CARDIOVASCULAR MEDICINE

Comparison of the haemodynamics of different pacing sites in patients undergoing resynchronisation treatment: need for individualisation of lead localisation

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Background: Biventricular pacing is a new therapy for the treatment of heart failure. However, a substantial number of patients do not respond to this therapy.

Hypothesis: Individually determined maximal pacing sites will improve the haemodynamic response and increase the number of responders.

Methods: In 48 patients with heart failure, the acute haemodynamic effects of nine different pacing configurations were studied, using two right and left ventricular pacing sites and their combinations. Cardiac index was measured using Doppler echocardiography. For further analysis, the combination with the highest cardiac index improvement was compared with baseline. Moreover, the number of responders was calculated using a cut-off value of 10% increase in cardiac index.

Results: The mean (SD) increase in cardiac index ranged between 3.8% (6.0%) and 11.1% (8.6%). The pacing site with maximal cardiac index was highly variable between patients, and here the cardiac index increased to 14.8% (7.6%; $p < 0.001$). The number of responders varied between 15% and 64%, increasing to 75% at the site with maximal increase in cardiac index. In a subset of patients, the haemodynamic improvement after pacemaker implantation correlated well with the acute haemodynamics.

Conclusion: Individualisation of pacing configuration for biventricular pacing leads to further haemodynamic improvement in patients with heart failure and reduces the number of patients not responding to this therapy.

It has long been recognised that patients with heart failure and a wide QRS complex have a very poor prognosis.^{1–2} A novel therapeutic approach in these patients is resynchronisation therapy, which is associated with improved prognosis and functional status.^{3–9} Earlier studies have shown that about one third of the patients may not haemodynamically improve by this form of therapy.^{10–11}

It has previously been observed by Butter *et al*¹² that the location of the left ventricular lead may largely determine the haemodynamic improvement of left ventricular pacing.

Data available on haemodynamic responses of different pacing sites are limited. Most studies try to achieve a posterolateral position for the left ventricular lead on the basis of the assumption that this part of the left ventricle is always the latest part to be activated in left bundle branch block.^{5–13} However, it may be hypothesised that the degree of haemodynamic improvement is in part dependent on the localisation of the left ventricular leads and, therefore, lead localisation determines the percentage of responding and non-responding patients. Furthermore, limited data are available on right ventricular lead placement (right ventricular apex pacing or right ventricular outflow tract (RVOT) pacing) in relation to haemodynamic improvement.

The aims of this study were (1) to investigate the acute haemodynamic response with different pacing configurations, (2) to determine the number of non-responding and responding patients with the different pacing configurations and (3) to determine the pacing site with the highest haemodynamic improvement in individual patients. This site

with maximal increase in cardiac index was compared with the traditionally used posterolateral site combined with right ventricular apical pacing.

PATIENTS AND METHODS

Forty eight consecutive patients with heart failure, who were candidates for biventricular pacemaker implantation as per New York Heart Association (NYHA) class III–IV or IV, QRS duration >120 ms and left ventricular ejection fraction $<35\%$, were studied. Only patients with sinus rhythm were included in the study because (1) in patients with atrial fibrillation, overdrive pacing would increase the heart rate and thus influence the primary parameter, cardiac index, and (2) overdrive pacing with a regular rhythm may offer a haemodynamic benefit itself in these patients. Before the haemodynamic study (about 1 week before the acute study), baseline echocardiography was carried out, to assess the left ventricular ejection fraction, mitral regurgitation severity and early to late transmitral flow velocity ratio (E/A).

Before pacemaker implantation, patients underwent haemodynamic measurements during temporary pacing at different sites in the right and left ventricles. The medical ethical committee of the VU University Medical Center, Amsterdam, approved the study protocol. All patients gave informed consent before entering the study.

