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Journal of Electrocardiology 38 (2005) 19–27

JOURNAL OF Electrocardiology

QT dispersion failed to estimate the global dispersion of ventricular repolarization measured using monophasic action potential mapping technique in swine and patients

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Abstract The aim of this study was to evaluate whether the QT dispersion measured from 12-lead electrocardiogram (ECG) can estimate the global dispersion of ventricular repolarization (DVR) measured using a monophasic action potential (MAP) mapping technique. Monophasic action potentials were recorded from 75 ± 12 left ventricular sites in 10 pigs and from 48 ± 16 left or right ventricular sites in 15 patients using the CARTO mapping system. The maximum DVRs in both end-of-repolarization and MAP duration among all the mapped sites were calculated and termed as global DVR for each measurement. QT intervals, QT_{peak} and QT_{end}, were measured from the 12-lead ECG, and QT dispersions; namely the differences between the maximum and the minimum of the QT_{peak} and QT_{end} were calculated. We found that QT dispersions were significantly smaller than ($P < .05$) and poorly correlated with the global DVRs both in pigs and patients. Bland-Altman agreement analysis demonstrated a marked variation of the differences and an obvious lack of agreement between the results obtained using the ECG and the MAP methods. In our patients, the global DVR increased markedly during ventricular tachycardia as compared with that during sinus rhythm ($P < .05$), whereas there was no significant difference in QT dispersion between these 2 subgroups. In conclusion, QT dispersion on the surface ECG could not estimate the global DVR measured using the MAP mapping technique. These findings are not consistent with some previously reported observations, suggesting the need for reappraisal of the electrophysiological implications of QT dispersion.

Keywords: QT dispersion; Monophasic action potential; Repolarization; Global dispersion

1. Introduction

Increased dispersion of ventricular repolarization (DVR) has been recognized as an important mechanism underlying the genesis of tachyarrhythmias [1]. Within the last decade, QT dispersion has been widely adopted as an index of DVR and a potential prognostic tool in the detection of future ventricular tachyarrhythmic events and sudden death. However, the results of various prognostic studies have been conflicting [2,3]. It remains unsettled whether QT dispersion bears any prognostic value. In addition, QT dispersion has never been compared to the global DVR because of difficulties in obtaining global information on myocardial repolarization.

Heterogeneity of ventricular repolarization can be invasively determined using monophasic action potential (MAP) recordings [4,5]. However, the global DVR has not been well evaluated using MAP recording technique. We have recently developed a novel MAP mapping technique, which combines MAP recording and electroanatomical mapping techniques and yields global information on myocardial repolarization [6,7].

To evaluate if QT dispersion measured from the 12-lead surface electrocardiogram (ECG) could estimate the global DVR, we compared QT dispersion with the global DVR in

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doi:10.1016/j.jelectrocard.2004.09.012

10 healthy pigs and 15 patients with tachyarrhythmias using the MAP mapping technique and the CARTO mapping system (Biosense, Waterloo, Belgium).

2. Methods

2.1. Subjects

Ten healthy pigs, 47 to 53 kg, were premedicated with pancuronium bromide (0.1 mg/kg), thiopental (5 mg/kg), and atropine (0.015 mg/kg). Anesthesia was maintained with an infusion of 10 mL/h of 1 mg fentanyl and 20 mg pancuronium bromide mixture. The pigs were intubated and artificially ventilated during the study. Volume-controlled ventilation of 8 L/min, 20 breaths/min, positive end-expiration pressure of 5 cm H_2O, and FiO_2 of 0.5 were used.

Fifteen patients (13 men and 2 women; mean age, 55.4 ± 15.4 years) referred for electrophysiological study and/or radiofrequency catheter ablation were recruited (9 patients with sustained ventricular tachycardia, 2 patients with a history of ventricular fibrillation, and 4 patients with supraventricular tachycardias). None had amiodarone treatment within the previous 3 months. All other antiarrhythmic drugs had been withdrawn for a period equivalent to at least 5 half-lives before the study. None of the patients had electrolyte abnormalities. Informed consent was obtained from all patients. The study was approved by the local ethics committee, and the electrophysiological procedures were in accordance with the local institutional guidelines.

