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Right ventricular lead placement and ventricular dyssynchrony in a pacemaker population: An acute analysis from the evaluation of apical and non-apical position (right pace) study☆,☆☆

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Since the advent of intravenous pacing leads, the apex has become the standard site for right ventricular (RV) implantation, as it ensures simple placement and greater lead stability and reliability. However, in subjects with normal left ventricular systolic function who require permanent pacing, RV apical stimulation is associated with an increased risk of atrial fibrillation, morbidity and even mortality [1]. These observations have raised questions regarding the appropriate pacing site. RV septal placement has been proposed as an alternative approach for the safe implantation and possible easy extraction of pacemaker and implantable defibrillator leads [2,3]. Moreover, several findings [4,5], suggested that non-apical pacing might have beneficial effects on systolic function, though it also confirmed inconclusive results with respect to other outcome measures, such as exercise capacity, functional class, quality of life and survival. Despite the lack of strong evidence in favor of non-apical pacing and the difficulty of placing the lead and accurately classifying [6] the final lead position, pacing at non-apical RV sites seems to have become a standard procedure at many implanting centers [7].

The RIGHT PACE study is a multi-center, prospective, single-blind, non-randomized trial [8]. The study was approved by the Institutional Review Boards of the participating centers and all subjects provided written consent.

Patients underwent implantation of a dual-chamber pacemaker with standard right atrial and RV leads. The target location for the RV lead tip was the apex or the inter-ventricular septum, according to the clinical practice of the center. Indeed, investigators were divided on the basis of their prior experience of non-apical pacing-lead implantation and the clinical practice adopted in their centers. No complication was reported by the investigators in both groups.

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In the present analysis, we evaluated the agreement between the classification at the implanting centers and that determined by central adjudication and the acute electrographic and echocardiographic effects of RV pacing. 437 patients indicated for dual-chamber pacemaker implantation with high percentage of RV pacing were included. Demographic data, clinical and pacing parameters according to the study groups at the time of enrollment are showed in Table 1. X-rays in the Antero-posterior, Right Oblique and Left Oblique projections (>30°) were available for core laboratory adjudication of the lead position in 409 patients. The apical positioning of the RV lead was not confirmed in 56 (20%) patients in the Apex group. Similarly, in 21 (16%) patients in the Non-apical group, the adjudicated pacing site was the apex. Agreement between the classification at the implanting centers and that determined by central adjudication was only moderate (kappa = 0.601; standard error = 0.040). The proportion of patients with non-apical lead positioning confirmed by X-rays Core-Lab was higher among patients who received an active fixation than a passive fixation lead (90% versus 70%, $p = 0.015$). After X-rays central adjudication, the comparison between Adjudicated RV apical (239 patients) and Adjudicated non-apical lead position (170 patients) showed significant left ventricular mechanical delay during stimulation in similar proportions of patients in the Apex and Non-apical groups. Indeed, 110 (46%) patients in the Adjudicated Apex group and 88 (52%) patients in the Adjudicated Non-apical group ($p = 0.252$) showed a difference of 41 ms or more between the septal and lateral delays (SLD) determined by means of tissue Doppler imaging [9]. By contrast, the QRS duration was shorter on non-apical pacing. (Fig. 1) On multivariate regression analysis, the only factor associated with the presence of significant left ventricular mechanical delay (SLD ≥ 41 ms) during RV pacing was the presence of pre-existing dyssynchrony during spontaneous conduction (odds ratio = 5.29; 95% CI = 2.60–10.76; $P < 0.001$).

Table 1
Demographics, baseline clinical parameters, pacing parameters and pharmacological treatment of the study population.