Abbreviations: AV, atrioventricular; NYHA, New York Heart Association; RVOT, right ventricular outflow tract

Haemodynamic measurements during multisite stimulation

An 8-French guiding catheter (Cordis, USA) was introduced under fluoroscopy for access to the coronary sinus from the femoral approach. After access, a balloon-occlusive venogram of the coronary sinus and its tributaries was carried out. Subsequently, two specially prepared percutaneous transluminal coronary (balloon) angioplasty guidewires suitable for unipolar pacing (Biotronik, Berlin, Germany) were introduced in two separate branches of the coronary sinus: the anterior and posterolateral branches. Furthermore, three temporary bipolar pacing catheters were positioned in the right atrial appendage, right ventricular apex and RVOT.

Pacing was carried out at nine different pacing sites as follows:

1. Right ventricular apex
2. RVOT
3. Bifocal right: right ventricular apex and RVOT
4. Coronary sinus (postero-lateral)
5. Right ventricular apex and coronary sinus (postero-lateral)
6. RVOT and coronary sinus (posterolateral)
7. Coronary sinus (anterolateral)
8. Right ventricular apex and coronary sinus (antero-lateral)
9. RVOT and coronary sinus (anterolateral)

Pacing was performed in the VDD mode, with an atrioventricular (AV) delay of 100 ms. At baseline and during each pacing configuration, an echo-Doppler study was conducted with an HP 4500 Sonos using an S3 transducer (Hewlett-Packard, Andover, California, USA). Measurements were taken after 1 min stabilisation.³ At baseline, the left ventricular outflow tract diameter was measured and Doppler flow measurements, determining the aortic valve area, were obtained.

All images were recorded on videotapes and analysed offline. For analysis, the mean of three consecutive beats was taken. Stroke volumes were calculated from the time-velocity integral of the aortic valve, corrected for the aortic valve area.¹⁴ Cardiac index was calculated by multiplying stroke volume by heart rate and corrected for body surface area. Finally, at baseline, a 12-lead electrocardiogram was recorded to measure QRS duration.

Identification of responders and non-responders

The percentage increase in cardiac index compared with baseline was calculated for each pacing site or combination. We used the site with maximal increase in cardiac index for further analysis. Patients were divided into a group of responders and non-responders on the basis of the variation in the cardiac index: the variation in the cardiac index between the baseline and acute haemodynamic study was 3.6%. On the basis of this variation between the baseline and acute haemodynamic study, a value of 10% (± 2.5 standard deviation (SD)) variation in cardiac index was chosen for a responder.

The intraobserver variation in the calculation of the cardiac index during the acute study was 1.6%. This variation was used to compare the improvement in the conventional coronary sinus (posterolateral) and right ventricular apex site with that in the other sites during the acute study. A variation in cardiac index of 5% (± 2.5 SD) between the coronary sinus (posterolateral) and right ventricular apex, and another site was considered to be significant.

Follow-up

In a subgroup of 17 patients, for comparison with acute study measurements, tests were repeated at the pacing combination tested with maximum haemodynamic result 8 weeks after implantation of a biventricular pacemaker. In these patients, lead positioning was attempted at the optimal pacing site combination. In 2 of 17 (12%) patients the second best lead position was reached, in one patient owing to phrenic nerve stimulation and in the other as a result of high thresholds and unstable lead position.

Statistical analysis

Data are presented as mean (SD), and in figures as a scatter plot and as a box and whisker plot. Groups were compared using the two-sided t test for unpaired data, and the data of the whole group were compared using the two-sided t test for paired data. Distribution between groups were compared using χ^2 test. $p < 0.05$ was considered to be significant.

RESULTS

Table 1 shows the baseline characteristics (37 men and 11 women; mean age 68 (SD 11) years) of the patients. Of the 48 patients, 27 had a previous myocardial infarction and 31 had undergone a revascularisation procedure before inclusion (mean interval 5.2 (SD 2.5) years). The mean (SD) NYHA class was III. Mean (SD) QRS duration was 165 (39) ms and mean (SD) left ventricular ejection fraction was 27% (9%).

Comparison of all pacing sites

Table 2 shows the different haemodynamics of all pacing sites. Haemodynamics were not obtained in all patients at all sites owing to failure to reach the specific branch (tortuous or sharp angle), absence of a specific branch, phrenic nerve stimulation, unacceptably high pacing thresholds or incomplete echo data.

