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Comparison of the haemodynamic effects of right ventricular outflow-tract pacing with right ventricular apex pacing

A quantitative review

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The right ventricular apex has been used for cardiac stimulation because this position is easily accessible and is associated with a stable position of the electrode with a low dislodgement rate. This position, however, is associated with a dyssynchronous left ventricular contraction with subsequent deleterious haemodynamic effects. Alternative stimulation sites have been studied extensively because of a potentially better haemodynamic effect compared with right ventricular apex pacing.

Using a Cochrane search strategy, nine studies were selected to analyze the haemodynamic effects of right ventricular outflow-tract pacing. The results of these studies ($n = 217$) were pooled and indicated a significantly better haemodynamic effect (odds ratio 0.34, confidence interval 0.15–0.53) compared with right ventricular apex pacing. Therefore, these data suggest that right ventricular outflow-tract pacing may offer a modest but significant benefit over right ventricular apex pacing in patients selected for pacemaker implantation on the basis of symptomatic bradyarrhythmias.

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Introduction

Since the introduction of permanent right ventricular pacing[1], the right ventricular apex was used mainly because pacing from this site was easily accessible and was associated with a stable position with a relatively low dislodgement rate. In the early 1980s some of the haemodynamic consequences of cardiac pacing were recognized which subsequently lead to the introduction of AV sequential pacing[2–4]. Several studies, however, provided evidence that pacing from the right ventricular apex was associated with dyssynchronous activation of the left ventricle, resulting in impaired haemodynamic function[5–7]. With the introduction of active fixtion electrodes, alternative sites of stimulation in the right ventricle were evaluated which resulted in a number of studies focussing on the haemodynamic benefits associated with pacing from the right ventricular outflow tract[8–24].

The purpose of this review is to summarize all studies reported and to perform a quantitative analysis of the two stimulation sites on haemodynamic outcome. Because each study was relatively small, this quantitative analysis adds substantial statistical power to detect differences between pacing sites.

Methods

Search strategy and eligibility criteria

The Cochrane search strategy[25] was performed using the terms outflow-tract pacing, septal pacing from a Medline and Embase database (1984–2000) supplemented by visual searches for relevant recent journal articles.

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To be included, studies had to be prospective and should include measurements of systolic left ventricular function. When several indices of left ventricular function were reported, the single index that was most common throughout all screened articles was selected. In addition, studies on pacing for reasons other than symptomatic bradyarrhythmias (e.g. for patients with hypertrophic obstructive cardiomyopathy) and studies on selected patients (e.g. patients with heart failure) were excluded.

All studies were sequentially screened independently by two authors (C.C. de C. and M.C.G.) for exclusion criteria and were subsequently analysed for a standardized pooled effects size. Two studies were not included because the study population was restricted to patients with heart failure in association with bradyarrhythmias[12,13] while three studies[7,21,23] were excluded because pacing was initiated from the epicardial position. In addition, two studies were excluded because right ventricular outflow-tract pacing was compared with various electrode positions outside the right ventricular apex[8,9]. Finally, one study was excluded because only patients with impaired left ventricular function were selected[10]. Principal investigators were contacted to verify unpublished data and to provide exact data on the number of patients and haemodynamic findings. Nine studies met the inclusion criteria for the systematic review and were used for a quantitative analysis.

Outcome definitions

Outcomes for comparison were haemodynamic variables reported in each study. When several haemodynamic parameters were reported the variables that were selected were those most commonly reported throughout all selected studies and included cardiac output using Echo-Doppler measurements (five studies)[11,14,15,20,22], ejection fraction using radionuclide measurements (two studies)[18,19], dP/dt (one study)[24] and cardiac output using thermodilution (one study)[16].

Statistical analysis

Because the haemodynamic variables of the different studies were measured in different scales, standardized effect sizes were calculated for each of the reported studies. Each study was weighted according to inverse variance weighting[26]. Based on standardized effect sizes and the weights of the separate studies included a standardized pooled effects size and the corresponding confidence intervals were calculated.

Results

A total number of 217 patients (77% male) were included in the final analysis. The underlying heart disease reported was ischaemic in 46%.

