Influence of Cardiopathy Etiology on Responses to Cardiac Resynchronization Therapy

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Introduction and objectives. Little is known about how responses to cardiac resynchronization therapy (CRT) are affected by the nature of the underlying cardiopathy. The aim of this study was to investigate how cardiopathy etiology influences the effect of CRT on reverse left ventricular remodeling.

Methods. The study included 106 patients with left ventricular systolic dysfunction and left bundle branch block (LBBB) who were receiving CRT. Clinical and echocardiographic investigations were performed at baseline before implantation and at 6 and 12 month follow-up to determine left ventricular diameter, volume, and systolic function, and to quantify mitral regurgitation.

Results. During follow-up, it was observed that CRT reduced left ventricular volume and diameter, increased left ventricular ejection fraction (LVEF), and reduced mitral regurgitation severity irrespective of the etiology of the cardiopathy. In patients with ischemic dilated cardiomyopathy, LVEF increased by 34% and end-diastolic and end-systolic volumes decreased by 4% and 12%, respectively; in those with idiopathic dilated cardiomyopathy, LVEF increased by 38% and end-diastolic and end-systolic volumes decreased by 13% and 19%, respectively (*P*=NS for ischemic vs non-ischemic disease). Nor were differences observed between the groups in clinical outcome: 74% of the ischemic group responded compared with 62% of the non-ischemic group (*P*=NS).

Conclusions. At 12-month follow-up, patients with left ventricular systolic dysfunction and LBBB treated by CRT showed clinical improvements and demonstrated reverse ventricular remodeling, irrespective of the etiology of their cardiopathy.

Key words: *Echocardiography. Imaging. Pacemaker. Ventricular remodeling.*

Influencia de la cardiopatía subyacente en la respuesta a la terapia de resincronización cardiaca

Introducción y objetivos. La influencia del tipo de cardiopatía en la respuesta a la terapia de resincronización cardiaca (TRC) es poco conocida. El objetivo de este estudio fue analizar el efecto de la TRC en el remodelado, en función de la etiología de la cardiopatía subyacente.

Métodos. Se incluyó a 106 pacientes con disfunción sistólica del ventrículo izquierdo (VI) y bloqueo de rama izquierda del haz de His (BRIHH) tratados con TRC. Se les realizó una evaluación clínica y ecocardiográfica para estudiar los diámetros, los volúmenes y la función sistólica del VI y cuantificar la insuficiencia mitral, antes del implante y a los 6 y los 12 meses de seguimiento.

Resultados. La TRC indujo en el seguimiento una reducción de los volúmenes y diámetros ventriculares, aumentó la fracción de eyección (FE) y se redujo la insuficiencia mitral independientemente de la etiología de la cardiopatía: los pacientes isquémicos (MCD-CI) incrementaron la FE del VI (FEVI) un 34% y los volúmenes telediastólico y telesistólico se redujeron en el 4 y el 12% frente a un incremento de la FE del 38% y una reducción de volúmenes del 13 y el 19% en los pacientes con miocardiopatía dilatada idiopática (MCD) (sin diferencia significativa entre MCD-CI y MCD). Tampoco se encontraron diferencias en el número de respondedores clínicos: el 74% en los pacientes con MCD-CI y el 62% de los portadores de una MCD (sin diferencia significativa).

Conclusiones. A los 12 meses de seguimiento, los pacientes con disfunción sistólica del VI y BRIHH tratados con TRC presentaron mejoría clínica y un remodelado ventricular inverso independientemente de la etiología de su cardiopatía.

Palabras clave: *Ecocardiografía. Imagen. Marcapasos. Remodelado ventricular.*

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ABBREVIATIONS

CRT: cardiac resynchronization therapy
DCM: nonischemic dilated cardiomyopathy
EF: ejection fraction
IDCM: ischemic dilated cardiomyopathy
LBBB: left bundle branch block
LV: left ventricular
LVEF: left ventricular ejection fraction
MR: mitral regurgitation

INTRODUCTION

Cardiac resynchronization therapy (CRT) is an effective treatment for patients with advanced heart failure and left bundle branch block (LBBB). It improves their symptoms and reduces mortality.[1,2] In addition, it causes reverse ventricular remodeling,[1-3] with a progressive reduction of ventricular diameters and volumes, which is more evident in patients who respond clinically to CRT.[2,4-6]

However, this benefit is not observed in all patients and all series report a lack of response in 30% of the cases.[6,7] A range of echocardiographic and clinical variables have been proposed as possible markers of non-response, including the etiology of the underlying heart disease of the patient. It is still a point of discussion whether the ischemic origin of the disease is a predictor of non-response,[8] as the few studies on the subject are inconclusive.[9-11]

In view of this lack of information, the main aim of this study was to analyze whether there were any differences in clinical response and the extent of ventricular remodeling according to the etiology of the underlying heart disease in our series of patients treated with CRT.