We found no significant differences in heart rate between baseline and all pacing sites and also no significant difference in cardiac index between the baseline measurements and pacing at the right ventricular apical site. All other sites showed significantly higher cardiac index compared with baseline ($p < 0.001$).

With respect to single-site pacing, coronary sinus (posterolateral) showed a greater increase in cardiac index than coronary sinus (anterolateral) pacing (fig 1; $p < 0.01$). Multisite pacing has always been haemodynamically superior to single-site pacing ($p < 0.01$). Comparison of the multisite

Table 1 Baseline demographics (n = 48)

Age in years (mean (SD, range))	68 (11, 37–86)
Male:female	37:11
LBBB:RBBB:aspecific conduction delay	28:1:19
Idiopathic cardiomyopathy	12
Coronary artery disease	36
0-1:2:3-vessel disease	6:7:23
Prior myocardial infarction	27
Inferior infarction	8
Anterior infarction	17
Multiple infarctions	2
Prior CABG:PTCA	18:13
Prior pacemaker implantation	10
NYHA classification I:III:IV	3:39:6
QRS duration in ms (mean (SD, range))	165 (39, 120–240)
PR time in ms (mean (SD, range))	223 (24, 180–290)
Left ventricular ejection fraction in %	27 (9, 12–40)
Mitral regurgitation severity (mean (SD))	1.8 (0.8)
E:A ratio (mean (SD, range))	1.8 (1.3, 0.4–5.9)

CABG, coronary artery bypass graft; E:A, early to late transmitral flow velocity; LBBB, left bundle branch block; NYHA, New York Heart Association; PTCA, percutaneous coronary (balloon) angioplasty; RBBB, right bundle branch block.

Table 2 Haemodynamic results at different pacing sites

Pacing site	CI	Δ CI (%)	Heart rate (beats/min)
Baseline (n = 48)	1.75 (0.40)	—	76 (17)
RV apex (n = 48)	1.74 (0.42)	−0.9 (4.6)	76 (16)
RVOT (n = 48)	1.84 (0.42)*	5.6 (5.5)	76 (15)
CS-AL (n = 47)	1.82 (0.43)*	3.8 (6.0)	76 (15)
CS-PL (n = 44)	1.86 (0.41)*	6.6 (7.0)	76 (15)
Bifocal right (n = 46)	1.90 (0.42)*	8.9 (5.8)	76 (15)
CS-AL+RV apex (n = 47)	1.90 (0.43)*	9.0 (8.5)	77 (16)
CS-AL+RVOT (n = 47)	1.89 (0.43)*	8.2 (7.4)	76 (15)
CS-PL+RV apex (n = 44)	1.94 (0.42)*	11.1 (8.6)	76 (15)
CS-PL+RVOT (n = 44)	1.94 (0.44)*	10.8 (9.3)	76 (16)
Site with highest CI increase (n = 48)	2.00 (0.43)*	14.8 (7.6)	—

AL, anterolateral; CI, cardiac index; CS, coronary sinus; PL, posterolateral; RV, right ventricular; RVOT, right ventricular outflow tract.

* $p < 0.001$ compared with baseline measurements. Values are mean (SD).

pacing showed no significant differences between bifocal right pacing, coronary sinus (anterolateral) and right ventricular apex, and coronary sinus (anterolateral) and RVOT pacing. Between coronary sinus (posterolateral) and right ventricular apex, and coronary sinus (posterolateral) and RVOT pacing, we found no significant difference. The percentage increase in cardiac index increase with respect to baseline of the two coronary sinus (posterolateral) combinations was significantly greater than the two coronary sinus (anterolateral) combinations and the bifocal right pacing site ($p < 0.01$).

The highest increase in cardiac index was 14.8% (SD 7.6%). The site with maximal increase in cardiac index was the coronary sinus–coronary sinus (posterolateral) and right ventricular apex configuration in 14 (29%) patients, the coronary sinus (posterolateral) and RVOT configuration in 10 (21%), the bifocal right configuration in 10 (21%), the coronary sinus (anterolateral)+right ventricular apex configuration in 9 (19%), and the coronary sinus (anterolateral) and RVOT configuration in 5 (10%) patients.

