Comparison of right ventricular apex and right ventricular outflow tract septum pacing in the elderly with normal left ventricular ejection fraction: long-term follow-up

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Abstract

Background: Whether right ventricular outfow tract septum (RVOTS) pacing is superior to right ventricular apex (RVA) pacing with respect to left ventricular synchrony, cardiac function, and remodelling in the elderly with normal left ventricular ejection fraction (LVEF), is still unknown.

Aim: To assess the impact of RVOTS vs. RVA pacing on the cardiac performance of the elderly with normal LVEF during a long-term observation.

Methods: From 2007 to 2010, 65 patients with standard pacing indications for permanent pacing were recruited and randomised to receive RVA (32 patients) or RVOTS pacing (33 patients). Over a median 28 months' follow-up, available data was summarised, including New York Heart Association (NYHA) functional class, echocardiographic and pacing parameters, axis, QRS duration and plasma B-type natriuretic peptide (BNP) level. Then these values were compared between the RVA group and the RVOTS group, as well as between pacemaker pre- and post-implantation in the RVA group and in the RVOTS group, respectively.

Results: There were no significant differences in baseline characteristics between the RVA group and the RVOTS group. The median pacing durations did not differ significantly between the groups (31.5 months in the RVA group vs. 28 months in the RVOTS group, $p = 0.728$). Compared to the baseline values, LVEF decreased with RVA pacing (from 59.5 ± 6.21 to 54.22 ± 8.73, $p = 0.001$), but LVEF did not markedly vary in the RVOTS group (57.82 ± 6.06 and 56.94 ± 5.54, $p = 0.152$). The number of patients with moderate tricuspid valve regurgitation remarkably increased in the RVA group, from six (18.75%) patients to 10 (31.3%) patients, preoperatively to postoperatively ($p = 0.046$), but this change was not statistically significant in the RVOTS group. Compared to the RVOTS group, NYHA functional class had a deteriorated tendency in the RVA group ($p = 0.071$). After the implantation, the increase of median BNP level was observed in the RVA group (35 pg/mL at pre-implantation and 50 pg/mL at the end of follow-up, $p = 0.007$); No significant change was obtained in the RVOTS group (36.4 pg/mL at pre-implantation vs. 38 pg/ml at the end of follow-up, $p = 0.102$). Compared to the RVA pacing group, the mean QRS width narrowed substantially in the RVOTS pacing group (from 143.56 ± 12.90 to 105.52 ± 15.21, $p = 0.000$). In terms of the end diastolic and systolic diameters of the left ventricular, there were no statistical variations observed during the follow-up.

Conclusions: Permanent RVA pacing in elderly patients with normal LVEF led to left ventricular systolic function deterioration denoted by lower LVEF and higher BNP level. When compared to RVA pacing, RVOTS pacing had no remarkable benefit in terms of preventing cardiac remodelling.

Key words: right ventricular apex, right ventricular outflow tract septum, pacing

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INTRODUCTION

Since the dawn of transvenous cardiac pacing introduced by Furman in 1959 [1], the right ventricular apical region has represented the classical pacing site. Owing to the ease of placement, excellent lead stability and reliability, and lower capture thresholds in the apical trabeculae, right ventricular apex (RVA) pacing has been widely used as the most appropriate pacing site for decades. However, previous studies have validated that conventional RVA pacing is deleterious to patients with permanent pacing [2, 3]. Apart from myocardial cell modification in left ventricular (LV) myofibril disarray and hypertrophy, intracellular vacuolisation, degenerative fibrosis, fat deposits, mitochondrial size changes and dystrophic calcification [4], RVA pacing can result in an increase of mitral regurgitation [2], LV remodelling, myocardial perfusion defects and regional wall motion abnormalities [5–8], histological remodelling [9], quality-of-life reduction [8], increasing incidence of atrial fibrillation [7, 8, 10] and incremental tendency of mortality [11, 12].

The proven detrimental effects of classical pacing have prompted research into alternative sites of ventricular stimulation. Some studies have shown that right ventricular outflow tract septum (RVOTS) pacing seems to be better in improving haemodynamic, LV systolic and diastolic functions, producing a better stroke volume and cardiac output compared to RVA pacing in acute and short-term studies [13–16]. However, some chronic [17–19] studies of RVOTS pacing have provided controversial efficacy of this approach in general, the cause of which may result from the difficulty with consistent, accurate, and reliable placement of leads in the selected position [20] and the basic cardiac function state of patients [21]. As for the literature, no data is available regarding the effects of prevention on adverse haemodynamic consequences of permanent RVA pacing in the elderly with normal left ventricular ejection fraction (LVEF) who have undergone chronic RVOTS pacing.

The present study aimed to investigate RVOTS pacing in comparison with RVA pacing in the elderly with standard indications for permanent ventricular pacing and detected left ventricular end-diastolic diameter (LVEDD), LVEF, New York Heart Association (NYHA) functional class and plasma B-type natriuretic peptide (BNP) level to evaluate whether RVOTS pacing could be superior to RVA pacing in the protection of cardiac structure and function in the long term.

