Mechanism of Cardiac Resynchronization Therapy by Real-time Three-dimensional Echocardiography in Patients with Heart Failure

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We report the case of a 66-year-old man with heart failure NYHA class IV treated with biventricular pacing for cardiac resynchronization. The patient was evaluated by real-time three-dimensional transthoracic echocardiography before and 48 hours after pacemaker implantation. The use of three-dimensional echocardiography contributed to understanding the underlying mechanism involved in cardiac resynchronization therapy by demonstrating enhanced synchrony of myocardial segments, which resulted in the patient's clinical improvement.

Cardiac resynchronization using biventricular pacing (CRT) has been recommended as an adjuvant therapy for patients with symptomatic, advanced heart failure and under optimized drug therapy.[1,2] Indication for CRT takes into account clinical aspects, the presence of severe left ventricular contractile dysfunction, and either electrical or mechanical dyssynchrony. We report a patient with drug-refractory heart failure submitted to real-time three-dimensional transthoracic echocardiography (3D echo) for assessment of ventricular dyssynchrony and who progressed satisfactorily during hospitalization.

CASE REPORT

A sixty-six-year-old male patient with history of orthotopic heart transplantation for ischemic cardiomyopathy complicated by graft vasculopathy, in 1999, was admitted with decompensated heart failure. At presentation, he complained of dyspnea at rest, paroxysmal nocturnal dyspnea, and right hypochondrium pain.

On physical examination, the patient showed regular heart rate of 106 bpm, respiratory rate of 20 breaths/min, blood pressure of 112/66 mmHg, axillary temperature of 36.6 °C, abdominal bloating with liver edge palpable up to 8 cm from the right costal margin and weight gain of 12 kg in the previous two months, despite optimization of oral drug therapy. Cardiovascular examination revealed jugular venous distention up to the mandibular angle, evidence of ventricular gallop due to a third heart sound (S_3), and grade 3/6+ holosystolic murmur loudest at the ventricular apex. Resting ECG showed sinus tachycardia, right bundle-branch block (QRS duration = 143 ms).

Two-dimensional transthoracic echocardiogram showed mild left ventricular dilation (diastolic diameter of 58 mm), marked diffuse hypokinesia (ejection fraction estimated using biplane method/Simpson's rule of 0.25). This patient underwent both right and left heart catheterization, displaying right atrial filling pressures of 22/19 mmHg, pulmonary capillary pressure of 26 mmHg, pulmonary artery pressure of 53/34 mmHg, cardiac index of 1.82 L/min/m2, marked diffuse left ventricular hypokinesia, and diffuse coronary lesions that could not be approached by therapeutic hemodynamic procedures. He was also given intravenous therapy for heart failure management, and had multiple episodes of unsustained ventricular tachycardia, reverted acute renal failure, and gout. The patient underwent implantation of a biventricular pacemaker for cardiac resynchronization and a defribillator (MedTronic InSync II Marquis 7289, MedTronic, California, USA) due to advanced heart failure, recurrent hospitalization in the previous months despite drug therapy optimization, marked left ventricular contractile dysfunction, recurrent unsustained ventricular

tachycardia, and widened QRS complex. Biventricular pacing was performed endocardially via de coronary sinus, according to the cardiac venous anatomy. A left ventricular electrode was implanted in the lateral wall. Real-time three-dimensional transthoracic echocardiography was performed (Philips Sonos 7500, Andover, USA) before and 48 hours after biventricular pacing (Table I). Three-dimensional echocardiographic analysis was performed in workstation using a special software (TomTec Imaging Systems, 4D CardioView software 1.3, Munich, Germany). The patient was discharged clinically improved three days after pacing and is currently under outpatient follow-up.

DISCUSSION

Biventricular pacing for cardiac resynchronization in patients with advanced heart failure has therapeutic benefits, resulting in clinical and laboratory improvement. This is due to enhanced intra- and interventricular synchrony, as well as increased ventricular filling time[1]. Clinical and functional improvement following biventricular pacing is evidenced by increased LVEF and oxygen consumption (VO_2), enhanced quality of life (Minnesota score), decreased mitral regurgitation, reduced number of hospital admissions, lower serum neurohormone levels, and decreased QRS complex duration[2-6].

