Twenty-millisecond interventricular difference as assessed by body surface potential mapping identifies patients with clinical improvement after implantation of cardiac resynchronization device

Nelson Samesima, Roberto Douglas, Nancy Tobias, Anísio Pedrosa, Martino Martinelli Filho, José Antonio Ramires, Carlos Alberto Pastore

Electrocardiology Service, Heart Institute of the University of São Paulo Medical School, São Paulo, Brazil

ABSTRACT

Objective: There is little research on the ventricular electrical aspects following cardiac resynchronization therapy (CRT). This study sought to establish electrocardiographic criteria associated to the ventricular electrical activation process that could identify patients with functional class (FC) improvement after CRT, by using the noninvasive method of body surface potential mapping (BSPM).

Methods: Fifty-six patients with chronic heart failure and left bundle-branch block (LBBB), who had undergone CRT, with mean age 59.9±10.8 years, left ventricular ejection fraction 30.9±8.3%, QRS 184±35ms, FC (NYHA) II – 16%, III – 68% and IV – 16%, were selected. Through the 87-lead BSPM isochronous maps, ventricular activation times (VAT) of both right (RV) and left ventricles (LV) were analysed, in two situations: (1) native LBBB and (2) during biventricular pacing. After CRT, patients were divided in two groups: with and without FC improvement. The VATs were compared by the Mann-Whitney's test. The ratio of patients with and without FC improvement who showed RV-to-LV VAT difference ≤20ms, and >20ms, was compared using the Fisher's test. Significance level was accepted as p≤0.05.

Results: Clinical characteristics of patients before CRT were similar in the groups. Patients with FC improvement (47) had RV-to-LV VAT difference during biventricular pacing shorter than those without FC improvement (14.40±13.0ms vs 23.8±9.4ms, p=0.0151). Moreover, the majority of patients with FC improvement had an RV-to-LV VAT difference ≤20ms during biventricular pacing (70% vs 22%, RR 5.8, CI 95% 1.334–25.517, p=0.01).

Conclusion: The RV-to-LV ventricular activation time difference of less than or equal to 20 milliseconds, as characterised by BSPM, could identify patients who presented with improved functional class after undergoing CRT. *(Anadolu Kardiyol Derg 2007: 7 Suppl 1; 213-5)*

Key words: body surface potential mapping, functional class, ventricular electrical activation

Introduction

Management of heart failure (HF) has greatly improved during the last decades with the introduction of the angiotensin converting enzyme inhibitors, beta-blockers and spironolactone. From the observation that the presence of a bundle-branch block or an intraventricular delay of the electrical impulse transmission could worsen HF due to a deteriorated systolic function (1-3), studies were conducted using the simultaneous stimulation of both ventricles in the attempt to promote ventricular resynchronization (1-5). Based on these results, the 2005 ACC/AHA Consensus has since recommended cardiac resynchronization therapy (CRT) for HF patients in sinus rhythm, with left ventricle ejection fraction lower than or equal to 35%, evidence of left ventricle dyssynchrony, mild to severe symptoms (New York Heart Association (NYHA) functional class III or IV) despite an optimal drug therapy (6). Notwithstanding the good results CRT has yielded, 20% to 30% of patients still do not show clinical improvement (7-9). Therefore, some methods have been employed aiming to better evaluate an accurate indication for CRT, thereby trying to reduce the amount of "nonresponders" (8-12). This study sought to establish electrocardiographic criteria associated to the ventricular electrical activation process, which could be capable of identifying patients with functional class (FC) improvement after undergoing cardiac resynchronization therapy, with basis on the noninvasive method of the body surface potential mapping (BSPM).

Methods

Inclusion criteria: patients with HF, left bundle-branch block, who had a cardiac resynchronization device implanted.

Exclusion criteria: Presence of an atrial fibrillation (AF) and/or a right bundle-branch block, and/or a hypertrophic cardiomyopathy, and/or a congenital cardiopathy.

Study population: Initially, ninety patients who had undergone CRT had a body surface potential mapping assessment performed. Among them, 28 patients were excluded due to:

Address for Correspondence: Nelson Samesima, MD, Electrocardiology Service, Heart Institute of the University of São Paulo Medical School, São Paulo, Brazil
Phone: +55 11 3069 5598 Fax: +55 11 3062 0343 E-mail: nsamesima@hotmail.com

Anatol J Cardiol 2007: 7 Suppl 1; 213-5
Anadolu Kardiyol Derg 2007: 7 Özel Sayı 1; 213-5

AF (19 patients), hypertrophic cardiomyopathy (3 patients), right bundle-branch block (3 patients), congenital cardiopathy (1 patient), lack of pre-implantation data (2 patients). Other 6 patients were lost to follow-up. Table 1 displays the clinical characteristics of the remainder 56 patients. These patients were allocated in two groups after CRT: those with NYHA functional class improvement, and those without FC improvement. Cardiopathy was of idiopathic (25 patients), Chagasic (16 patients), ischemic (10 patients) and hypertensive origin (5 patients).

