Ventricular Electrical Activation in Cardiac Resynchronization as Characterized by Body Surface Potential Mapping

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Summary

Objectives: To assess cardiac electrical activation by using body surface potential mapping (BSPM), in patients with congestive heart failure (CHF) and left bundle branch block (LBBB) undergoing cardiac resynchronization therapy (CRT) with biventricular pacemaker (BIV-PM) implantation.

Methods: Mean cardiac electrical activation times were analyzed in the right ventricle (RV) (mean RV activation time = mRV), anteroseptal area (mAS), and left ventricle (mLV) of 28 patients (mean age 61.2 ± 9.5 years; NYHA class III-IV CHF; ejection fraction <40%; LBBB of mean QRS 181.2±19.4ms, SÂQRS –8.5º±68.6º), as shown in their BSPM isochronous maps, before and after implantation of atriobiventricular pacemaker, comparing those with values obtained from a control group of normal individuals [CG], in three situations: (1) native LBBB; (2) RV pacing; and (3) atriobiventricular pacing.

Results: Situation (1): mRV and mAS values were similar (41.0±11.8ms x 43.6±13.4ms), with delayed mLV (81.0±12.5ms, p<0.01) and asynchronous with RV and AS areas; situation (2): mRV was greater than in CG (86.8±22.9ms, p<0.001), with greater difference between mAS and mLV (63.4±20.7ms vs. 102.7±20.3ms; p<0,001); situation (3): mLV and mRV were similar (72.0±32.0ms vs. 71.6±32.3ms), mRV was greater than in CG and native LBBB (71.6±32.3ms vs. 35.1±10.9ms and 41.0±11.8ms; p<0.001), and mAS was close to CG and native LBBB values (51.3±32.8ms vs. 50.1±11.4ms and 43.6±13.4ms).

Conclusion: The body surface potential mapping showed that RV and LV activation times which are similar, and are close to those of the AS area, suggest patterns of synchronized ventricular activation in patients with CHF and LBBB during atriobiventricular pacing.

Key words: Bundle-branch block; heart failure, congestive; cardiac pacing, artificial; body surface potential mapping.

Introduction

The treatment of heart failure is still a major challenge in medicine. Despite the advance of pharmacological therapy, patients not controlled with optimized medical treatment have an important option in the non-pharmacological treatment. Heart transplantation has shown significant improvement in the quality of life with reduction in mortality. The different surgical procedures for the treatment of CHF were not very successful. The development of atriobiventricular cardiac pacing introduced in the 1990's with the objective of resynchronizing ventricles in the presence of left bundle branch block (LBBB) has changed the natural history of CHF[1]. This technique, known as cardiac resynchronization therapy (CRT), showed significant improvement of the functional class and ejection fraction in individuals with severe ventricular dysfunction and LBBB[2-5].

Echocardiographic studies revealed that the hemodynamic consequences of abnormal conduction patterns in patients with dilated cardiomyopathy are closely related to QRS complex widening and apparently may result from an interventricular asynchrony and delayed septal contraction[6,7]. Considering that CRT is an expensive invasive procedure, and that approximately 30% of the patients derive no proven benefit from it, the great current challenge is to define the characteristics of optimal candidates to undergo CRT[8].

The electroanatomic mapping assessment, in turn, demonstrated the importance of the correct positioning of the leads of the pacemaker system for a better resynchronization and favorable responses to CRT[9-11].

Thus, body surface potential mapping (BSPM) may be useful in the assessment of biventricular pacing, facilitating the understanding of the mechanisms of cardiac electrical activation, and separating the activation of the right and left chambers, as well as contributing to other methods already described in the identification of the patients more likely to respond to CRT.

The objective of the present study was to investigate different patterns of cardiac electrical activation in patients with CHF and LBBB, using isochronous maps of BSPM to elucidate the possible mechanisms responsible for the great number of patients non-responsive to CRT.