CRT is currently indicated for symptomatic patients despite drug therapy optimization when they present NYHA functional class IV, QRS complex duration > 130 ms, LBBB morphology, LVEF < 35% (as shown on echocardiography by Simpson' method), and left ventricular diastolic diameter > 55 mm (Degree of recommendation IIa, level of evidence A).[7] However, about 30% of the patients with ventricular dyssynchrony seen on ECG do not benefit from CRT[5]. Hence, electrical

dyssynchrony on ECG alone seems to be inadequate to identify patients who will respond to treatment. It should be also noted that CRT is costly, in addition to presenting complication rates of up to 8%[2]. Therefore, electromechanical inter- and/or intraventricular dyssynchrony should be observed for CHF patients to be indicated for CRT.

Electromechanical ventricular asynchrony may be evidenced by using radiopharmaceuticals, nuclear magnetic resonance or echocardiography. Echocardiography is a simple, highly reproducible and easy-to-perform technique that provides information not only for CRT indication, but also for drug therapy optimization and clinical follow-up. Accordingly, echocardiography provides data regarding atrioventricular, inter- and intraventricular synchrony and contributes to CRT optimization through optimization of atrioventricular interval and its relationship to diastolic filling. Also, during clinical follow-up it allows the determination of LVEF and yields information on LV negative remodeling by the calculation of ventricular volumes, ventricular mass index, mass/volume ratio, and ventricular sphericity index.

Different echocardiographic modalities have been used for the assessment of ventricular synchrony. From conventional techniques, such as M-mode and pulsed Doppler, to more advanced modalities, such as tissue Doppler, strain and strain rate, plus 3D real-time echo, they can provide information on ventricular synchrony. Using M-mode, LV septal-to-posterior wall motion delay is measured. Patients considered most likely to respond to CRT are those with a delay >130 ms[8]. Pulsed Doppler provides information on cardiac synchrony by measuring the ventricular pre-ejection period (intraventricular synchrony) and ventricular filling time (atrioventricular synchrony), and also the differences between the onset of the QRS complex and the pulmonary flow and the beginning of the QRS complex and the aortic flow (interventricular synchrony)[5]. Tissue Doppler and strain imaging are reliable indicators of regional ventricular contraction, making echocardiographic analysis more accurate and close to reality. The use of tissue Doppler allows measurement of the Q-S interval, which represents the time elapsed between the beginning of the QRS complex and peak of the S-wave (ventricular contraction) on the four LV walls and on the free wall of RV. The QS interval is usually measured at basal segments (at atrioventricular ring level) of the four LV walls and the RV free wall. Then, the greatest difference between left ventricle QS intervals and also right ventricle QS intervals is taken. In the case of this patient, only left ventricle QS intervals were measured, because that was the hospital protocol. Prior to CRT, the greatest difference of left ventricle QS intervals was 90 ms, and after CRT, 40 ms (Table I), showing intraventricular synchrony improvement.

Three-dimensional echo allows calculation of LV dyssynchrony index (SDI), corresponding to the standard deviation of the mean time of systolic contraction for each of the 16 left ventricular segments (fig. I), with normal

Table I - Real-time three-dimensional transthoracic echocardiographic and tissue Doppler studies before and two days following biventricular pacing

	Prepacing	Postpacing (2º day)
LV ejection fraction (3D) (%)	27.2	32.3
LV end-diastolic volume (3D)(ml)	166.8	161.2
LV end-systolic volume (3D)(mL)	113.3	109.1
LV mass (3D)(g)	161.8	160.9
LV mass/volume ratio (3D)	1.03	1
LV diastolic diameter (2D) (cm)	5.6	5.6
Q-S interval (Tissue Doppler) (ms)		
Anterior wall	200	200
Inferior wall	230	220
Septal wall	180	190
Lateral wall	270	230
Index of LV dyssynchrony (%)	24.8	12.8

3D - real-time three-dimensional transthoracic echocardiography; 2D - two-dimensional transthoracic echocardiography; LV - left ventricle; Q-S - interval between the beginning of Q-wave on the ECG and the peak of S-wave on tissue Doppler

value < 8%. SDI may also be calculated taken into account only 12 ventricular segments, leaving out the 4 apical segments. In this patient, SDI was 24.8% pre-CRT and 12.8% post-CRT, characterizing great improvement in left ventricular synchrony (Table I).

