

Benefits of Cardiac Resynchronization Therapy in Patients With Atrial Fibrillation Who Have Not Undergone Atrioventricular Node Ablation

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The aim of this study was to compare the effects of cardiac resynchronization therapy on left ventricular function and reverse remodeling in patients in sinus rhythm with the effects in patients with atrial fibrillation who have not undergone atrioventricular node ablation. Echocardiographic and clinical parameters were evaluated at baseline and after 6 months of cardiac resynchronization therapy in 55 patients: 15 had atrial fibrillation and 40 were in sinus rhythm. Device programming was similar in the 2 groups, as were the reductions in QRS interval and echocardiographic measures of asynchrony observed after implantation. However, although significant improvements in end-systolic volume and ejection fraction were seen in both groups, reverse remodeling was greater in patients in sinus rhythm (reduction in end-systolic volume 30.9% [24.6%] vs 12.5% [18.6%]; $P=0.024$), as was the relative increase in ejection fraction (15.4% [12.6%] vs 5.0% [7.2%]; $P=0.010$). Cardiac resynchronization therapy in patients with atrial fibrillation who had not undergone atrioventricular node ablation resulted in significant improvements in ejection fraction and reverse remodeling, but these were less than those observed in patients in sinus rhythm.

Key words: Atrial fibrillation. Cardiac resynchronization. Reverse remodeling. Remodeling.

Beneficio de la terapia de resincronización cardiaca en la fibrilación auricular sin ablación del nodo

El objetivo fue comparar el efecto de la terapia de resincronización cardiaca en la función ventricular y el remodelado inverso en pacientes en ritmo sinusal y fibrilación auricular sin ablación del nódulo auriculoventricular. Se analizaron parámetros clínicos y ecocardiográficos antes y 6 meses tras la resincronización de 55 pacientes: 15 en fibrilación auricular y 40 en ritmo sinusal. La programación del dispositivo, el estrechamiento del QRS y la asincronía ecocardiográfica tras el implante fueron similares en ambos grupos. Sin embargo, aunque en ambos grupos se observó mejoría significativa del volumen telesistólico y la fracción de eyección, los pacientes en ritmo sinusal presentaron mayor remodelado inverso (reducción del volumen telesistólico del 30,9% \pm 24,6% contra el 12,5% \pm 18,6%; $p = 0,024$) y aumento relativo en la fracción de eyección (el 15,4% \pm 12,6% y el 5% \pm 7,2%; $p = 0,010$). La terapia de resincronización en pacientes con fibrilación auricular sin ablación del nódulo mejora significativamente la fracción de eyección y el remodelado inverso, pero menos que en ritmo sinusal.

Palabras clave: Fibrilación auricular. Resincronización cardiaca. Remodelado inverso. Remodelado.

INTRODUCTION

Control of cardiac rhythm by atrioventricular node (AVN) ablation and pacemaker implantation in patients with atrial fibrillation (AF) refractory to pharmacological treatment provides better quality of life and functional

capacity.¹ In addition, regularization of cardiac rhythm improves systolic function.² This benefit, as well as the reduction in the severity of mitral regurgitation, is greater in cases with left ventricular^{2,3} or biventricular⁴⁻⁶ pacing. The change from right ventricular to biventricular pacing in patients with AF and AVN ablation improves the symptoms of advanced heart failure and ventricular dysfunction.⁷ This appears to be due to the fact that right ventricular pacing produces dyssynchrony in almost half the patients, a problem associated with clinical deterioration, worsening of systolic function, and ventricular dilatation.⁸

Based on the available data, cardiac resynchronization therapy (CRT) is considered indicated in patients with

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significant ventricular dysfunction in NYHA functional class II-III and undergoing AVN ablation for persistent AF. There is little information, however, on the benefits of CRT in patients with ventricular dysfunction, advanced heart disease and AF, without AVN ablation.⁹⁻¹¹

This study was undertaken to determine whether the effects of CRT on inverse remodeling in patients with advanced heart failure and left bundle branch block differs between those who are in sinus rhythm (SR), and those with pharmacologically controlled AF.

METHODS

A retrospective study was performed in a cohort of 55 patients treated with CRT at our hospital and fulfilling the following criteria: low ejection fraction ($\leq 35\%$), wide QRS interval (≥ 120 ms), and advanced functional class (NYHA $>II$), despite optimized medical treatment. Echocardiographic criteria of asynchrony were not required to indicate the therapy. Patients were excluded if they had an indication for ventricular pacing because of high-grade atrioventricular block (AVB) or needed AVN ablation. The effects of CRT on left ventricular size and function, mitral dyssynchrony and regurgitation, and clinical status were compared between patients with AF and those in SR. Functional grade was considered a quantitative variable.

