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CLINICAL RESEARCH

Additional value of three-dimensional echocardiography in patients with cardiac resynchronization therapy

Apport de l'échographie cardiaque 3-dimensionnelle chez les patients bénéficiant d'une resynchronisation biventriculaire

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Summary
Background. — There is no gold standard technique for quantification of ventricular dyssynchrony.
Aim. — To investigate whether additional real-time three-dimensional morphologic assessment of ventricular dyssynchrony affects response after biventricular pacing.
Methods. — Forty-one patients with severe heart failure were implanted with a biventricular pacing device and underwent two-dimensional (time dispersion of 12 left ventricular electromechanical delays) and three-dimensional echocardiographic assessment of ventricular dyssynchrony (dispersion of time to minimum regional volume for 16 left ventricular segments),

before implantation, 2 days postimplantation with optimization of the pacing interventricular delay and 6 months postimplantation.

Results. — Individual optimization of sequential biventricular pacing based on three-dimensional ventricular dyssynchrony provided more improvement ($p < 0.05$) in left ventricular ejection fraction and cardiac output than simultaneous biventricular pacing. During the different configurations of sequential biventricular pacing, the changes in three-dimensional ventricular dyssynchrony were highly correlated with those of cardiac output ($r = -0.67$, $p < 0.001$) and ejection fraction ($r = -0.68$, $p < 0.001$). The correlations between two-dimensional ventricular dyssynchrony and cardiac output or ejection fraction were significant but less ($r = -0.60$, $p < 0.01$ and $r = -0.56$, $p < 0.05$, respectively). After 6 months, 76% of patients were considered responders (10% decrease in end-systolic volume). Before implantation, we observed a significant difference between responders and non-responders in terms of three-dimensional ($p < 0.05$) — but not two-dimensional — ventricular dyssynchrony.

Conclusion. — This prospective study demonstrated the additional value of three-dimensional assessment of ventricular dyssynchrony in predicting response after biventricular pacing and optimizing the pacing configuration.

Résumé
Introduction. — Dans cette étude prospective, nous avons évalué l'intérêt d'une évaluation de l'asynchronisme ventriculaire gauche par échographie tridimensionnelle (3D) chez les patients ayant bénéficié de l'implantation d'une resynchronisation biventriculaire (BV).

Méthodes. — Quarante et un patients insuffisants cardiaques ont été implantés d'un pacemaker ou d'un défibrillateur triple-chambre et ont bénéficié d'une échographie bidimensionnelle (2D) et tridimensionnelle avec mesure de l'asynchronisme ventriculaire gauche (1) avant implantation, (2) deux jours après l'implantation avec optimisation des délais interventriculaires et (3) six mois après l'implantation.

Résultats. — (1) L'optimisation du délai interventriculaire basée sur l'évaluation de l'asynchronisme 3D a permis un bénéfice significatif ($p < 0,05$) en termes de fraction d'éjection et de débit cardiaque. (2) Les variations d'asynchronisme ventriculaire gauche 3D étaient hautement corrélées aux variations de débit cardiaque ($r = -0,67$; $p < 0,001$) et de fraction d'éjection ($r = -0,68$; $p < 0,001$). Ces mêmes corrélations étaient significatives mais moindres entre asynchronisme 2D et débit cardiaque ou fraction d'éjection ($r = -0,60$; $p < 0,01$ and $r = -0,56$; $p < 0,05$, respectively). (3) Après six mois de stimulation biventriculaire, 76 % des patients étaient considérés comme répondeurs à la resynchronisation (réduction d'au moins 10 % du volume télésystolique). Avant l'implantation, les répondeurs présentaient un asynchronisme 3D significativement ($p < 0,05$) supérieur que les non répondeurs. En revanche, cette différence n'était pas significative pour l'asynchronisme 2D.

Conclusion. — Cette étude prospective démontre un intérêt important de la mesure de l'asynchronisme 3D pour prédire la réponse après resynchronisation et pour permettre l'optimisation des réglages de l'appareil.

Introduction

CRT has an established role in the management of symptomatic drug-refractory heart failure in patients with prolonged QRS complexes [1—3]. Despite the application of established selection electrocardiographic criteria, up to one-third of patients do not respond to the therapy [3,4]. In single-centre studies, direct assessment of echocardiographic mechanical ventricular dyssynchrony has been found to be useful in selecting appropriate patients for CRT, predicting a favourable response and optimizing device programming [5—9]. Currently, an array of echocardiographic parameters for quantification of ventricular dyssynchrony is available but a gold standard technique has yet to be accepted. A recent, prospective, multicentre study found

that some indices of 2D dyssynchrony were associated with high inter- and intraobserver variability, and that no 2D echocardiographic measurement alone improved the process of patient selection for CRT reliably [10]. Real-time 3D echocardiography has already shown a high level of accuracy in determining LVEF and left ventricular volume [11,12]. 3D echocardiography with appropriate software for segmental wall motion analysis allows the quantification of mechanical dyssynchrony, taking all myocardial segments into account [13]. The present study was designed to examine whether the measurement of left ventricular synchronicity by 3D echocardiography, using regional volumetric changes, could quantify the effect of CRT on global left ventricular function and mechanical asynchrony in patients with refractory chronic heart failure, and provide additional information to

Methods

Reproducibility of 3D echocardiographic measurements

Interobserver and intraobserver reproducibility of 3D echocardiographic measurements was assessed with linear regression analysis and the Bland-Altman method in 32 patients (28 men; mean age: 53 ± 16 years). These patients were selected to demonstrate different levels of left ventricular dysfunction from normal heart to severe cardiomyopathy.

Study population

Consecutive patients with drug-resistant heart failure undergoing implantation of a BVP device were enrolled prospectively on the following basis: LVEF less than 35%,

optimize CRT device programming and distinguish between responders and non-responders.

sinus rhythm, QRS duration more than 120 ms, and NYHA functional class III or IV, despite optimal medical therapy. The presence of echocardiographic evidence of ventricular dyssynchrony was not an inclusion or exclusion criterion. Patients with a history of atrial arrhythmias, complete atrioventricular block or ongoing symptoms of myocardial ischaemia were excluded from the study protocol. All patients provided written, informed consent to the study, which was approved by the institutional clinical research and ethics committee. Of the 46 patients who met the inclusion criteria, five had to be excluded because of a poor ultrasonic window that did not allow exploitable 3D acquisitions.