METHODS
Study population

A total of 65 patients with conventional pacing indications for permanent pacing were enrolled in the study from 2007 to 2010, and prospectively randomised to receive RVA or RVOTS pacing. A dual-chamber pacemaker (models 5286 and 5356, St. Jude Medical, MN, USA) along with two bi-polar active fixation pacing leads (models TENDRIL™ST 1888TC, St. Jude Medical) was referred to implant for patients. The inclusion criteria were as follows: (1) the subjects should be from 65 to 85 years of age; (2) the subjects should not have clinical manifestations of congestive heart failure (HF) and chronic renal insufficiency; and (3) all subjects did not have atrial fibrillation diagnosed prior to pacemaker implantation. The patients were divided into an RVOTS-paced group (n = 33) and an RVA-paced group (n = 32). All recruited patients gave written consent to participate in the study. The study protocol was accepted by the clinical research and Ethics Committees of the hospital.

Leads implantation

All implantations were performed in a sterile manner with a conscious state under local anaesthesia by an experienced operator. In the RVA group, the passive fixation electrodes were positioned toward the RVA. In the RVOTS group, the active helix electrodes were positioned against the septum of the RVOT. In both groups, the passive fixation electrodes were used for right atrial appendage. In the RVOTS group, stylet was preformed to an S-shaped. The RVOTS lead guided by the stylet was introduced through the tricuspid valve into the right ventricle (RV) and further into the pulmonary artery. It was then withdrawn slowly with a counter-clockwise movement until the tip of the electrode dropped below the pulmonary valve. The RVOTS was approved according to the tip of the electrode directing to spine in 45° left anterior oblique (LAO) view using high-quality fuoroscopic radiographs (HQFR) and producing a negative or isoelectric vector in lead I [22], and a positive QRS in leads II, III, and AVF [23] in pacemaker electrocardiogram (ECG) (Fig. 1). HQFR were performed in three standard views: postero-anterior (PA), 30° right anterior oblique (RAO), and 45° LAO projections. Figure 2 displayed the ventricular lead positions at the RVOTS and RVA in PA, RAO 30° and LAO 45° views, respectively.

Echocardiography

A transthoracic echocardiographic examination was separately performed at baseline and at the end of follow-up using a SONOS 5500 (Philips, the Netherlands) ultrasound machine with 2.5 MHz transducer. All echocardiographic examinations were done and analysed by the same experienced echocardiographer, who was blinded to clinical data and group division. The measured parameters with the M-mode technique included left ventricular end-systolic diameter (LVESD), LVEDD, left atrium diameter (LA), interventricular septum (IVS) and posterior wall (PW) thickness. The measurement of LVEF was undertaken by the Simpson's biplane method. Early and late mitral peak inflow velocity and
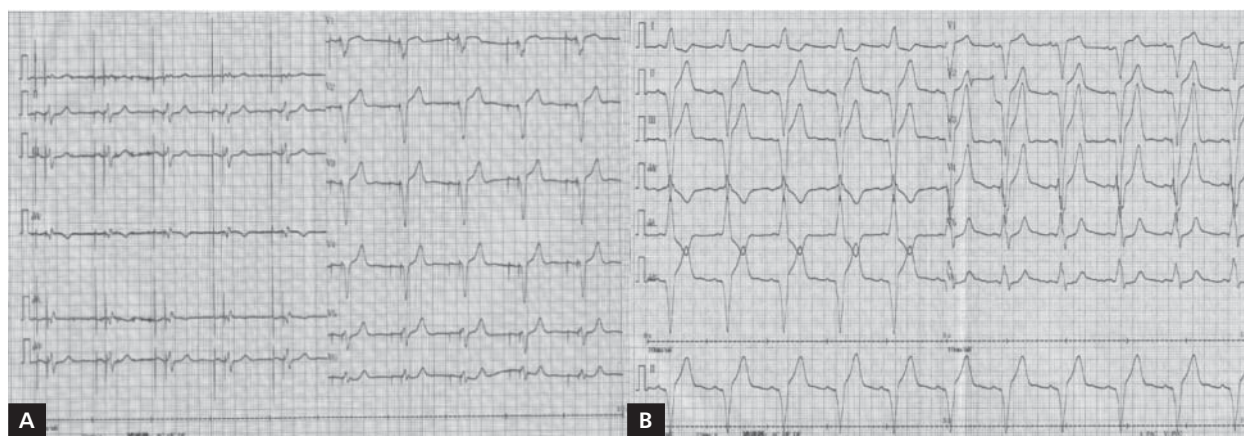
Figure 1. Twelve-lead electrocardiograms indicating the site of right ventricular outflow tract septum (RVOTS) and right ventricular apex (RVA) pacing from different patients; **A.** RVOTS pacing; **B.** RVA pacing
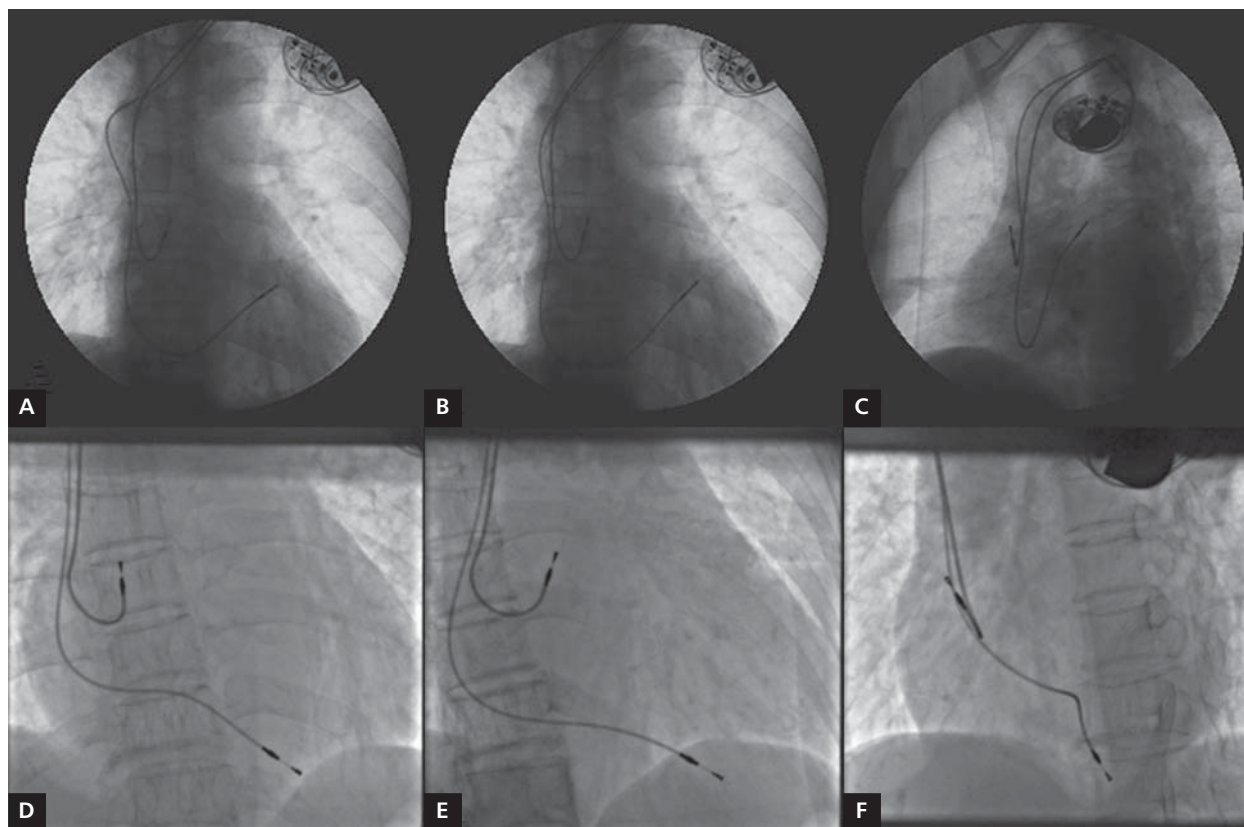

