Mechanisms Behind Hemodynamic Benefits of Right Ventricular Outflow Tract Pacing Compared to Right Ventricular Apex Pacing

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Summary

Several investigators have already proven that right ventricular outflow tract (RVOT) pacing is superior to right ventricular apex (RVA) pacing. We tried to eludicate the physiological phenomena responsible for the observed hemodynamic improvement by using electrocardiography and echocardiographic measurements. Eighteen patients with a symptomatic complete heart block were studied (11 male, mean age 65 ± 8 years).The patients had a left ventricular ejection fraction of 44 % ± 4 %. We used sequential atrioventricular pacing with an atrioventricular delay of 120 ms at the RVOT and RVA, and performed measurements at 80, 100, and 120 beats/min. On the electrocardiogram, RVOT pacing showed more septal activation compared to RVA pacing: 13/18 vs. 7/18. RVOT pacing was associated with less mitral regurgitation compared to RVA on color Doppler: 3/18 vs. 8/18. The cardiac index was significantly higher in the RVOT position: an improvement of 20 % at 80 beats/min, 19 % at 100 beats/min, and 14 % at 120 beats/min was observed. RVOT pacing had significantly improved transmitral flow on echocardiography, as compared to RVA pacing. Only at 120 beats/min were no significant differences found. We deem that multiple factors can be attributed to the superiority of RVOT pacing: abnormal depolarization with an increase in mitral valve incompetence in RVA pacing, and decreased mitral inflow in RVA pacing, which results in differences in the left ventricular preload and the left ventricular function.

Key Words

Hemodynamics, echocardiography, right ventricular outflow tract (RVOT) pacing

Introduction

When endocardial implantable pacemaker systems were introduced into clinical practise, the right ventricular apex (RVA) was used for sensing and stimulation due to the stable positioning of the lead [1]. With several possibilities for active fixation, alternative pacing sites became feasible [2,3]. Right ventricular outflow tract (RVOT) pacing may lead to a more physiologic excitation of the myocardium and a more synchronized contraction of both ventricles, which has a beneficial hemodynamic effect [4-24].

The aim of this study was to clarify the physiological phenomena responsible for the observed increased cardiac output during RVOT pacing as compared to RVA pacing through the use of echocardiography.

Materials and Methods

The study included 11 men and 7 women with a symptomatic complete heart block and a mean age of 65 ± 8 years (Table 1). Nine of the patients had a prior myocardial infarction. The left ventricular function was relatively well-preserved with a mean ejection fraction of 44 % ± 4 %. Patients with significant valvular disease, unstable angina pectoris, and coronary artery bypass grafting were previously excluded.

The hemodynamic study preceded the implantation of a permanent DDD pacemaker. Patients received 2 g of intravenous flucloxacillin an hour before, and 1 g of intravenous flucloxacillin 6 and 12 hours after implantation. During the implantation procedure one of the temporary pacing leads was kept in place as a backup.

Number of patients	18
Male/female	11/7
Prior myocardial infarction (coronary artery disease)	9
Age	65 ± 8 years
Ejection fraction	44 % ± 4 %

Table 1. Baseline characteristics of the study group.

For positioning of the three pacing leads, the left and right femoral and the right subclavian approach were used. With the aid of fluoroscopy, standard bipolar temporary pacing leads (TC 116, Biotronik, Germany) were located in the right atrium, RVA, and RVOT. The leads were connected to an external pacing threshold analyzer (ERA 300, Biotronik). The first site of pacing among patients was randomized. Patients were paced at 80 beats/min, 100 beats/min, and 120 beats/min, respectively. Atrioventricular (AV) delay was 120 ms. Pacing in the RVOT and RVA was performed in an alternating fashion. Pacing in each position and at each heart rate was continued for 3 min before all measurements were made, including blood pressure, electrocardiogram, and echo-Doppler measurements. Between pacing periods, a 5-min interval was allowed for sinus rhythm to return to its baseline value (± 10 %). Systolic and diastolic blood pressure and mean arterial pressure were measured using a Dynamap 1846 automatic monitor (Critikon, UK).

