ONE YEAR FOLLOW-UP OF CONVENTIONAL ECHOCARDIOGRAPHIC PARAMETERS FOR DYSSYNCHRONY IN PATIENTS WITH CARDIAC RESYNCHRONIZATION THERAPY

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Abstract: *Cardiac resynchronization therapy (CRT) has been shown to be effective in patients with drug-refractory heart failure and wide QRS complexes. The aim of our study was to analyze the one year evolution of conventional echocardiographic measurements along with dyssynchrony parameters in patients with cardiac resynchronization therapy. Serial examination data from 31 patients with CRT devices were analyzed. There were significant differences (p<0,05) between values of dyssynchrony parameters measured before and after implantation. Septal to posterior wall motion delay values (SPWMD) showed significant regression (p<0,01) at six and twelve months after implantation. Ejection fraction improved beginning from the first month, mainly by progressive reduction of end-systolic left ventricular volumes. In patients with cardiac resynchronization therapy, improvement of echocardiographic dyssynchrony parameters is a process that begins immediately after device implantation, and continues in the next months, expressing the fact that reverse remodeling takes time and sometimes needs pacing protocol adjustments.*

INTRODUCTION

Despite important advances in non-invasive therapies of patients with severe heart failure, high mortality and hospital readmissions stimulated the need for additional therapies. Patients with persistent left ventricular systolic dysfunction and symptomatic heart failure, refractory to maximal medical therapy, complicated with interventricular conduction delay, expressed by QRS widening, have a consensus recommendation for cardiac resynchronization therapy- CRT.(1) By atrioventricular sequential biventricular pacing, with or without implantable cardioverter defibrillator, the correction of ventricular electromechanical dyssynchrony might be achieved.(2)

This therapy considerably reduces symptoms and hospitalizations due to worsening of heart failure, by improving ventricular function in over 70% of patients, and also significantly reducing the risk of death.(3)

Beneficial effects of CRT rise from the interplay of several important factors related to patients selection, lead placement and device programming. Echocardiography plays a major role in providing important information on the ventricular contraction sequence and the hemodynamic consequences of asynchrony that may help identifying suitable patients, most beneficial lead placement and optimizing CRT device settings during follow-up.

MATERIALS AND METHODS

We analyzed echocardiographic data collected from 42 patients with severe heart failure and wide QRS complexes who fulfilled the European Society of Cardiology recommendations and underwent cardiac resynchronization therapy. Eleven patients were excluded (seven due to poor acoustic window that did not allow reproducible measurements, two of them failed to reach scheduled visits and two of them died). The remaining 31 patients had serial echocardiographic examinations: prior to device implantation, at 48-72 hours after implantation and at one, three, six and twelve months, respectively. A written consent had been signed before device implantation, stating the fact that patients agreed with all invasive and non invasive procedures from the study protocol. All transthoracic echocardiographic examinations were made using a Vivid-S5 scanner (version BT 10, GE Medical Systems, Israel). Complete chamber and valvular evaluation, as well as synchronicity measurements comprising atrioventricular, interventricular and radial and longitudinal intraventricular dyssynchrony were assessed, using conventional bidimensional, M-mode and Doppler echocardiography, as well as tissue Doppler imaging (TDI) and tissue tracking (TT).

The echo-Doppler examination included parasternal long and short axis views and three standard apical views. For each view, four consecutive cycles were recorded during quiet respiration. From the apical views, separate bidimensional and colour tissue Doppler acquisition were recorded at a mean frame rate of 110/s with adequate underlying grey-scale frame rate. Using pulsed wave Doppler recordings across the aortic and pulmonary valves, the aortic and pulmonary pre-ejection times were recorded. Interventricular mechanical delay (IVMD) is the difference in left and right preejection times. Using M- mode in parasternal short or long axis views of the left ventricle, septal to posterior wall motion delay (SPWMD) was measured.

Conventional echocardiography techniques were used to assess left ventricle systolic and diastolic function, by measuring end-systolic and end-diastolic volumes and analyzing mitral inflow patterns. Ejection fraction was calculated using Simpson biplane formula. Parameters for each examination were included in a chart, along with the CRT device settings. This allowed appropriate evaluation of mechanical dyssynchrony before and after device implantation and adjustments of

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programmable atrio-ventricular (AV) and interventricular (VV) delays. Collected data were analyzed using graphpad Prism 5.0.

Means are expressed as mean ± standard deviation. In order to compare the central tendency of two samples we used several tests: paired t test or Wilcoxon test for paired data, unpaired t test or Man-Whitney test for unpaired data. Normality test used was Kolmogorov-Smirnov. For three or more samples, central tendency was compared using Kruskal-Wallis test. The significance level for all the tests used is alpha=0.05.

RESULTS

Baseline clinical characteristics of patients included in the study are presented in table no. 1.