We found no difference in cardiac index increase between patients with an inferior ($n = 8$) and those with an anterior ($n = 17$) myocardial infarction (16% (SD 9%) versus 14% (SD

6%); $p = \text{NS}$), and also no difference in site localisation, with maximal increase in cardiac index between the two groups with infarcts.

Number of responders at different sites

For the eight pacing configurations (excluding the right ventricular apex; table 3), the percentage of responders varied between 15% and 64% and that of the non-responders between 85% and 36%. When using the site with maximal increase in cardiac index, the number of responders increased to 75%. The percentage increase in cardiac index varied between 13% and 19% in responders.

Comparison between the posterolateral position and other sites

As the posterolateral site in combination with the right ventricular apex is the preferred combination in most clinical studies, the haemodynamics of the other sites were compared with that of this posterolateral site.

In four patients of the total group, a posterolateral position of the coronary sinus lead was not reached. In three of these patients, a cardiac index increase of 10% was found with another pacing combination (75%). In 28 patients, an increase of 10% was found in cardiac index at the coronary sinus (posterolateral) and right ventricular apex site. In this group, 5 (18%) patients showed a 5% increase in cardiac index at another site compared with the coronary sinus (posterolateral) and right ventricular apex site. In 16 patients, the increase in cardiac index was below 10% at the coronary sinus (posterolateral) and right ventricular apex site. In this patient group, 9 (56%) patients showed a 5% increase in cardiac index at another site compared with the coronary sinus (posterolateral) and right ventricular apex site. Thus, in 14 of 44 (32%) patients, a more favourable pacing combination than the coronary sinus (posterolateral) and right ventricular apex combination could be used. Figure 2 shows the 14 patients with a 5% increase in cardiac index at another site compared with the coronary sinus (posterolateral) and right ventricular apex site. The number of alternative sites varied between 1 and 3.

Follow-up

For the subgroup of patients with haemodynamic follow-up, the improvement in cardiac index at the acute pacing study was 16% (SD 8%) compared with 16% (SD 10%) for the improvement in cardiac index at the follow-up study ($p = \text{NS}$). Figure 3 shows the correlation between the improvements in cardiac index, comparing the results of the temporary pacing study with those after device implantation, which was highly significant ($p < 0.001$).

Figure 1 Scatter plot and a box and whisker plot of the mean increase in cardiac index (CI) of all pacing sites compared with baseline. AL, anterolateral; Bif R, bifocal right pacing; CS, coronary sinus; PL, posterolateral; RV, right ventricular; RVOT, right ventricular outflow tract.

Table 3 Responders versus non-responders for all sites

	Non-responders		Responders	
	CI (%) ^a	n (%)	CI (%) ^a	n (%)
RVOT (n = 48)	4.0 (4.4)	40 (83)	13.4 (3.4)	8 (17)
CS-AL (n = 47)	2.1 (4.3)	40 (85)	13.9 (4.2)	7 (15)
CS-PL (n = 44)	3.8 (4.6)	34 (77)	16.0 (5.3)	10 (23)
Bifocal right (n = 46)	4.8 (2.9)	27 (59)	14.4 (3.9)	19 (41)
CS-AL+RV apex (n = 47)	3.0 (4.4)	26 (55)	16.0 (6.0)	21 (45)
CS-AL+RVOT (n = 47)	3.6 (4.0)	29 (62)	15.7 (5.2)	18 (38)
CS-PL+RV apex (n = 44)	2.5 (5.0)	16 (36)	18.8 (7.5)	28 (64)
CS-PL+RVOT (n = 44)	5.1 (6.0)	26 (59)	19.2 (6.5)	18 (41)
Site with highest CI increase (n = 48)	6.1 (2.5)	12 (25)	20.6 (7.9)	36 (75)

AL, anterolateral; CI, cardiac index; CI (%), increase in cardiac index compared with baseline; CS, coronary sinus; PL, posterolateral; RV, right ventricular; RVOT, right ventricular outflow tract.