Implantation of the Device

Pacemaker implantation was performed through an intravenous approach. The electrodes were inserted through the subclavian vein using standard implantation techniques. In all cases, the electrode for left ventricular pacing was placed in a posterolateral or lateral vein. Programming of atrioventricular delay in patients in SR was optimized by echocardiography. Programming of biventricular pacing was based on the criterion of QRS narrowing.

Echocardiographic Examination

Doppler echocardiography (Acuson CV70, Siemens) was performed in the month before and 6 months after device implantation. End-systolic and end-diastolic volumes, and the ejection fraction (EF) were measured according to the guidelines of the American Society of Echocardiography.¹² Mitral regurgitation was quantitatively estimated by calculating the area of the regurgitant orifice with the proximal isovelocity surface area method.¹³ Interventricular asynchrony was calculated as the difference between the aortic and pulmonary pre-ejection time periods. Intraventricular asynchrony was assessed as the time difference between the interventricular septal and lateral free wall velocity peaks on spectral tissue Doppler analysis, and the time difference between maximum systolic motion from the septum to posterior

wall in M mode (Pitzalis index). Atrioventricular asynchrony was assessed as the relationship between diastolic filling time and length of the cycle.

Inverse remodeling was defined as a relative reduction in end-systolic volume (ESV) of at least 10%, a cut-off point with proven diagnostic value.¹⁴

Statistical Analysis

Continuous variables are expressed as the mean (standard deviation) and categorical variables as percentages. The χ^2 test or Fisher's exact test were used to compare qualitative variables, and Student *t* test to compare quantitative variables. Comparisons of data from the same sample before and after CRT were done with Student's *t* test for paired data for the quantitative variables and the Mann-Whitney *U* test for qualitative variables. Significance was set at a 2-tailed *P* value of $<.05$. All statistical analyses were performed with SPSS (version 12.0, SPSS Inc, Chicago, Illinois, USA).

RESULTS

Among the 55 patients included in the study (64 [9] years of age), 15 had AF, and 40 were in SR. The 2 groups of patients presented similar demographic characteristics (Table 1), ischemic etiology, and preimplantation treatment. There were no significant differences between the groups in QRS interval width, EF results, mitral regurgitation, or grade of echocardiographic asynchrony before pacemaker implantation. In addition, the stimulated QRS width, relative reduction in QRS width, and programming for biventricular (VV) pacing were similar between groups and there were no differences in the percentage of biventricular pacing recorded by the device.

Analysis of CRT response (Table 2) showed a significant reduction in intraventricular and interventricular asynchrony, with improved EF and ESV and reductions in severe mitral regurgitation. Nonetheless, inverse remodeling was seen to be less marked in the group of patients with AF (53.3% and 75%; $P=.021$), with a lower relative ESV reduction (12.5 [18.6] and 30.9 [24.6]; $P=.024$) and relative EF increase (5.0 [7.2] and 15.4 [12.6]; $P=.010$).

The functional grade improvement (NYHA) was significant in both the AF group ($P=.033$) and the SR group ($P<.001$), with no differences in either baseline or follow-up values between the groups.

DISCUSSION

In patients with AF and pharmacological control of rhythm undergoing CRT in this series, we observed an improvement in the systolic function parameters, such as the EF and inverse remodeling, with a decrease in the ESV, as well as a significant reduction in severe mitral regurgitation. These findings were produced in a group

TABLE 1. Comparative Analysis of Baseline Characteristics and Those Derived From Biventricular Pacing

	AF (n=15)	SR (n=40)
Clinical data		
Age, mean (SD), y	65 (7)	64 (10)
Sex, women	20%	25%
Beta-blockers	93.2%	90%
ACEI/ARA-II	93.2%	95%
Diuretics	100%	100%
Spironolactone	73.3%	72.5%
Ischemic heart disease	46.6%	37.5%
QRS, ms	170.1 (36)	170.9 (22.4)
Echocardiographic data		
EF, %	20.9 (8.2)	21.6 (6.4)
EDV, mL/m ²	128.1 (31.2)	122.8 (51.6)
ESV, mL/m ²	101.7 (26.2)	96.4 (43.8)
MR (>0.40 cm ²)	26.6%	22.5%
sPAP, mm Hg	48.2 (8.4)	45.2 (6.6)
Filling/RR, %	33.6 (4.7)	37.7 (8.2)
Pitzalis index, ms	231.6 (57)	216.2 (60.7)
Sep-lat, ms	107.2 (15.1)	89.7 (31)
Aortopulmonary, ms	79.3 (22.2)	69.5 (21.6)
Programming data		
Paced QRS	132.1 (13.2)	125.4 (16.4)
R-QRS, %	21.6 (16.5)	25.4 (13.4)
Programmed VV, ms	-16.9 (27.5)	-17.3 (29.3)
Biventricular pacing, %	93.3 (3.5)	96.1 (2.1)