2.2. The CARTO system

The CARTO system has been previously described in detail [8]. In brief, the torso of the subject is covered by 3 magnetic fields of different frequencies. A location reference (Ref-Star, Biosense Webster) is fixed on the back of the subject, whereas a mapping catheter (Navi-Star, Biosense Webster) navigates within the heart chambers. The magnetic sensors equipped in the tip of the mapping catheter and the location reference continuously compare the intensities of the 3 magnetic fields, ensuring that the location of the mapping catheter can be accurately determined and displayed in real-time. Color-coded 3-dimensional maps of anatomical structure and endocardial activation/repolarization sequence are constructed from accurately localized electrograms recorded using the mapping catheter, allowing display from any view projection. The accuracy of spatial localization has been verified to be within 0.7 mm in vivo [8].

2.3. MAP recording

In patients, MAP recording was performed using a 7F Navi-Star catheter (Biosense Webster) before a clinical electrophysiology and/or radiofrequency catheter ablation procedure. The catheter was introduced into the right ventricle via the femoral vein (n = 10) or into the left ventricle via femoral artery (n = 5), depending on the location of the arrhythmogenic substrate. Right ventricular mapping was performed during sinus rhythm in 6 patients and during ventricular tachycardia in 4 patients. In the remaining 5 patients, left ventricular mapping was performed during sinus rhythm in 3 patients and during ventricular tachycardia in 2 patients. In the pigs, MAP recordings were all from the left ventricular endocardium during constant pacing at the lateral right atrium at 130 beats/min using a modified-tip 7F Navi-Star catheter (Biosense Webster), which has a contact ball of 0.5-mm length and 1-mm diameter at the end of the tip electrode [9].

Monophasic action potential signals were recorded between the 4-mm tip electrode (exploring electrode) and the 2-mm ring electrode proximal to the tip (indifferent electrode) at a filter bandwidth of 0.05 to 400 Hz. Unipolar electrograms from the tip and the indifferent electrode were simultaneously recorded at a filter bandwidth of 0.5 to 120 Hz.

When the amplitude and morphology of the MAP in the real-time monitor window of the CARTO system were within acceptable limits [4], it was captured in a sampling window for further inspection (Fig. 1B,D). The accepted signals and the 12-lead ECG were stored simultaneously at a sampling frequency of 1 kHz. Caution was taken to place the mapping catheter perpendicularly against the endocardium and to avoid “ST segment” elevation, that is, greater than 20% amplitude of the ventricular deflection, on the unipolar electrogram from the indifferent electrode [4]. To estimate global information of DVR accurately, at least 1 MAP was recorded in an area of 2 cm^2 in both pigs and human beings. To avoid the influence of variations in heart rate, the cycle length stability monitor function of the CARTO system was used and MAP sampling was performed when the cycle length was stable and its variation was 5% or less of the initial cycle length in patients.

2.4. MAP analysis

Monophasic action potential analysis was performed off-line using the double annotation feature of the CARTO system by an independent investigator. The first annotation was defined as the onset of the rapid phase of the MAP upstroke, representing local activation. The second was defined as the intersection between the baseline and the tangent to the steepest slope on phase 3 of the MAP, representing the local end-of-repolarization (EOR) (Fig. 1B,D). The 2 annotation lines were both manually set and carefully checked with display time scales of 200 and 100 mm/s.

The activation time was defined as the time interval from the earliest recorded ventricular activation on the surface ECG to the local activation on the MAP, the EOR time as the period from the earliest activation time to the local EOR, and the MAP duration as that from the local activation to the local EOR. At each site, these 3 values were obtained, taking the peak of an upright QRS complex on the surface ECG as time reference (Fig. 1A,C). On the basis of these values, 3-dimensional maps of the EOR (Fig. 1E,F) and the