Pacemaker implantation

All patients had successful implantation of a CRT device and all leads were positioned transvenously. The atrial lead was positioned at the right atrial appendage and the right ventricular lead was positioned at the apex. The left ventricular lead (Attain OTW 4194, Medtronic, Minneapolis, MN, USA) was positioned in a posterior ($n = 7$), lateral
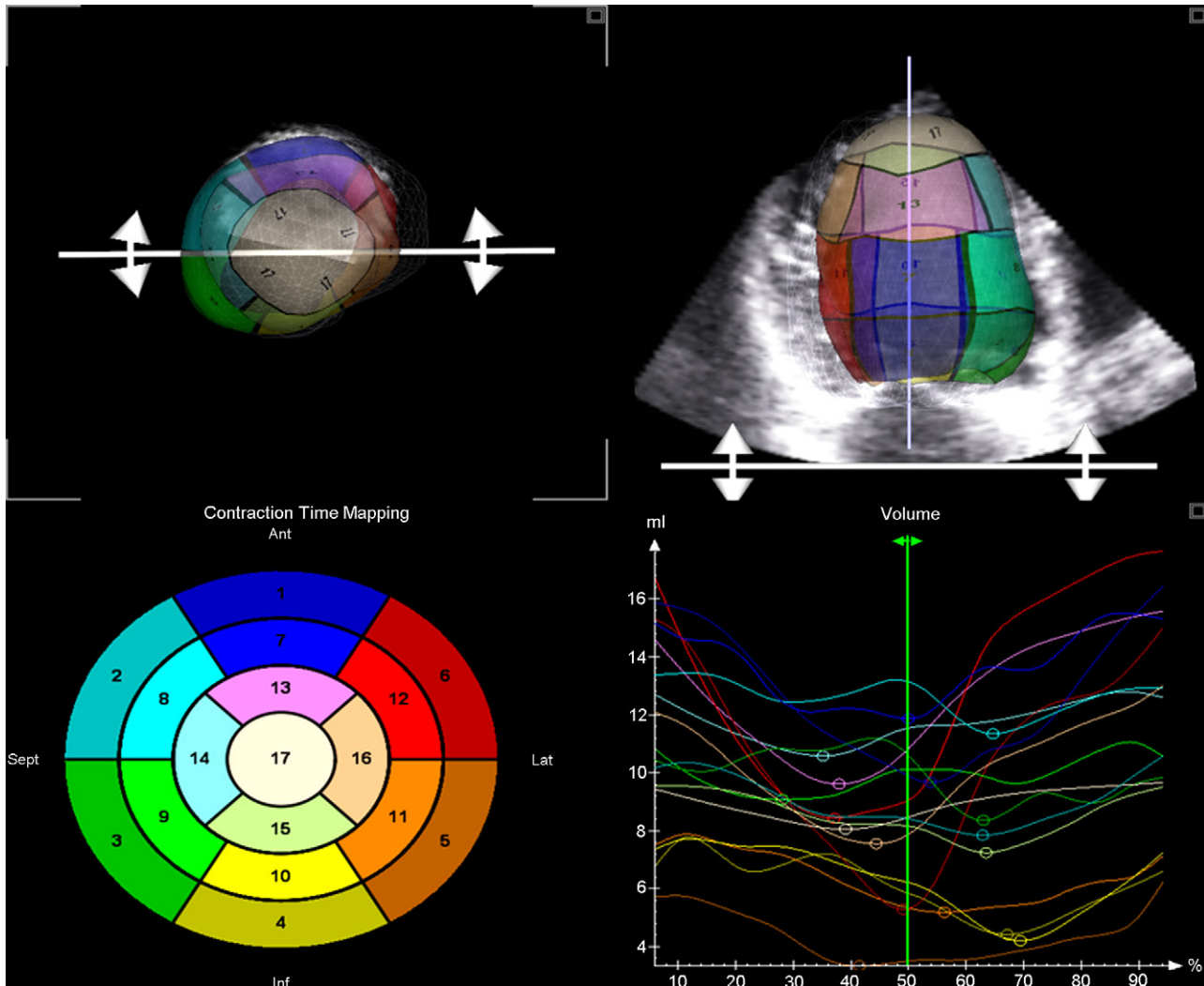
Figure 1. Upper part: left ventricle cast produced by quantitative offline analysis. Lower part and right side: regional volume curves in a patient with severe intraventricular dyssynchrony.

($n = 24$) or anterior ($n = 10$) cardiac vein. The leads were connected to a CRT device (Insync SENTRY 7298, Medtronic, Minneapolis, MN, USA or CONTAK RENEWAL 4 HE, Boston Scientific/Guidant, Natick, MA, USA) that allowed programming of interventricular stimulation delay from 0 to 80 ms.

Study protocol

All patients underwent clinical evaluation at baseline before CRT implantation and after 6 months of simultaneous BVP. During clinical evaluation, a 6-minute hall-walk test, a quality of life assessment using the Minnesota Living with Heart Failure test and a maximal treadmill exercise test with measurement of peak exercise oxygen consumption were performed. To minimize variability between examinations, all echocardiographic recordings were performed by one experienced echocardiographer. All images were recorded digitally and analysed offline. Each parameter was measured and averaged over three consecutive beats during sinus rhythm. The offline analysis was performed by a blinded observer.

2D echocardiography was performed using a 2.5 to 5.0 MHz imaging probe connected to an ultrasound system (Vivid 7, Vingmed-General Electric, Horten, Norway) in accordance with the American Society of Echocardiography guidelines. Gain, filter and depth settings were adjusted to eliminate background noise and to allow for a clear tissue signal. The cardiac output was determined by the left ventricular outflow method that has been applied reproducibly in individuals with heart failure [14]. Evidence of left intraventricular dyssynchrony was determined using colour-coded tissue Doppler imaging to assess segmental wall motion in the middle of the basal and mid-segmental portions of the septal, lateral, inferior, anterior, posterior and anteroseptal walls. The variation in the peak of segmental left ventricular contraction was evaluated by measuring the interval between the onset of the QRS complex and the peak of each segmental systolic velocity. The index of systolic dyssynchrony was defined as the standard deviation of the 12 time to peak electromechanical delay values obtained.

3D echocardiography was performed using a 3D probe connected to an iE-33 ultrasound system (Philips, Amsterdam, The Netherlands). Real-time 3D echocardiography used the 4S or X4 matrix array transducer to provide a pyramidal volume in real time. Four smaller real-time volumes, acquired from alternate cardiac cycles during a short-breath hold, were necessary to provide a pyramidal volume covering the whole left ventricular volume. LVEF was determined using four-dimensional left ventricular analysis software (TomTec, Unterschleissheim, Germany). A 3D index of intraventricular dyssynchrony was obtained by calculating the time interval from the onset of QRS until the time of appearance of the minimum regional volume in each of the 17 segments. The 3D dyssynchrony index was defined as the standard deviation of these 17 time intervals. To allow comparison between patients with significantly different heart rates, systolic dyssynchrony was expressed as a percentage of the duration of the cardiac cycle (Fig. 1).