For all echocardiographic and Doppler studies, a Sonos 2500 (Hewlett Packard, USA) with a 3.5 MHz continuous wave transducer was utilized. The highest audio signal and the sharpest outline were used as the maximum envelope to assess optimal recording of blood flow velocities in the ascending part of the aorta. Evaluation of Doppler recordings was performed offline by using a computer-assisted digitalization system. The area under the Doppler flow velocity curve was determined by digitizing the signal from baseline to baseline. An average of 6 consecutive cycles were used to calculate cardiac output. Cardiac output was calculated as the systolic velocity integral multiplied by the aortic root area, multiplied by the heart rate. The aortic root area was measured by M-mode echocardiography using the parasternal long-axis view. Color Doppler tracings were performed on the mitral valve, and a mitral regurgitation of more than one third of the left atrium was considered significant.

Transmitral flow was analyzed by Doppler measurement of the E-wave and the A-wave, i.e. parameters for the early and late diatole respectively. The E/A ratio is defined as the ratio between the maximum E-wave peak velocity and the A-wave peak velocity (physiological E/A > 1.6, pathological E/A < 1.0). To measure the time-velocity integral, we used the darkest portion of the waveform. The integral areas under the E- and A-wave were evaluated by measuring at the end of the E- and A-waves for the outer border of the velocity profile. For detailed description of E- and A-wave variables see echocardiographic literature, e.g. [25].

Heart rate was measured using two consecutive spikes on the ECG. An R-wave > 0.1 mV in standard surface ECG lead V1 or V2 was considered a marker of septal activation. All measurements were performed by two experienced echocardiographers, who were not informed of which pacing mode was being used.

Differences in functional parameters for different pacing sites were assessed using the Student's t-test. For differences between subgroups of patients, an analysis of variance was used. All data were expressed as a mean ± standard deviation. A P-value less than 0.05 was considered statistically significant.

Results

Hemodynamic and echocardiographic results were independent of the pacing site randomisation. The

	RVOT-pacing No. of patients	RVA-pacing No. of patients	P-value
Septal activation	13 (72 %)	7 (39 %)	< 0.01
Systolic mitral regurgitation	3 (17 %)	8 (44 %)	< 0.001
Diastolic mitral regurgitation	5 (27 %)	6 (33 %)	ns

Table 2. Hemodynamic and echocardiographic findings for right ventricular outflow tract (RVOT) pacing and right ventricular apex (RVA) pacing.
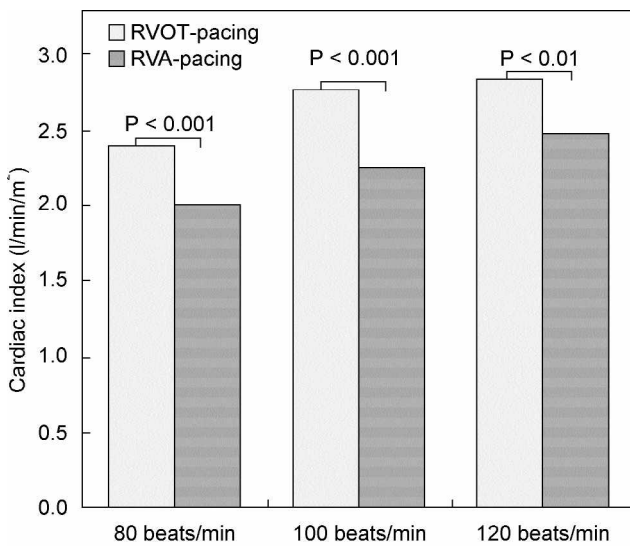
Figure 1. Cardiac index (cardiac output over body surface area) for pacing at 80, 100, 120 beats/min for right ventricular outflow tract (RVOT) pacing and right ventricular apex (RVA) pacing.

findings are shown in Figure 1 and Table 2. On the 12-lead ECG, septal activation was observed in 13/18 (72 %) of patients with RVOT pacing, compared to only 7/18 (39 %) of patients with RVA pacing. On color-Doppler tracing, 3/18 (17 %) of patients with RVOT pacing compared to 8/18 (44 %) of patients with RVA pacing showed significant mitral regurgitation.

We measured the cardiac index (cardiac output over body surface area, physiological level 5.5 ± 0.5 l/min/m^2) for three different pacing rates. Although cardiac index in each patient was intraindividually significantly higher at all pacing rates during error stimulation the difference in the cardiac index between RVT and RVA ranges 20 % at 80 beats/min to 19 % at 100 beats/min and 14 % at 120 beats/min (Figure 1).

Table 3 shows the Doppler echocardiographic data with respect to left ventricular inflow. It illustrates the differences in E/A ratio at different heart rates and pacing sites. During pacing at 80 and 100 beats/min, respectively, a high E/A ratio was observed for RVOT position. No significant difference was found during pacing at 120 beats/min.