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Methods

Body surface potential mapping (BSPM) - BSPM records the sequence of ventricular activation times (VAT) obtained from 87 electrodes placed on the anterior and posterior surface of the chest. The system allows the automatic translation of data into isochronous maps that characterize ventricular activation times in milliseconds (ms), which can be analyzed separately or together, characterizing a cardiac area. The 87 unipolar electrodes of the Fukuda Denshi BSPM instrument (Fukuda Denshi, Tokyo, Japan) model 7100, with 59 electrodes distributed on the anterior chest and 28 on the back, made simultaneous records. Electrical potentials were digitalized, processed and visualized in the BSPM matrix as PQRST complexes (Fig. 1A), distributed according to the orientation of the electrode system and defined by letters with their respective numeric indexers. In addition to assessing the traditional electrovectorcardiographic variables (rhythm, PR interval, axes, QRS complex width, orientation and direction of the loops in the horizontal and frontal planes), the system also generates isochronous maps which record cardiac electrical activation times (in ms) automatically and sequentially[12] (Fig. 1B).

Atriobiventricular pacemakers - Atriobiventricular pacemakers were implanted in 28 patients: 20 through the coronary sinus, and eight via thoracotomy (Pulsar M, Discovery, Guidant; Insync ICD)[13].

The patients studied had their ventricular electrical activation sequence assessed in three different situations: 1) native LBBB (baseline, pre-implantation); 2) right ventricle pacing (PM-RV; post-implantation); and 3) atriobiventricular pacing (PM-BIV; post-implantation). No modification in the V-V interval was made for the BSPM analysis.

Population studied - Twenty eight patients of which 71% were males (20), with mean age of 61.2 ± 9.5 years, idiopathic CHF (61%), New York Heart Association (NYHA) functional class III and IV, ejection fraction ≤ 40% (mean 28.2% ± 7.9%), LBBB with QRS ≥ 140 ms (mean 181.2ms ± 19.4ms) and SÂQRS – 8,5º ± 68,6º were studied. All patients underwent BSPM before and after implantation of atriobiventricular pacemakers.

Inclusion criteria were: age above 18 years, sinus rhythm, moderate to severe heart failure (NYHA functional class III-IV) refractory to drug therapy, ejection fraction ≤ 40% (as determined by radionucleotide ventriculography), and intraventricular conduction disturbance (LBBB) with QRS ≥ 140ms. Exclusion criteria were: severe systemic diseases (neoplasia, chronic renal failure, unstable ischemic syndrome, severe pulmonary disease), life expectancy lower than 6 months, age under 18 years, any contraindication to atriobiventricular pacemaker implantation, or impossibility to undergo pre- or postoperative tests for whatever clinical reason.

All patients included in the study gave their written consent approved by the Ethics Committee of Universidade de São Paulo.

Control group - We chose to include in the study a control group, which underwent BSPM to obtain reference values and identification of the normal pattern of ventricular electrical activation. It is important to point out that to date no "normal" pattern has been established by the BSPM in the literature. Twenty healthy patients, 11 (55%) males, mean age of 56 ± 10.1 years, with normal values of clinical tests, electrocardiogram (ECG) and echocardiography were selected to comprise a control group of individuals with normal hearts.

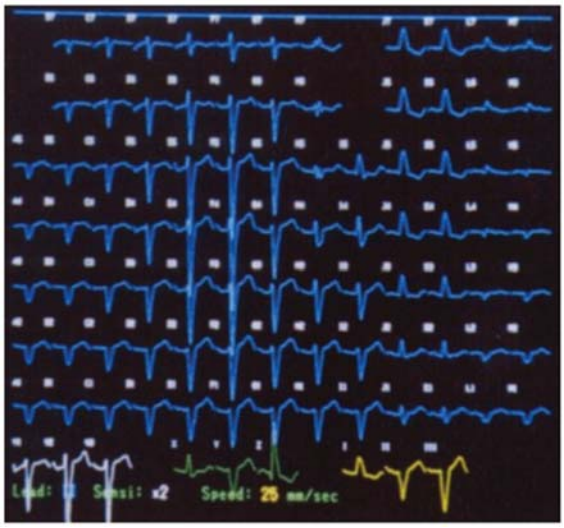

Fig. 1A - *PQRST complexes recorded by the 87 Body Surface Potential Mapping leads.*

