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Analysis of left ventricular function in patients with heart failure undergoing cardiac resynchronization

Análise da função ventricular esquerda de pacientes com insuficiência cardíaca submetidos à ressincronização cardíaca

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Resumo

Fundamentos: **O tratamento cirúrgico da insuficiência cardíaca padrão-ouro é o transplante cardíaco, porém, em decorrência das dificuldades desse tratamento, outras propostas cirúrgicas têm sido relatadas, entre elas o implante de ressincronizador cardíaco.**

Objetivo: **Analisar a função ventricular esquerda, por meio da ecocardiografia, de pacientes portadores de insuficiência cardíaca avançada com dissincronia interventricular submetidos a implante de ressincronizador cardíaco.**

Métodos: **Entre junho de 2006 a junho de 2012, foram avaliados 24 pacientes com idade média de 61,5 ± 11 anos, portadores de insuficiência cardíaca congestiva avançada em classe funcional III e IV (NYHA), dissincronia interventricular e tratamento medicamentoso otimizado. Esses pacientes foram submetidos ao implante de ressincronizador cardíaco e avaliados ecocardiograficamente no pós-operatório de seis meses.**

Resultados: **Houve melhora significativa dos parâmetros ecocardiográficos analisados. A média dos diâmetros diastólicos ventriculares esquerdos reduziu de 69,6 ± 9,8 mm para 66,8 ± 8,8 mm, diâmetros sistólicos de 58,6 ± 8,8 mm para 52,7 ± 8,8 mm e a fração de ejeção, média de 31 ± 8% para 40 ± 7% com nível de significância, respectivamente, de 0,019, 0,0004 e 0,0002, estatisticamente significativos com nível de significância de 0,05.**

Conclusão: **Houve melhora da função ventricular esquerda analisada por meio da ecocardiografia, em seis meses, de pacientes portadores de insuficiência cardíaca avançada submetidos a implante de ressincronizador cardíaco.**

Descritores: **Insuficiência cardíaca. Terapia de Ressincronização Cardíaca. Ecocardiografia.**

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Abbreviations, acronyms & symbols	
AAS	Acetylsalicylic acid
ACE	Angiotensin converting enzyme
CRT	Cardiac resynchronization therapy
DCM	Dilated cardiomyopathy
ECG	Electrocardiogram
EF	Ejection fraction
HF	Heart failure
LBBB	Left bundle branch block
LVDD	Left ventricle diastolic diameter
LVEF	Left ventricular ejection fraction
LVSD	Left ventricle systolic diameter
NYHA	New York Heart Association
RV	Right ventricle
SD	Standard deviation
SUS	Unified Health System
UFMS	Federal University of Mato Grosso do Sul

Abstract

Background: **The gold standard surgical treatment for heart failure is cardiac transplantation, however, due to difficulties of this treatment, other surgical proposals have been reported, including the implantation of cardiac resynchronizer.**

Objective: **To analyze the left ventricular function by echocardiography in patients with advanced heart failure with interventricular dyssynchrony undergone implantation of cardiac resynchronizer.**

Methods: **Between June 2006 and June 2012, 24 patients with average age of 61.5 ± 11 years were evaluated, carriers of advanced congestive heart failure functional class III and IV (NYHA), interventricular dyssynchrony and optimal drug therapy, and submitted implantation of cardiac resynchronizer and postoperative echocardiographically evaluated in six months.**

Results: **There was significant improvement of the analyzed echocardiography parameters. The average left ventricular diastolic diameter decreased from 69.6 ± 9.8 mm to 66.8 ± 8.8 mm, systolic diameters from 58.6 ± 8.8 mm to 52.7 ± 8.8 mm, and ejection fraction, average of 31 ± 8% to 40 ± 7% with level of significance, respectively, of 0.019, 0.0004 and 0.0002, statistically significant with a significance level of 0.05.**

Conclusion: **There was a significant improvement of left ventricular function analyzed by echocardiography at six months, in patients with advanced heart failure undergone implantation of cardiac resynchronizer.**

Descriptors: **Heart failure. Cardiac resynchronization therapy. Echocardiography.**

INTRODUCTION

Heart failure (HF) one of the greatest clinical challenges in the current public health, and it is considered an epidemic on progress, diagnosed in 1% to 2% of developed countries population [1,2].