METHODS

We included 106 consecutive patients with ischemic dilated cardiomyopathy (IDCM) or nonischemic dilated cardiomyopathy (DCM) treated with CRT (between June 2003 and December 2005). The etiology of the heart disease was considered ischemic when significant disease was found (stenosis ≥50%) in 1 or more epicardial arteries in a recent coronary angiogram (perfomed < 6 months earlier).[12]

The criteria for the indication of CRT were as follows: *a)* functional class III-IV heart failure according to the New York Heart Association (NYHA) classification despite medical treatment or NYHA class II failure if the patient had covered <350 m in the 6-minute walk test and met criteria b and c; *b)* left ventricular ejection fraction (LVEF) ≤35%; and *c)* QRS >120 ms regardless of cardiac rhythm. Patients were excluded on the following grounds: *a)* treatable heart disease; *b)* heart transplantation scheduled within 6 months; or *c)* short life expectancy.

The study was approved by the ethics committee and informed consent was obtained from all patients.

Study Design and Objectives

The study protocol included a baseline evaluation of the patient by transthoracic echocardiography to analyze left ventricular (LV) morphology and function; a clinical evaluation to determine the functional class according to the NYHA classification, the distance covered in the 6-minute walk test; and the patient's quality of life with the Minnesota Living With Heart Failure questionnaire for assessing the well-being of such patients (lower score, higher quality of life) translated into Spanish and duly validated were also performed.[13] The same echocardiographic study was repeated between 24 and 72 hours after device placement and at 6 and 12 months of follow-up. The same clinical assessment was also undertaken at 6 and 12 months. Patients were considered as clinical responders if they were alive without having received a heart transplant and had increased the distance covered in the 6-minute walk test by at least 10%. Reverse remodeling was considered to have occurred when LVEF increased by 5 points (Δ5%) and/or end-systolic volume decreased by 15%.[14-17]

Device Placement

Each patient received a 3-chamber pacemaker with or without defibrillator in line with the clinical indication according to the current guidelines.[18] One electrode was placed in the right atrium if the patient was in sinus rhythm, 1 at the apex of the right ventricle, and 1 in a posterolateral branch through the coronary sinus.

Echocardiography

Echocardiographic studies were done with a conventional commercially available device (Vivid 7; General Electric-Vingmed, Milwaukee, Wisconsin, USA). In each study, the same variables were assessed: LV end-diastolic and end-systolic diameters were measured with M mode in the long axis parasternal view, LVEF and volumes were quantified with the Simpson method in the 4- and 2-chamber apical view, and cardiac load was calculated using quantitative Doppler technique in accordance with the recommendations of the American Society of Echocardiography.[19] If the patient showed mitral regurgitation (MR), this was quantified with the proximal isovelocity surface area method,[20] and if tricuspid regurgitation allowed an atrioventricular gradient to be obtained by quantitative Doppler measurement, the

systolic pressure in the pulmonary artery was estimated. Likewise, we studied whether interventricular asynchrony was present with pulsed Doppler techniques, calculating the difference between the pulmonary and aortic preejection times. Intraventricular asynchrony, was also assessed with M mode, by measuring the time elapsed from maximum septal contraction to peak contraction of the posterior wall.[21]

Inter- and intraobserver variations in our laboratory for measurement of different cardiac dimensions were 4.6% (2.8%-5.3%) and 3.5% (2%-4.5%), respectively.

All studies were stored in digital format and analyzed off-line by experienced echocardiographers who, not being involved in the clinical follow-up of the patient, were unaware of whether the patients were clinical responders to CRT or not.

Statistical Analysis

A general descriptive analysis was undertaken. Quantitative variables were expressed as mean (SD) and qualitative ones as absolute frequencies, and percentages. For comparison of the echocardiographic variables before and after starting CRT, a Student *t* test was used for paired data with a Bonferroni correction when multiple comparisons were made. Qualitative variables were compared with the χ^2 test. The functional class before and after CRT was analyzed with the Wilcoxon test. A *P* value less than .05 was considered significant. Data were analyzed with the SPSS software package, version 11.0.