All 2D and 3D echocardiographic parameters were measured successively, 2 days before implantation, 2 days after implantation and after 6 months of simultaneous BVP. Two days after implantation, various predetermined pacing configurations were assessed using spontaneous atrial synchronized pacing: right ventricular pacing; left ventricular pacing; simultaneous BVP; sequential BVP with right ventricular pre-activation with interventricular intervals of 20 and 40 ms; and sequential BVP with left ventricular pre-activation with interventricular intervals of 20 and 40 ms. These configurations were performed in a random order. The optimal interventricular delay was defined as the one that resulted in maximal decrease in 3D dyssynchrony. As described previously, the atrioventricular delay was optimized for each configuration to provide the longest transmitral filling time without truncation of the A-wave from pulsed Doppler analysis of the left ventricular filling [15].

Statistical analysis

All data are presented as mean values ± standard deviations. Sequential data measurements were analysed by repeated measures of analysis of variance. Spontaneous rhythm was considered as the reference pacing configuration for the comparison of all sequential BVP configurations and to assess the correlations between the percentage change in cardiac output and LVEF on the one hand, and markers of ventricular dyssynchrony on the other. Pearson's correlation coefficient was used to quantify correlations between quantitative variables. Reproducibility of measurements was assessed with linear regression analysis and the Bland-Altman method. Statistical significance was established at $p < 0.05$.

Results

The baseline characteristics of the 41 patients are presented in Table 1. All patients had implantation of an effective BVP device and completed the entire study protocol. No patient died during the 6-month follow-up period.

Table 1 Demographic and clinical variables.	
	Patients ($n = 41$)
Age (years)	67.6 ± 7.6
Men (%)	85
Ischaemic heart disease (%)	56
Primitive dilated cardiomyopathy (%)	44
NYHA class	3.1 ± 0.3
Ejection fraction (%)	7.6 ± 6.7
QRS width (ms)	159 ± 29
Concomitant therapy (%)	
Angiotensin-converting enzyme inhibitor	73
Angiotensin type 1 receptor antagonist	17
Beta-blockers	90
Diuretics	100
Aldosterone antagonists	78

Results are given as mean values ± standard deviations or percentages.
NYHA: New York Heart Association.
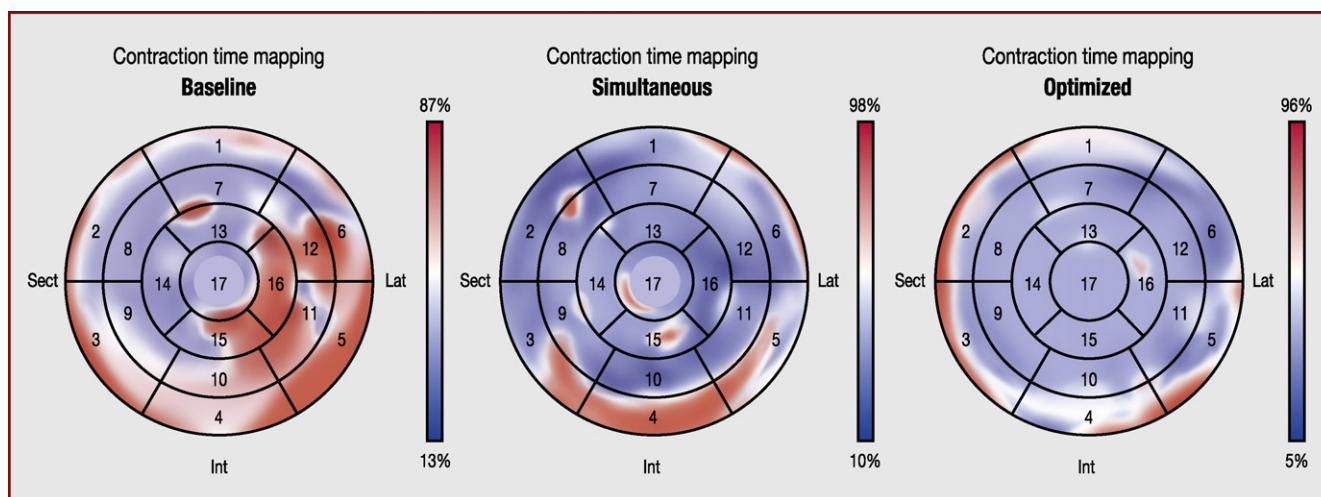
Figure 2. Interobserver reproducibility in terms of 3D left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV).

Reproducibility of echocardiographic measurements

Interobserver variability mean average error (and 95% confidence interval value) obtained from the Bland-Altman analysis of 3D LVEF and 3D left ventricular end-systolic and end-diastolic volumes were −0.2% (3.3%), −1.2 mL (13.7 mL) and −0.2 mL (16.1 mL), respectively (Figs. 2 and 3).

Intraobserver variability mean average error (and 95% confidence interval value) obtained from the Bland-Altman analysis of 3D LVEF and 3D left ventricular end-systolic and end-diastolic volumes were 0.1% (2.8%), −0.1 mL (8.4 mL) and 0.3 mL (9.6 mL), respectively.

Acute impact of biventricular pacing

Compared with baseline evaluation, simultaneous BVP increased LVEF significantly from 27.6 ± 6.7 to $31.0 \pm 6.7\%$ ($p < 0.05$), increased cardiac output significantly from 2.2 ± 0.4 to 2.8 ± 0.6 L/min ($p < 0.01$), reduced 2D left ventricular dyssynchrony significantly from 32.0 ± 8.9 to 23.7 ± 10.0 ms ($p < 0.01$) and reduced 3D left ventricular dyssynchrony significantly from 10.0 ± 2.8 to $6.9 \pm 2.3\%$ ($p < 0.01$) (Table 2) (Figs. 4–7).

