly applied via surface electrodes. In brief, a constant sinusoidal alternating current I\textsubscript{0} of 400 μA and 40 kHz were passed through the thorax between short-band electrodes placed on the neck and on the lower thorax aperture. The baseline impedance (Z\textsubscript{0}) and the maximum rate of change in impedance (dZ/dt) were used to estimate stroke volume by modification of the method of Kubicek et al.\textsuperscript{16)} All patients gave
informed consent before entering the study and the local ethics committee approved the study.

Results

QRS duration increased as the pacing rate was raised and no change in polarity at QRS by the pacing rate was observed at the same pacing site. QRS duration was shortest when pacing in AAI mode without ventricular pacing. When pacing in DDD mode with ventricular pacing, the QRS duration became shorter with MS pacing than with RVOT or AP pacing (Figure 1); however, the change ratio of the QRS duration was not correlated in each case at each pacing site.

At the MS pacing site, the pacing catheter was situated at the periphery of the coronary sinus at the right anterior oblique X-ray projection and turned in a posterior direction at the left anterior oblique projection (Figure 2). A feature of the configuration of the 12-lead electrocardiogram with MS pacing was that an Rs or rS pattern was shown in II, III, and aVF leads (Figure 2). Output and LV dp/dt did not show an apparently significant difference at each pacing site but showed an increasing tendency with MS pacing (Figure 3). As with pacing at RVOT, the earliest site of excitation conduction at the ventricle recorded by His and Cs catheters was His bundle distal and was then conducted to Cs. Excitation conduction in Cs was different in each case but the earliest site of excitation conduction at Cs distal occurred in six-nine. With MS pacing, excitation conduction occurred at His bundle distal and Cs proximal at a similar time and was then conducted from Cs proximal to distal (Figure 4).

Discussion

It remains uncertain why the pacing site at the periphery of the coronary sinus at the right anterior oblique X-ray projection and turned in a posterior direction at the left anterior oblique projection makes the QRS duration shorter. Burri et al. indicated that the optimal pacing site was situated at the periphery of the morphology of the coronary sinus at the right anterior oblique X-ray projection and turned in a posterior direction at the left anterior oblique X-ray projection, and is reported to avoid being positioned on the anterior free wall. It is thought that pacing stimuli at that point divide above and below the right
ventricle. Stimuli that head downward enter the right bundle branch through the working myocardium around the pacing site and excite the ventricle. Stimuli that head upward enter the His bundle through the working myocardium around the pacing site, enter the left branch and excite the ventricle. The QRS wave is thought to be formed by the fusion of stimuli of the right and left bundle branches and the velocity of the conducting system of the heart is faster than the working myocardium.\(^{18}\) If the pacing

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**Figure 2** Positional relation among His bundle, coronary sinus and pacing site that made the QRS duration shortest. Three typical cases are presented. No. 2, 5, 7

Pacing catheter was situated at periphery of coronary sinus at right anterior oblique of X-ray illumination and turned in a posterior direction at left anterior oblique of X-ray illumination in all patients. The configuration of the 12-lead electrocardiogram showed an Rs or rS pattern in II, III, and aVF leads with MS pacing.

P: pacing site in right ventricle, H: His bundle, C: coronary sinus
site is as close as possible to the conducting system of the heart and His bundle, the QRS duration should be shorter. From this point of view, a pacing site situated at the periphery of the coronary sinus and turned in a posterior direction is situated near the His bundle and right bundle branch, corresponding to this theory. It is thought that backward stimuli from this pacing site enter the left bundle branch earlier than other pacing sites, making the QRS duration shorter. The difference in excitation conduction from the ventricle recorded at the Cs catheter is thought to depend on the pacing site of RVOT.

In fact, when a ventricular pacing lead is placed at pacemaker implantation, a Cs catheter is not inserted. For this reason, it is thought that the ventricular pacing lead should be placed at the periphery of the morphology of the coronary sinus and turned in a posterior direction in the right ventricle. In this study, patients with bundle branch block were not enrolled and their results would not be the same as in patients with normal conduction. For patients with right bundle branch block, pacing just in front of the block is considered to make the QRS duration shorter. For left bundle branch block, the pacing site in the right ventricle possibly did not change the QRS duration.