Figure 2. Chest X-ray showing the position of the right ventricular lead from a case at the right ventricular outflow tract septum in postero-anterior (PA) (**A**), right anterior oblique (RAO 30°) (**B**) and left anterior oblique (LAO 45°) (**C**), as well as from another case at the right ventricular apex in PA (**D**), RAO 30° (**E**) and LAO 45° (**F**)

E wave deceleration time (EDT) were assessed in apical four-chamber views using pulsed wave Doppler beam at the level of mitral valve leaflet tips. A three-degree scale was adopted to evaluate the degree of mitral and tricuspid valve regurgitation.

Electrocardiography

A 12-lead surface ECG was obtained before the procedure of pacemaker implantation and immediately after the implantation, and one and six months afterwards, and at the end of follow-up. The QRS axis was measured and the QRS

duration was calculated using the first to the last sharp vector crossing the isoelectric line in all leads. The mean of these quantitative values was computed and used for statistical analysis.

B-type natriuretic peptide assay

Levels of BNP were assayed before implantation and at the last follow-up. Venous blood samples were taken after 30 min at rest in the supine position. BNP level was assessed in an immunochemical fashion using an Elecsys BNP device (Roche Diagnostics).

Follow-up

The pacemakers were programmed with a base rate of 60 bpm and an upper rate of 140 bpm. The atrio-ventricular delay of the model 5286 or 5356 pacemakers was initially programmed to the standard value of 160 ± 30 ms. Follow-up examinations were performed by an experienced electrophysiological physician at one, three, six and 12 months after implantation, and subsequently twice a year. Additional examinations were conducted when patients had uncomfortable symptoms probably caused by pacemaker implantation. While in the process of follow-up, all data was analysed and recorded into a database. This data was retrieved from the examination of programme-controlled devices, including percentage of ventricular pacing, pacing threshold, sensitivity and electrode impedance. In addition, it contained the evaluation of patient's NYHA status based on clinical symptoms, the presence of permanent atrial fibrillation, 12-lead ECG recordings, 24 h Holter monitoring, chest X-ray to confirm location of the implanted electrode (in PA, LAO 45° and RAO 30° projections), echocardiography to describe the cardiac structure and function, as well as BNP plasma level measurements. The final examination data was used for statistical analyses, including the average values of percentage of ventricular pacing, the median pacing durations and NYHA functional class, whereas statistical analyses were carried out using the first and last data from the QRS axis, QRS complex, BNP measurements and echocardiography parameters. During the whole follow-up period, appropriate medical treatment was administered to the patients to remedy underlying diseases and control clinical symptoms.