After optimization of the interventricular delay according to the level of 3D dyssynchrony, simultaneous BVP was the optimal pacing configuration for three patients (7%). Pre-activation of the left ventricle was optimal for 23 patients (56%) with an interventricular interval of 20 ms for eight patients, 40 ms for five patients, and with left ventricular pacing alone for 10 patients. For the 15 remaining patients (37%), pre-activation of the right ventricular lead was optimal with an interventricular interval of 20 ms for seven patients and 40 ms for eight patients. Compared with simultaneous BVP, individually optimized sequential BVP increased LVEF significantly from 31.0 ± 6.7 to $33.5 \pm 6.9\%$ ($p < 0.05$), increased cardiac output significantly from 2.8 ± 0.6 to 3.1 ± 0.6 L/min ($p < 0.05$) and decreased 3D left ventricular dyssynchrony significantly from 6.9 ± 2.3 to $4.9 \pm 1.8\%$ ($p < 0.01$). 2D left ventricular dyssynchrony was not decreased significantly (23.7 ± 10.0 ms versus 21.5 ± 9.9 ms; $p =$ not significant).

Changes in 3D left ventricular dyssynchrony between simultaneous BVP, right ventricular pacing, left ventricular pacing and sequential BVP exhibited highly significant correlation with changes in cardiac output and LVEF ($r = -0.67$, $p < 0.001$ and $r = -0.68$, $p < 0.001$, respectively). Changes in 2D left ventricular dyssynchrony correlated significantly with changes in cardiac output and LVEF, but with lower

Table 2 Echocardiographic data: baseline, simultaneous and optimized sequential biventricular pacing.

|	Baseline	Simultaneous BVP	Optimized sequential BVP
Cardiac output (L/min)	2.2 ± 0.4	2.8 ± 0.6[b]	3.1 ± 0.6[b,c]
LVEF (%)	27.6 ± 6.7	31.0 ± 6.7[a]	33.5 ± 6.9[b,c]
3D left ventricular dyssynchrony (%)	10.0 ± 2.8	6.9 ± 2.3[b]	4.9 ± 1.8[b,d]
2D left ventricular dyssynchrony (ms)	32.0 ± 8.9	23.7 ± 10.0[b]	21.5 ± 9.9[b]

Results are given as mean values ± standard deviations.
2D: two-dimensional; 3D: three-dimensional; BVP: biventricular pacing; LVEF: left ventricular ejection fraction.
[a] $p < 0.05$ versus baseline.
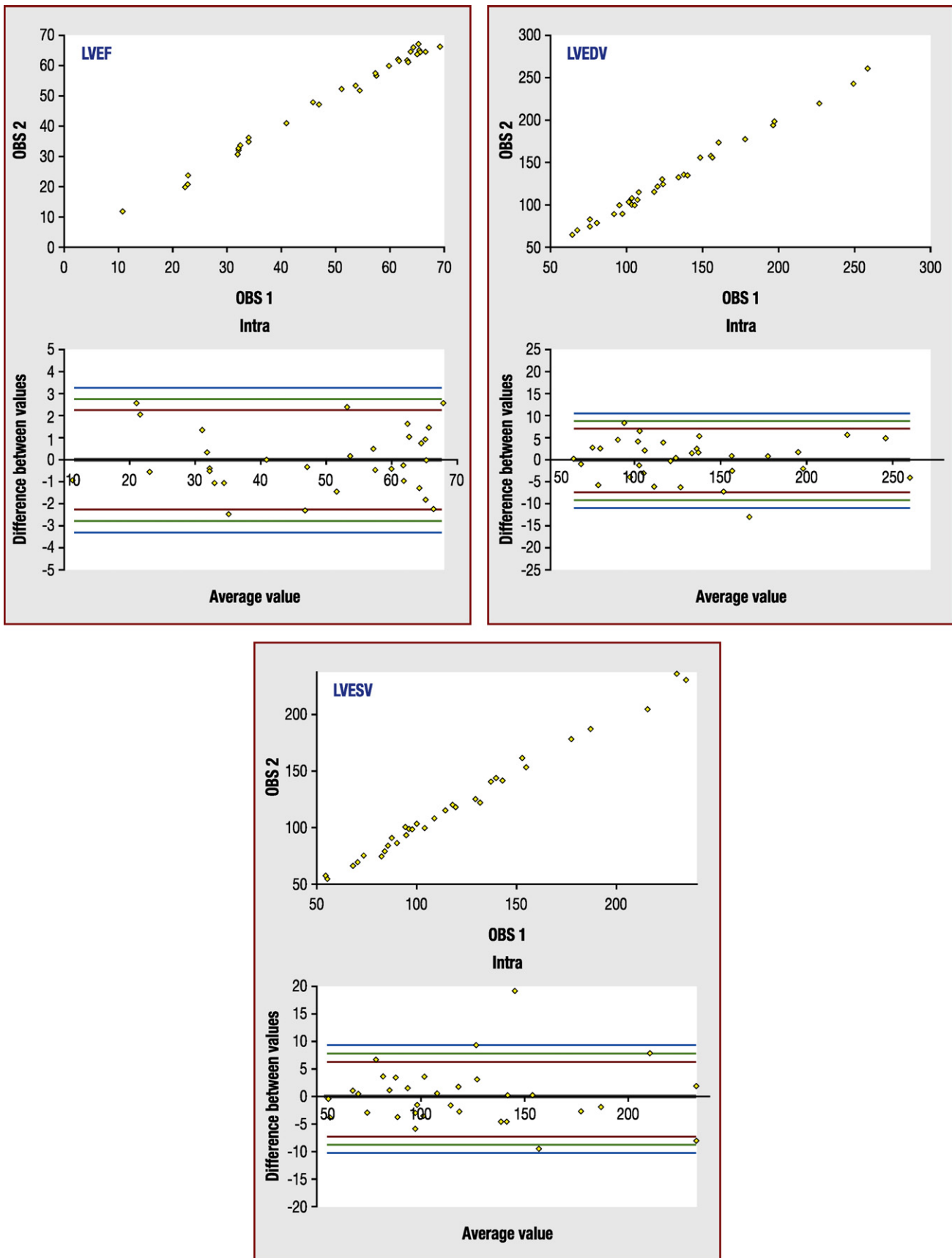[b] $p < 0.01$ versus baseline.
[c] $p < 0.05$ versus simultaneous BVP.
[d] $p < 0.01$ versus simultaneous BVP.
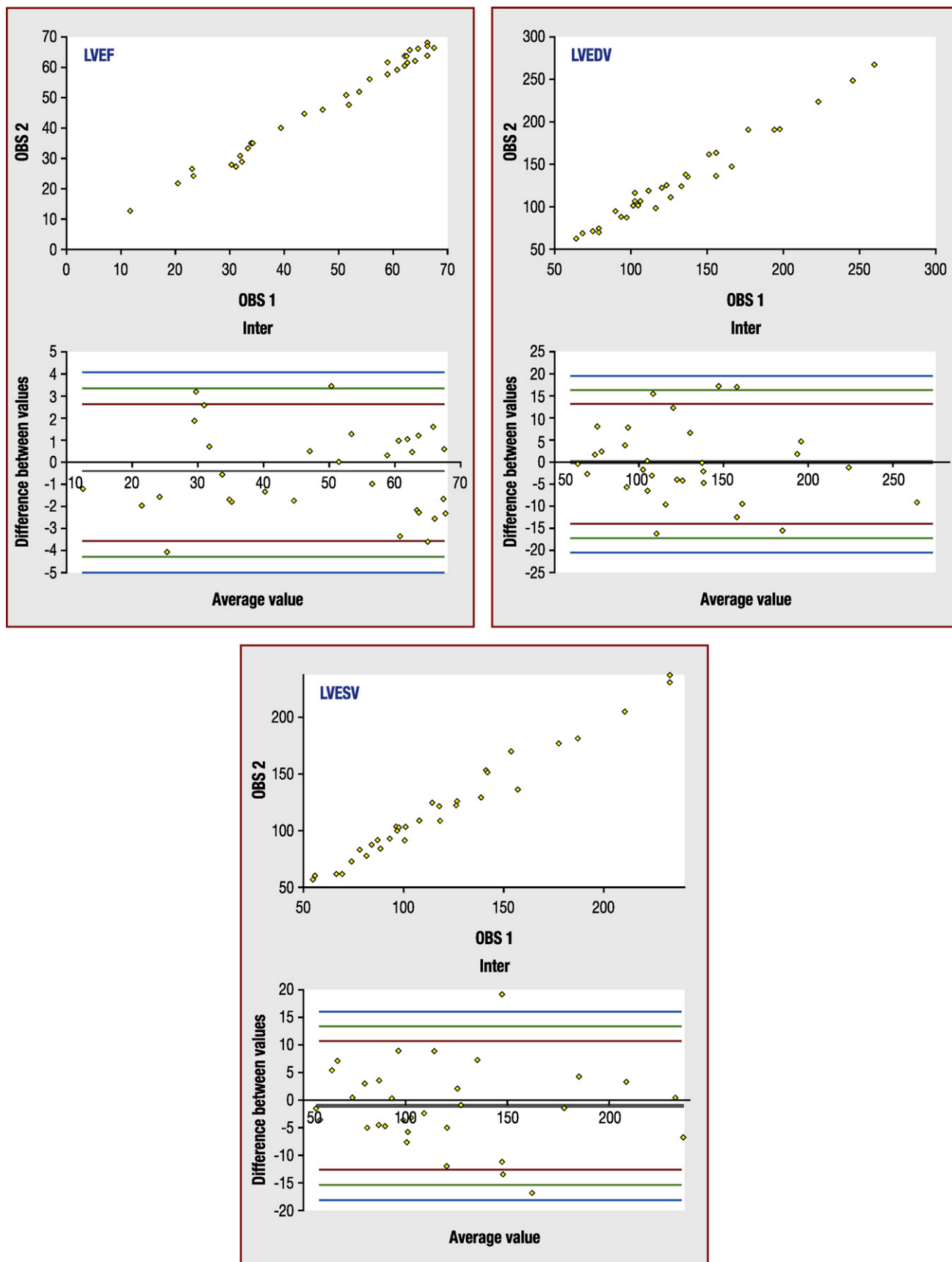
Figure 3. Intraobserver reproducibility in terms of 3D left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV).