^aValues are mean (SD).

DISCUSSION

This study shows several important results: the haemodynamic response varied between patients, and the site with the highest increase in cardiac index was highly variable between patients. Considering the patient group as a whole, the individually optimised pacing site showed the highest improvement in cardiac index, which was considerably higher than those of the nine pacing sites, including the posterolateral pacing combinations ($p < 0.001$). Moreover, in about half of the patients, the RVOT lead, instead of the right ventricular apex lead, was used for site optimisation. Finally, the ratio of responders to non-responders varied greatly between the different pacing sites, again with the lowest number of non-responders if the pacing site was optimised per patient. These data therefore suggest a demand for individual optimisation of pacing sites. On the other hand, despite optimisation, 25% of the patient population did not respond to this therapy.

Improvement in cardiac index at different pacing sites

To our knowledge, this is the first study that compared all different multisite pacing combinations with respect to haemodynamic outcome (nine pacing sites with five multisite combinations). Kass *et al*¹³ compared four pacing sites with only one multisite combination, and Varma *et al*¹⁵

compared five pacing sites, including two multisite combinations. In several studies, the coronary sinus lead was implanted at both anterior and posterior positions, possibly because of difficulties in achieving an acceptable final posterior position.^{8 12 15-24} However, a limited number of studies have compared the haemodynamics of the different pacing sites. Butter *et al*¹² compared anterior wall pacing with free wall pacing, and found that although both pacing modalities increased haemodynamics, free wall pacing was superior to anterior pacing, in line with our data. Varma *et al*²⁵ studied only one posterior left ventricular and two right ventricular positions, and found no differences between the groups.

A few studies have also compared univentricular left-sided pacing with biventricular pacing. Our study showed that, although significant improvement in univentricular posterolateral pacing was found over univentricular anterolateral or RVOT pacing ($p < 0.05$), these results were much inferior when compared with results obtained on multisite pacing. Two studies showed a slight superiority of left ventricular to biventricular pacing.^{5 13} Several studies showed a clear superiority of biventricular over left ventricular univentricular pacing,^{23 26 27} in line with our study. However, some studies found no difference in improvement in subjective and objective parameters.^{3 22}

Patients were randomised to either univentricular or biventricular pacing only in the Pacing Therapies for Congestive Heart Failure I Study.⁵ In this study, the location of the left ventricular pacing site was fixed as the left ventricular lead was implanted by thoracotomy.⁵ Left

Figure 2 Haemodynamic results of 14 patients in whom pacing at other sites resulted in a 5% increase in cardiac index (CI) compared with the "standard" coronary sinus (posterolateral) and right ventricular apex site. AL, anterolateral; Bif R, bifocal right pacing; CS, coronary sinus; PL, posterolateral; RV, right ventricular; RVOT, right ventricular outflow tract.

Figure 3 The correlation of the improvement in cardiac index (CI) during the acute pacing study compared with the results after device implantation.

ventricular pacing had a better haemodynamic improvement than biventricular pacing, and both improved considerably compared with conventional right ventricular pacing.

Use of a pacing site with highest improvement in cardiac index

Studies on different pacing sites in the same patient are very few.^{12–15} Butter *et al*¹² compared free wall pacing with anterior wall pacing combined with one right ventricular lead position. Both were haemodynamically superior to baseline, but an opposite response (increase in LV+dP/dt at the free wall, with a decrease at the anterior wall) could be found in 37% of patients tested.

Although we showed that all pacing sites improved cardiac index compared with baseline and right ventricular apex pacing, more importantly, it was shown that the pacing site with maximal increase in cardiac index varied considerably between patients. The traditionally used coronary sinus (posterolateral) and right ventricular apex configuration was the site with maximal increase in cardiac index in only 29% of patients. Also, the site with maximal increase in cardiac index was superior to the coronary sinus (posterolateral) site in terms of haemodynamic improvement and the number of responders (fig 2). Moreover, our data show that the haemodynamics are sustained 3 months after definite pacemaker implantation (fig 3).