Statistical analysis

Continuous variables which conformed to the normal distribution were expressed as mean ± standard deviation. Non-normal distribution continuous data were presented as median. Categorical data are summarised as frequencies and percentages. Student's t-test was employed for comparisons of the normal distribution continuous variables. Additionally, comparisons of two independent samples of ordinal or non-normal distribution continuous variables were conducted using the Mann-Whitney U test. Contrastingly, Wilcoxon si-

gned-rank test was adopted to compare the statistical differences of matched data of ordinal or non-normal distribution continuous variables. A two-sided p value < 0.05 was considered statistically significant. Statistical analyses were performed with SPSS Version 19.

RESULTS

Sixty-five patients were randomised to participate in the study (32 patients to the RVA group and 33 to the RVOTS group), whose baseline characteristics are shown in Table 1. There were no major differences between the groups. No patients were lost during the follow-up. In all 65 patients, leads were successfully implanted. No serious complications related to the operation were detected during the implantation or the follow-up, such as pneumothorax, pacemaker pocket infection or pericardial tamponade. However, two cases of atrial lead dislodgement were observed (one patient in the RVA group and one in the RVOTS group) by HQFR at discharge.

ECG and pacing parameter changes during the follow-up

In the present study, no difference was observed in the pacing duration between the RVA and RVOTS groups, in which the median pacing durations were 31.5 and 28 months, respectively (Table 2). The mean QRS complex increased with the RVA pacing in comparison with the QRS widening of baseline and the RVOTS pacing (143.56 ± 12.90 and 106.25 ± 18.36, $p < 0.001$; 143.56 ± 12.90 and 105.52 ± 15.21, $p = 0.001$, respectively), whereas the mean QRS interval with RVOTS pacing was similar to the baseline QRS complex. The final examination axis had a tendency to left-axis deviation compared to the initial at the RVA pacing (–11.5° vs. 42.5°, $p = 0.003$). In contrast, the frontal plane axis returned to approximately normal axis as the pacing site at the RVOTS (56° vs. 35°, $p = 0.000$) (Table 3). Detailed pacing parameters, including atrial and ventricular pacing threshold, sensitivity and electrode impedance, were recorded for statistical analyses without obvious differences intergroup or intragroup.

Patients᾽ clinical assessment

Seven cases of new onset chronic atrial fibrillation (CAF) occurred in total during the follow-up in the RVA group (6/32, 18.7%) and the RVOTS group (4/33, 3.3%), $p = 0.043$ (Table 2). Compared to the RVOTS group, the qualitative evaluation of HF, namely, NYHA class status, declined in the RVA group. At the end of follow-up, the numbers of patients with NYHA class II and III were higher in the RVA group, although the difference was not statistically significant ($p = 0.071$) (Table 2). After the implantation, the median BNP level increased in the RVA group (35 pg/mL at pre-implantation and 50 pg/mL at the end of follow-up, $p = 0.007$); however, the median BNP level of final examination had no marked variation in comparison with the median of pre-implantation in

Table 1. Baseline characteristics of patients included in the study

	RVA pacing (n = 32)	RVOTS pacing (n = 33)	P
Age [years], median	75 (65–85)	73 (65–85)	0.768
Male gender	18 (56%)	22 (67%)	0.527
Hypertension	21 (66%)	20 (61%)	0.677
Coronary artery disease	6 (19%)	6 (18%)	0.953
Diabetes mellitus	3 (9%)	5 (15%)	0.482
Renal failure	4 (13%)	6 (18%)	0.529
NYHA class II	5 (16%)	3 (9%)	0.426
LA [mm]	36.56 ± 4.94	37.00 ± 5.63	0.741
IVS [mm]	10.00 ± 1.34	9.94 ± 1.34	0.964
PW [mm]	9.91 ± 1.38	10.00 ± 1.59	0.639
IVS/PW	1.01 ± 0.11	1.01 ± 0.18	0.637
LVESD [mm]	34.13 ± 5.04	33.56 ± 4.88	0.639
LVEDD [mm]	47.16 ± 3.63	46.67 ± 4.01	0.608
A peak [cm/s]	73.63 ± 20.51	72.70 ± 18.19	0.847
E peak [cm/s]	92.97 ± 25.35	85.79 ± 23.36	0.239
EDT [ms]	210.91 ± 29.68	204.94 ± 27.08	0.400
LVEF [%]	59.5 ± 6.21	57.82 ± 6.06	0.273
QRS axis [°], median	42.5 (–45–100)	35 (–50–105)	0.828
QRS duration [ms]	106.25 ± 18.36	105.00 ± 18.58	0.786
Indications for pacemaker implantation:			
AV block II°/III°	21 (66%)	20 (61%)	0.677
SSS	11 (34%)	13 (39%)	
Pacemaker mode:			
DDD	23 (72%)	21 (64%)	0.481
DDDR	9 (18%)	12 (36%)	
BNP [pg/mL]	35.78 ± 15.52	36.50 ± 16.85	0.849
MVR:			
Mild	16 (50%)	19 (58%)	0.643
Moderate	8 (25%)	6 (18%)	
Normal	8 (25%)	8 (18%)	
TVR:			
Mild	20 (62.5%)	19 (57.5%)	0.765
Moderate	6 (18.75%)	8 (24.2 %)	
Normal	6 (18.75%)	6 (18.3 %)	
Diuretic	17 (53%)	14 (42%)	0.897
ACE-I/ARB	15 (47%)	16 (48%)	0.543
Beta-blocker	12 (38%)	10 (30%)	0.543
Calcium channel blocker	20 (62.5%)	17 (51.5%)	0.375