Figure 4. Static front map of mechanical activation during spontaneous rhythm, and simultaneous and optimal biventricular pacing configuration based on 3D left ventricular dyssynchrony. In blue, segmental volumes in diastolic time; in red, segmental volumes still in systolic time.
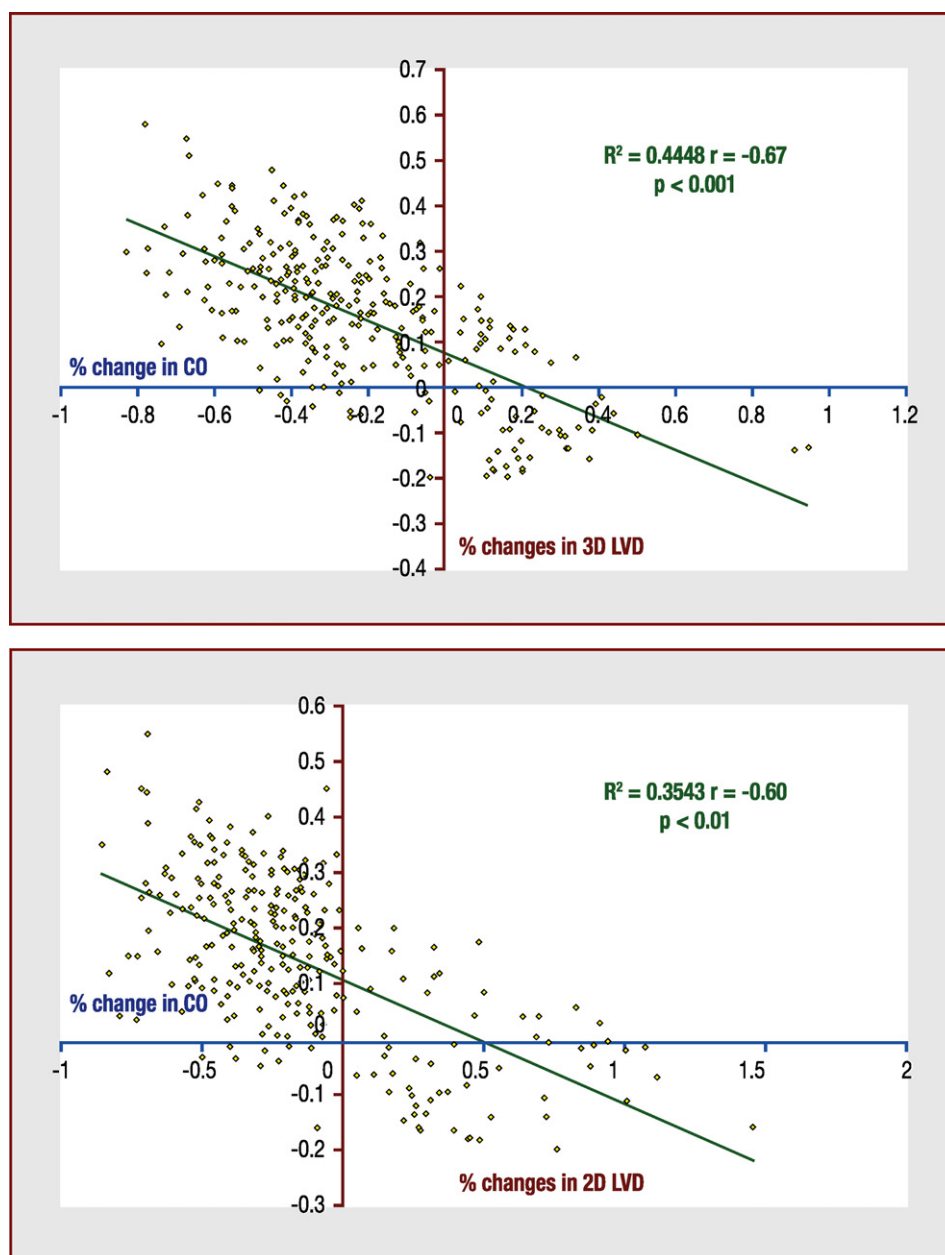
Figure 5.   Correlation between percentage changes in 3D or 2D left ventricular dyssynchrony (LVD) and percentage changes in cardiac output (CO).

