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Ventricular repolarization during uni and biventricular pacing in normal subjects

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ABSTRACT

Background: The cardiac depolarization–repolarization process (D-REPP) may differ among various modes of cardiac pacing depending on the paced chamber(s) and lead position. We intended to assess the effect of different modes of cardiac pacing (left, right and biventricular) on the D-REPP as expressed in QRS, QT, peak-to-end of the T wave (PETW) and PETW/QT intervals and their dispersion. These intervals were compared during pacing and sinus rhythm.

Methods: We studied 31 patients without structural heart disease and with normal ventricular function who underwent right, left and biventricular pacing. Simultaneous 12-leads were recorded and electronic calipers were used for measurement of the QRS, QT, corrected QT (cQT), PETW, and PETW/QT ratio.

Results: cQT duration, PETW, standard deviation of the PETW, PETW/QT, and QRS duration were shorter during sinus rhythm. Isolated stimulation of the right or the left ventricle produced a similar increase in all the intervals and did not display significant differences in terms of cQT duration, PETW, PETW/QT, or QRS duration. Biventricular pacing produced a significant increase in cQT, QRS, PETW and PETW/QT, but these values were shorter than those obtained during isolated right or left ventricular stimulation.

Conclusion: In subjects without structural heart disease, cardiac pacing produces a significant increase of the D-REPP. No differences were found when comparing right or left univentricular pacing. Biventricular stimulation induces less perturbation of the D-REPP.

1. Introduction

The cardiac depolarization–repolarization process (D-REPP) is not uniform across the myocardial cells that make up the ventricles. The ventricular wall is composed of different types of myocardial cells: epicardial, endocardial and M cells [1]. These cells exhibit substantial differences in their repolarization characteristics, pharmacological profiles, and response to pathophysiologic states [1]. Indeed, epicardial cells complete their repolarization first, and M cells are the last to complete repolarization. Full repolarization of the epicardial cells coincides with the peak of the T wave, and repolarization of the M cells coincides with the end of the T wave.

D-REPP duration may be calculated by measuring the QT interval. However, the QT interval includes both depolarization (which is prolonged during pacing) and repolarization [1–3]. In a normal setting, D-REPP is relatively homogenous and depends on the length of the previous cardiac cycle. This is why the QT interval should be corrected for heart rate. One of the most frequently used formula for that purpose was proposed by Bazett [1,2]. QT interval dispersion is considered to be an index of heterogeneity of the D-REPP, and this heterogeneity is related to an increase in the risk of suffering severe ventricular arrhythmias and sudden death [2]. The final part of repolarization and its transmural dispersion can be evaluated by measuring the interval from the peak to the end of the T wave (PETW) [1,4,5]. This interval shows differences related to heart rate and ventricular mass. Indeed, the PETW shortens when heart rate increases and lengthens when ventricular mass increases [5]. When the PETW interval is related to the total duration of the D-REPP, it remains unaffected by either heart rate or ventricular mass [5]. It has been suggested that PETW/QT ratio is a good index of transmural dispersion of repolarization [1,4,5].

In pathological conditions, the D-REPP may differ when comparing different parts of the heart, and this difference is supposed to be expressed in the dispersion of the QT interval and the PETW/QT when they are simultaneously measured in all electrocardiographic leads [1–5]. It is generally accepted that patients with a prolonged QT interval, an augmented QT interval dispersion or an increase of transmural dispersion of repolarization are prone to suffer from potentially lethal ventricular arrhythmias, i.e., *torsades de pointe* and ventricular fibrillation [2–5].

Cardiac resynchronization therapy (CRT) was introduced in clinical practice in 1994 for the treatment of heart failure [6]. In order to achieve CRT, both ventricles should be stimulated simultaneously (biventricular pacing). Cardiac pacing is delivered in the endocardium of the right ventricular apex and (through a coronary vein) in the epicardium of the lateral wall of the left ventricle. CRT has been shown to improve the functional capacity and ventricular function and to reduce the overall morbidity and mortality of patients with heart failure NYHA III-IV, ejection fraction ≤ 0.35 and QRS ≥ 130 ms[7]. However, some recent reports have raised concern about the possibility that CRT could induce

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ventricular repolarization dispersion and potentially lethal ventricular arrhythmias [8,9].

Cardiac pacing induces a QRS prolongation and an abnormal pattern of repolarization. During right ventricular apical endocardial pacing, the ventricular activation pattern resembles that occurring in patients with left bundle branch block (LBBB). In such cases, left ventricular dysfunction has been reported [10]. The D-REPP delay that is observed in LBBB may be accompanied by an increase in the dispersion of the repolarization. In an animal model, Prinzen et al. [10] demonstrated that the left ventricular dysfunction associated with LBBB was corrected by means of left ventricular apical pacing. Ventricular D-REPP could thus be different during right ventricular apical pacing, left ventricular epicardial pacing and biventricular pacing.

In a Medline review of the literature, we did not find any study reporting an effect from left, right and/or biventricular stimulation over the D-REPP in subjects without structural heart disease as expressed by the above mentioned ECG indexes of these intervals. We then decided to measure QRS, QT, QT dispersion, PETW and PETW/QT in patients submitted to right, left and biventricular pacing. Our hypothesis was that ventricular pacing prolongs these intervals, and that biventricular pacing produces a smaller perturbation.

2. Methods

2.1. Population

A detailed explanation was offered and informed consent was obtained from the patients who accepted to be enrolled in the study. Patients without structural heart disease, who were going to be submitted to an electrophysiological evaluation for diagnostic or therapeutic purposes, were included. We excluded patients with hypertension, hyperlipidemia, history of tobacco use, structural heart disease, heart failure, left ventricular dysfunction, bundle branch block, implanted devices, and those who were receiving drugs that affect cardiac electrophysiological properties.