RESULTS

Baseline Clinical and Echocardiographic Characteristics

In total, 106 consecutive patients treated with CRT were prospectively included (age, 69 [8] years; 84 [78%] were men). Eleven patients (10%) were in atrial fibrillation. The patients completed 12 months of follow-up. Baseline echocardiography showed a severe systolic dysfunction with a mean LVEF of 23 [7]%—and severe LV dilation (end-systolic and end-diastolic diameters, 73 [8] mm and 60 [9] mm, respectively). Mitral regurgitation was reported in 44 (41%) patients. Significant (nontrivial) regurgitation was considered when the regurgitant volume was 10 mL/beat. Overall, 71 patients (67%) were in NYHA functional class II; 10 (9%) in functional class IV; and 25 (23%) in functional class II. Of those in functional class II, all covered less than 350 m in the 6-minute walk test. Patients covered on average 309 [139] m in the 6-minute walk test. The baseline characteristics are shown in Table 1.

43 (40%) patients had IDCM and 63 (60%) had nonischemic DCM. The baseline clinical and echocardiographic characteristics of the 2 groups are shown in Tables 2 and 3, respectively. Among the patients with IDCM, 39 (90%) had a history of myocardial infarction with no other clinically significant differences compared to patients with IDCM (Table 2). In addition,

TABLE 1. **Overall Baseline Clinical and Echocardiographic Characteristics at 6 and 12 Months**

	Baseline OFF (n=106)	Baseline ON (n=106)	6 Months (n=99)	12 Months (n=94)
DCM	63 (60%)			56 (59%)
Ischemic DCM	43 (40%)			38 (41%)
NYHA FC				
I	0			19*
II	25			41*
III	71			33*
IV	10			1*
Atrial fibrillation, %	11 (10%)			
6-minute walk test	307 (149)		422 (170)*	472 (157)*
Quality-of-life score, points	39 (20)		25 (18)*	25 (20)*
Echocardiography				
LVEF, %	23 (7)	25 (7)*	30 (8)*	31 (10)*
LVEDD, mm	73 (8)	73 (8)	71 (9)*	70 (9)*
LVESD, mm	60 (10)	58 (9)*	55 (13)*	55 (10)*
LVEDV, mL	221 (91)	218 (82)	200 (81)*	204 (72)
LVESV, mL	165 (76)	169 (76)	143 (70)*	141 (62)*
LV cardiac load, L/min	3.9 (2.1)	3.5 (1)	4 (1.2)	4.2 (1)*
Mitral regurgitation orifice, mm^2, (n=44)	30 (17)	20 (15)*	25 (15)*	20 (17)*
Mitral regurgitation volume, mL/beat, (n=44)	48 (22)	34 (26)*	34 (19)*	30 (22)*
Pulmonary artery systolic blood pressure, mm Hg	39 (12)	36 (9)	37 (8)	38 (11)

LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; DCM, idiopathic dilated cardiomyopathy; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume.

*$P<.05$ compared with OFF.

TABLE 2. **Clinical Differences in Baseline and Follow-Up Variables According to the Etiology of the Underlying Heart Disease**

	Dilated Cardiomyopathy (n=63)				Ischemic Dilated Cardiomyopathy (n=43)			
	Baseline OFF	Baseline ON	6 Months	12 Months	Baseline OFF	Baseline ON	6 Months	12 Months
Age	69 (8)				69 (7)			
QRS, ms	154 (29)				140 (28)			
Atrial fibrillation, %	7 (11%)				4 (9%)			
History of AMI, %	0				39 (90%)[a]			
NYHA FC								
I		0	13 (21%)[b]	13 (23%)[b]	0	8 (19%)[b]	9	(24%)[b]
II		11 (17%)	30 (50%)[b]	24 (43%)[b]	15 (35%)	24 (59%)[b]	22 (58%)[b]	
III		49 (78%)	17 (28%)[b]	17 (30%)[b]	21 (49%)	8 (20%)[b]	7 (18%)[b]	
IV		3 (5%)	0b	2 (3%)[b]	7 (16%)	1 (2%)[b]	0[b]	
6-minute walk test, m	290 (140)	416 (164)[b]	445 (160)[b]	291 (165)	419 (188)[b]	510 (143)[b]		
Quality-of-life score, points	42 (19)	26 (21)[b]	27 (23)[b]	40 (22)	25 (16)[b]	23 (13)[b]		
ACEI or ARA-II, %	52 (83%)			33 (78%)				
β-Blockers, %	40 (64%)			29 (68%)				

NYHA FC indicates New York Heart Association Functional Class; AMI, acute myocardial infarction; ACEI or ARA-II, angiotensin converting enzyme inhibitor or angiotensin II receptor antagonists.
[a]*P*<.05 in baseline OFF of IDCM versus baseline OFF of DCM.
[b]*P*<.05 compared with baseline OFF.

patients with DCM had significantly larger ventricular volumes than those patients with IDCM (Table 3).

