Acute biventricular pacing after cardiac surgery has no influence on regional and global left ventricular systolic function

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Received 28 September 2006; accepted after revision 20 February 2007; online publish-ahead-of-print 13 April 2007

KEYWORDS
Biventricular pacing;
Heart failure;
Heart surgery;
Left ventricular systolic function;
Tissue Doppler imaging

Background Cardiac resynchronization therapy has been shown to improve systolic function in patients with advanced chronic heart failure and electromechanical delay (QRS width >120 ms). However, the effect of acute biventricular (BiV) pacing on perioperative haemodynamic changes is not well defined. In the present study, acute changes in regional left ventricular (LV) systolic function determined by tissue Doppler imaging (TDI) and global LV systolic function determined by the continuous cardiac output method were measured during various pacing configurations in patients with depressed LV systolic function undergoing heart surgery.

Methods Twenty-six patients (age 68 ± 8 years, 15 males) with depressed systolic LV function (LV ejection fraction <35%), symptomatic heart failure, and a QRS duration of >120 ms undergoing temporary epicardial BiV pacing after aortocoronary bypass and valve surgery were included. QRS duration on surface electrocardiogram (ECG), TDI (systolic velocities of septal and lateral mitral annulus), cardiac index (CI), right atrial pressure, pulmonary artery pressure (PAP), and pulmonary capillary wedge pressure (PCW) were measured during various pacing configurations [no pacing (intrinsic rhythm), right atrial–biventricular (RA–BiV pacing), right atrial–left ventricular (RA–LV), right atrial–right ventricular (RA–RV), and AAI pacing].

Results There were no differences in QRS duration during intrinsic rhythm, RA–BiV pacing, and AAI pacing. However, RA–LV and RA–RV stimulations showed a longer QRS duration (P < 0.01 vs. intrinsic rhythm, RA–BiV pacing, and AAI, respectively). Tissue Doppler velocities of the septal and lateral mitral annulus were comparable in all pacing modes. Neither CI nor PAP or PCW showed significant differences during the various pacing configurations. There was a positive correlation between regional (TDI) and global (CI) parameters of LV systolic function.

Conclusions Biventricular pacing after heart surgery does not improve parameters of regional and global LV systolic function acutely in patients with heart failure and intraventricular conduction delay and, thus, may not reflect changes observed with chronic BiV pacing.

Introduction

Long-term multisite pacing in end-stage heart failure is associated with haemodynamic improvement.¹ The main purpose of biventricular (BiV) pacing is to restore ventricular contraction and relaxation sequences homogeneously by simultaneously pacing both ventricles from the right apex and the left lateral wall, respectively. The encouraging preliminary results of the acute setting¹ in cardiac resynchronization therapy (CRT) in patients with heart failure and electromechanical delay of left ventricular (LV) activation have recently been confirmed in several randomized, controlled trials during chronic BiV pacing.² ³ In these studies patients showed a significant improvement of symptoms, quality of life, exercise tolerance and systolic function after implantation of a CRT system.² ³ Whether these promising data could be reproduced in the early post-operative setting in patients with impaired LV function and prolonged QRS duration undergoing coronary bypass grafting or valve surgery is not yet clear.

Tissue Doppler imaging (TDI) is a new echocardiographic technique using the Doppler principle to measure the
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regional velocity of any myocardial segment. TDI has been shown to be a valuable diagnostic tool to determine systolic and diastolic LV function. The aim of the present study was to evaluate the acute changes in regional systolic function determined by TDI and in global systolic function determined by continuous cardiac output (CCO) method with temporary multisite pacing and various pacing configurations after heart surgery in patients with depressed LV function and symptomatic heart failure.