A subgroup analysis of patients with an anterior and inferior myocardial infarction showed no significant differences in either increase in cardiac index or the used optimal pacing configuration between the two patient groups with infarcts. To our knowledge, no study has compared patients with an inferior or anterior myocardial infarction and the use of resynchronisation therapy. However, only a small group of patients were analysed and the results need confirmation in a larger population.

Possibly, the implantation of leads at an optimised right and left ventricular pacing site will further improve functional capacity, haemodynamics and ultimately the prognosis in these patients. Therefore, studies on mechanisms, identification and effect on outcome are needed to further refine resynchronisation therapy.

Responders and non-responders

Previous studies have shown that a substantial number of patients do not respond to resynchronisation therapy.^{3 5 9–11 23 28–34} Data on the number of non-responding patients are described in a minority of studies, and different criteria have been used to define the response—for example, wedge pressure,³ LV+dP/dt,^{5 10 28} pulse pressure,^{5 10} end-systolic volume on echocardiography,^{11 29} Quality-Of-Life Score,^{30 31 35} NYHA classification^{23 30–32} or tissue Doppler imaging synchrony.³³ By using these different criteria, the percentage of non-responders has been found to vary between 18% and 50%.^{3 5 9–11 23 28–34}

The mechanisms underlying a response or non-response are not clear. However, Reuter *et al*³⁰ carried out a multivariate analysis on his patient group and found that a considerably increased risk for non-response was the presence of a myocardial infarction, the presence of mitral regurgitation <grade 2, an aortic velocity–time integral <12 cm (comparable to a low cardiac output state) and the ischaemic origin of the cardiomyopathy.

In addition to these predictors, we showed that the ratio of number of responders to that of non-responders was dependent on the stimulation site. At the different multisite combinations, the percentage of non-responders varied between 36% and 62%. After choosing for individual lead optimisation, the non-response rate decreased to 25%.

Limitations

These data are the results of an acute haemodynamics study and of a substudy with short-term follow-up, in which the functional outcome was not determined. However, Kim *et al*³⁶ showed a correlation between the acute haemodynamic improvement and the change in walking distance during follow-up, indicating that acute haemodynamic improvements are associated with improved functional capacity during follow-up. Recent data also suggest that the changes in haemodynamics and functional class occur early, and that there is no or minimal further improvement during long-term follow-up.^{31 37} However, the effect of pacing site optimisation on prognosis needs to be determined.

Despite using continuous-wave Doppler echocardiography for the determination of cardiac index, to minimise measurement variation,¹⁴ several pacing combinations could provide a similar haemodynamic response as a result of measurement variation. In these cases, the choice of the definite implantation site may be determined by other factors such as procedure time and complication chance.

In our study, a fixed AV delay of 100 ms was used. Variation in the AV delay may have influenced the haemodynamics. Studies on AV delay optimisation in biventricular pacing show improvement in cardiac index with VDD pacing with short AV delay.^{13 28} Breithardt *et al*²⁸ found that the most optimal haemodynamic results were achieved with short and intermediate AV delays between 80 and 120 ms. These findings are in line with those of Auricchio *et al*,⁵ who reported that the optimal AV delay depended on the PR interval of the patient. The mean AV delay was around 100 ms, in line with our study. Patients with atrial fibrillation were excluded, because of the probability that by overdrive pacing the heart rate would be considerably higher than that at baseline, which would influence cardiac index measurements. In addition, by overdrive pacing, the regular rhythm may offer a haemodynamic benefit of itself.

Clinical implications

Firstly, the pacing site with the highest increase in cardiac index is variable between patients. This indicates that multiple haemodynamic measurements have to be taken at the available pacing sites. Both right-sided and left-sided pacing sites have to be explored for an optimal haemodynamic response.

Secondly, we established that compared with standard biventricular pacing, optimisation using the posterolateral region of the coronary sinus ensures a superior haemodynamic response and a larger group of patients with a positive response to this therapy.