During follow-up, devices with programming capability became available. Therefore, in the last 31 patients in the series (18 with DCM and 13 with IDCM; *P*=NS) programming of the device was carried out using echocardiographic optimization. The study of the transmitral flow with pulsed Doppler was used for the AV interval optimization and the assessment of the intraventricular asynchrony with tissue Doppler techniques were used for the interventricular interval (VV) optimization; this programming was not modified during follow-up.

Echocardiographic Evolution

At 6 and 12 months of follow-up, there was an overall reverse ventricular remodeling, with the reduction of both left ventricular diameters and volumes, as well as a progressive increase in LVEF. There was also a reduction in the severity of mitral regurgitation, with a decrease of the mitral regurgitation orifice and regurgitant volume, although there were no significant changes in the severity of pulmonary hypertension (Table 1).

TABLE 3. **Differences in Baseline and Follow-Up Echocardiographic Variables According to the Etiology of the Underlying Heart Disease**

	Dilated Cardiomyopathy (n=63)				Ischemic Dilated Cardiomyopathy (n=43)			
	Baseline OFF	Baseline ON	6 Months	12 Months	Baseline OFF	Baseline ON	6 Months	12 Months
LVEF, %	22 (8)	25 (6)[a]	29 (8)[a]	31 (9)[a]	26 (9)	28 (8)[a]	32 (10)[a]	35 (2)[a]
LVEDD, mm	76 (9)	74 (8)	72 (8)[a]	70 (9)[a]	72 (7)	70 (8)	70 (12)	69 (9)[a]
LVESD, mm	61 (9)	60 (9)	56 (14)[a]	55 (10)[a]	57 (11)	55 (11)	52 (15)[a]	53 (12)[a]
LVEDV, mL	232 (100)	234 (100)	218 (91)[a]	205 (81)[a]	202 (13)[b]	213 (85)	190 (62)	193 (11)
LVESV, mL	181 (81)	179 (86)	158 (78)[a]	149 (73)[a]	149 (12)[b]	154 (78)	125 (56)[a]	130 (9)[a]
LVCL, L/min	3.6 (1)	3.6 (1.2)	4.2 (1.4)[a]	4.1 (0.9)[a]	3.7 (1.4)	3.6 (1.2)	4 (1)[a]	3.9 (0.9)
Mitral RO, mm^2	36 (19)	20 (15)[a]	27 (15)	22 (20)[a]	29 (13)	21 (14)[a]	20 (14)[a]	15 (8)[a]
Mitral RV, mL/beat	51 (25)	32 (24)[a]	37 (18)[a]	33 (25)[a]	43 (16)	37 (29)	29 (19)[a]	25 (15)[a]
PAP, mm Hg	38 (9)	33 (12)	40 (11)	36 (10)	37 (13)	34 (16)	37 (12)	26 (15)[a]
s-pw, ms	159 (98)	103 (84)[a]	92 (62)[a]	98 (61)[a]	144 (124)	106 (83)[a]	103 (65)[a]	95 (75)[a]
IV-D, ms	54 (28)	29 (28)[a]	33 (24)[a]	27 (25)[a]	42 (35)	24 (23)[a]	32 (30)	40 (37)
Echo resp., %				45 (72%)				32 (74%)

LVEDD indicates left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; LVCL, left ventricular cardiac load; RO, regurgitation orifice; PAP, pulmonary artery systolic pressure; Echo resp., echocardiographic responder: 5-point increase in LVEF and/or 15% decrease in LVESV; IV-D, interventricular delay; s-pw, distance between the septum and posterior wall; RV, regurgitation volume; LVEDV, left ventricular end-diastolic volume; LVESV left ventricular end-systolic volume.
[a]*P*<.05 compared with baseline OFF.
[b]*P*<.05 in baseline OFF of IDCM versus baseline OFF of DCM.