Methods
Study population
Patients undergoing elective aortocoronary bypass grafting and valve replacement were selected on the basis of a LV ejection fraction ≤35% in a preoperative levocardiography during angiography and a QRS duration of >120 ms on surface electrocardiogram (ECG) after having given informed consent, which was approved by the institutional Ethics Committee. Patients were studied in the intensive care unit after cardiac surgery while they were in a haemodynamically stable condition without positive inotropic agents. During the study, intravenous drug infusions were not changed and no additional medications were started. Patients who were haemodynamically unstable or who required an intra-aortic balloon counterpulsation were excluded from the study.

Pacing procedure
During surgery, epicardial leads were attached to the right atrium and the right ventricle as part of the standard management. Two additional epicardial leads were attached to the left ventricle at the lateral free wall. The haemodynamically stable patients were stimulated with an external constant-current dual-chamber demand pacemaker (Medtronic 5388, Medtronic Inc., Minneapolis, MN) in the following predetermined pacing modes: no pacing (intrinsic rhythm), right atrial–BIV pacing (RA–BIV pacing), right atrial–LV pacing (RA–LV), right atrial–right ventricular pacing (RA–RV), and atrial pacing (AAI). These configurations were performed in each patient in the same order. Biventricular pacing was achieved by connecting the ventricular leads with a Y bifurcated adapter to the ven-tricular port of the pacemaker. The pacing rate was set at 10 bpm above the underlying rhythm (90 ± 6 bpm), and the AV delay (150 ms) was unchanged in all AV-sequential pacing modes. The presence of complete ventricular capture during the various pacing configurations was confirmed by the analysis of the paced QRS complex morphology recorded simultaneously on the surface ECG. TDI and haemodynamic parameters were evaluated during all the predefined pacing modes. Data were collected after 10 min of stimulation in each mode to ensure data acquisition after achieving equilibrium. All epicardial leads were removed transcutaneously before discharge of the patient.

ECG, echocardiographic, and haemodynamic analysis
A 12-lead ECG was recorded with each of the pacing configurations. QRS duration was measured for each intervention. Echocardiography was performed using a 2.5–5.0 MHz imaging probe connected to a commercially available ultrasonographic system (System 5, Vingmed, General Electric, Horten, Norway). TDI was performed in the pulsed-wave Doppler mode to measure velocities of the septal (medial) and lateral mitral annulus in the apical four-chamber view. The sample volume was placed in the middle of the basal and lateral walls. Gain and filters were adjusted to eliminate background noise and to allow for a clear tissue signal. Care was taken to keep the incidence angle between the direction of the Doppler beam and the analysed vector of myocardial motion as small as possible and to maintain the probe at the identical level throughout the protocol. All studies were recorded on super-VHS videotapes and analysed off-line by an experienced echocardiographer who was not aware of the pacing mode. For each parameter, three consecutive beats of sinus rhythm or AV paced complexes were measured and the average value was taken. The normal TDI profile consists of a systolic myocardial (Sm) wave and an early (Em) and late (Am) myocardial diastolic waves. The systolic wave consists of two peaks: S1 and S2. S1 reflects isovolumic contraction, whereas S2 occurs during ejection. The S2 velocity was measured during the various pacing configurations.

Mitral regurgitation jets were imaged using colour Doppler echocardiography in two imaging planes (parasternal long-axis and four-chamber view). Doppler Nyquist limits and gain settings were optimized to demonstrate regurgitant jets. Semi-quantitative measurements of mitral regurgitation jet size were performed off-line. The maximal regurgitant jet area and the regurgitant jet diameter at the vena contracta were determined during intrinsic rhythm and during the various pacing configurations. The severity of mitral regurgitation was graded visually on a scale from 1 to 4 (mild or moderate = grade 1 or 2, moderate to severe = grade 3, and severe = grade 4).

Haemodynamic studies were performed in a supine, non-sedated condition after 10 min in each pacing mode and during intrinsic rhythm. Midchest position was used for the zero reference level. Continuous cardiac output was measured by the automated thermodilution method (Baxter Vigilance, Edwards Critical Care Division, Irvine, CA). Compared to the standard iced bolus thermodilution technique, the use of the validated, automated CCO method allows the documentation of rapid changes in cardiac output (e.g. when switching into various pacing modes). Haemodynamic measurements included pulmonary artery pressure (PAP), right atrial pressure (RAP), pulmonary capillary wedge pressure (PCW), and cardiac index (CI).