2.2. Electrophysiological evaluation

Before the procedure, conscious sedation was achieved with midazolan. Two femoral vein and one subclavian vein introducers were placed in order to insert the catheters for stimulation and recording. Through the subclavian vein, one decapolar catheter was inserted into the coronary sinus (CS). The femoral catheters were alternatively placed in the high right atrium, His recording position and the right ventricular apex. After completing the electrophysiological study and/or ablation, a 12-lead ECG was recorded in order to corroborate sinus rhythm and a normal ECG morphology. Thereafter, catheters were placed in the right ventricular apex and in a left lateral coronary vein for uni and biventricular stimulation. A simultaneous, 12-lead ECG was obtained while the patient was in sinus rhythm and during right ventricular apical, left ventricular epicardial (through the CS), and biventricular pacing at a rate of 100 beats per minute. Pacing was performed at a stimulus amplitude that was twice that of the diastolic threshold. Recordings were electronically saved for further analysis.

2.3. Measurements and calculations

The ECG recordings were measured by an independent observer who was not aware of the patient's identification or of the results obtained in each one of the different pacing settings.

QT interval was measured from the beginning of the QRS complex to the end of the T wave. The peak-to-final portion of the T wave interval was measured from the point of maximal voltage of the T wave to its intersection with the base-line. The QT interval was corrected for heart rate with the Bazett formula [1]. The measurements of each lead were saved in an Excel data sheet were cQT and PETW/QT were computed.

2.4. Statistical analyses

The statistical comparisons were done with the SPSS, Excel and Statgraph computer programs. Means and standard deviation were computed. Quantitative comparisons were performed by means of analyses of variance and Kruskal–Wallis according to the type of data distribution. Tukey–HSD and Games–Howell post-tests were applied to identify the groups responsible for differences when these appeared. Qualitative comparisons were made using the χ^2 or Fisher test as appropriate. Alpha value was set up at p value less than 0.05 with confidence intervals of 95%. According to the normal values of our laboratory, a minimal sample of 28 individuals was estimated to detect significant differences for a normal QT value of 0.398 s and a standard deviation of 0.02 s, with a power of 95%.

3. Results

Thirty one 27.3 ± 12.3 year-old consecutive patients (13 males) were included. No patient suffered complications from the procedure or had associated structural heart disease. Left ventricular ejection fraction was normal (0.62 ± 0.03) in all the patients. In one case it was not possible to achieve left ventricular capture stimulating in the CS. That patient was excluded from the study. Nineteen (70%) patients had AV reentrant tachycardias mediated by accessory pathways, and 6 (20%) suffered AV nodal reentrant tachycardia. All these patients had a successful radio-frequency (RF) ablation and the ECG was normal after the RF application. The other 5 patients (10%) were studied because of frequent supraventricular premature beats, sinus tachycardia, and Mobitz I supradivisional second degree AV block secondary to an increased vagal tone. In these 5 patients the ECG was also normal and in sinus rhythm when the ECG was being recorded.

Ventricular capture and the corresponding QRS morphology according to the paced chamber(s) were systematically verified before the recordings were performed. As expected, during right ventricular apical stimulation, the QRS morphology resembled the LBBB. Left ventricular stimulation produced a QRS morphology that looked like right bundle branch block, and biventricular pacing produced a mixed QRS morphology (see Fig. 1). Ventricular pacing (either uni or biventricular) did not induce any type of arrhythmia.

D-REPP indexes are displayed in Table 1. The QT, cQT, PETW, and PETW/QT duration values exhibited a normal distribution. Their differences were compared by using a one-way analysis of variance, homogeneity of variances, robust test of equality of means, Tukey HSD and Games–Howell post-hoc tests. The other indexes did not have a normal distribution, and their means were compared by means of the Kruskal–Wallis test.

3.1. QRS duration

It was normal during sinus rhythm and significantly prolonged during all types of cardiac pacing. QRS duration was significantly shorter during biventricular pacing when compared to both right and left ventricular pacing. There was no significant QRS duration difference between right and left ventricular pacing.

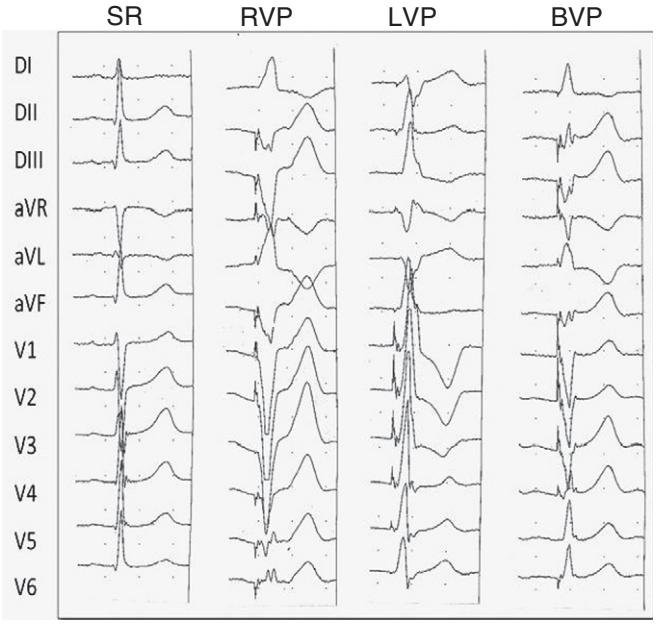

Fig. 1. QRS morphology in the 12 ECG leads (DI through V6) during the different phases of the study. SR = sinus rhythm. RVP = right ventricular pacing, LVP = left ventricular pacing. BVP = biventricular pacing.