r and p values ($r = -0.60$, $p < 0.01$ and $r = -0.56$, $p < 0.05$, respectively). Changes in 2D left ventricular dyssynchrony also correlated significantly with changes in 3D ventricular dyssynchrony ($r = 0.49$; $p < 0.05$).

Mid-term impact of biventricular pacing

After 6 months of simultaneous BVP, NYHA functional class, quality of life score, exercise capacity assessed by the 6-minute walk test and peak exercise oxygen consumption improved significantly compared with baseline. Similarly, 3D echocardiography revealed a significant increase in LVEF ($33.6 \pm 7.2\%$ versus $27.6 \pm 6.7\%$; $p = 0.001$) associated with a significant decrease in left ventricular end-diastolic volume ($144.1 \pm 60.3\,\text{cm}^3$ versus $175.6 \pm 80.2\,\text{cm}^3$; $p < 0.01$),

left ventricular end-systolic volume ($95.7 \pm 48.4\,\text{cm}^3$ versus $127.1 \pm 69.7\,\text{cm}^3$; $p < 0.01$), 3D left ventricular dyssynchrony ($4.9 \pm 1.2\%$ versus $10.0 \pm 2.8\%$; $p < 0.001$) and 2D left ventricular dyssynchrony ($23.6 \pm 8.3\,\text{ms}$ versus $32.0 \pm 8.9\,\text{ms}$; $p < 0.01$) after 6 months of simultaneous BVP.

Thirty-one patients had a 10% reduction in left ventricular end-systolic volume and were considered to be responders to the therapy. NYHA class, quality of life score, exercise capacity and echocardiographic volumes were significantly more improved in responders than in non-responders (Tables 3 and 4). At baseline, the only parameter that differed between responders and non-responders was the level of 3D left ventricular dyssynchrony. Similarly, the reduction in the magnitude of 3D dyssynchrony after implantation was significantly more pronounced in responders than
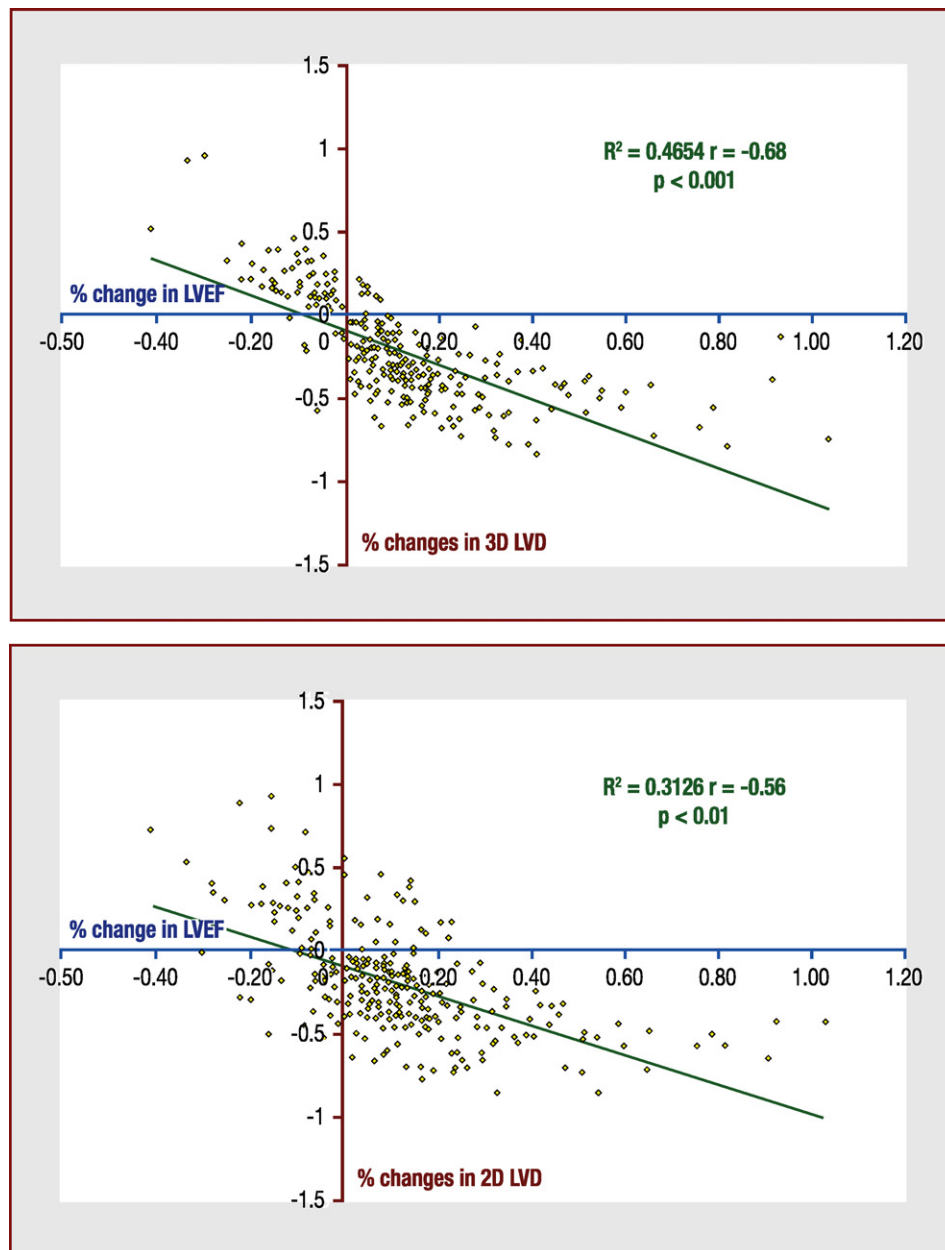
Figure 6. Correlation between percentage changes in 3D or 2D left ventricular dyssynchrony (LVD) and percentage changes in left ventricular ejection fraction (LVEF).

in non-responders. In contrast, neither the pre-implantation magnitude of 2D dyssynchrony nor its reduction after CRT was significantly different in responders versus non-responders.