Body surface potential mapping: This noninvasive method comprises 87 electrocardiographic electrodes to be distributed 58 on the anterior, and 29 on the posterior surface of the body. It provides maps of isochronous lines, which enable the visualization of the global ventricular activation times (Fig. 1). Furthermore, it is possible to individualize the right ventricle (RV) and left ventricle (LV) areas, thereby characterizing the regional ventricular activation times (VAT) (Fig. 2). Measurement of VATs was semi-automatically performed in each patient by the Fukuda Denshi model 7100 BSPM equipment (Fukuda Denshi Co., Inc., Tokyo, Japan) during two clinical study situations, (1) in their own baseline rhythm (i.e., with native left bundle-branch block), and (2) in the rhythm induced by biventricular pacing.

Statistical analysis: Continuous variables are presented as mean±standard deviation. Mean VATs of groups with and without functional class improvement were compared through the nonparametric Mann-Whitney's test. Fisher's test was used for comparing the group who showed RV-to-LV VAT difference shorter than or equal to 20 ms and the group with greater than 20 ms VAT difference. Significance level was set at $p<0.05$.

Table 1. Clinical characteristics

Age, years	60+11
Male gender, n (%)	37 (62)
LVEF, %	31±8
QRS duration, ms	186+35
Functional class, n (%)	
II	9 (16)
III	38 (68)
IV	9 (16)

LVEF- left ventricular ejection fraction

Table 2. Baseline clinical characteristics of patients with different response to CRT

Variables	Functional class improvement (47)	Worsened functional class (9)
Age, years	60.43±11.45	57.33±9.42
Male gender, n (%)	30 (64)	4 (44)
LVEF before CRT, %	31.4±8.2	28.6±8.7
QRS duration, ms	185.5±35.6	177.8±23.3
SÂQRS, °	-27.4±79.7	-10.0±60.1
Functional class, n (%)		
II	7 (15)	2 (22)
III	33 (70)	5 (56)
IV	7 (15)	2 (22)

CRT- cardiac resynchronization therapy, LVEF- left ventricular ejection fraction, SAQRS- spatial angle of QRS

Results

The clinical characteristics of patients were similar in the groups before CRT (Table 2). All 56 patients were clinically evaluated (NYHA FC), before and after implantation (1051±746 days). Patients with FC improvement (47) evidenced a shorter RV-to-LV VAT difference during biventricular pacing than the group without FC improvement (14.40±13.0 ms x 23.8±9.4 ms, p=0.0151). Furthermore, the majority of the patients with FC improvement had an RV-to-LV VAT difference of ≤20 ms during biventricular stimulation (70% vs 22%, RR 5.8, CI 95% 1.334–25.517, p=0.01).

Discussion

The advent of the CRT brought great advancement to the management of HF, with significant results over morbidity and mortality. However, a reasonable percentage of patients does not benefit from this therapy. Therefore, complementary methods such as the electrocardiogram, tissue Doppler echocardiogram and electroanatomic mappings attempt at identifying parameters capable of distinguishing the best candidates for CRT (8-14). In the present study, the BSPM was employed to assess and

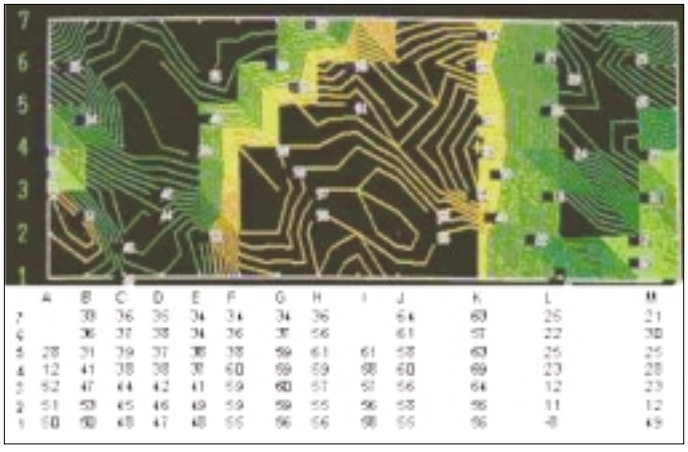

Figure 1. Map of isochronous lines forwarded by body surface potential mapping

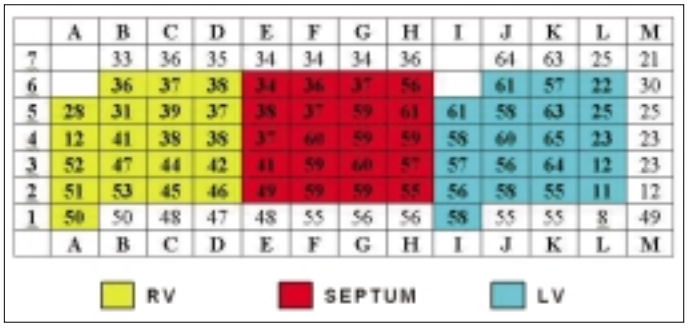

Figure 2. Regional disposition of ventricular electrical activation times
LV- left ventricle, RV- right ventricle