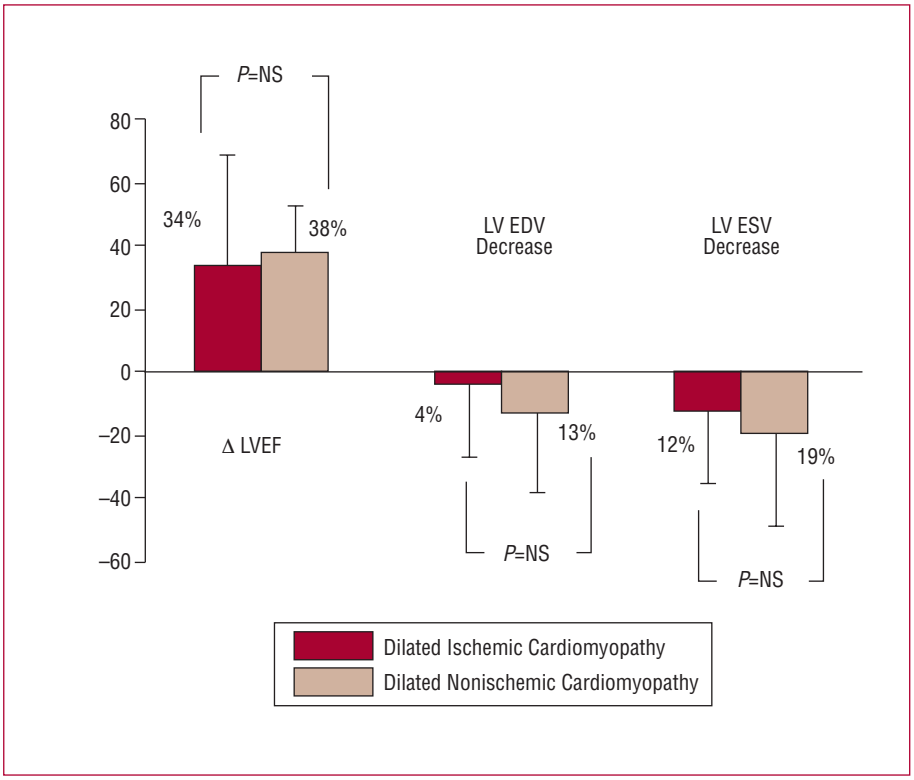

Figure 1. Reduction in left ventricular LV end-diastolic volume (EDV) and end-systolic volume (ESV) and increase in LV ejection fraction (Δ FEVI) according to the cause of the underlying heart disease after 12 months follow-up (DCM vs IDCM, *P*=NS).

When the extent of LV remodeling was analyzed according to the etiology of the underlying heart disease, we found a reduction in LV volumes and an increase in LVEF after CRT in both groups of patients (Table 3). Although ischemic patients tended to present less reverse remodelling than non-ischemic patients, there were no statistically significant differences between the groups with IDCM and DCM. Thus, after 12 months follow-up, patients with IDCM presented an absolute reduction of 4% and 12% in the LV end-diastolic and end-systolic volumes whereas the corresponding reduction was 13% and 19%, respectively, in patients with DCM (with no significant differences between IDCM and DCM in either case). Likewise, LVEF increased 34% in the IDCM group compared to 38% among patients with DCM (*P*=NS) (Figure 1).

From the echocardiographic point of view, 77 patients (73%) in the overall group showed a response to CRT (increase of 5 points of LVEF and/or decrease of 15% in LV end-systolic volume) after 12 months follow-up: 69 patients (65%) showed a 5-point increase in LVEF, 43 (40%) showed a 15% decrease in LV end-systolic volume, and 35 (33%) showed both. The proportion of echocardiographic responders was similar in both groups: 32 (74%) in the IDCM group and 45 (72%) in the DCM group (*P*=NS). Likewise, the proportion of patients with a decrease in LV end-systolic volume of more than 15% was 72% in the IDCM group and 67% in the DCM group (*P*=NS). Finally, the percentage of patients with a 5-point increase in LVEF after 12 months follow-up was also similar for both groups: 38% in the IDCM patients and 40% in the DCM patients (*P*=NS).

Clinical Evolution

At 6 months follow-up, 76 patients (72%) had responded clinically to CRT and 30 (28%) had not. Of those who failed to respond, 2 had received a heart transplant and 5 had died; the remaining patients (23) were considered nonresponders because the distance covered in the 6-minute walk test had not increased by at least 10%. At 12 months, a further 2 patients had received a transplant and another 3 patients died. There was still a group of 23 patients who could not walk 10% further in the 6-minute walk test. In general, therefore, clinical response to CRT at 12 months follow-up was favorable in 71 patients (67%), whereas there was no response in the remaining 35 (33%) in accordance with our previously described criterion.[4,8] Furthermore, after 12 months, 60 patients (64%) were in NYHA functional class I or II, whereas only 33 (35%) remained in functional class III and 1 (1%) was in functional class IV. Similarly, the distance covered in the 6-minute walk test increased and the score on the quality-of-life questionnaire improved (Table 1).