RVOTS — right ventricular outflow tract septum; RVA — right ventricular apex; NYHA — New York Heart Association; LA — left atrium diameter; IVS — interventricular septum; PW — posterior wall; LVESD — left ventricular end-systolic diameter; LVEDD — left ventricular end-diastolic diameter; EDT — E wave deceleration time; LVEF — left ventricular ejection fraction; AV — atrio-ventricular; BNP — plasma B-type natriuretic peptide; MVR — mitral valve regurgitation; TVR — tricuspid valve regurgitation; ACE-I — angiotensin converting enzyme inhibitor; ARB — angiotensin receptor blocker

Table 2. Characteristics of the two groups according to the final examination

	RVA	RVOTS	P
Pacing duration [months], median	31.5 (13–58)	28 (12–56)	0.728
Percentage of ventricular pacing [%]	82.91 ± 13.32	81.79 ± 13.95	0.742
New onset CAF	6 (18.7%)	1 (3.3%)	0.043
NYHA class:			
II	8 (25%)	4 (12%)	0.071
III	3 (9%)	1 (3.3%)	

RVOTS — right ventricular outflow tract septum; RVA — right ventricular apex; CAF — chronic atrial fibrillation

Table 3. Changes of electrocardiogram and BNP level in both groups obtained during the follow-up

	RVA		RVOTS		P		
	Initial	Final	Initial	Final	RVA Initial vs. final	RVOTS Initial vs. final	Final RVA vs. RVOTS
QRS duration [ms]	106.25 ± 18.36	143.56 ± 12.90	105.00 ± 18.58	105.52 ± 15.21	< 0.001	0.902	< 0.00
QRS axis [°], median	42.5 (–45–100)	–11.5 (–45–54)	35 (–50–105)	56 (25–105)	0.003	0.019	< 0.00
BNP level, median [pg/mL]	35 (16.3–78.6)	50 (16–563)	36.4 (10.6–70.8)	38 (10–485)	0.007	0.102	0.282
100–400	0	3 (9.38%)	0	3 (9.09%)	0.083	0.083	0.969
> 400	0	4 (12.5%)	0	1 (3.03%)	0.046	0.317	0.155

RVOTS — right ventricular outflow tract septum; RVA — right ventricular apex; BNP — plasma B-type natriuretic peptide

the RVOTS group. Meanwhile, there was no statistically significant difference in the final median BNP level between the RVOTS group and the RVA group. The number of patients with a BNP level ranging between 100 pg/mL and 400 pg/mL was six (three patients in the RVA group and three patients in the RVOTS group). In four patients with RVA pacing, BNP level was > 400 pg/mL but this was the case only in one patient in the RVOTS pacing group. A remarkable increase of BNP level with RVA pacing, which ranged > 400 pg/mL, was observed (p = 0.046, Table 3).

Echocardiography evaluation

Compared to the baseline values, LVEF decreased with RVA pacing (from 59.5 ± 6.21 to 54.22 ± 8.73, p = 0.001) and did not vary with RVOTS pacing (from 57.82 ± 6.06 to 56.94 ± ± 5.54, p = 0.152) (Fig. 3A). The IVS and PW mean values with RVOTS pacing at the end of follow-up was statistically raised compared to the initial results (9.94 ± 1.34 vs. 10.97 ± ± 1.51, p = 0.000; 9.97 ± 1.57 vs. 10.48 ± 1.56, p = = 0.002, respectively) (Fig. 3B). Conversely, the mean value of IVS/PW with RVOTS pacing had no discrimination when compared to baseline in statistics (1.01 ± 0.18 vs. 1.06 ± 0.17, p = 0.171) (Fig. 3C). During final echocardiographic measurements in the RVA group in comparison with the initial values, a variation was not noted in IVS; however, notable chan-

ges were observed in PW thickness as well as IVS/PW values (9.91 ± 1.38 vs. 10.97 ± 1.80, p = 0.001; 1.01 ± 0.11 vs. 0.94 ± 0.12, p = 0.004, respectively) (Fig. 3B, C). Between initial and final echocardiography examination in the RVA group, variations were not detected in EDT, the size of LA, LVEDD and LVESD, or in the velocity of E and A peak. With regard to cardiac valve regurgitation, apart from the proportional increase of moderate tricuspid valve regurgitation with RVA pacing (31.3% vs. 18.75%, p = 0.046) (Fig. 3D), there were no statistically significant changes between initial and final echocardiography examinations in the RVA or the RVOTS group.