Statistical methods
Data are presented as mean ± SD. Between-group comparisons were performed by a one-way analysis of variance (ANOVA) for continuous variables followed by the Scheffe’s procedure if the P-value was significant (P < 0.05). A simple linear regression was used to determine the relation between CI and TDI.

Results
Twenty-six consecutive patients (mean age 68 ± 8 years, 15 males) with symptomatic heart failure due to ischemic (n = 20) and valvular heart disease (n = 6) with a mean LVEF of 27 ± 7% and a widened QRS complex of 132 ± 25 ms on the pre-operative surface ECG were included in the present study. All patients underwent elective aortocoronary bypass grafting. Additional aortic valve replacement was performed in two patients and mitral valve reconstruction in four patients with mitral regurgitation grade 3 or 4; thus, no patient showed grade 3 or 4 mitral regurgitation post-operatively. Six patients had a history of myocardial infarction with some degree of myocardial scarring (three patients had LV akinesia apical and three had anteroseptal akinesia), all other patients had diffuse hypokinesia. There were no differences in QRS duration between intrinsic rhythm, RA–BIV pacing, and AAI pacing, respectively. However, RA–LV and RA–RV pacing showed a longer QRS duration (P < 0.01 vs. intrinsic rhythm, RA–BIV pacing, and AAI, respectively) (Tables 1 and 2).

In nine patients, TDI could not be performed because of poor image quality. Biventricular pacing did not induce significant improvement in regional systolic function since
systolic tissue Doppler velocities of septal and lateral mitral annulus were comparable in all pacing modes (Table 1). To compare regional with global systolic LV function, a regression analysis between mean TDI velocities (septal and lateral) and CI was performed for all pacing modes that showed a positive correlation ($y = 2.2 + 13 \times x; r = 0.31, P = 0.017$).

No statistically significant changes in the grade of mitral regurgitation or in haemodynamic parameters between the various pacing sites or combination of sites could be documented (Tables 1 and 2). Compared with intrinsic rhythm, improvements in CI (increase $>20\%$) were observed in two patients with RA–BiV pacing and in four patients with AAi, RA–LV, and RA–RV pacing, respectively. Three patients with RA–RV and one with RA–LV pacing showed a decrease in CI of $20\%$ compared with baseline. No intra- or post-operative complications were observed with the placement or removal of the epicardial pacing leads or with the completion of the pacing protocol.

**Discussion**

In the present study, the effect of acute BiV pacing on regional (TDI) and global (CI) systolic function in patients with depressed LV function undergoing heart surgery was assessed. There were two important findings. First, parameters in regional and global systolic function are comparable in all pacing modes and, second, there is a positive correlation between regional and global parameters of LV systolic function.

Cardiac resynchronization therapy has been demonstrated to improve haemodynamics in selected patients with symptomatic heart failure and widened QRS. Results from registries and controlled randomized studies of the long-term effects of chronic BiV pacing are consistent with a significant and sustained benefit to symptoms, exercise tolerance, quality of life, as well as a reduction in mortality. Alonso et al. revealed a mean reduction of 1.3 in the functional NYHA class and a 50% increase in peak oxygen consumption in patients with the greatest shortening of QRS duration during chronic BiV pacing. However, in the present study of acute BiV pacing, there was no significant QRS narrowing and improvement in LV function. This is in accordance with the previous studies of acute BiV pacing in which the QRS width did not reflect any improvement in the LV performance and cardiac output. Also, Saxon et al. did not find a significant difference in the QRS width between the paced QRS durations achieved with intraoperative, simultaneous RV and LV pacing and the native QRS duration. However, the mean native QRS duration in our patients was only 132 ms, and it has been suggested that patients only with an average QRS width of 150 ms improved from additional LV pacing, whereas those with a smaller QRS width did not benefit. Furthermore, it could be demonstrated that the only independent predictor of a clinical response was the degree of QRS shortening associated with resynchronization therapy that was shortened by 37 ms in responders and by 11 ms in non-responders.