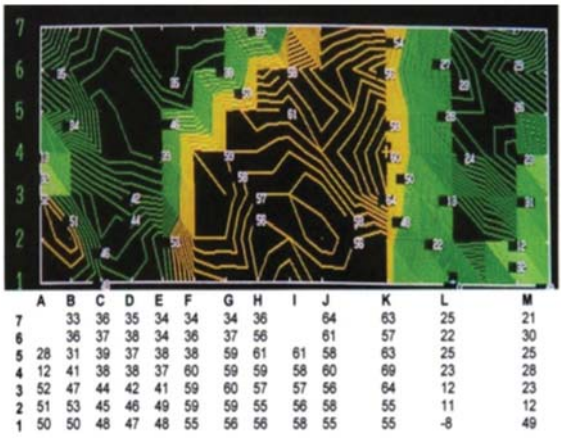

Fig. 1B - *Isochronous map of cardiac electrical activation.*

Statistical analysis - The matrixes of ventricular electrical activation times recorded in the isochronous maps were statistically analyzed, and three distinct areas resulted from this analysis, corresponding approximately to the right ventricle (RV), anteroseptal area (AS), and left ventricle (LV) (Fig. 2). From them, the mean values (mean activation times) were calculated for each area: right ventricle (mRV), anteroseptal area (mAS), and left ventricle (mLV). The analysis of variance (ANOVA) was used to compare these mean values in the three study situations: (1) native LBBB, (2) PM-RV, and (3) PM-BIV, and all these values were compared with reference values of the normal control group (CG). The Bonferroni correction was used for multiple comparisons. The significance level was established at $p \leq 0.05$.

	A	B	C	D	E	F	G	H	I	J	K	L	M
7		33	36	35	34	34	34	36		64	63	25	21
6		36	37	38	34	36	37	56		61	57	22	30
5	28	31	39	37	38	37	59	61	61	58	63	25	25
4	12	41	38	38	37	60	59	59	58	60	65	23	23
3	52	47	44	42	41	59	60	57	57	56	64	12	23
2	51	53	45	46	49	59	59	55	56	58	55	11	12
1	50	50	48	47	48	56	56	56	58	55	55	-8	48
	A	B	C	D	E	F	G	H	I	J	K	L	M

RV AS LV

Fig. 2 - *Study areas: Right Ventricle (RV), Anteroseptal area (AS), and Left Ventricle (LV).*

Results

Clinical characteristics - Among the clinical variables studied after CRT, a 19.1% reduction in QRS duration (181.2 ms ± 19.4 ms vs. 145.7 ms ± 20.5 ms), a 7.6% increase in ejection fraction (28.2% ± 7.0% vs. 31.4% ± 10.8%), and improvement in functional class in 75% of the patients were observed.

Analysis of ventricular activation times - The values of mean ventricular activation times found were:

1. In the control group – CG (reference values): mRV = 35.1 ms ± 10.9 ms; mAS = 50.1 ms ± 11.4 ms; and mLV = 53.2 ms ± 10.8 ms.

2. In the group of patients with LBBB, ventricular activation times were assessed in three situations:

• situation 1 – native LBBB: mRV = 41.0 ms ± 11.8 ms; mAS = 43.6ms ± 13.4 ms; and mLV = 81.0ms ± 12.5 ms.

• situation 2 - PM-RV (induced LBBB): mRV = 86.8 ms ± 22.9 ms; mAS = 63.4 ms ± 20.7 ms; and mLV = 102.7 ms ± 20.3 ms.

• situation 3 - PM-BIV: mRV = 71.6 ms ± 32.3 ms; mAS = 51.3 ms ± 32.8 ms; and mLV = 72.0 ms ± 32.0 ms.

In situation 1 (native LBBB), the activation of RV and AS regions was similar (p = NS). In the LV region it was more precocious (p < 0,001), and lost synchronism with the anteroseptal area. In relation to the control group, the left ventricular activation was delayed (p < 0,001).

After implantation of the atriobiventricular pacemakers, the system was set to pace only the RV or both ventricles. In situation 2, with RV pacing only (PM-RV), a significant increase in mRV, mAs, and especially in mLV in comparison with the control group (p < 0.001) was verified. In this situation, activation times in the two ventricles were not significantly different; however, significant differences were verified between the RV and the AS region (p < 0.05), as well as between the AS region and the LV (p < 0.001).

