**Introduction and objectives.** Cardiac resynchronization therapy has been shown to be an option in the treatment of patients with congestive heart failure. The current indication for this treatment is based on clinical and electrocardiographic criteria, although echocardiography has also been shown to be a useful tool for the diagnosis of ventricular dyssynchrony. The aim of this study was to assess left ventricular dyssynchrony by echocardiography and to evaluate the effect of the stimulation site on the magnitude of resynchronization.

**Patients and method.** We studied 25 patients with biventricular stimulation (left ventricular lead located in a lateral position in 13 patients, and in an anterior position in 12). A complete echo-Doppler evaluation, including left ventricular ejection fraction, ventricular diameters and parameters of inter- and intraventricular dyssynchrony, was performed before implantation and 3 months after the procedure, with the device connected and disconnected.

**Results.** Left ventricular ejection fraction increased significantly from 23.7 (6.5) to 27.8 (5.5) \( (P=0.007) \) at 3 months. In the group as a whole, biventricular pacing was associated with a significant decrease in all intraventricular dyssynchrony parameters (septal-to-lateral wall motion delay and septal-to-posterior wall motion delay). This decrease in septal-to-posterior wall motion delay and septal-to-lateral wall motion delay was significantly greater in patients with the electrode implanted in the lateral position (58.1 ms vs 118 ms; \( P=0.02 \)) than with the lead in the anterior position (39.5 ms vs 86.5 ms; \( P=0.04 \)). Three patients, all with the electrode in an anterior location, were considered non-responders.

**Conclusions.** Left lateral free wall stimulation provided significantly better intraventricular resynchronization compared to stimulation at an anterior site. Echocardiography is a useful tool to evaluate changes in intra- and interventricular synchrony related to the pacing site.

**Key words:** Heart failure. Cardiac resynchronization therapy. Biventricular pacing. Pacemaker. Echocardiography.

**Effecto de la localización del electrodo ventricular izquierdo sobre los parámetros ecocardiográficos de asincronía en pacientes sometidos a terapia de resincronización cardíaca**

**Introducción y objetivos.** La terapia de resincronización ha mostrado su eficacia como alternativa al tratamiento de pacientes con insuficiencia cardíaca. Las indicaciones actuales se basan en criterios clínicos y electrocardiográficos, aunque la ecocardiografía es una herramienta útil para el diagnóstico de asincronía. El objetivo de este estudio es valorar la asincronía ventricular mediante ecocardiografía, así como el efecto resincronizador según la localización del electrodo ventricular izquierdo.

**Pacientes y método.** Se estudió a los primeros 25 pacientes (13 con el electrodo en posición lateral y 12, anterior) sometidos a terapia de resincronización. Se valoraron ecocardiográficamente, además de la fracción de eyeción y los diámetros ventriculares, los parámetros de asincronía inter e intraventricular antes del implante y a los 3 meses, con el dispositivo conectado y desconectado.

**Resultados.** La fracción de eyeción mejoró de 23,7 ± 6,5% hasta 27,8 ± 5,5% a los 3 meses \( (p = 0.007) \). La estimulación biventricular en cualquier localización se asoció a una mejora significativa de todos los parámetros de asincronía intraventricular (retraso septo-pared posterior y retraso septo-pared lateral). Se observó una disminución significativa, tanto del retraso septo-pared posterior (58,1 frente a 118 ms; \( p = 0.02 \)) como del retraso septo-pared lateral (39,5 frente a 86,5 ms; \( p = 0.04 \)), en los pacientes con el electrodo en posición anterior. Tres pacientes, todos con el electrodo en posición anterior, fueron considerados no respondedores.

**Conclusiones.** La estimulación desde la región lateral del ventriculo izquierdo se asocia a una mejor corrección de los parámetros de asincronía intraventricular que la estimulación desde la zona anterior. La ecocardiografía es una técnica útil para valorar los cambios de la sincronía intra e interventricular según las diferentes zonas estimuladas.
unacceptable electrical parameters in the target area or other technical difficulties. The lateral or post-lateral part of the left ventricle has been identified as the site that provides greatest acute hemodynamic benefit, particularly for $dp/dt$, but the effect of left ventricular electrode site on echocardiographic parameters after resynchronization has yet to be determined.

The objective of the present study was to assess intra- and interventricular dyssynchrony with Doppler echocardiography before and at 3 months after implantation of an atrio-biventricular pacing device and to quantify how the degree of resynchronization varies according to site of left ventricular pacing in patients with advanced heart failure who underwent CRT.