The HF is one of the most prevalent causes of hospital admissions in Brazil, on the Unified Health System (SUS). In 2007, there were 1.156.136 hospital admissions for cardiovascular diseases, representing the third leading cause of hospital admissions on the SUS, and HF is the main one [3].

The HF treatment has the purpose of symptoms improvement, reduction of mortality, hospital costs decreasing and prevention of readmissions. The treatment of heart failure consists of: nonpharmacological steps (diet, exercising, stress management, and others), drug therapy and surgery [3].

Studies show that medical treatment should always include a beta blocker and an inhibitor of the angiotensin converting enzyme (ACE), composing the optimized medical treatment. For symptomatic patients, diuretics and digitalis are added. But if there is a disabling symptoms persistence, it is necessary to introduce aldosterone antagonists (functional class III heart failure by Criteria Committee of the New York Heart Association - NYHA) with strict control of serum potassium and combination of hydralazine + nitrate [3-6].

The search for alternative or complementary methods to drug treatment, which could change the course of the disease, is a major challenge of the researchers [7].

Surgical treatment should be considered for patients resistant to optimized medical treatment. Cardiac transplantation is the main treatment for patients with severe clinical and hemodynamic conditions, which represent significant changes in the prognosis of HF, but there are major obstacles to its achievement, as the low amount of donors, adverse responses to immunosuppressants, unfavorable clinical conditions and surgical risk, and other factors that are against the surgery [8].

Therefore, other alternative surgical techniques to heart transplantation, including surgical intervention of mitral valve in dilated cardiomyopathy [9], left ventricular aneurysmectomy and implanting a pacemaker of cardiac resynchronization [10,11] are given being performed to improve the clinical conditions and reduce morbidity and mortality of HF patients.

The cardiac interventricular dyssynchrony is presented

as electromechanical regional change, leading to delays in both contraction and relaxation in cardiac muscle. Among the possible mechanisms of biventricular function worsening, the dyssynchronous contraction of the right ventricle stands out, leading to a septal bulging towards the left ventricle. This can unleash a delay in the papillary muscles activation with consequent mitral valve insufficiency [11].

The interventricular dyssynchrony can be analyzed by echocardiography, using the pulsed Doppler, calculating the electromechanical delay between the ventricles by measuring the time interval between the R wave of the electrocardiogram and the beginning of the curve of flow speed and aortic pulmonary flow. In case the difference between the two intervals is greater than 40 milliseconds, it is an indicative of interventricular dyssynchrony [12,13].

A cardiac resynchronization therapy plays an important role in treating patients with severe heart failure with conduction abnormalities and prolongation of the QRS complex, having as the main representative the left bundle branch block (LBBB), found in about 25-50% of patients [14].

Among the indications for implantation of cardiac resynchronizer with or without internal defibrillator, patients with dilated cardiomyopathy with depressed left ventricular ejection fraction (LVEF) less than 35% are included, patients with ischemic heart disease without surgical or interventional treatment conditions, irreversible structural changes, functional class III or IV with electrocardiogram (ECG) showing QRS>150 milliseconds or QRS 120 to 150 milliseconds with dyssynchrony [15].

Studies show that biventricular resynchronization therapy provides a significant medical improvement with a reduction in the number of hospital admissions, improvement in functional class and quality of life. The assessment of ventricular function by echocardiography demonstrates improvement in systolic and diastolic function and ejection fraction [16-20].

The echocardiographic analysis, a cost-effective favorable, reproducible and affordable examination reveals itself as a method not only for indication, but also for postoperative evaluation of patients who underwent cardiac resynchronization therapy, evaluating parameters such as ejection fraction, cardiac synchrony, ventricular remodeling, reducing the degree of mitral valve incompetence and reversal of interventricular electromechanical delay [21-24].