AF indicates atrial fibrillation; EDV, left ventricular end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; MR, mitral regurgitation; R-QRS, QRS reduction relative to baseline; SR, sinus rhythm; Sep-lat, septal-to-lateral wall delay by spectral tissue Doppler; sPAP, systolic pulmonary artery pressure.

of patients whose only baseline difference from those in SR and undergoing CRT was that they had AF. Moreover, both groups were resynchronized with a reduction in the QRS interval width, both had similar VV programming, and both showed a comparable decrease in parameters of ventricular and interventricular asynchrony. We found,

however, that EF improved to a greater degree and there was more inverse modeling in patients with baseline SR than in patients with baseline AF.

As has been seen in other studies,¹⁵ CRT produced inverse remodeling with an EF increase and mitral regurgitation decrease in this series of patients. These benefits have also been reported in patients with AF and AVN ablation.^{4,6} In contrast to the series of Gasparini et al,¹⁰ however, in which the improvement in functional capacity and EF seen in patients in SR was comparable in patients with AF only when AVN ablation was performed, the present series showed that patients who did not undergo AVN ablation also present inverse remodeling, reduced mitral regurgitation, and better functional capacity, although to a lesser degree. Similar findings have been reported recently, although the study groups showed some baseline differences: specifically, significantly greater previous right ventricular pacing in patients with AF and no AVN ablation than in the SR group (39.4% and 18.8%; $P<.001$),¹¹ a fact that limits the conclusions.

The differences seen between the group of patients in SR and those with AF may be due, at least in part, to better restoration of atrioventricular synchrony. Furthermore, although the percentage of paced beats recorded by the devices was similar between the groups, we are unaware of what percentage corresponded to fusion beats and what percentage to pseudofusion beats, and their contribution to the results obtained.

Limitations

The series presented is small and there is no control group, with the bias these factors may produce, although data described in these patients is scant. The absence of baseline differences between the patient groups stands out in this study.

TABLE 2. Comparative Analysis of Response to Cardiac Resynchronization Therapy

	AF (n=15)		SR (n=40)	
	Baseline	Post-CRT	Baseline	Post-CRT
EF, %	20.9 (8.2)	26.0 (7.9) ^a	21.6 (6.4)	37.8 (11.7) ^{a,b}
EDV, mL	242.2 (72.5)	207.8 (61.0)	221.8 (93.2)	176.6 (80.2) ^a
ESV, mL	192.0 (58.2)	157.8 (55.2) ^a	174.3 (79.6)	115.3 (73.9) ^{a,b}
MR (>0.4 cm ²)	26%	13.3% ^a	22.5%	7.5% ^a
sPAP, mm Hg	48.4 (8.4)	37.6 (10.6) ^a	45.2 (6.6)	35 (7) ^a
NYHA	3.07 (0.26)	1.83 (0.25) ^a	3.05 (0.22)	2.13 (0.24) ^a
Filling/RR, %	33.6 (4.7)	44.1 (11.5) ^a	37.7 (8.2)	48.4 (8.7) ^a
Sep-lat, ms	107.2 (15.1)	3.2 (32) ^a	89.7 (31.6)	13.3 (40.2) ^a
Aortopulmonary, ms	79.3 (22.2)	21.4 (23.9)	69.5 (21.6)	30.6 (28.5) ^a

AF indicates atrial fibrillation; CRT, cardiac resynchronization therapy; EDV, left ventricular end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; MR, mitral regurgitation; R-QRS, QRS reduction relative to baseline; Sep-lat, Sep-lat, septal-to-lateral wall delay by spectral tissue Doppler; sPAP, systolic pulmonary artery pressure; SR, sinus rhythm.

^a $P<.05$ with respect to baseline.

^b $P<.05$ with respect to post-CRT in AF.

The percentage of biventricular pacing can include fusion beats or pseudofusion beats; thus the percentage of effective pacing may be overestimated.

CONCLUSIONS

CRT in patients with AF without AVN ablation provides significant benefits in terms of inverse remodeling and EF increase, but these effects are smaller than those seen in patients in SR.

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