PATIENTS AND METHODS

Study Population

From a series of 49 patients who underwent CRT, we selected the first 13 with lateral left ventricular implantation of the electrode and the first 12 with the electrode implanted in the anterior position. All had chronic heart failure of NYHA functional class III or IV despite maximum tolerated medication, left ventricular dysfunction (ejection fraction <35%), sinus rhythm and left bundle branch block with a QRS complex duration >120 ms. Patients with acute heart failure, valve disease or ischemic heart disease treatable by surgery, those indicated for conventional pacemakers, and those with permanent atrial fibrillation were excluded from the study.

Study Procedures

Clinical history, a 12-lead electrocardiogram (ECG) and a Doppler echocardiogram were recorded, and a physical examination was performed for all patients before implantation of the device. All had chronic heart failure of NYHA functional class III or IV despite maximum tolerated medication, left ventricular dysfunction (ejection fraction <35%), sinus rhythm and left bundle branch block with a QRS complex duration >120 ms. Patients with acute heart failure, valve disease or ischemic heart disease treatable by surgery, those indicated for conventional pacemakers, and those with permanent atrial fibrillation were excluded from the study.

Echocardiographic Study

The echocardiographic study (Sonos 5500, Hewlett-Packard, 3 MHz probe) was performed in left lateral decubitus before implantation of the resynchronization device (baseline conditions) and after 3 months with atrio-biventricular pacing (device connected) and without pacing (device disconnected). Images were taken in the parasternal long- and short-axis views, two- and four-chamber apical views, and subxiphoid
Device Implantation

Implantation was performed in an electrophysiology laboratory equipped with a Hicor digital angiography system (Siemens). The procedure was performed under local anesthetic with normal venous approaches (subclavian and/or cephalic vein) using previously described techniques.

All patients underwent angiography of the coronary venous system, and the left ventricular electrode was implanted preferably in the lateral region. An anterior site was chosen as a last resort if lateral implantation was not possible or if a lateral site produced unacceptable pacing thresholds.

The atioventricular interval was optimized by echo-Doppler technique and by previously described methods in all patients. We checked that the generator was functioning correctly on discharge from hospital by measurement of thresholds and radioscopic control of the electrodes.

An observer, who did not participate in any other way in the study, analyzed the difference between maximum width of the QRS complex during pacing and width of the complex at baseline in each patient.

Site of Left Ventricular Electrode

The anterior zone was defined as lying between 10 and 1 o’clock and the lateral zone as lying between 2 and 5 o’clock in the 45° left anterior oblique projection (Figure 1).

The first 13 consecutive patients with the ventricular electrode in the lateral or posterolateral position and the first 12 consecutive patients with the electrode in the anterior position were included.

The parameters at baseline and after resynchronization were first compared for all 25 consecutive patients.
patients of the overall population and then analyzed by the final left ventricular pacing site.

**Statistical Analysis**

The numerical results from the study are expressed in the study as mean±standard deviation. The Kolmogorov-Smirnov test, with the Lillefors correction, was used to evaluate how well the data fitted a normal distribution. The differences in percentages between groups were compared with the exact test (PEPI statistics package, Abramson and Gahlinger, 1993-2000). The differences between different variables were compared by the Student t-test for dependent and independent samples as appropriate. Statistical significance was set at \( P < .05 \).

**RESULTS**

All devices were pacing correctly when the patients were discharged from hospital and after 3 months. The demographic and clinical characteristics of the overall patient group are presented in Table 1.

Twenty patients received a Guidant TR 1241 resynchronization device and 5 an automatic defibrillator with biventricular pacing capability (Guidant H135 and 1823). The mean acute pacing threshold was 1.4±0.6 volts, with mean left ventricular electrode impedance of 1.082±307 Ohms and amplitude of 11.1±5.7 millivolts.

At 3 months, an improvement in ejection fraction (23.7±6.5 at baseline vs 27.8±5.5% after 3 months) and a decrease in end-diastolic diameter of the left ventricle were observed after CRT (72.9±8.2 mm at baseline vs 65.6±6.6 mm at 3 months). This was associated with an increase in the aortic flow velocity integral (19.6±4.3 at baseline vs 21.3±4.9 at 3 months) and a decrease in the ratio of mitral flow to mitral annulus velocity (E/E’) (15.7±5.7 at baseline vs 10.7±5.3 at 3 months). The ejection fraction and aortic flow velocity integral improved significantly only in the group of patients with lateral pacing, whereas end-diastolic diameter and E/E’ ratio improved with both lateral pacing and anterior pacing (Table 2).

**Electrocardiographic Parameters**

The mean duration of the baseline QRS complex was 159.9±29.4 ms. After biventricular stimulation, this duration was 157.8±20.2 ms (\( P = .77 \)).