Overall, it appeared that not necessarily all patients implanted with a pacemaker and paced at the right apex at a high rate developed heart failure or atrial fibrillation. In fact, it was reported that heart failure developed a few years after pacemaker implantation and accounted for only a few percent,\(^\text{19}\) and Carmine Muto et al. reported that RV septum pacing could improve ejection fraction (EF) and quality of life (QOL) in patients with AF and low EF needing a pacemaker.\(^\text{20}\) In this study, output and LV dp/dt did not show apparently significant differences at each pacing site but showed an increasing tendency with MS pacing, indicating that the effects of pacing on heart function did not cease soon after pacemaker implantation and were impossible to assess in the acute stage.

Moreover, pacing from this site made the conduction time from the atrium to ventricular lead shorter than pacing from the apex, and was thought to inhibit unnecessary ventricular pacing.

**Study limitations**

This study was performed after ablation and the spontaneous rates were over 80 bpm in some cases and sympathetic tone might have increased. The QRS duration for a control therefore could not be measured in all cases.

QRS duration could be measured but output and dp/dt could not be calculated if a spontaneous or premature beat occurred during the measurement periods of one second because reliable measure-
ments of output or dp/dt could only be calculated over at least 1 full second under the same conditions. As a spontaneous or premature beat occurred at 80 ppm, reliable measurements could not be calculated or obtained.

The intracardiac electrocardiogram was examined in retrospect because it examines the width of QRS by the pacing site; therefore, examination of the relation between excitation conduction at the ventricle and the pacing site of RVOT could not be examined.

In this study, using an RF catheter, the catheter was inserted from the inferior vena cava. In practice, a pacemaker lead will be inserted from the superior vena cava, and another strategy to situate the lead in that position must be studied.

Clinical implications
The indication for MS pacing is limited to conditions without so-called dissynchrony or bundle branch block below the His bundle and using stimuli heading upward in a retrograde fashion from the right branch of the pacing site, entering the His bundle and the left branch. It was necessary to meet these conditions even for sick sinus syndrome or...

Figure 4 Intracardiac electrogram during pacing in AAI mode, RVOT, MS, and RVA
Above left: Case 5
The earliest site of excitation conduction of the ventricle was seen in His 1-2 with RVOT pacing (stimulation-His 1-2: 27 ms), and in the ventricular activation of Cs, Cs 9-10 was early, followed by Cs 1-2. Ventricular activation occurred with His 1-2 immediately after stimulation with MS pacing and was conducted to 1-2 in Cs from Cs 9-10. His 1-2 of ventricular activation was early with RVA pacing (stimulation-His 1-2: 38 ms), and was conducted in Cs from Cs 9-10 to Cs 1-2.
Below left: Case 2
Excitation conduction of the ventricle was almost identical to case 5, but excitation conduction in Cs was different and was conducted from Cs 1-2 to Cs 9-10.
Right: Case 8
Excitation conduction of Cs with RVOT and MS pacing
Excitation conduction in Cs was conducted from Cs 1-2 to Cs 9-10 with RVOT pacing and from Cs 9-10 to Cs 1-2 with MS pacing.
Con: pacing in AAI mode, His: His bundle, His 1-2: His distal, His 7-8: His proximal, Cs: coronary sinus, Cs 1-2: Cs distal, Cs 9-10: Cs proximal, TA: tricuspid annulus
atrioventricular block, but conversely, when meeting these conditions, MS pacing would act effectively on heart function even in patients with low EF or permanent AF with low EF.

Conclusion

For patients with normal QRS duration and without bundle branch block, the pacing site where the ventricular lead is situated at the periphery of the coronary sinus at the right anterior oblique X-ray projection and turned in a posterior direction at the left anterior oblique X-ray projection was found to be the optimal site for ventricular pacing, and output and LV dp/dt showed an increasing tendency at this site. The biphasic pattern in II, III, and aVF leads according to the configuration of the 12-lead electrocardiogram on pacing could be an index parameter for the optimal pacing site.

References

1) Andersen HR, Nielsen JC, Thomsen PE, Thuesen L, Mortensen PT, Vesterlund T, Pedersen AK: Long-term follow-up of patients from a randomized trial of atrial versus ventricular pacing for sick-sinus syndrome. Lancet 1997; 350: 1210–1216
17) Burri H, Sunthorn H, Dorsza PA, Viera I, Shan D: Thresholds and complications with right ventricular septal pacing compared to apical pacing. PACE 2007; 30: S57–78