DISCUSSION

In the present study, we have demonstrated that pacing of different right ventricle areas affects the cardiac function in elderly patients with normal LVEF over a long-term follow-up. For a median 31.5 months' observation, the results suggested that RVA pacing reduced the mean of LVEF and increased the median value of BNP level, which are routinely used to evaluate cardiac function and haemodynamic status in clinical practice. Moreover, prolonged RVA pacing significantly increased the incidence of CAF in this study. Nevertheless, we found pacing of RVOTS had no significant influence on LVEF, BNP level or new onset CAF during a relatively long investigation.
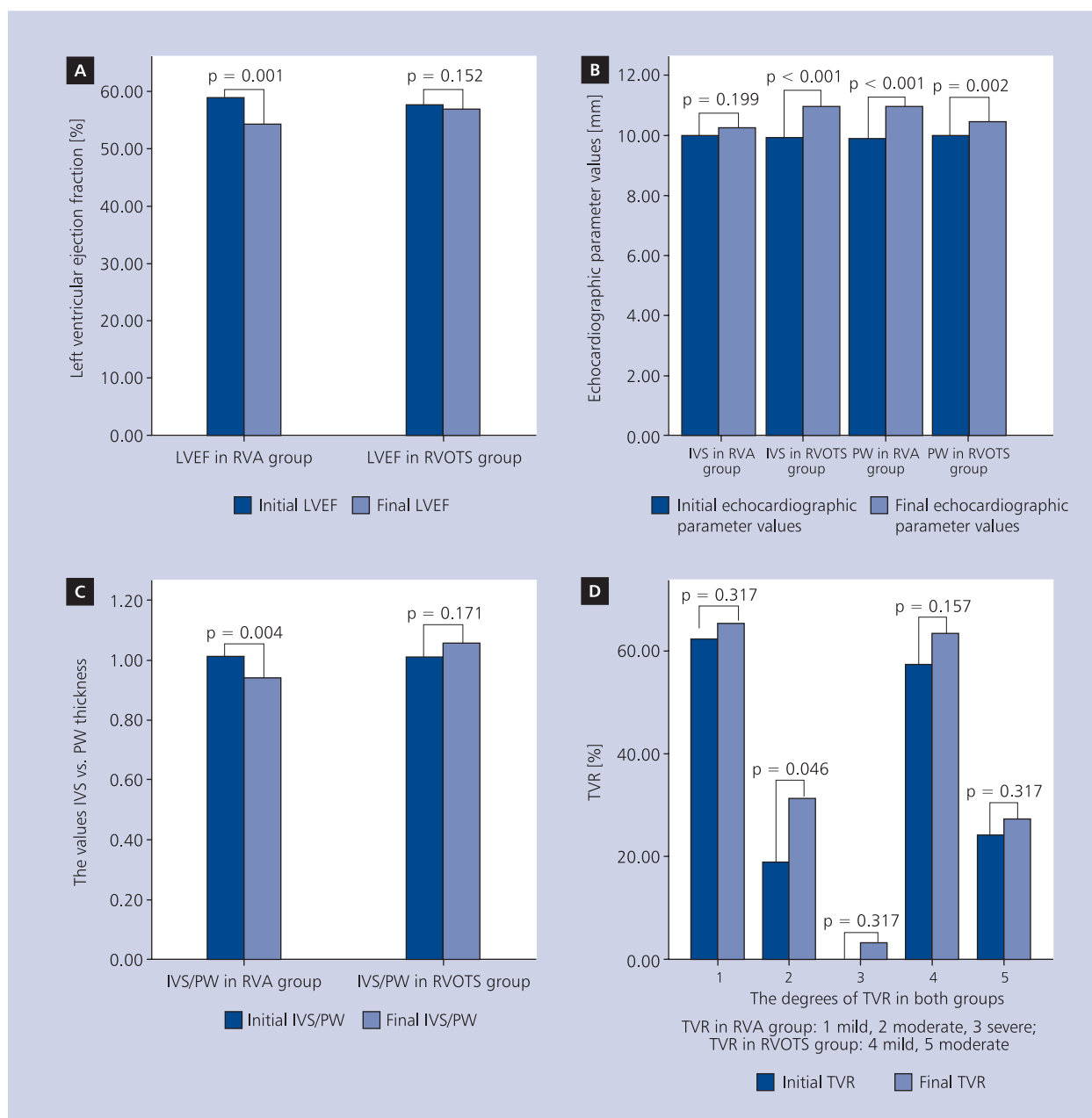
Figure 3. Differences of echocardiographic parameters in both groups obtained during initial and final echocardiographic examinations; **A.** Compared to the baseline values, left ventricular ejection fraction (LVEF) decreased with right ventricular apex (RVA) pacing (p = 0.001); **B.** The interventricular septum (IVS) and posterior wall (PW) mean values with right ventricular outflow tract septum (RVOTS) pacing at the end of follow-up were statistically raised compared to the initial results (p < 0.001, p = 0.002, respectively). In the RVA group, a notable change was observed in PW thickness (p = 0.001); **C.** When compared to baseline in statistics, a notable change was observed in IVS/PW values in the RVA group (p = 0.004); **D.** Tricuspid valve regurgitation (TVR) in two groups: apart from the proportionate increase of moderate TVR with RVA pacing (p = 0.046), there were no statistically significant changes between initial and final echocardiography examinations