In situation 3, atriobiventricular pacing (PM-BIV), the mRV increased significantly and was delayed in relation to the control group and to the native LBBB (p < 0.001). In this situation, mAS was close to the values observed in the control group and in the native LBBB (p = NS); the mLV was significantly delayed when compared to the control group (p < 0.05) and had a value similar to that of RV (p = NS). This fact indicates that the electrical activation of both ventricles occurred simultaneously.

Figure 3 shows a graphical comparison of the values obtained in the three areas (RV, AS, and LV) in each of the study situations (native LBBB, PM-RV, and PM-BIV) and the reference values obtained in the control group (CG).

Figure 4 shows isochronous activation line maps in the frontal and horizontal planes with the matrixes of the mean ventricle and anteroseptal area activation times in, which the difference brought by the atriobiventricular activation (PM-BIV) in relation to the study group in the situation of native LBBB is shown.

Figure 5 compares the LV-to-anteroseptal-area conduction delay in the three study situations and in the control group, characterizing the better electrical synchronism of the ventricles provided by the atriobiventricular pacing.

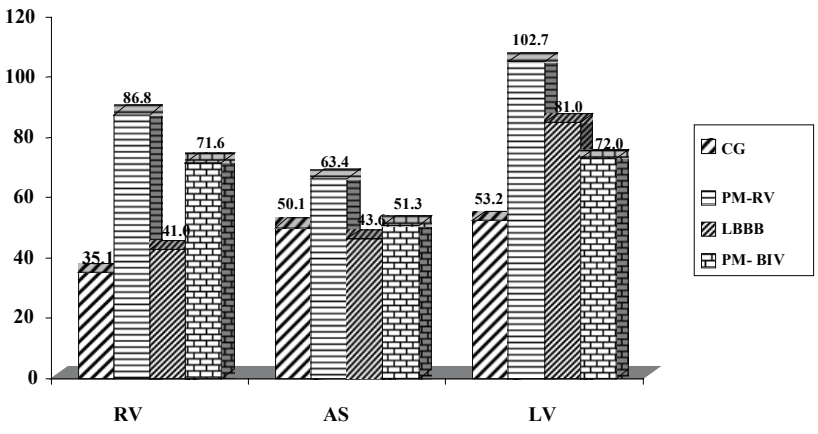

Fig. 3 - *Graph comparing mean ventricular activation times in the three study areas (RV, AS, and LV), in the three study situations (native LBBB, PM-RV, and PM-BIV), and with reference values of the normal control group (CG).*

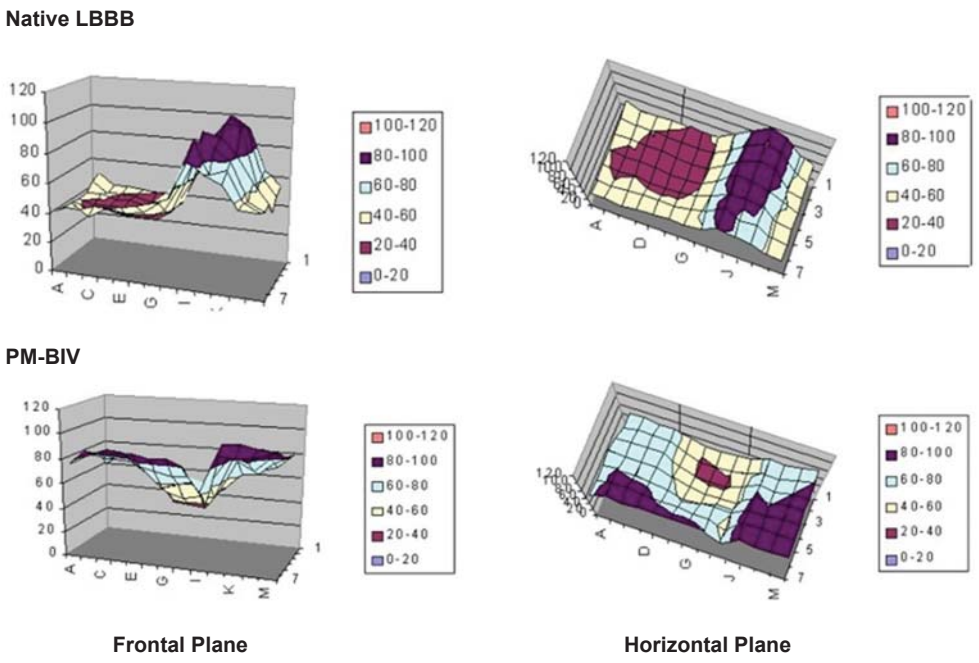

Fig. 4 - 3-D graphic representation in the frontal and horizontal planes of the matrixes of mean electrical activation times in the ventricles and in the anteroseptal region observed in the isochronous maps constructed with values of the LBBB group in two of the study situations, native LBBB and atriobiventricular pacing (PM-BIV).