Considering the severity of patients with advanced heart failure with optimized medical treatment in need of surgical treatment and wtih electrocardiographic criteria, medical and echocardiographic for implantation of cardiac resynchronizer. The goal of this research is to analyze left ventricular function through of echocardiography in patients with advanced heart failure who underwent implantation of cardiac resynchronizer.

METHODS

Casuistry

The echocardiographic data of 24 patients with severe congestive heart failure were analyzed, classified as NYHA functional class III and IV according to the Criteria Committee of the NYHA, underwent implantation of transvenous cardiac resynchronizer, by Cardiovascular Surgery Service of the discipline of Cardiothoracic Surgery of the Helio Mandetta Faculty of Medicine-Federal University of Mato Grosso do Sul (UFMS), between June 2006 to June 2012, with the approval of the UFMS Ethics Committee in humans in the approval letter - protocol number 2235-CAAE 0354.0.049.000 11, on November 9, 2011.

The patients were between 34 and 86 years old, average 61.5 ± 11.1 years old, eight (33%) were female and sixteen (67%) males, according to Table 1. All patients were on maximum allowable drug therapy.

Concerning etiology, idiopathic dilated cardiomyopathy, valvular diseases from mild to severe functional impairment and ischemic cardiomyopathy have been demonstrated.

Table 1. General data of patients.

Patients	Gender	Age (years)	Functional Class
1. E.M.S.	M	65	III
2. E.S.P.	M	61	III
3. H.R.S.	F	60	III
4. J.B.S.	M	60	III
5. J.C.C.	M	66	III
6. M.D.L.	F	57	III
7. M.L.A.T.	F	57	IV
8. M.R.M.	F	54	IV
9. P.M.L.	M	69	III
10.C.C.N.	F	81	III
11. D.B.K.	F	60	IV
12. J.S.R.	M	69	IV
13. S.R.O.	M	63	III
14. N.O.S.	M	56	III
15. S.L.	M	61	IV
16. E.C.L.	F	74	III
17. B.F.S.	M	86	IV
18. I.F.M.	M	56	IV
19. E.L.F.	M	42	III
20. A.M.	F	69	III
21. M.A.S.	M	34	IV
22. J.G.I.	M	63	IV
23. E.A.O.S.	M	48	III
24. U.R.S.	M	66	III
		61.5 ± 11.1 years	

M: male; F: female

Inclusion Criteria

The inclusion criteria were: 1) patients with dilated cardiomyopathy (DCM) and congestive heart failure functional class (NYHA) III or IV refractory to optimized drug therapy; 2) patients with DCM without possibility of surgery (coronary artery bypass grafting, valve replacement, left ventricular aneurysm resection or correction of congenital heart disease); 3) left and right bundle branch block standard interventricular conduction disturbance, associated with anterosuperior or left branch induced right ventricular cardiac pacing exclusive block; 4) interventricular dyssynchrony documented on echocardiography; 5) QRS complex duration higher or equal to 120 ms.

Echocardiographic assessment

Echocardiographic evaluation was performed by the same examiner preoperatively and postoperatively with Medson EX 8008 Apparatus, transducers of frequency 2 and 3 MHz in conventional evaluation plans.

Table 2. Preoperative echocardiographic assessment of patients who underwent implantation of cardiac resynchronizer.

Patients	LVDD (mm)	LVSD (mm)	EF %
E.M.S.	80	70	26%
E.S.P.	79	69	23%
H.R.S.	63	53	30%
J.B.S.	85	72	31%
J.C.C.	65	50	45%
M.D.L.	65	51	43%
M.L.A.T.	56	48	28%
M.R.M.	72	62	29%
P.M.L.	81	64	48%
C.C.N.	68	54	43%
D.B.K.	49	44	25%
J.S.R.	80	70	24%
S.R.O.	65	53	37%
N.O.S.	67	55	33%
S.L.	77	62	33%
E.C.L.	78	65	34%
B.F.S.	64	54	20%
I.F.M.	70	64	20%
E.L.F.	78	64	36%
A.M.	55	47	30%
M.A.S.	86	74	29%
J.G.I.	69	62	22%
E.A.O.S.	58	53	19%
U.R.S.	72	61	31%
Mean	69.6	58.6	31%
SD	9.8	8.7	8%