analyze patients implanted with a cardiac resynchronization device as to their clinical evolution regarding the functional class presented before and after undergoing CRT. In previous publications we characterized through the BSPM the ventricular electrical activation of normal individuals and of patients with left bundle branch block,, and additionally we identified the activation of areas associated with the right ventricle, the septum and the left ventricle (15-17). Thus, in applying the same methodology to patients with a cardiac resynchronizing device, we showed that those patients who evolved to a better functional class after CRT also showed a difference of up to 20 milliseconds between the right ventricle and left ventricle electrical activation times. On the other hand, those who showed a worsened functional class after CRT, had that difference greater than 20 milliseconds.

Conclusion

The BSPM demonstrated that a difference of up to 20 milliseconds between the electrical activation times of the right and left ventricles could identify those patients with functional class improvement after CRT.

References

1. Leclercq C, Kass DA. Retiming the failing heart: principles and current clinical status of cardiac resynchronization. J Am Coll Cardiol 2002; 39: 194-201.
2. Auricchio A, Abraham WT. Cardiac resynchronization therapy: current state of the art: cost versus benefit. Circulation 2004; 109: 300-7.
3. Leclercq C, Hare JM. Ventricular resynchronization: current state of the art. Circulation 2004; 109: 296-9.
4. Abraham WT, Hayes DL. Cardiac resynchronization therapy for heart failure. Circulation 2003; 108: 2596-603.
5. Jarcho JA. Resynchronizing ventricular contraction in heart failure. N Engl J Med 2005; 352: 1594-7.
6. Hunt SA, Abraham WT, Chin M, Feldman AM, Francis GS, Ganiats TG, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). J Am Coll Cardiol 2005; 46: e1-82.
7. Saxon, LA, Ellenbogen, KA. Resynchronization therapy for the treatment of heart failure. Circulation 2003; 108:1044-8.
8. Bax JJ, Ansalone G, Breithardt OA, Derumeaux G, Leclercq C, Schalij MJ, et al. Echocardiographic evaluation of cardiac resynchronization therapy: ready for routine clinical use? A critical appraisal. J Am Coll Cardiol 2004; 44:1-9.
9. 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.
10. Mehra MR, Greenberg BH. Cardiac resynchronization therapy: caveat medicus! J Am Coll Cardiol 2004; 43:1145-8.
11. Achilli A, Sassara M, Ficili S, Pontillo D, Achilli P, Alessi C, et al. Long-term effectiveness of cardiac resynchronization therapy in patients with refractory heart failure and "narrow" QRS. J Am Coll Cardiol 2003; 42: 2117-24.
12. Kass DA. Predicting cardiac resynchronization response by QRS duration: the long and short of it. J Am Coll Cardiol 2003; 42: 2125-7.
13. Auricchio A, Fantoni C, Regoli F, Carbucicchio C, Goette A, Geller C, et al. Characterization of left ventricular activation in patients with heart failure and left bundle branch block. Circulation 2004; 109: 1133-9.
14. Fantoni C, Kawabata M, Massaro R, Regoli F, Raffa S, Arora V, et al. Right and left ventricular activation sequence in patients with heart failure and right bundle branch block: a detailed analysis using three-dimensional non-fluoroscopic electroanatomic mapping system. J Cardiovasc Electrophysiol 2005; 16: 112-9.
15. Pastore CA, Moffa PJ, Tobias NM, de Moraes AP, Kaiser E, Cuoco MA, et al. Left bundle branch block analysis by body surface mapping. Comparison with electrocardiographic and vectorcardiographic findings. Arq Bras Cardiol 1996; 66: 253-6.
16. Pastore CA, Tobias N, Samesima N, Martinelli FM, Pedrosa A, Nishioka S, et al. Body surface potential mapping investigating the ventricular activation patterns in the cardiac resynchronization of patients with left bundle-branch block and heart failure. J Electrocardiol 2006; 39: 93-102.
17. Pastore CA, Tobias N, Samesima N, Martinelli FM, Pedrosa A, Nishioka S, et al. Ventricular electrical activation in cardiac resynchronization as characterized by body surface potential mapping. Arq Bras Cardiol 2007; 88: 251-7.