No statistically significant differences were seen in the width of the QRS complex before and after implantation of the resynchronization device regardless of whether pacing was lateral (156.0±33.8 ms vs 154.7±18.2 ms; \( P = .58 \)) or anterior (161.9±25.3 ms vs 160.9±22.6 ms; \( P = .23 \)).

**Interventricular Dyssynchrony**

The electromechanical delay between left and right ventricle was similar on comparison of baseline with

3 months pacing regardless of whether the device was connected (38.3±22.3 ms at baseline vs 31.1±24.2 ms after 3 months; *P*=.35) or disconnected (38.3±22.3 ms at baseline vs 37.8±21.8 ms after 3 months; *P*=.42). Similarly, when the same parameters were compared according to anterior or lateral pacing, no statistically significant differences were observed (Table 3).

**Intraventricular Dyssynchrony**

Septal-posterior-wall motion delay was significantly lower after 3 months of pacing when measured with the pacing device connected (86.6±35.4 ms at 3 months; Figure 2) compared to measurement with the device disconnected (218.3±44.7 ms; Figure 2) in the overall patient population (*P*<.001). When the device was disconnected, baseline SPWMD and SPWMD at 3 months showed no significant differences (218.3±44.7 vs 211.6±34.7 ms; *P*=.56).

Similarly, resynchronization was also associated with a statistically significant decrease (*P*=.007) in SLWMD at baseline (111.4±30.9 ms) compared to SLWMD at 3 months with the device connected (61.9±21.3 ms; Figure 3). Baseline SLWMD was similar to SLWMD with the device disconnected at the end of follow-up (111.4±30.9 vs 115.3±28.6; *P*=.58).

Both SPWMD and SLWMD were significantly smaller in patients with lateral pacing compared to those with anterior pacing (Table 3).

**Events During Follow-Up**

Of the 25 patients, 3 (16%) were considered non-responders to treatment because their NYHA functional class remained unchanged and/or the number of meters covered in the 6-minute walk test did not increase by >10%. All 3 non-responders had anterior pacing of the left ventricle.

**DISCUSSION**

The tissue echo-Doppler technique in M-mode used in this study shows that SPWMD and SLWMD return to normal after implantation of a cardiac resynchronization device. These findings agree with other studies in which intraventricular electromechanical delay (SPWMD and SLWMD) improves after resynchronization, and such parameters may even be useful for predicting benefit from CRT. Maximum systolic velocity of the septum and the left ventricular free wall and the delay in contraction between these areas were assessed by...
tissue echo-Doppler techniques. The specificity and sensitivity of the delay was approximately 90% for prediction of clinical improvement after CRT.18 This study specifically shows the influence of the left ventricular electrode site on the correction of intraventricular dyssynchrony. We are not aware of any studies that assess medium-term response to CRT by site of ventricular stimulation. The parameters that were measured in our population improved after 3 months with both lateral and anterior pacing. For lateral pacing, the improvement was large and statistically highly significant, in contrast to the small improvements with anterior pacing that were not statistically significant. Likewise, the improvement in ejection fraction and aortic flow velocity integral was only significant for lateral pacing, which reinforces the results for resynchronization. The effectiveness of resynchronization may be greater when the electrode is in a lateral position because there is a larger distance between the right and left ventricular electrodes. The two fronts of activation are therefore further apart, in contrast to anterior implantation, which places the left ventricular electrode much closer to the right ventricular electrode. Similarly, our findings might explain the improved hemodynamic effects (indicated by dp/dt) for lateral implantation of the electrode compared to anterior implantation.19 A recent observational study found a similar clinical effect for patients with lateral and anterior implantation of the electrode,20 but there are no randomized studies to compare the effect on medium-term clinical outcome of the two sites in patients who undergo resynchronization.

The importance of the site of the electrode in determining which patients are non-responders remains to be clarified. The 3 non-responders in our patient population had anterior pacing. Our conclusions are necessarily limited by the low number of patients, but these results do suggest that it is advisable to choose lateral implantation of the left ventricular electrode whenever possible despite the greater technical difficulties.21 Unfortunately, lateral implantation may not be possible in more than 30% of the patients because of unfavorable venous anatomy, high pacing thresholds, instability of the electrode, or the presence of phrenic pacing.20 No differences in interventricular dyssynchrony were found and device implantation seemed to have little effect, possibly because of the low degree of interventricular dyssynchrony observed in our patients. These results agree with some studies,22 but

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**TABLE 3. Intra- and Interventricular Dyssynchrony According to Pacing Site**