LVDD: left ventricle diastolic diameter; LVSD: left ventricle systolic diameter; EF: ejection fraction; mm: millimeters; SD: standard deviation

The study used the echocardiographic data with, a maximum of one month before the pacemaker implantation multisite to evaluation before, and after six months for postoperative evaluation, shown respectively on Tables 2 and 3. The following variables were used: Left Ventricular Diastolic Diameter, Left Ventricular Systolic Diameter and Ejection Fraction, in the standardized methods in the literature.

Operative technique

The operative technique for implantation of cardiac resynchronizer starts with cardiac monitoring and degermation and antisepsis of the anterior chest wall and neck. Local anesthesia is performed with 2% lidocaine in an area located in the middle third of the right infraclavicular fossa, of approximately 4 cm^2. An incision of approximately 4 cm at the place above 1 cm below the right clavicle is made, with careful hemostasis.

The first electrode was placed in the right ventricle (RV), followed by the right atrium lead, both by puncture of the right subclavian vein in which the guide wires were inserted, and on them, inserting of the sheaths through which the endocavitary electrodes were passed (active fixation). They were placed in traditional sites (atrium into the right auricle and right ventricle at the end of it) or where the initiation of stimulation was obtained, with acceptable sensing and impedance. The last electrode was placed in the coronary sinus for left ventricular pacing. The electrodes used were: Corox OTW 75 DP (Biotronik®).

The position obtained by the use of radiological anatomy with fluoroscopy in left anterior oblique, at an angle of 35 degrees in order to position the electrode of passive fixation on the lateral or posterior vein of the left ventricle. Afterwards, electrophysiological tests took place to verify basic viability and stability. The final stimulus generator is connected, and it immediately starts its activity verified by electrocardiogram tracing. Then the closing of plans was held.

Postoperative follow-up

The days of observation and monitoring varied from November 2006 until June 2012. All patients were medicated in order to maintain the optimization of drug therapy for heart failure.

The postoperative evaluation was performed by the Doppler echocardiogram in six months postoperatively.

Statistical analysis

The analysis of quantitative variables was performed by comparing average (previously checked the normality of distributions), using the Student t test. The level of significance was $P < 0.05$.

RESULTS

The patients were discharged without complications during the perioperative and no death on the early postoperative.

According to the needs of each patient, there was drug use in their highest tolerated doses, with frequent use of digoxin, furosemide, carvedilol, acetylsalicylic acid (AAS), amiodarone, enalapril, losartan, warfarin and espironalactona.

Regarding postoperative data, according to Table 3, the mean left ventricular diastolic diameters were 66.8 ± 8.8 mm, systolic diameters, 52.7 ± 8.8 mm and ejection fraction 40 ± 7%.

Comparing the pre-and postoperatively data, according to Table 4, there was significant reduction in echocardiographic parameters and increase in the analyzed ventricular function. The average left ventricular diastolic diameter decreased from 69.6 ± 9.8 mm to 66.8 ± 8.8 mm, systolic diameters of 58.6 mm ± 8.8 to 52.7 ± 8.8 mm and there was an increase in ejection fraction, an average of 31% ± 8 to 40 ± 7% significance level, respectively, 0.019, 0.0004 and 0.0002, statistically significant with a significance level of 0.05.