For decades, RVA pacing has been accepted as a traditional and convenient site of implantation of ventricular leads for permanent cardiac pacing. However, RVA pacing produces an abnormal late activation of the lateral wall of the LV [24]. RVA pacing also leads to disturbances of perfusion, ad-renergic innervation and segmental LV contractile function, which in turn leads to the deterioration of its systolic and diastolic function. This induces LV myofibril disarray and hypertrophy, cellular abnormalities, involving intracellular vacuolisation, degenerative fibrosis, fat deposits, mitochondrial size

changes, dystrophic calcification [4], and fibre shortening, which ultimately may lead to ventricular remodelling resulting from neuro-hormonal and electrophysiological changes. More recent studies have shown that chronic RVA pacing may impair LV systolic function [2, 8, 18, 19]. Yet, we found few results indicating whether cardiac function of chronically RVA pacing-treated aged patients with normal LVEF had been impaired. In this clinical study, permanent RVA pacing yielded a significant reduction in mean LVEF, a remarkable increment in median BNP level, and new onset CAF. Our findings are in agreement with other studies that have demonstrated a decrease of LV systolic function with RVA pacing [2, 19, 25, 26] and an increase of new onset CAF [2, 7]. On the other hand, our results contradict the findings of previous investigators, [2] in terms of comparing final BNP levels between RVA and RVOTS groups. This revealed that in contrast to the final BNP level in the RVOTS group, the RVA group's final BNP level had no significant difference, although the number of patients with a final BNP level of > 400 pg/mL was higher in patients on RVA pacing than in patients with RVOTS pacing. The possible cause was that the duration of follow-up was shorter in our study, and normal cardiac function before enrollment in this study may be another reason [21].

In the clinical study, we found that RVOTS pacing was associated with a notable increase of IVS and PW thickness, although the IVS/PW ratio did not vary. Compared to the RVOTS group, prolonged RVA pacing contributed to the asymmetric PW hypertrophy, which was demonstrated by the markedly statistical variation between the final and initial IVS/PW ratio. The possible mechanism is that the early activated portion of LV close to the pacing site contracts at low chamber pressure and stretches the opposing noncontracting wall. As a result, the late activated portion elicits contraction at higher wall stress, in turn, which leads to the asymmetric PW hypertrophy and LV dyssynchrony [27]. While we did not observe a variation of the IVS/PW ratio with RVOTS pacing, it has been postulated that pacing at RVOTS results in a shorter LV activation time and possibly less ventricular dyssynchrony [27].

Patients with spontaneous left bundle branch block (LBBB) generally convey a poor prognosis [28]. Cardiac resynchronisation therapy (CRT) has been demonstrated to improve patients' cardiac function and clinical course, and advance their survival by restoring LV synchrony [29, 30]. Recently, it has become known that iatrogenic LBBB has similar harm produced by permanent RVA pacing. In essence, the harm incurred by such a type of pacing may more specifically relate to the abnormal axis conferred by apical pacing rather the LBBB [31].

RVOTS pacing area is close to physiologic conduction system. Hence, in contrast to RVA pacing, it would promote depolarisation in a more physiological fashion through the rapid conduction and diffuse propaganda of the specialised muscle,

by which RVOTS pacing produces the presence of narrower QRS width and approximately normal axis in ECG. These hypotheses were supported by the findings in our study, in which we validated the mean QRS complex significantly increased and the axis presented left-axis deviation when paced in RVA. Nevertheless, the mean QRS interval with RVOTS pacing was similar to the baseline QRS complex, and with RVOTS pacing patients' axes had immediately restored to approximately normal. The study of Trimble et al. [32] documented that patients with prolonged QRS durations had, on average, higher levels of mechanical dyssynchrony as described by median phase standard deviation (54.1° vs. 34.7°, p < 0.0001) and bandwidth (136.5° vs. 99.0°, p = 0.0005) than patients with normal QRS durations. Presumably, restoring normal axis and narrower QRS duration may in part explain why early chronic RVOTS pacing is associated with protective effects on cardiac function in individuals depending on permanent pacing.

In the present study, we observed that RVA pacing was associated with a significant exacerbation of moderate tricuspid valve regurgitation. This may be partly explained by apex lead contributing to mal-coaptation of the tricuspid valve leaflets. Consequently, worsening of cardiac function over time may be partly caused by the exacerbation of tricuspid valve regurgitation [33]. In terms of the end diastolic and systolic diameters of the LV, there were no statistical variations observed during the follow-up. Nevertheless, the LVEDD had a deteriorated tendency in the RVA group (47.16 ± 3.63 and 49.22 ± 5.16, p = 0.071). Probably, the adverse LV remodelling effect of RVA pacing may take a longer period to manifest, especially in patients with normal LVEF.