In addition, it is increasingly recognized that identification of candidates for BiV pacing solely on the basis of the QRS duration is inadequate, whereas inclusion of some direct measurements of inter- or intraventricular dysynchrony by echocardiography may be helpful in identifying potential long-term responders.

In the present study, a positive correlation was found between the systolic TDI velocities and CI and, therefore, regional systolic function reflects global LV function. In accordance with the haemodynamic data, TDI also showed no benefit from BiV pacing. This positive correlation is in

| Table 1 | Electrocardiographic, haemodynamic, and TDI data at baseline (intrinsic rhythm) and with different pacing configurations in 17 patients |
|---------|-------------------|-------------------|-------------------|-------------------|
| ECG (QRS in ms) | CI (L/min/m²) | TDI Sm septal (cm/s) | TDI Sm lateral (cm/s) | MR (grade) |
| Intrinsic | 137 ± 26 | 2.7 ± 0.5 | 4.9 ± 1.3 | 5.1 ± 1.4 | 1.9 ± 0.3 |
| RA–BiV | 136 ± 21 | 2.7 ± 0.5 | 4.8 ± 1.5 | 5.0 ± 1.5 | 1.8 ± 0.2 |
| RA–LV | 161 ± 37* | 2.8 ± 0.7 | 4.6 ± 1.5 | 4.2 ± 1.3 | 1.8 ± 0.3 |
| RA–RV | 165 ± 35* | 2.8 ± 0.6 | 4.8 ± 1.5 | 5.1 ± 1.1 | 2.0 ± 0.4 |
| AAi | 134 ± 27 | 2.9 ± 0.6 | 4.7 ± 1.5 | 4.8 ± 1.5 | 1.9 ± 0.3 |

CI, cardiac index; TDI, tissue Doppler imaging; MR, mitral regurgitation.

*P < 0.01 vs. ECG intrinsic rhythm, RA–BiV pacing, and AAi, respectively.

| Table 2 | Electrocardiographic and haemodynamic data at baseline (intrinsic rhythm) and with different pacing configurations in 26 patients |
|---------|-------------------|-------------------|-------------------|-------------------|-------------------|
| ECG (QRS in ms) | CI (L/min/m²) | PAP (mmHg) | RAP (mean, mmHg) | PCW (mean, mmHg) |
| Intrinsic | 132 ± 25 | 2.8 ± 0.5 | 38 ± 8/19 ± 4 | 11 ± 3 | 16 ± 4 |
| RA–BiV | 140 ± 19 | 2.7 ± 0.4 | 38 ± 8/19 ± 4 | 10 ± 3 | 16 ± 6 |
| RA–LV | 162 ± 32* | 2.8 ± 0.6 | 37 ± 7/19 ± 4 | 10 ± 3 | 15 ± 4 |
| RA–RV | 167 ± 29* | 2.9 ± 0.6 | 37 ± 7/19 ± 4 | 10 ± 3 | 16 ± 5 |
| AAi | 140 ± 24 | 2.9 ± 0.5 | 36 ± 7/19 ± 4 | 10 ± 4 | 15 ± 4 |

CI, cardiac index; PAP, pulmonary artery pressure; PCW, pulmonary wedge pressure; RAP, right atrial pressure.