Analysis of the clinical response to CRT in the 2 groups of patients divided according to etiology of the underlying heart disease also failed to reveal significant differences:

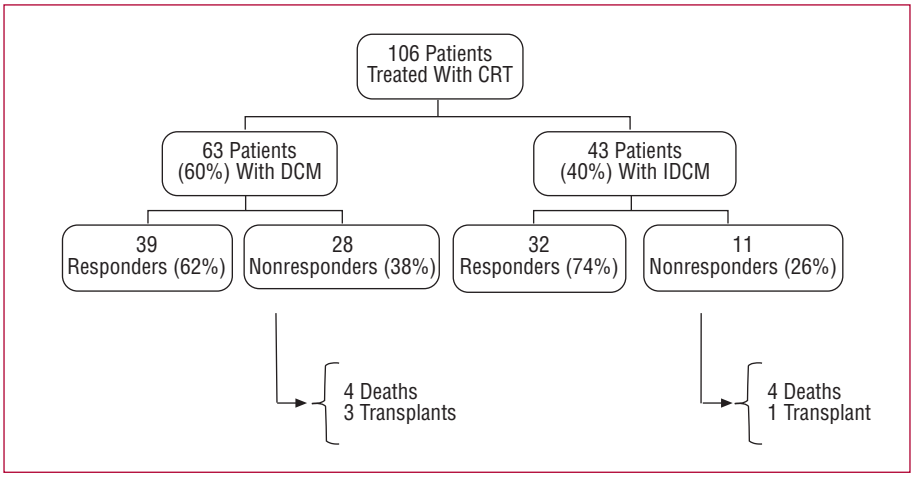

Figure 2. Clinical response at 12 months follow-up according to the underlying heart disease.

after 12 months follow-up, of the 63 patients with DCM, 39 (62%) had responded to CRT and 24 (38%) had not, compared to 32 (74%) and 11 (26%), respectively, in the population with IDCM (DCM vs IDCM, *P*=NS) (Figure 2). There were no significant differences between the 2 groups in the increase in the distance covered in the 6-minute walk test: after 12 months the patients with DCM walked 143 (183) m further than at baseline and the patients with IDCM walked 175 (144) m further (*P*=NS) (Table 2). With regard to the quality-of-life questionnaire, the patients with DCM showed a 12-point improvement in the score on the test and the patients with IDCM showed a 15-point improvement after 12 months follow-up (*P*=NS).

DISCUSSION

The present study shows the clinical benefit of treating patients with CRT. It also points to the reverse ventricular modeling that occurs with this therapy, with a progressive and sustained decrease in LV size, increase in LVEF, and decrease of the severity of mitral valve regurgitation. In addition, this study shows that the clinical an echocardiographic benefit occurs in patients with DCM as well as in patients with IDCM.

CRT and Ventricular Remodeling

It is hypothesized that the neurohormonal activation induced by heart failure is the main mechanism favoring LV remodeling and that this mechanism is the target for both medical treatments and CRT.[22,23] It is likely that CRT favors reverse remodeling by several different mechanisms which act both on improving the synchrony of contraction of the different myocardial segments and on normalization of LV diastolic filling time, which tends to normalize the neurohormonal profile.[24-28] CRT acts by producing changes in LV morphology and these changes confer a hemodynamic benefit that translates into a clinical improvement of the patient.[29,30]

If there is limited information on how exactly CRT acts in the pathophysiology of LV remodeling, there is still less information on whether the patient's heart disease etiology can determine or limit the extent of the benefit obtained with this therapy. Thus, it is not yet clear whether this morphological change that should hypothetically provide clinical benefit in patients treated with CRT occurs to the same extent in hearts with substantial scars as sequelae of a previous infarction.

CRT and Etiology of the Underlying Heart Disease

Previous studies, such as the SCARS registry,[7,8] show that having a dilated cardiomyopathy of ischemic origin, particularly if advanced and associated with a severely dilated left ventricle and severe mitral valve regurgitation, is a predictor of poorer response to CRT. Likewise, Sutton et al[10] showed in a population of 228 patients included in the Multicenter Insync Randomized Clinical Evaluation that reverse ventricular remodeling after CRT implantation occurred mainly in nonischemic patients and the authors attributed the differences to progression of ischemic disease. Contrary to those findings, Molhoek et al,[9] comparing a population of 74 patients, 34 with ischemic heart disease and 40 with DCM, over a 2-year follow-up, did not find any significant differences.[31-33]

In our series, we also failed to find any differences in the extent of clinical or echocardiographic response between patients with IDCM and those with DCM. However, patients with DCM had significantly higher baseline LV volumes than ischemic patients (Table 3), a factor which is associated with worse prognosis.[7,8] Despite this, we found a similar proportion of clinical

and echocardiographic responders among patients with DCM or with ischemic etiology. This could indicate that the extent of reverse remodeling is greater in patients with DCM than in ischemic patients, in agreement with the results of Sutton et al.[10] Probably, the response to CRT is limited by large regions of scar tissue in patients with a history of infarction, an observation which serves to highlight the growing interest in undertaking viability studies to better select patients with IDCM who might respond to CRT.[34,35]

Limitations

The last 31 patients of the series received an optimization of the AV and VV intervals although there were no significant differences in the number of optimized patients in each group. However, the programing was not subsequently reviewed, and this could have influenced the subsequent evolution of these patients.