SDI calculation enables not numerical determination of ventricular dyssynchrony, but also identification of the site of greatest dyssynchrony, where the left electrode should ideally be placed. In this case, pre-CRT synchrony pattern is quite heterogeneous, but the greatest conduction delay was found on the lateral wall (Fig. 2, red line), where the left ventricular electrode was implanted. Implantation of left electrode in a site other than that where the greatest conduction delay occurs and the ensuing ventricular contraction may be one of the mechanisms that account for failure to appropriate response following CRT.

By determining SDI immediately after pacemaker implantation, three-dimensional echo provides an insight into the mechanism involved in ventricular resynchronization therapy. In the reported case, an increase in LVEF (from 27.2% to 32.3%) 48 hours following CRT was noted, with maintenance of ventricular

volumes, ventricular mass index, LV diastolic diameter and LV mass/volume ratio. Therefore, the mechanism associated with the improvement in LV contractile performance was enhanced left intraventricular synchrony, as shown by lower SDI 48 hours after CRT. A further characteristic of this patient was the presence of prolonged QRS and RBBB morphology, as with most Brazilian patients with Chagas' disease. Larger studies are needed to determine whether CRT may be a promising treatment for this group of patients with CHF class III and IV (NYHA) and RBBB.

The use of real-time three-dimensional echocardiogram has advantages regarding CRT, namely: to allow real-time, simultaneous, fast analysis of all ventricular segments, facilitate and standardize communication between cardiac electrophysiologists or surgeons who perform biventricular pacing, enable quantification of pre-implantation ventricular dyssynchrony (dyssynchrony index) imme-diately after the procedure and during clinical follow-up. Its disadvantages, however, include the high cost of 3D echocardiography equipment, the need of cardiologists trained in and familiar with the technique, and the limited quality of images acquired for three-dimensional analysis.
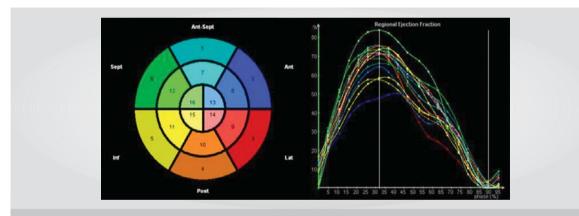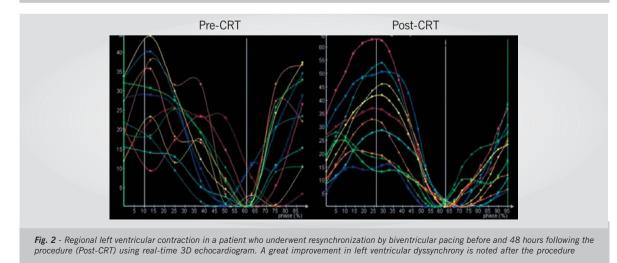

Fig. 1 - *Regional left ventricular contraction in a 16-segment model of the left ventricle using real-time 3D echocardiogram. Normal volunteer*

Fig. 2 - *Regional left ventricular contraction in a patient who underwent resynchronization by biventricular pacing before and 48 hours following the procedure (Post-CRT) using real-time 3D echocardiogram. A great improvement in left ventricular dyssynchrony is noted after the procedure*

CONCLUSION

The use of three-dimensional echocardiography allowed evaluation of cardiac resynchronization after biventricular pacing in this patient with RBBB and CHF class II and IV (NYHA). This technique may be a valuable adjuvant not only to CRT indication for patients with advanced CHF, but also to determination of the implantation site for the left electrode and evaluation of reverse ventricular remodeling during the patient's clinical evolution.

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