80 beats/min	RVA-pacing (n = 16)	RVOT-pacing (n = 16)	P-value
E/A ratio	1.4 ± 0.6	1.8 ± 0.7	< 0.05
$E_{int\ area}$ (a.u.)	8.5 ± 1.9	9.0 ± 2.2	< 0.05
$A_{int\ area}$ (a.u.)	4.9 ± 1.0	4.1 ± 0.8	ns
$A_{int\ area}/(E_{int\ area} + A_{int\ area})$	0.37 ± 0.05	0.32 ± 0.05	< 0.05
100 beats/min			
E/A ratio	1.2 ± 0.5	1.7 ± 0.7	< 0.05
$E_{int\ area}$ (a.u.)	8.1 ± 1.7	8.9 ± 2.2	< 0.05
$A_{int\ area}$ (a.u.)	4.8 ± 1.0	4.0 ± 0.7	ns
$A_{int\ area}/(E_{int\ area} + A_{int\ area})$	0.36 ± 0.04	0.31 ± 0.05	< 0.05
120 beats/min			
E/A ratio	1.1 ± 0.5	1.4 ± 0.7	ns
$E_{int\ area}$ (a.u.)	8.1 ± 1.7	8.4 ± 2.0	ns
$A_{int\ area}$ (a.u.)	4.8 ± 1.0	4.1 ± 0.9	ns
$A_{int\ area}/(E_{int\ area} + A_{int\ area})$	0.34 ± 0.04	0.32 ± 0.05	ns

Table 3. Transmitral flow data from echocardiographic Doppler measurements for right ventricular outflow tract (RVOT) pacing and right ventricular apex (RVA) pacing. E/A ratio = ratio of E-wave and A-wave velocity amplitude; $E_{int\ area}$ = integral under the E-wave time-velocity curve; $A_{int\ area}$ = integral under the A-wave time-velocity curve in arbitrary units (a.u.).

Discussion

Although the influence of the ventricular pacing site on left ventricular contraction and hemodynamic parameters has been studied in a number of animal studies, only a few studies have investigated this issue in humans. Previous interventions provided evidence for hemodynamic improvement during RVOT pacing compared to conventional RVA pacing [18,19]. Several factors may be responsible for the improved cardiac performance during RVOT pacing. As we found in our study, pacing from the RVA may effect the competence of mitral valve closure. This may alter left ventricular, end-diastolic volume with a subsequent effect on cardiac output [10]. Grover et al. demonstrated in dogs an altered, transient, inward, wall motion at end-diastole with different pacing sites, causing an increase in mitral regurgitation or impaired diastolic filling resulting in altered end-diastolic volumes. Thus RVA pacing may be associated with substantial mitral regurgitation, resulting in a decrease in left ventricular performance [7]. Lister et al. correlated the electrophysiologic and hemodynamic effects of pacing at different ventricular sites in dogs. They found that alteration of ventricular depolarization resulted in an activation of the papillary muscle late in systole, resulting in marked atrioventricular regurgitation [11]. Kosowsky et al. compared hemodynamic consequences of direct His bundle pacing and epicardial right ventricular pacing at various PR intervals in dogs. They demonstrated impaired performance during abnormal depolarization, with a further decrease in function at shorter PR intervals [12]. Park et al. performed experiments in ten dogs. Ventricular epicardial and endocardial pacing resulted in a significant decrease in left ventricular end-diastolic and end-systolic pressures, as well as in max/min pressure gradients dp/dt [6]. The rightward shift of the left-ventricular end-systolic pressure-volume relation that occurs during pacing appears to be related to the degree of dyssynchronous activation. Furthermore, it indicates a depression of left ventricular pumping performance independent of changes in preload. In this regard, Park demonstrated that stroke volume during pacing can decrease for two reasons:

- Left ventricular preload measured by end-diastolic volume is decreased;
- Left ventricular pump function independent of filling status is decreased by pacing because of the rightward shift of the left ventricular end-systolic pressure volume relation.

Conclusion

The present study indicates that multiple factors can be attributed to an increase in cardiac output during RVOT pacing as compared to RVA pacing. Abnormal depolarization during RVA pacing is associated with incompetence of the mitral valve, which can be partly prevented by RVOT pacing. In addition, mitral inflow is decreased during RVA pacing, which affects left ventricular preload and function.

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