In Table 1 all studies identified by the comprehensive search are listed in addition to the outcome with respect to haemodynamic variables analyzed. The selected studies were subsequently assessed for a standardized pooled effect size (Fig. 1). Pooled data demonstrated a modest but definite effect size in favour of right ventricular outflow-tract pacing compared with apex pacing (odds ratio 0.34, confidence intervals 0.15–0.53).

From all selected studies that entered the standardized pooled effect size analysis, only two studies reported long-term haemodynamic effects[18,20] while all other studies reported only acute haemodynamic effects.

Table 1 Haemodynamic variable from the studies identified by comprehensive search

Author	Publication/year	No. of patients	Parameter	Results
Benchimol[8]	Circulation/1966	6	CO[T]	±
Barold[9]	Am J Cardiol/1969	52	CO[T]	±
Raichlen[23]	Circulation/1984	18	CO[T]	−
Cowell[10]	PACE/1994	15	CO[T]	+
Giudici[11]	Am J Cardiol/1997	89	CO[E]	+
Gold[13]	Am J Cardiol/1997	13	CO[T]	±
Karpawich[24]	PACE/1997	22	LVEDP	+
Blanc[12]	Circulation/1997	14	PCWP	±
Buckingham[14]	PACE/1997	11	CO[E]	±
De Cock[15]	PACE/1998	17	CO[E]	+
Saxon[17]	J Card Electr/1998	11	FAC[E]	+
Buckingham[16]	PACE/1998	14	CO[T]	±
Mera[18]	PACE/1999	12	EF[N]	+
Buckingham[21]	PACE/1999	37	CO[T]	±
Schwaab[19]	JACC/1999	14	EF[N]	+
Victor[20]	JACC/1999	16	CO[T]	±
Kolettis[22]	Chest/2000	20	CO[E]	+

CO, cardiac output; T, thermodilution; E, Echo-Doppler study; N, nuclear study; FAC, fractional area change. PACE, Pacing Clin Electrophysiol; JACC, Journal of the American College of Cardiology. For details of publications see reference list. Results: +, positive effect; −, negative effect; ±, no effect of right ventricular outflow-tract pacing as compared with apex pacing.

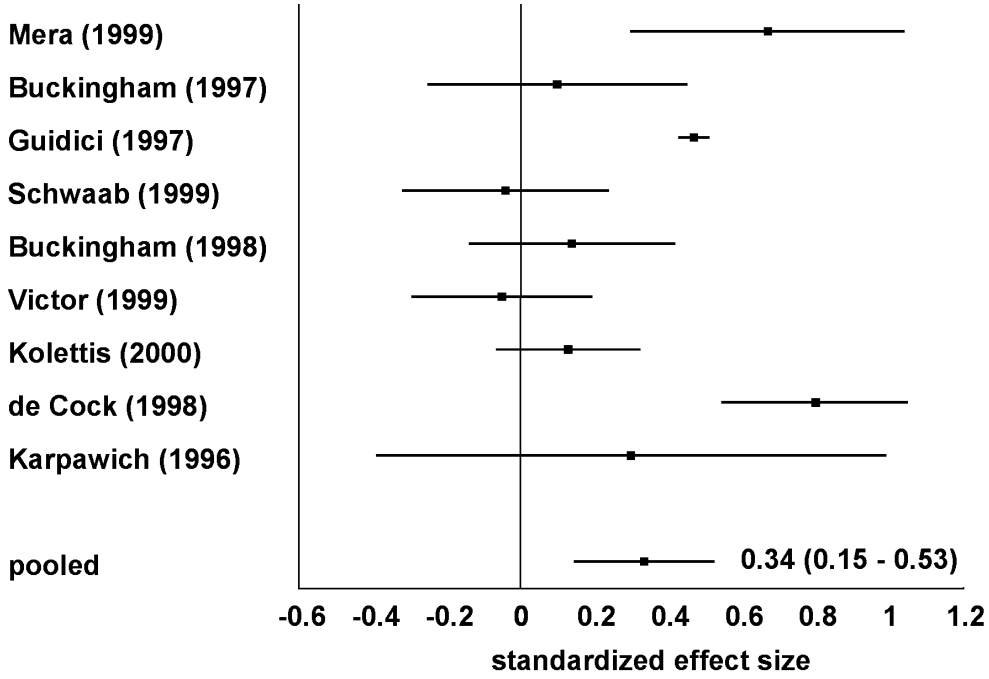

Figure 1 **Standardized effect size of all selected studies including the standardized pooled effect.**