<table>
<thead>
<tr>
<th></th>
<th>Lateral (n=13)</th>
<th>Anterior (n=12)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Posterior septal wall motion delay, ms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>189.3±51.2</td>
<td>231.4±39.8</td>
<td>.47</td>
</tr>
<tr>
<td>3 months CRT “on”</td>
<td>58.1±28.4</td>
<td>118.0±54.1</td>
<td>.02</td>
</tr>
<tr>
<td>3 months CRT “off”</td>
<td>194.1±75.0</td>
<td>254.2±81.2</td>
<td>.22</td>
</tr>
<tr>
<td><strong>Lateral septal wall motion delay, ms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>120.6±24.6</td>
<td>112.8±21.2</td>
<td>.65</td>
</tr>
<tr>
<td>3 months CRT “on”</td>
<td>39.5±13.3</td>
<td>86.5±27.5</td>
<td>.04</td>
</tr>
<tr>
<td>3 months CRT “off”</td>
<td>115.4±22.3</td>
<td>107.0±33.3</td>
<td>.79</td>
</tr>
<tr>
<td><strong>Interventricular dyssynchrony, ms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>37.6±8.4</td>
<td>36.5±9.3</td>
<td>.81</td>
</tr>
<tr>
<td>3 months CRT “on”</td>
<td>35.3±16.1</td>
<td>28.1±10.3</td>
<td>.32</td>
</tr>
<tr>
<td>3 months CRT “off”</td>
<td>38.1±9.8</td>
<td>38.5±9.0</td>
<td>.97</td>
</tr>
</tbody>
</table>

Data are expressed as mean±standard deviation.

*CRT indicates cardiac resynchronization therapy; CRT “off,” without cardiac resynchronization therapy; CRT “on,” with cardiac resynchronization therapy; 3 months, evaluation after 3 months of follow-up.
others find a clear improvement in interventricular
dys synchrony during CRT.23 This discrepancy might
arise because the difference in the electromechanical
delays of the 2 ventricles does not fully correlate with
the dys synchrony of the left ventricular free wall.24
In agreement with other studies, CRT was associat-
ed with an improvement in ejection fraction and a
reduction in end-diastolic diameter at 3 months in
patients with lateral pacing, suggesting that regression
of ventricular remodeling may occur in these
patients.25 The same dys synchrony persists at 3
months with the device disconnected. We might
expect improvement in dys synchrony after a positive
change in ventricular remodeling, but the persistence
of conduction disorders may counteract the improved
ventricular remodeling so the degree of dys synchrony
remains unchanged. We also found that CRT
decreased the ratio of E/E'. Values for this ratio above
15 have been associated with increased ventricular
filling pressures as assessed by echocardiography.26
Currently, the main criterion for diagnosis of
dys synchrony is left bundle branch block as evidenced
by QRS complex duration >120 ms. However, left
bundle branch block does not always lead to
alterations in ventricular synchrony and may be the
result of other anomalies such as actual conduction
defects or slowing of propagation of the electrical
impulse in ischemic or necrotic tissue.27 In fact, our
study showed no differences in the width of the QRS
complex before and after resynchronization. This
width does not correlate with the degree of
resynchronization after implantation even though a
width of around 150 ms has been shown to
discriminate between responders and non-responders
to CRT.28 Our findings agree with other studies which
show little association between the number of
responders and narrowing of the QRS complex with
biventricular pacing.29 Given that the width of the
QRS complex, the degree of dys synchrony and
response to CRT are poorly correlated, the echo-
Doppler technique may prove a useful tool for
diagnosis of dys synchrony in order to reduce the
proportion of non-responders. This potential
application should be investigated in prospectively
designed studies.

Study Limitations

The pacing site was not randomly assigned but
rather chosen according to accessibility and electrical
parameters. We therefore cannot separate the effects of
the site of electrode implantation from other factors
(whether anatomical or of some other kind) that
prevented implantation in the lateral site.

The electromechanical and ejection delays of the
different chambers were recorded from different heart
cycles and so were inevitably subject to beat-to-beat
variations.

The methods available at present for quantifying
dys synchrony are limited in a number of ways. First,
tissue Doppler techniques do not differentiate between
passive and active movement of the myocardial wall.
Deformation measures known as the strain rate would
be needed for better quantification. Second, for the
measurement of SPWMD in M-mode, 2 small areas of
the myocardium were compared on the assumption
that they were representative of the entire wall
movement. A further source of error may lie in the
assumption that exactly the same wall segment was
used for with and without resynchronization. Finally,
the limitations of the calculation of the ejection
fraction with the Teichholtz formula, particularly in
patients with segmental contraction disorders, are well
known.

CONCLUSIONS

Lateral pacing of the left ventricle is associated with
greater intraventricular resynchronization than anterior
pacing after implantation of a cardiac
resynchronization device. Measurement of SPWMD
and SLWMD by echocardiography is useful for
diagnosis of intraventricular dys synchrony, can help
assess changes in synchrony according to the pacing
site and may contribute to an evaluation of the
effectiveness of CRT.

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