Table no. 1. Baseline clinical characteristics of patients

Mean age (years)		**60 ± 8.37**
Gender	Male (no.)	**24**
	Female (no.)	**7**
Underlying condition	Idiopathic cardiomyopathy (no.)	**22**
	Ischaemic heart disease (no.)	**6**
	Valvular cardiomyopathy (no.)	**3**
Associated conditions	Atrial fibrillation (no.)	**6**
	CRT-D (no.)	**3**
NYHA functional class	IV	**17**
	III	**13**
	II	**1**
Conduction disturbance	Left bundle branch block (LBBB) (no.)	**29**
	Right bundle branch block (RBBB) (no.)	**2**
Mean QRS duration (ms)		**163.2±3.2**

In all patients, echocardiographic parameters of atrio-ventricular, interventricular and intraventricular dyssynchrony showed improvement after device implantation. As expected, there were significant differences (p<0,05) between values of dyssynchrony parameters measured before and after implantation Main dyssynchrony parameters evaluated were IVMD and SPWMD.

Values for both were significantly reduced 48 hours after resynchronization therapy (p<0,0001), showing that mechanical dyssynchrony is alleviated immediately after device implantation (table no. 2).

Table no. 2. Evolution of main echocardiographic parameters

Parameter	Pre CRT	Post CRT	1 month	3 months	6 months	12 months
IVMD (ms)	54.9	28.5	23.1	26.3	24.1	36.8
SPWMD (ms)	247.7	116.9	86.3	88.1	67.4	73.8
EDV (ml)	282.1	278.8	278.0	262.0	269.0	245.0
ESV(ml)	234	222.5	215.0	192.0	192.0	171.0
EF (%)	17.55	21.5	25.0	28.8	31.2	35.8

No significant differences were noted related to age, sex or underlying condition. Interventricular mechanical delay was maintained within normal values for the next 12 months, in some cases by adjustments of pacing protocols, when needed. Septal to posterior wall motion delay values showed significant regression (p<0,01) at six and twelve months after implantation, along with decrease of mitral regurgitation.

Values for end diastolic volumes showed a slow, progressive reduction, but with no statistical significance. (figure no. 1) Meanwhile, end systolic volumes decreased significantly beginning with the third month (figure no. 2). Ejection fraction improved beginning from the first month, and the improvement was highly significant (p=0,0003) after three months, significance being maintained for the entire follow-up period (figure no. 3) mainly by progressive reduction of end-systolic left ventricular volumes.

Figure no. 1. Evolution of end diastolic volume values

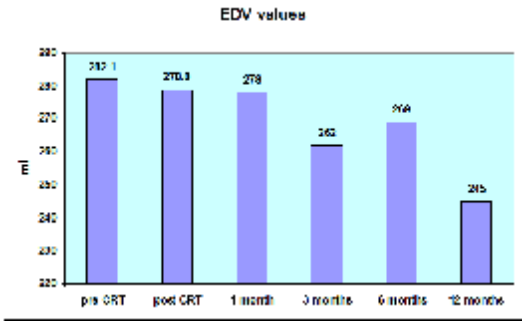


Figure no. 2. Evolution of end systolic volume values (*statistical significance (p<0,05)

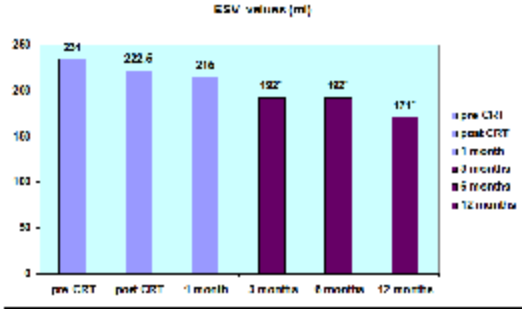
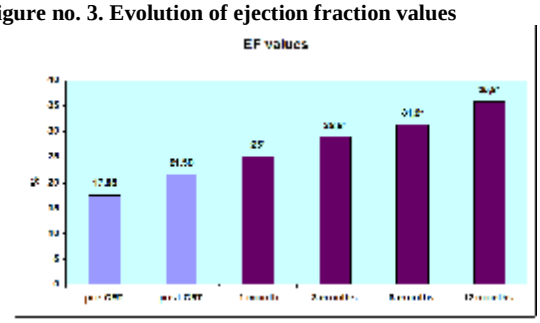


Figure no. 3. Evolution of ejection fraction values



DISCUSSIONS

Cardiac resynchronization therapy aims at reverse remodeling by biventricular pacing and has been demonstrated to remarkably improve morbidity and mortality in patients with severe heart failure.(4) Ventricular dyssynchrony has been shown to contribute to clinical deterioration of Heart Failure and resynchronization therapy has proved the opposite.(5) Patients included in our study had shown a significant response to CRT, expressed by rapid alleviation of dyssynchrony parameters. As shown previously, LV segmental and global dyssynchrony can easily be assessed by Doppler echocardiography (6), with its parameters not only predicting prognosis but also the extent of exercise tolerance. Consecutively, a gradual reduction of left ventricular end systolic volumes, along with slightly reduction of end diastolic volumes, determined a slow, but progressive augmentation of left ventricular ejection fraction beginning with the third month after device implantation. This was considered a significant response to CRT, in accordance with the assumption

that the presence of a correctable abnormality evaluated by conventional echocardiography is associated with LV reverse remodeling and better survival at midterm follow-up.(7) Conventional echocardiographic exams were able to asses response to therapy and also provided tools for device programming for functional adjustments.

CONCLUSIONS

In patients with cardiac resynchronization therapy, improvement of echocardiographic dyssynchrony parameters is a process that begins immediately after device implantation, and continues in the next months, expressing the fact that reverse remodeling takes time and sometimes needs pacing protocol adjustments.

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