The definition of IDCM according to the presence of at least one lesion >50% in one artery can be debated as a sole cause of cardiomyopathy, and in fact this continues to be the object of discussion in the literature.[12] In our case, we decided to follow what has been widely accepted in recent years and published in studies similar to our own.[9]

CONCLUSIONS

CRT is an effective alternative therapy in patients with dilated heart disease whether of ischemic or nonischemic origin, although the echocardiographic response in terms of reverse remodeling tends to be slightly lower in ischemic patients. Therefore, at present, no patient should be ruled out of CRT due to the etiology of the cardiopathy.

REFERENCES

1. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002;346:1845-53.
2. Cleland JGF, Daubert J-C, Erdmann E, Freemantle N, Gras D, Kappenberger L, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005;352:1539-49.
3. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, de Marco T, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004;350:2140-50.
4. Vidal B, Sitges M, Marigliano A, Diaz-Infante E, Azqueta M, Tamborero D, et al. Relation of response to cardiac resynchronization therapy to left ventricular reverse remodeling. Am J Cardiol. 2006;97:876-81.
5. Bleeker GB, Schalij MJ, Molhoek SG, Boersma E, Steendijk P, van der Wall EE, et al. Comparison of effectiveness of cardiac resynchronization therapy in patients <70 versus > or =70 years of age. Am J Cardiol. 2005;96:420-22.
6. Bradley DJ, Bradley EA, Baughman KL, Berger RD, Calkins H, Goodman SN, et al. Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials. JAMA. 2003;289:730-40.
7. Díaz-Infante E, Berruezo A, Mont L, Osorio P, García-Moran E, Marigliano A, et al. Predictores de ausencia de mejoría clínica a medio plazo con la terapia de resincronización cardíaca. Rev Esp Cardiol. 2004;57:306-12.
8. Diaz-Infante E, Mont L, Leal J, Garcia-Bolao I, Fernandez-Lozano I, Hernandez-Madrid A, et al. Predictors of lack of response to resynchronization therapy. Am J Cardiol. 2005;95:1436-40.
9. Molhoek SG, Bax JJ, van Erven L, Bootsma M, Boersma E, Steendijk P, et al. Comparison of benefits from cardiac resynchronization therapy in patients with ischemic cardiomyopathy versus idiopathic dilated cardiomyopathy. Am J Cardiol. 2004;93:860-3.
10. Sutton MG, Plappert T, Hilpisch KE, Abraham WT, Hayes DL, Chinchoy E. Sustained reverse left ventricular structural remodeling with cardiac resynchronization at one year is a function of etiology: quantitative Doppler echocardiographic evidence from the Multicenter InSync Randomized Clinical Evaluation (MIRACLE). Circulation. 2006;113:266-72.
11. Saxon LA, De Marco T, Schafer J, Chatterjee K, Kumar UN, Foster E. Effects of long-term biventricular stimulation for resynchronization on echocardiographic measures of remodeling. Circulation. 2002;105:1304-10.
12. Richardson P, McKenna W, Bristow M, Maisch B, Mautner B, O'Connell J, et al. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies. Circulation. 1996;93:841-2.
13. Rector TS, Tschumperlin LK, Kubo SH, Bank AJ, Francis GS, McDonald KM, et al. Use of the Living With Heart Failure questionnaire to ascertain patients' perspectives on improvement in quality of life versus risk of drug-induced death. J Card Fail. 1995;1:201-6.
14. Bleeker GB, Bax JJ, Fung JW, van der Wall EE, Zhang Q, Schalij MJ, et al. Clinical versus echocardiographic parameters to assess response to cardiac resynchronization therapy. Am J Cardiol. 2006;97:260-3.
15. Bax JJ, Bleeker GB, Marwick TH, Molhoek SG, Boersma E, Steendijk P, et al. Left ventricular dyssynchrony predicts response and prognosis after cardiac resynchronization therapy. J Am Coll Cardiol. 2004;44:1834-40.
16. Yu CM, Bleeker GB, Fung JW, Schalij MJ, Zhang Q, van der Wall EE, et al. Left ventricular reverse remodeling but not clinical improvement predicts long-term survival after cardiac resynchronization therapy. Circulation. 2005;112:1580-6.
17. Cintron G, Johnson G, Francis G, Cobb F, Cohn JN. Prognostic significance of serial changes in left ventricular ejection fraction in patients with congestive heart failure. The V-HeFT VA Cooperative Studies Group. Circulation. 1993;6:VI17-23.
18. Swedberg K. Effective implementation of the new ESC guidelines for the management of chronic heart failure in routine clinical practice. J Renin Angiotensin Aldosterone Syst. 2005;6:S6-10.
19. Schiller NB, Shah PM, Crawford M, deMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr. 1989;2:358-67.
20. Bargiggia GS, Tronconi L, Sahn DJ, Recusani F, Raisaro A, de Servi S, et al. A new method for quantitation of mitral regurgitation based on color flow Doppler imaging of flow convergence proximal to regurgitant orifice. Circulation. 1991;84:1481-9.
21. Pitzalis MV, Iacoviello M, Romito R, Massari F, Rizzon B, Luzzi G, et al. Cardiac resynchronization therapy tailored by echocardiographic evaluation of ventricular asynchrony. J Am Coll Cardiol. 2002;40:1615-22.
22. Doughty RN, Whalley GA, Walsh HA, Gamble GD, Lopez-Sendon J, Sharpe N. Effects of carvedilol on left ventricular remodeling