Victor *et al.*[20] found no difference between the two pacing sites after 3 months of follow-up in patients with chronic atrial tachyarrhythmias and complete AV block. In contrast Mera *et al.*[18] reported a significant increase in LV fractional shortening during right ventricular outflow-tract pacing after 2 months of follow-up in a comparable group of patients. Group size varied considerably among the studies, ranging from 11 to 92 patients.

The study of Giudici *et al.*[11] reported 92 patients demonstrating a significant improvement in cardiac output during right ventricular outflow-tract pacing, which represents by far the largest study included in the standardized effect size analysis. When this study is excluded the overall effect was of borderline statistical significance (0.20 ± 0.22, confidence intervals -0.02 to 0.42).

Discussion

The present review demonstrates a modest but significant haemodynamic beneficial effect of right ventricular outflow-tract pacing compared with apex pacing in a wide range of patients.

Patient selection is very likely an important factor responsible for the divergent outcomes among the selected studies. Three studies[11,15,19] reported on post-defined subsets of patients more likely to benefit from right ventricular outflow-tract pacing. Two studies suggested that a decrease in QRS duration or a normalization of the QRS axis is associated with a more efficient contraction of the left ventricle[11,19]. In the study of Giudici *et al.*[11] patients with a low baseline cardiac output had a greater relative improvement with right-ventricular outflow-tract pacing compared with apex pacing. De Cock *et al.*[15] demonstrated a significantly better outcome from right ventricular outflow-tract pacing in patients with important coronary artery disease and/or left ventricular dysfunction whereas in patients with less coronary artery disease and/or normal ventricular function ($EF \geq 0.50$) no beneficial haemodynamic effect could be detected.

Some studies excluded specific subsets of patients, which may have modified haemodynamic response during pacing. Victor *et al.*[20] who found no difference between the two pacing sites included only patients with chronic atrial arrhythmias.

In the study of Kolettis *et al.*[22] who reported improved cardiac output during right ventricular outflow-tract pacing only patients without left ventricular dysfunction or coronary artery disease were eligible for the study.

The selection criteria used in this review were prespecified and were based on the applicability of right ventricular outflow-tract pacing to a wide range of patients selected for pacemaker implantation for symptomatic bradyarrhythmias.

Therefore, studies that used epicardial stimulation[8,9,17,21,23] and studies in selected patients[10,12,13] were not included in the final analysis.

There are several important limitations of this retrospective meta-analysis that need to be emphasized. There was a marked heterogeneity of pacing effects across the studies but it should be recognized that the power of these results to detect differences in pacing site is low due to the small sample size. In addition, the methodology to assess haemodynamic changes varies

widely among the studies. Five studies used Echo-Doppler measurements[11,14,15,20,22], two studies used radionuclide techniques[18,19], one study used thermodilution measurements[16] and in one study invasive dP/dt was recorded[24] which may all have potential limitations. Furthermore, the exact stimulation site during right ventricular outflow-tract pacing was not standardized and may vary among studies. Finally, studies reporting both acute and long-term effects were included as well as data from both randomized and non-randomized series. Given these substantial limitations more data from randomized trials are clearly needed before any recommendations for the use of this alternative stimulation site can be given. However, right ventricular outflow-tract pacing is relatively simple with a dislocation rate and pacing and sensing parameters reported to be comparable with right ventricular outflow-tract pacing[27].

In conclusion, the present review suggests that right ventricular outflow-tract pacing is associated with a modest but significant improvement in haemodynamic function. This pacing site should be considered a valid alternative for right ventricular apex pacing particularly in patients with impaired left ventricular function.

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