Limitations of the study

The present study was not a double-blind design, but a prospective, randomised, open-label and single-centre design. The shortcomings of this study design may bring selection and information biases. Prospective, randomised, double-blind and multicentre trials would further explore whether RVOTS pacing is superior to RVA pacing in a longer follow-up. The limited samples may also cause random error, which probably contributed to a deviation from the true results. We only measured partial parameters to evaluate cardiac function, and the obtained parameters could not contain all information which was capable of measuring cardiac synchrony, disynchrony and function, accurately and reliably. In a future investigation, tissue Doppler imaging or phase analysis of gated-myocardial perfusion single-photon emission computed tomography should be adopted to precisely evaluate cardiac function and left ventricular synchrony.

CONCLUSIONS

1. Classical RVA pacing in elderly patients with normal LVEF leads to a LV systolic function deterioration, denoted by lower LVEF and higher BNP levels.

2. When compared to RVA pacing, RVOTS pacing had no remarkable benefit in terms of preventing cardiac remodelling. It is worth noting that in elderly patients with permanent RVOTS pacing, increases of IVS and PW thickness were also observed.

3. We noted similar safety, reliability and operability of RVOTS pacing, compared to RVA pacing, over a long-term follow-up.

Conflict of interest: *none declared*

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Porównanie stymulacji koniuszkowej i stymulacji części przegrodowej drogi odpływu prawej komory u osób w podeszłym wieku z prawidłową frakcją wyrzutową lewej komory: obserwacja długookresowa

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Streszczenie

Wstęp: Jak dotąd nie ustalono, czy stymulacja części przegrodowej drogi odpływu prawej komory (RVOTS) jest bardziej skuteczna niż stymulacja koniuszkowa prawej komory (RVA) pod względem synchronizacji pracy prawej i lewej komory, czynności serca i remodelingu u osób w podeszłym wieku z prawidłową frakcją wyrzutową lewej komory (LVEF).

Cel: Badanie przeprowadzono w celu porównania wpływu stymulacji RVOTS i stymulacji RVA u starszych pacjentów z prawidłową LVEF podczas obserwacji długookresowej.

Metody: W latach 2007–2010 zrekrutowano do badania 65 chorych ze wskazaniami do stałej stymulacji serca i przydzielono ich losowo do stymulacji RVA (32 chorych) lub RVOTS (33 chorych). Po okresie obserwacji, którego mediana wynosiła 28 miesięcy, zebrano dostępne dane, obejmujące klasę czynnościową wg *New York Heart Association* (NYHA), parametry echokardiograficzne i parametry stymulacji, oś serca, czas trwania zespołu QRS oraz stężenie peptydu natriuretycznego typu B (BNP) w osoczu. Następnie porównano te dane między grupami RVA i RVOTS oraz między okresami przed i po wszczepieniu stymulatora, odpowiednio w grupach RVA i RVOTS.

Wyniki: Nie stwierdzono znamiennych różnic między grupą RVA i grupą RVOTS pod względem wyjściowej charakterystyki badanych. Mediana czasu stymulacji nie różniła się istotnie między grupami (31,5 miesiąca w grupie RVA *vs*. 28 miesięcy w grupie RVOTS; p = 0,728). W grupie RVA wartość LVEF zmniejszyła się w stosunku do wartości wyjściowych (od 59,5 ± ± 6,21 do 54,22 ± 8,73; p = 0,001), natomiast w grupie RVOTS nie uległa znaczącej zmianie (57,82 ± 6,06 i 56,94 ± 5,54; p = 0,152). Liczba chorych z umiarkowaną niedomykalnością zastawki trójdzielnej zwiększyła się wyraźnie w grupie RVA [od 6 (18,75%) przed wszczepieniem stymulatora do 10 (31,3%) chorych po wszczepieniu urządzenia; p = 0,046], jednak w grupie RVOTS ta zmiana nie była istotna statystycznie. W porównaniu z grupą RVOTS w grupie RVA stwierdzono tendencję do pogarszania się klasy wg NYHA (p = 0,071). W grupie RVA zaobserwowano zwiększenie mediany stężenia BNP po wszczepieniu stymulatora (35 pg/ml przed wszczepieniem urządzenia i 50 pg/ml w momencie zakończenia obserwacji; p = 0,007); w grupie RVOTS nie stwierdzono istotnych zmian w tym zakresie (36,4 pg/ml przed wszczepieniem urządzenia i 38 pg/ml w momencie zakończenia obserwacji; p = 0,102). Średnia szerokość zespołu QRS znacznie bardziej zmniejszyła się w grupie RVOTS (od 143,56 ± 12,90 do 105,52 ± 15,21; p = 0,000) niż w grupie RVA. W okresie obserwacji nie stwierdzono istotnych statystycznie zmian w zakresie poprzecznych wymiarów skurczowych i rozkurczowych lewej komory.

Wnioski: Stała stymulacja RVA u chorych w podeszłym wieku z prawidłową LVEF prowadziła do pogorszenia czynności skurczowej lewej komory przejawiającej się zmniejszeniem LVEF i podwyższonym stężeniem BNP w osoczu. Stymulacja RVOTS nie wiązała się z zauważalnymi korzyściami w zakresie zapobiegania przebudowie mięśnia sercowego w porównaniu ze stymulacją RVA.

Słowa kluczowe: koniuszek prawej komory, część przegrodowa drogi odpływu prawej komory, stymulacja

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