Discussion

Our study brings new information about the potential impact of 3D echocardiographic software in the measurement of ventricular dyssynchrony. First, 3D measurement of left ventricular volumes and ventricular dyssynchrony in the same acquisition is feasible and reproducible. Second, after implantation of a CRT device, optimization of interventricular delay based on 3D ventricular dyssynchrony allows

greater improvement than simultaneous BVP in terms of acute haemodynamic parameters. Third, changes in 3D dyssynchrony are correlated with changes in haemodynamic parameters, suggesting that this measurement of dyssynchrony is of haemodynamic importance. These correlations are higher than the correlations obtained with 2D dyssynchrony. Finally, we demonstrated significant differences between responders and non-responders in terms of pre-implantation level of 3D dyssynchrony and reduction of ventricular dyssynchrony after BVP. These differences were not significantly different in terms of 2D dyssynchrony.

To reduce the number of non-responders, attempts to identify and quantify mechanical dyssynchrony (the target of the therapy) led to the investigation of the possible role of echocardiography. Conventional and sophisticated
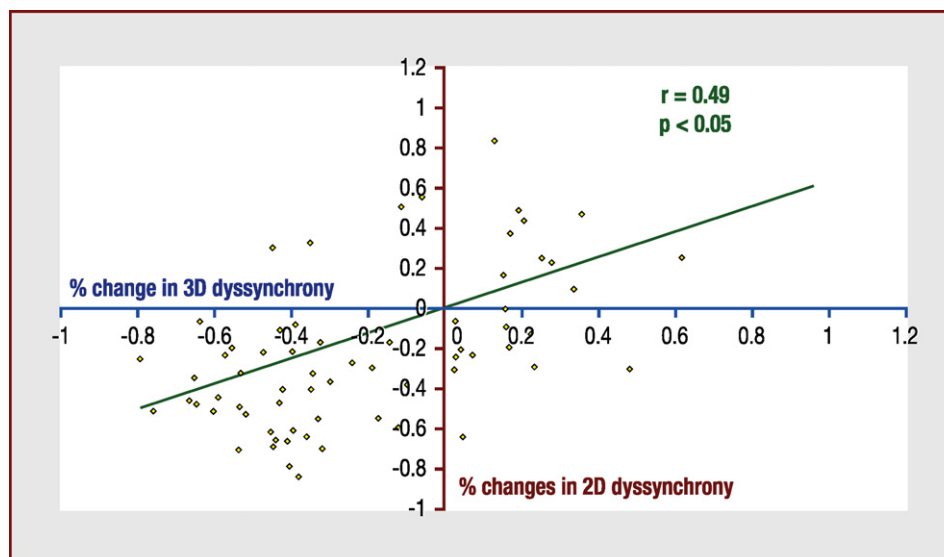
Figure 7. Correlation between percentage changes in 2D ventricular dyssynchrony and percentage changes in 3D ventricular dyssynchrony.

Table 3 Differences in baseline characteristics between responders and non-responders.

Characteristic	Responders($n = 31$)	Non-responders($n = 10$)	p
NYHA class	3.2 ± 0.4	3.0 ± 0.5	0.31
Quality of life score	51.3 ± 14.8	58.4 ± 23.6	0.27
Six-minute walk test (m)	291.1 ± 68.5	312.8 ± 72.3	0.33
Peak exercise oxygen consumption (mL/kg/min)	13.2 ± 4.8	13.9 ± 5.9	0.36
Left ventricular end-diastolic volume (mL)	186.5 ± 86.8	141.7 ± 40.1	0.08
Left ventricular end-systolic volume (mL)	139.5 ± 76.1	100.3 ± 30.5	0.07
LVEF (%)	26.9 ± 6.8	29.7 ± 6.2	0.11
2D left ventricular dyssynchrony index (ms)	33.3 ± 9.2	27.2 ± 6.5	0.11
3D left ventricular dyssynchrony index (%)	11.0 ± 2.4	6.5 ± 1.1	< 0.01
QRS duration (ms)	160.7 ± 19.7	153.5 ± 23.1	0.57

Results are given as mean values ± standard deviations.
LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

Table 4 Comparison of percentage change in baseline characteristics after 6 months of BVP in responders and non-responders.

Characteristic	Percentage change after 6 months		
	Responders($n = 31$)	Non-responders($n = 10$)	p
NYHA class	-37.5 ± 13.1	-10.0 ± 8.2	< 0.01
Quality of life score	-48.5 ± 23.6	-19.0 ± 17.5	< 0.05
Six-minute walk test	$+57.5 \pm 19.8$	$+6.8 \pm 13.7$	< 0.01
Peak exercise oxygen consumption	$+16.6 \pm 6.2$	$+4.3 \pm 4.9$	< 0.05
Left ventricular end-diastolic volume	-21.1 ± 6.9	-3.4 ± 7.3	< 0.01
Left ventricular end-systolic volume	-28.3 ± 7.4	-6.8 ± 4.8	< 0.01
LVEF	$+28.5 \pm 22.2$	$+11 \pm 19.5$	0.24
2D left ventricular dyssynchrony index	-37.5 ± 19.6	-23.1 ± 21.4	0.18
3D left ventricular dyssynchrony index	-54.5 ± 16.3	-17.5 ± 19.8	< 0.01

Results are given as mean values ± standard deviations.
LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

echocardiographic techniques have been investigated extensively but, to date, there is still no gold standard echocardiographic parameter for use in clinical practice [5—9]. Some tissue Doppler imaging parameters of dyssynchrony have clearly been shown to correlate with haemodynamic parameters, to help in optimization of device programming and to predict response after CRT, and are therefore used widely in the literature [5,7,9,16,17]. However, the widespread adoption of these techniques in clinical practice has been limited by aspects of acquisition and analysis, low reproducibility, poor spatial resolution and non-simultaneous evaluation of segmental motion. Only the longitudinal function in the basal and mid-segments are studied. Moreover, the PROSPECT study concluded that no single 2D echocardiographic measurement improved the process of patient selection for CRT reliably [10].