*P < 0.01 vs. intrinsic rhythm, RA–BiV pacing, and AAi, respectively.
accordance with previous studies in which patients with impaired and preserved LV systolic function showed a close correlation between the systolic velocity of mitral annular displacement (Sm) obtained by TDI and LV ejection fraction measured by different methods, including two-dimensional echocardiography,23 cineangiogram,24 radionuclide ventriculography,25–27 or pulmonary haemodynamics.28 The absolute systolic velocity measured by TDI may differentiate between normal and decreased LV function in healthy subjects and patients with heart failure, which has been shown by a number of experimental and clinical studies.27–29 The wide range of absolute velocities described in the literature is due to the different TDI techniques used (pulsed-wave TDI records peak velocities, colour-coded TDI provides mean velocities) and the location of the measurements (velocities increase from the apex towards the base).3 In contrast to the present study, previous studies showed that acute BiV pacing improved haemodynamics.12,36,37 Foster et al.,36 revealed an increased CI during acute BiV pacing 12–36 h after elective coronary artery revascularization. However, these patients showed only slightly reduced baseline LV ejection fraction (>40%). In patients with heart failure, BiV pacing resulted in higher systolic blood pressure and lower PCW; however, the aetiology of impaired systolic function was not homogenous, comprising patients with ischemic as well as idiopathic cardiomyopathy.12 In a homogeneous study, population with idiopathic dilated cardiomyopathy peak systolic TDI values and LV ejection fraction increased significantly during acute BiV pacing.37 The discrepancy between the positive effect of acute BiV pacing on LV function in previous studies and the negative results of the present study may be explained by the patient selection. Patients with coronary artery disease and severe LV dysfunction after heart surgery may represent another patient population than those with non-ischemic chronic heart failure. In the presence of coronary artery disease and post-operative myocardial stunning, pacing may worsen ischemia in underperfused areas and influences regional contractility remote from ischemic regions.17,38 Cardiac remodelling after resynchronization therapy may take weeks to months in patients with coronary heart disease.19,39 and thus measurements of LV function in the acute phase of BiV pacing do only reflect the beginning of a long-term process. Finally, the optimal echocardiographic technique to measure changes in cardiac function during BiV pacing has yet to be determined in future studies. Strain rate imaging (in conjunction with three-dimensional echocardiography) may appear to be more useful and sensitive to evaluate myocardial function40 and to define echocardiographic parameters, which may allow to identify patients who will respond to resynchronization therapy more precisely.

Limitations

In the present study, no individually optimized atrio-ventricular (AV) or ventriculo-ventricular (VV) interval was programmed. The haemodynamic response to pacing may be affected by optimizing the synchronicity of atrial and ventricular contraction. In a prospective study by Sawhney et al.,41 an individually optimized AV interval showed greater improvement in NYHA class and quality of life at 3 months compared with a fixed AV interval of 120 ms. In addition, current BiV pacing devices have separate RV and LV channels that allow programming of a VV interval with RV or LV pre-exitation that may affect inter- and intra-ventricular synchrony. Sogaard et al.42 optimized VV settings by TDI. However, the clinical impact to optimize the device settings by this technique has not been assessed. Bordachar et al.43 showed that reduced inter-ventricular dysynchrony is not necessarily correlated with improved LV systolic function. Furthermore, landmark trials, which proved a benefit from CRT, randomized over 4000 patients based only on their ECG, functional NYHA class, and LV ejection fraction.2–5 The population in the present study was a cohort of severely ill heart failure patients in a critical post-operative period early after heart surgery with ongoing haemodynamic monitoring. Thus, additional echocardiographic measurements for individually optimizing the AV and VV intervals would have been difficult and too time-consuming in this situation. A further limitation of the present study may be the complex interactions of cardioplegia, ischemia, reperfusion, and anaesthetic drugs on cardiac haemodynamics. However, since every patient served as his own control, these effects may have been overestimated.

Conclusions

In the present study, no acute effect of temporary BiV pacing after heart surgery has been shown on regional and global parameters of systolic LV function. Acute pacing does not reflect changes observed with chronic BiV pacing. Further studies are needed to elucidate the complex mechanisms involved in BiV-induced changes in ventricular activation/contraction sequence with acute and chronic pacing systems in order to identify patients with depressed LV function, which benefit most from cardiac resynchronization therapy.

References