Table 3. Postoperative echocardiographic assessment of patients who underwent implantation of cardiac resynchronizer

Patients	LVDD (mm)	LVSD (mm)	EF %
E.M.S.	87	70	38%
E.S.P.	79	60	39%
H.R.S.	62	43	57%
J.B.S.	77	64	34%
J.C.C.	64	51	43%
M.D.L.	69	55	40%
M.L.A.T.	66	52	43%
M.R.M.	67	57	31%
P.M.L.	70	38	43%
C.C.N.	65	49	48%
D.B.K.	53	37	57%
J.S.R.	71	58	37%
S.R.O.	58	45	44%
N.O.S.	72	59	36%
S.L.	75	62	35%
E.C.L.	78	65	28%
B.F.S.	58	54	35%
I.F.M.	60	48	40%
E.L.F.	73	58	41%
A.M.	53	43	39%
M.A.S.	76	66	27%
J.G.I.	61	47	45%
E.A.O.S.	54	44	36%
U.R.S.	63	48	47%
Mean	66.8	52.7	40%
SD	8.8	8.8	7%

LVDD: left ventricle diastolic diameter; LVSD: left ventricle systolic diameter; EF: ejection fraction; mm: millimeters; SD: standard deviation

Table 4. Preoperative and postoperative echocardiographic assessment of patients who underwent implantation of cardiac resynchronizer.

Parameters	Preoperative	Postoperative	SD
LVDD	69.6± 9.8 MM	66.8 ± 8.8 MM	0.019
LVSD	58,6 ± 8,8 MM	52,7 ± 8,8 MM	0.0004
EF%	31 ± 8%	40 ± 7%	0.0002

LVDD: left ventricle diastolic diameter; LVSD: left ventricle systolic diameter; EF: ejection fraction; mm: millimeters; SD: standard deviation

DISCUSSION

Heart failure is a serious public health problem, with high annual mortality [25]. In order to decrease the symptoms, complications and increase life expectancy, several forms of treatment are considered, such as pharmacological and nonpharmacological steps with major therapeutic advances in recent decades. However, many patients remain with significant symptoms and a high number of hospital admissions, determining reserved prognosis and expensive treatments [26,27]. Where surgical treatment should be considered.

The cardiac resynchronization therapy (CRT) has an important role in the treatment of patients with advanced heart failure with conduction abnormalities and prolongation of the QRS complex, as main representative the left bundle branch block (LBBB), present in approximately 25-50% patients [14,15,28,29].

Studies have shown the medical benefits of CRT. The tests MIRACLE [30] and MUSTIC [31], CONTAK CD [32] showed that CRT determines functional class improvement of HF patients, exercise tolerance (6 minutes walking test peak VO_2), reduction in the rate of HF hospitalization and improved quality of life through the Minnesota questionnaire. However, decrease in mortality with CRT and echocardiographic parameters improving were not demonstrated.

A meta-analysis of the CARE-HF [33], MUSTIC [31] and MIRACLE [30] studies, comparing biventricular pacing with optimized medical treatment alone showed a significant reduction in hospitalization rates, reducing the risk of death.

McAlister et al. [34], in 2007, in 11 months follow-up, demonstrated the efficacy and safety of biventricular pacing in over 10,000 patients. They concluded that CRT reduced hospitalizations and all causes of mortality. An

increase in ejection fraction was observed, improving quality of life for the Minnesota questionnaire and improvement in functional class.

However, some studies have shown that CRT was able to significantly improve as from the third month of follow-up echocardiographic parameters, such as reduced stroke volume and left ventricular end-diastolic and increasing of ejection fraction [26-28].

In contrast with the controversy in the literature regarding the improvement in echocardiographic parameters, this research has demonstrated an increase in ejection fraction of 31% ± 8 to 40 ± 7%, reducing of diastolic and left ventricular systolic diameter from 69.6 ± 9.8 mm to 66.8 ± 8.8 mm and 58.6 mm ± 8.9 to 52.7 ± 8.8 mm, respectively, all parameters statistically significant.

This research may infer that transvenous CRT improves benefits in the biventricular systolic function with significant improvement in echocardiographic parameters such as ejection fraction and reduction of systolic and diastolic diameters.

CONCLUSION

In the present study, there was improvement in left ventricular function assessed by echocardiography in patients with advanced heart failure who underwent implantation of cardiac resynchronizer.

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