after acute myocardial infarction: the CAPRICORN Echo Substudy. Circulation. 2004;109:201-6.
23. Greenberg B, Quinones MA, Koilpillai C, Limacher M, Shindler D, Benedict C, et al. Effects of long-term enalapril therapy on cardiac structure and function in patients with left ventricular dysfunction: Results of the SOLVD Echocardiography Substudy. Circulation. 1995;91:2573-81.
24. Auricchio A, Stellbrink C, Block M, Sack S, Vogt J, Bakker P, 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.
25. Auricchio A, Stellbrink C, Butter C, Sack S, Vogt J, Misier AR, et al. Clinical efficacy of cardiac resynchronization therapy using left ventricular pacing in heart failure patients stratified by severity of ventricular conduction delay. J Am Coll Cardiol. 2003;42: 2109-16.
26. Breithardt OA, Sinha AM, Schwammenthal E, Bidaoui N, Markus KU, Franke A, et al. Acute effects of cardiac resynchronization therapy on functional mitral regurgitation in advanced systolic heart failure. J Am Coll Cardiol. 2003;41:765-70.
27. Breithardt OA, Stellbrink C, Kramer AP, Sinha AM, Franke A, Salo R, 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.
28. Kanzaki H, Bazaz R, Schwartzman D, Dohi K, Sade LE, Gorcsan J 3rd. A mechanism for immediate reduction in mitral regurgitation after cardiac resynchronization therapy: insights from mechanical activation strain mapping. J Am Coll Cardiol. 2004;44:1619-25.
29. Kim WY, Sogaard P, Mortensen PT, Jensen HK, Pedersen AK, Kristensen BO, et al. Three dimensional echocardiography documents haemodynamic improvement by biventricular pacing in patients with severe heart failure. Heart. 2001;85:514-20.
30. Lancellotti P, Melon P, Sakalihasan N, Waleffe A, Dubois C, Bertholet M, et al. Effect of cardiac resynchronization therapy on functional mitral regurgitation in heart failure. Am J Cardiol. 2004;94: 1462-5.
31. Gasparini M, Mantica M, Galimberti P, Genovese L, Pini D, Faletra F, et al. Is the outcome of cardiac resynchronization therapy related to the underlying etiology? Pacing Clin Electrophysiol. 2003;26: 175-80.
32. Reuter S, Garrigue S, Barold SS, Jais P, Hocini M, Haissaguerre M, 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.
33. Woo GW, Petersen-Stejskal S, Johnson JW, Conti JB, Aranda JA Jr, Curtis AB. Ventricular reverse remodeling and 6-month outcomes in patients receiving cardiac resynchronization therapy: analysis of the MIRACLE study. J Interv Card Electrophysiol. 2005;12:107-13.
34. Bleeker GB, Schalij MJ, van Der Wall EE, Bax JJ. Postero-lateral scar tissue resulting in non-response to cardiac resynchronization therapy. J Cardiovasc Electrophysiol. 2006;17:899-901.
35. Breithardt OA, Breithardt G. Quest for the best candidate: how much imaging do we need before prescribing cardiac resynchronization therapy? Circulation. 2006;113:926-8.