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REFERENCES

- 1 Braunwald E. Shattuck lecture—cardiovascular medicine at the turn of the millennium: triumphs, concerns, and opportunities. *N Engl J Med* 1997;**337**:1360–9.
- 2 The CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). *N Engl J Med* 1987;**316**:1429–35.
- 3 Blanc JJ, Etienne Y, Gilard M, *et al*. Evaluation of different ventricular pacing sites in patients with severe heart failure: results of an acute hemodynamic study. *Circulation* 1997;**96**:3273–7.
- 4 Cazeau S, Ritter P, Lazarus A, *et al*. Multisite pacing for end-stage heart failure: early experience. *Pacing Clin Electrophysiol* 1996;**19**:1748–57.

- 5 Auricchio A, Stellbrink C, Block M, et al. Effect of pacing chamber and atrioventricular delay on acute systolic function of paced patients with congestive heart failure. The Pacing Therapies for Congestive Heart Failure Study Group. The Guidant Congestive Heart Failure Research Group. *Circulation* 1999;**99**:2993-3001.
- 6 Leclercq C, Cazeau S, Le Breton H, et al. Acute hemodynamic effects of biventricular DDD pacing in patients with end-stage heart failure. *J Am Coll Cardiol* 1998;**32**:1825-31.
- 7 Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med* 2001;**344**:873-80.
- 8 Gras D, Mabo P, Tang T, et al. Multisite pacing as a supplemental treatment of congestive heart failure: preliminary results of the Medtronic Inc. InSync Study. *Pacing Clin Electrophysiol* 1998;**21**:2249-55.
- 9 Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002;**346**:1845-53.
- 10 Stellbrink C, Breithardt OA, Franke A, et al. Impact of cardiac resynchronization therapy using hemodynamically optimized pacing on left ventricular remodeling in patients with congestive heart failure and ventricular conduction disturbances. *J Am Coll Cardiol* 2001;**38**:1957-65.
- 11 Pitzalis MV, Iacoviello M, Romito R, et al. Cardiac resynchronization therapy tailored by echocardiographic evaluation of ventricular asynchrony. *J Am Coll Cardiol* 2002;**40**:1615-22.
- 12 Butter C, Auricchio A, Stellbrink C, et al. Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. *Circulation* 2001;**104**:3026-9.
- 13 Kass DA, Chen CH, Curry C, et al. Improved left ventricular mechanics from acute VDD pacing in patients with dilated cardiomyopathy and ventricular conduction delay. *Circulation* 1999;**99**:1567-73.
- 14 Kusumoto F, Venet T, Schiller NB, et al. Measurement of aortic blood flow by Doppler echocardiography: temporal, technician, and reader variability in normal subjects and the application of generalizability theory in clinical research. *J Am Soc Echocardiogr* 1995;**8**:647-53.
- 15 Varma C, O'Callaghan P, Mahon NG, et al. Effect of multisite pacing on ventricular coordination. *Heart* 2002;**87**:322-8.
- 16 Auricchio A, Kloss M, Trautmann SI, et al. Exercise performance following cardiac resynchronization therapy in patients with heart failure and ventricular conduction delay. *Am J Cardiol* 2002;**89**:198-203.
- 17 Piscione F, Perrone-Filardi P, De Luca G, et al. Low dose dobutamine echocardiography for predicting functional recovery after coronary revascularisation. *Heart* 2001;**86**:679-86.
- 18 Alonso C, Leclercq C, Victor F, et al. Electrocardiographic predictive factors of long-term clinical improvement with multisite biventricular pacing in advanced heart failure. *Am J Cardiol* 1999;**84**:1417-21.
- 19 Hamdan MH, Barbera S, Kowal RC, et al. Effects of resynchronization therapy on sympathetic activity in patients with depressed ejection fraction and intraventricular conduction delay due to ischemic or idiopathic dilated cardiomyopathy. *Am J Cardiol* 2002;**89**:1047-51.