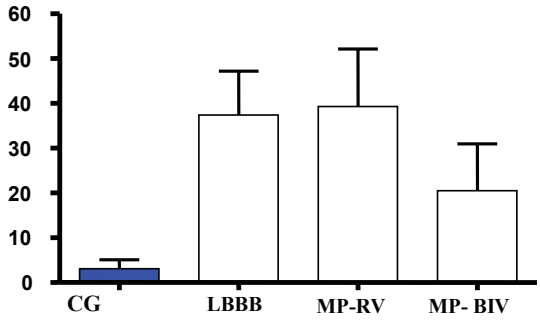

Fig. 5 - Comparison of the LV-septal region conduction delay in the three study situations and in the control group.

Discussion

Patients with wide QRS complexes are assumed to present both interventricular and intraventricular conduction delay during their cardiac electrical activation process. This conduction abnormality (LBBB) is an independent marker associated with a 70% higher risk of mortality and sudden death among patients with dilated cardiomyopathy[14]. The result of the abnormal electrical activation in one of the ventricles is an asynchronous chamber contraction with a decreased efficiency[13].

The present analysis using body surface potential mapping demonstrated that, from the electrical point of view, the atriobiventricular pacing improved the ventricular electrical activation sequence.

However, no improvement of the ventricular function was observed in approximately 30% of the patients after cardiac resynchronization. Recognizing the modifications resulting from the process described may help us to better understand the cardiac electrical activation phenomenon, and thus identify the patients responsive to the procedure, in addition to defining the best pacing sites to maximize CRT success rates.

In dilated cardiomyopathies progressing with LBBB, an earlier activation of the septal region can be observed in association with a lateral wall tension. Further, a delayed contraction of the lateral wall and an intense tension of the already activated septum occur. The term paradoxal motion of the septum is not the most suitable, because it is a consequence of the imbalance of forces of the septal region, unable to stand the delayed lateral wall tension contracting toward the right ventricle[8]. An analysis of patients with LBBB using BSPM sought to establish ventricular electrical activation patterns of this population[15].

Ventricular resynchronization obtained with the atriobiventricular pacemaker prevents the reciprocal tension of the walls. Conventional echocardiogram, and currently tissue Doppler echocardiography, as well as magnetic resonance have characterized these changes, mainly in retrieving the lateral wall delay[6,7,16].

Currently, the factors interfering with the cardiac response of patients undergoing CRT are: duration of the QRS complex, lack of interventricular and intraventricular synchronism, electrode positioning, adequate ventricular activation times, and adapted atrioventricular (A-V) activation time[8].

The importance of the lack of interventricular synchronism, as already demonstrated in previous studies, associated with the intraventricular asynchrony, brought the overall dynamics of activation in LBBB to light[17].

Ventricular contraction in the presence of intraventricular conduction block worsens the ventricular function. Conventional ECG may help identify approximately 70% of the patients with contractile alterations when the QRS complex is greater than 140 ms; however, it is unable to accurately predict the sites with altered contraction.

One of the explanations of the nonresponse to CRT is that 30% to 40% of the patients with CHF and QRS above 120ms lack LV asynchrony in the tissue Doppler echocardiography[18]. Additionally, patients with CHF and narrow QRS (<120ms) present LV asynchrony and are candidates for cardiac resynchronization therapy[18].

Recently, studies using electroanatomic mapping in CRT[9-11] showed a significant hemodynamic improvement when slow conduction sites of the LV are activated, reinforcing the importance of the optimized electrode placement as a crucial factor for CRT to bring clinical benefits. These studies illustrate the electrophysiological mechanisms responsible for inter and intraventricular conduction and which influence the synchronized LV contraction.