Parameter	Apex ($n = 274$)	Non-apical ($n = 163$)	p
Male gender, n(%)	171 (62)	104 (64)	0.770
Age, years	75 ± 9	73 ± 11	0.059
AV block—third degree, n(%)	45 (16)	39 (23)	0.054
AV block—second degree, n(%)	65 (24)	52 (32)	0.062
Coronary artery disease, n(%)	65 (24)	47 (29)	0.237
Myocardial infarction, n(%)	28 (10)	21 (13)	0.393
Previous CABG, n(%)	15 (5)	12 (7)	0.428
Previous angioplasty, n(%)	38 (14)	27 (17)	0.444
Previous valvular surgery, n(%)	12 (4)	5 (3)	0.493
History of atrial fibrillation, n(%)	66 (24)	33 (20)	0.353
Hypertension, n(%)	199 (73)	120 (74)	0.821
Diabetes, n(%)	65 (24)	53 (33)	0.045
Chronic obstructive pulmonary disease, n(%)	26 (9)	19 (12)	0.471
Chronic kidney disease, n(%)	56 (20)	29 (18)	0.499
LV ejection fraction, %	57 ± 9	58 ± 9	0.897
LVEDV, ml	101 ± 43	101 ± 30	0.992
LVESV, ml	44 ± 21	45 ± 18	0.695
LVEDD, mm	50 ± 21	48 ± 7	0.240
LVESD, mm	33 ± 17	32 ± 7	0.251
LAD, mm	41 ± 6	41 ± 13	0.495
Severe mitral regurgitation, n(%)	26 (9)	17 (10)	0.750
Patients with SLD >41 ms during spontaneous conduction	69 (25)	45 (28)	0.577
Procedure time, min	55 ± 16	53 ± 16	0.619
Fluoroscopy time, min	5 ± 4	5 ± 3	0.951
Sensed R wave amplitude, mV	12 ± 5	11 ± 5	0.170
RV lead impedance, Ohm	725 ± 269	635 ± 177	<0.001
RV pacing threshold amplitude, V	0.5 ± 0.4	0.6 ± 0.4	<0.001
RV pacing threshold duration, ms	0.4 ± 0.1	0.5 ± 0.1	<0.001

AV = Atrio-ventricular; CABG = Coronary artery bypass grafting; LV = Left ventricular; LVEDV = Left ventricular end-diastolic volume; LVESV = Left ventricular end-systolic volume; LVEDD = Left ventricular end-diastolic diameter; LVESD = Left ventricular end-systolic diameter; LAD = Left atrial diameter; SLD = Septal to lateral delay; RV = Right ventricular.

The main findings of the present analysis were that the currently adopted approach to non-apical pacing of the RV proved to be non-reproducible, owing to the difficulty of accurately classifying the final lead position and secondly, that pacing of the RV at apical or non-apical sites resulted in increased intraventricular dyssynchrony of left ventricular contraction whereas the degree of induced dyssynchrony was comparable between pacing sites.

We noticed a better agreement between local and central classification of non-apical positioning only when active fixation leads were used. This should suggest their adoption when non-apical positioning is attempted. Nonetheless, apical and non-apical approaches seemed equally feasible. Indeed, the pacing parameters were satisfactory in both study groups, the procedural and fluoroscopy times were comparable and no complication was reported by the investigators, who performed implantation procedures according to their prior experience and standard clinical practice. By contrast, in the recently published Protect-Pace study [4] placing the lead in the septal position required significantly more time, as lead implantation was performed by means of a specific steerable sheath/lead system.

The proportion of patients with abnormal mechanical delay (i.e. SLD ≥ 41 ms, as previously defined in a similar population with preserved systolic function) [9] increased on both pacing modalities. Although the Right Pace study included only patients with preserved ventricular function, about one fourth of them had significant spontaneous left ventricular mechanical delay, which turned out to be the only factor associated with the presence of pacing-induced dyssynchrony. Moreover, we cannot exclude that our population was affected by unrecognized diastolic abnormalities that were shown to be frequently associated with global mechanical dyssynchrony [10].

Pastore et al. [11] demonstrated that the degree of dyssynchrony induced by ventricular pacing is variable, and is higher in patients with higher baseline dyssynchrony, more dilated ventricles and more depressed ejection fraction. Our findings seem to confirm and extend this concept, which suggests that, even in the absence of patent ventricular dysfunction, the presence of pre-existing dyssynchrony may be more important in the response to RV pacing than the pacing mode and site, and may help to predict the risk of heart failure in pacemaker patients. Moreover, the electrical distribution of each patient may also determine the individual optimal pacing site [12].

Our planned 24-month analysis should confirm the safety and reliability of non-apical pacing over the long-term and will show whether the small differences in pacing parameters observed between the groups result in different longevity of the system.

The main limitation of the present study is the lack of randomization. However, the study was designed in order to obtain an unbiased representation of current clinical practice and to compare two approaches currently adopted as standard procedure at many implanting centers. In conclusion, we confirmed that the currently adopted approach to non-apical pacing of the RV is non-reproducible, and that pacing of the RV at apical or non-apical sites resulted in comparable dyssynchrony at acute assessment.

Disclosures

RIGHT PACE was an independent study. The Advisory Committee designed the trial. Boston Scientific provided technical support and supervised the implementation of the study, but had no access to the database and did not participate in the analysis of the results or the writing of the article. Boston Scientific representatives (M. Malacrida and S. Valsecchi) commented on the manuscript before its submission. The other authors report no conflicts.