- 20 Kerwin WF, Bolvinick EH, O'Connell JW, et al. Ventricular contraction abnormalities in dilated cardiomyopathy: effect of biventricular pacing to correct interventricular dyssynchrony. *J Am Coll Cardiol* 2000;**35**:1221-7.
- 21 Leclercq C, Cazeau S, Ritter P, et al. A pilot experience with permanent biventricular pacing to treat advanced heart failure. *Am Heart J* 2000;**140**:862-70.
- 22 Hamdan MH, Zagrodzky JD, Joglar JA, et al. Biventricular pacing decreases sympathetic activity compared with right ventricular pacing in patients with depressed ejection fraction. *Circulation* 2000;**102**:1027-32.
- 23 Garrigue S, Bordachar P, Reuter S, et al. Comparison of permanent left ventricular and biventricular pacing in patients with heart failure and chronic atrial fibrillation: prospective haemodynamic study. *Heart* 2002;**87**:529-34.
- 24 Nelson GS, Berger RD, Fetters BJ, et al. Left ventricular or biventricular pacing improves cardiac function at diminished energy cost in patients with dilated cardiomyopathy and left bundle-branch block. *Circulation* 2000;**102**:3053-9.
- 25 Varma C, O'Callaghan P, Rowland E, et al. Comparison between biventricular pacing and single site pacing in patients with poor ventricular function: a hemodynamic study. *Pacing Clin Electrophysiol* 2003;**26**:551-8.
- 26 Touiza A, Etienne Y, Gilard M, et al. Long-term left ventricular pacing: assessment and comparison with biventricular pacing in patients with severe congestive heart failure. *J Am Coll Cardiol* 2001;**38**:1966-70.
- 27 Etienne Y, Mansourati J, Touiza A, et al. Evaluation of left ventricular function and mitral regurgitation during left ventricular-based pacing in patients with heart failure. *Eur J Heart Fail* 2001;**3**:441-7.
- 28 Breithardt OA, Stellbrink C, Franke A, et al. Acute effects of cardiac resynchronization therapy on left ventricular Doppler indices in patients with congestive heart failure. *Am Heart J* 2002;**143**:34-44.
- 29 Yu CM, Fung WH, Lin H, et al. Predictors of left ventricular reverse remodeling after cardiac resynchronization therapy for heart failure secondary to idiopathic dilated or ischemic cardiomyopathy. *Am J Cardiol* 2002;**91**:684-8.
- 30 Reuter S, Garrigue S, Barold SS, et al. Comparison of characteristics in responders versus non-responders with biventricular pacing for drug-resistant congestive heart failure. *Am J Cardiol* 2002;**89**:346-50.
- 31 Molhoek S, Bax J, van Erven L, et al. Effectiveness of resynchronization therapy in patients with end-stage heart failure. *Am J Cardiol* 2002;**90**:379.
- 32 Oguz E, Dagdeviren B, Bilsel T, et al. Echocardiographic prediction of long-term response to biventricular pacemaker in severe heart failure. *Eur J Heart Fail* 2002;**4**:83-90.
- 33 Ansalone G, Giannantoni P, Ricci R, et al. Doppler myocardial imaging in patients with heart failure receiving biventricular pacing treatment. *Am Heart J* 2001;**142**:881-96.
- 34 Ricci R, Ansalone G, Toscano S, et al. Cardiac resynchronization: materials, technique and results. The InSync Italian Registry. *Eur Heart J* 2000;**2**(Suppl):j6-15.
- 35 Linde C, Braunschweig F, Gadler F, et al. Long-term improvements in quality of life by biventricular pacing in patients with chronic heart failure: results from the Multisite Stimulation in Cardiomyopathy study (MUSTIC). *Am J Cardiol* 2003;**91**:1090-5.
- 36 Kim WT, Sogaard P, Mortensen PT, et al. Three dimensional echocardiography documents haemodynamic improvement by biventricular pacing in patients with severe heart failure. *Heart* 2001;**85**:514-20.
- 37 Linde C, Leclercq C, Rex S, et al. Long-term benefits of biventricular pacing in congestive heart failure: results from the Multisite Stimulation in cardiomyopathy (MUSTIC) Study. *J Am Coll Cardiol* 2002;**40**:111-18.

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