3D echocardiography provides a more accurate determination of left ventricular volumes and systolic function than 2D echocardiography and may become very useful in the field of CRT [11—13]. Indeed, 3D echocardiography may overcome some of the limitations observed with 2D echocardiography. As demonstrated in this study, the reproducibility with a semi-automatic endocardial contour analysis was reliable and seemed superior than that obtained with the 12-segment analysis of 2D dyssynchrony. The reproducibility of an echocardiographic measurement is of major importance if it is to be included in a multicentre study as a selection criterion. Moreover, quantification of mechanical dyssynchrony with 3D echocardiography takes all myocardial segments into account by examining the composite effect of radial, circumferential and longitudinal contraction. 2D and 3D echocardiographic parameters explore different systolic periods (end-systole with 3D echocardiography, peak of systolic velocity with 2D echocardiography). This may explain the difference in terms of correlation of 2D and 3D echocardiographic parameters with haemodynamic status. Changes in 3D dyssynchrony were found to correlate highly with changes in cardiac output and ejection fraction.

Echocardiographic dyssynchrony parameters may help in the management of patients with heart failure, in terms of selecting the candidate for CRT and optimizing the programming of the pacing device after implantation. Before implantation, we demonstrated that future responders exhibited significantly higher 3D dyssynchrony than future non-responders. This seems promising in terms of optimizing the selection of candidates for CRT. In our study, the difference in terms of 2D dyssynchrony did not reach significance, in contrast with data published previously. The limited number of patients may be a possible explanation. Interestingly, responders had a significantly higher decrease in 3D dyssynchrony, suggesting that this parameter may help with the pre-implantation optimization of pacing sites based on an acute maximal reduction of 3D dyssynchrony. Similarly, individually optimized sequential BVP based on 3D dyssynchrony allowed a significant improvement in haemodynamic parameters. Pre-discharge optimization of the interventricular delay may be proposed, despite the need for definite proof of the clinical value of sequential BVP. However, as suggested by the PROSPECT study, no single-centre study can come to a definitive conclusion about the value of an echocardiographic technique in the field of CRT [10]. A multicentre study may be required to confirm our results.

There are limitations to this study and to a 3D assessment of ventricular dyssynchrony. The sample size ($n = 41$) was rather small to determine predictive factors of response, but the protocol, with seven different echocardiographic evaluations, provided enough data for a solid statistical analysis to estimate the haemodynamic significance of the parameters of dyssynchrony. We have demonstrated differences between responders and non-responders in terms of 3D dyssynchrony; however, we did not determine a cut-off value for this parameter that allows selection and/or exclusion of CRT candidates in everyday clinical practice. The semi-automated border detection algorithms are user-friendly, but their use is very limited in patients with a poor ultrasonic window, and the total procedure is still time-consuming. Improved automatic endocardial border detection and a segmental online volume analysis may help to establish the assessment of 3D dyssynchrony as a daily practice clinical method for selecting, monitoring and optimizing CRT. The fact that 2D and 3D dyssynchrony were measured on different echocardiographic machines may have interfered with our data. Finally, the rate of response was high in our study. Patients with a 10% reduction in left ventricular end-systolic volume were considered to be responders to the therapy; a threshold of 15% might have yielded different results.

Conclusion

This prospective echocardiographic study provides new information about the potential impact of 3D echocardiographic software in the measurement of ventricular dyssynchrony and demonstrates the additional value of 3D assessment of ventricular dyssynchrony in predicting the response after BVP and optimizing the pacing configuration.

References

[1] Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med 2002;346: 1845—53.

[2] Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med 2004;350:2140—50.

[3] Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med 2005;352:1539—49.

[4] Reuter S, Garrigue S, Barold SS, et al. Comparison of characteristics in responders versus nonresponders with biventricular pacing for drug-resistant congestive heart failure. Am J Cardiol 2002;89:346—50.

[5] Bax JJ, Marwick TH, Molhoek SG, et al. Left ventricular dyssynchrony predicts benefit of cardiac resynchronization therapy in patients with end-stage heart failure before pacemaker implantation. Am J Cardiol 2003;92:1238—40.

[6] Breithardt OA, Stellbrink C, Kramer AP, et al. Echocardiographic quantification of left ventricular asynchrony predicts an acute hemodynamic benefit of cardiac resynchronization therapy. J Am Coll Cardiol 2002;40:536—45.

[7] Sogaard P, Egeblad H, Kim WY, et al. Tissue Doppler imaging predicts improved systolic performance and reversed left ventricular remodeling during long-term cardiac resynchronization therapy. J Am Coll Cardiol 2002;40:723—30.

[8] Yu CM, Fung JW, Zhang Q, et al. Tissue Doppler imaging is superior to strain rate imaging and postsystolic shortening on the prediction of reverse remodeling in both ischemic and nonischemic heart failure after cardiac resynchronization therapy. Circulation 2004;110:66—73.

[9] 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 2003;91:684—8.

[10] Chung ES, Leon AR, Tavazzi L, et al. Results of the predictors of response to CRT (PROSPECT) trial. Circulation 2008;117:2608—16.

[11] Jenkins C, Bricknell K, Hanekom L, et al. Reproducibility and accuracy of echocardiographic measurements of left ventricular parameters using real-time three-dimensional echocardiography. J Am Coll Cardiol 2004;44:878—86.

[12] Sugeng L, Mor-Avi V, Weinert L, et al. Quantitative assessment of left ventricular size and function: side-by-side comparison of real-time three-dimensional echocardiography and computed tomography with magnetic resonance reference. Circulation 2006;114:654—61.

[13] Kapetanakis S, Kearney MT, Siva A, et al. Real-time three-dimensional echocardiography: a novel technique to quantify global left ventricular mechanical dyssynchrony. Circulation 2005;112:992—1000.

[14] Gola A, Pozzoli M, Capomolla S, et al. Comparison of Doppler echocardiography with thermodilution for assessing cardiac output in advanced congestive heart failure. Am J Cardiol 1996;78:708—12.

[15] Kindermann M, Frohlig G, Doerr T, et al. Optimizing the AV delay in DDD pacemaker patients with high degree AV block: mitral valve Doppler versus impedance cardiography. Pacing Clin Electrophysiol 1997;20:2453—62.

[16] Bader H, Garrigue S, Lafitte S, et al. Intra-left ventricular electromechanical asynchrony. A new independent predictor of severe cardiac events in heart failure patients. J Am Coll Cardiol 2004;43:248—56.

[17] Bordachar P, Lafitte S, Reuter S, et al. Echocardiographic parameters of ventricular dyssynchrony validation in patients with heart failure using sequential biventricular pacing. J Am Coll Cardiol 2004;44:2157—65.