Body surface potential mapping (BSPM) has the great advantage of being a non-invasive tool more precise than conventional ECG, and able to discriminate the best ventricular activation sites and to assess the efficacy of the therapy used to synchronize the heart chambers. Thus, it can be very useful in the treatment of these patients.

The present study using the BSPM assessed time sequences of ventricular electrical activation with the purpose of assessing the electrical activity, not only in the ventricles as a whole, but also regionally, as in the anteroseptal region, since it has a key role in the dynamics of cardiac contraction. These areas were analyzed in the three study situations - native LBBB, LV pacing, and during atriobiventricular pacing - comparing all with the control group of normal individuals. The comparative analysis of the three study situations provided evidence of the important alterations that occur in the presence of LBBB. The electrical activation of the septal region suffered little alteration; however, a clear and significant LV activation delay occurs, a fact that had already been previously studied, demonstrating the difficulty in the transmission of electrical impulses through a damaged conduction system[19].

An important finding during RV pacing was the increase in mRV (86.8ms), which got close to the characteristic RV delay with LBBB (102.7ms), significantly increasing the total duration of the ventricular activation. This alteration caused a longer delay between ventricle activation and AS activation, as shown in Figure 5, and provoked a more intense interventricular and intraventricular asynchrony, as already described in the DAVID study[20]. However, an electrotemporal characterization, as was evidenced by this study using BSPM, had not yet been demonstrated.

The analysis of the electrical activation time sequence with atriobiventricular pacing using the BSPM was able to demonstrate the efficacy of the resynchronization therapy. LV activation time was shorter than that of the native LBBB (mLV decreased from 81.0ms to 72,0ms). A smaller difference of the anteroseptal region was observed, and the mAS increased in comparison with the native LBBB (51.3ms vs. 43.6ms). This finding is, in itself, proof of a better matching of septal and LV activation, as seen in Figure 5. Reddy et al[9], using electroanatomic mapping, described an almost synchronous activation between the septal and lateral walls of the LV with PM-BIV, which resulted in an earlier activation of the posterior-lateral base of the LV, with a decrease of QRS from 211ms in the RV single-chamber pacing to 157ms with PM-BIV. In our study, the mRV increased significantly with PM-BIV and was almost equal to that of the LV (51.3ms vs. 43.6ms). This provides evidence of the occurrence of a synchronized electrical activation during contraction of the two chambers, a fact that, in our opinion, seems to be an original contribution of this study.

The characterization of the electrical activation pattern obtained by BSPM before and after atriobiventricular pacing reflects the change from an abnormal activation sequence in LBBB to the simultaneous activation of both ventricles, thus restoring the cardiac synchronism.

The study of ventricular electrical activation times using BSPM may contribute to guide the search of optimal sites to be activated by atriobiventricular pacemaker electrodes, thus increasing the likelihood of better patient responses to CRT.

Conclusion

Patients with CHF and LBBB undergoing CRT, present at the BSPM:

• increased electrical activation times in both ventricles during isolated RV pacing (induced LBBB), causing longer ventricle-to-AS region activation delay.

• similar electrical activation times in both ventricles, a shorter activation time of the AS region during PM-BIV, indicating simultaneous ventricular activation;

• evidence of a higher intraventricular asynchrony when greater differences of mean electrical activation times are found between the septal region and the lateral wall of the LV.

Study limitations - The definition of the study areas (RV, AS and LV) using BSPM electrodes has narrow limits, because these areas not always correspond to the anatomic areas described.

The positioning of the pacemaker electrodes conventionally implanted in the apex of the RV and in the lateral wall of the LV may vary due to the technical difficulties faced. A smaller margin of error has usually been obtained in patients undergoing electrode placement via thoracotomy. As a consequence, some pacing stimuli may have been applied in inadequate sites, thus modifying the electrical activation process in the ventricles, albeit without achieving the desired efficacy.

Tissue Doppler echocardiogram was not performed to confirm cardiac resynchronization following CRT.

No modification in the V-V interval was made after CRT.

The present study proposes a new procedure in the use of BSPM, which we expect will suffer modifications, in this initial phase, that may contribute to improve its efficacy.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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