Vectorcardiographic determinants of cardiac memory during normal ventricular activation and continuous ventricular pacing

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BACKGROUND Cardiac memory (CM) refers to persistent T-wave changes on resumption of normal conduction after a period of abnormal ventricular activation. Traditionally, to observe CM, normal ventricular activation had to be restored, limiting the exploration of this phenomenon in clinical practice.

OBJECTIVE This study sought to prove that CM can be detected during continuous aberrant activation and to establish factors affecting its magnitude using a vectorcardiographic technique.

METHODS Sixteen nonpacemaker-dependent patients (11 male, age 72 ± 8 years, mean ± SD) undergoing pacemaker/internal cardioverter-defibrillator implantation were paced in DDD mode with a short atrioventricular (AV) delay for 7 days to induce CM. Electrocardiograms were acquired during AAI and DDD pacing at a constant rate before and after CM induction. Dower transform–derived vectorcardiograms were reconstructed and analyzed.

RESULTS T vector during AAI pacing changed in both magnitude (baseline, 0.26 ± 0.10 mV; Day 7, 0.39 ± 0.13 mV, $P < .01$) and direction aligning with the paced QRS vector (baseline DDD QRS − AAI T angle 125° ± 36°; Day 7, 39° ± 21°, $P < .01$). During DDD pacing, there was no change in T-vector direction, but T amplitude decreased (baseline, 1.06 ± 0.32 mV; Day 7, 0.71 ± 0.26 mV, $P < .01$). CM measured as T-vector peak displacement (TPD) was identical in AAI and DDD mode (TPD 0.46 ± .0.17 mV and 0.46 ± 0.17 mV, respectively). Individual CM magnitude correlated with QRS/T-vector amplitude ratio during DDD pacing at baseline ($r = 0.90$).

CONCLUSION CM can be reliably shown during continuous ventricular pacing, expanding its application to situations in which abnormal ventricular activation persists. Its magnitude is determined by the QRS/T-amplitude ratio of the ventricular paced beat.

KEYWORDS Electrocardiography; Vectorcardiography; Pacing; Electrical remodeling; Repolarization

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Introduction

Cardiac memory (CM) has been traditionally described as persistent T-wave changes after the resumption of normal conduction after a period of abnormal ventricular activation.[1,2] It is believed to be an adaptive process allowing resynchronization of myocardial repolarization in the setting of a new activation sequence.[3,4] Molecular mechanisms underlying this phenomenon are complex[5] and involve changes in ion channel function,[6,7] calcium handling,[8,9] transcription factors,[10] and gap junction redistribution,[11] triggered by altered local myocardial strain.[12] In 1982, Rosenbaum et al[1] showed the alignment of T vector in sinus rhythm with QRS vector during the preceding period of abnormal activation (pacing, ventricular arrhythmia, transient left bundle branch block [LBBB]) and introduced the term CM. T-vector changes are known to accumulate with increased duration of aberrant activation and heart rate, but little is known about the interindividual variation and exact determinants of the CM magnitude in a given patient.

Conduction system disease leading to the development of LBBB or atrioventricular (AV) block requiring ventricular pacing (the 2 most common causes of CM) is usually progressive and irreversible. Restoration of normal ventricular conduction in this situation is relatively uncommon. As a result, CM cannot be evaluated in this large patient population, and its clinical significance beyond confounding myocardial ischemia[13] remains largely unexplored. The ability to detect CM during continuously abnormal ventricular activation would significantly expand applicability of this phenomenon to a much larger number of patients and facilitate clinically oriented CM research.

We hypothesized that by using a vectorcardiographic approach in a human pacing-induced model of CM, it would be possible to (1) demonstrate CM during continuous abnormal ventricular activation, and (2) extend the original qualitative concept of CM to develop quantitative vectorcardiographic predictors of its magnitude.

Dr. Shvilkin has received consulting fees from and owns stock options in NewCardio, Inc. Drs. Bojovic, Vajdic, and Gussak are employees of NewCardio, Inc. Dr. Josephson is the Chairman of the Scientific Advisory Board of New Cardio, Inc., and owns its stock options. Dr. Zimetbaum owns stock options in NewCardio, Inc. **Address reprint requests and correspondence:** Dr. Alexei Shvilkin, Baker 4/Cardiology, Beth Israel Deaconess Medical Center, 185 Pilgrim Road, Boston, Massachusetts 02215. E-mail address: ashvilki@bidmc.harvard.edu. (Received January 24, 2009; accepted March 13, 2009.)

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Methods

Patients

This study was approved by the Institutional Review Board of Beth Israel Deaconess Medical Center. All patients provided written informed consent for the study.

Patients >18 years of age in sinus rhythm with 1:1 AV conduction at physiologic heart rates undergoing pacemaker or implantable cardioverter-defibrillator (ICD) implantation for approved indications were included. Patients were excluded if they had one of the following: LBBB, history of sustained ventricular arrhythmia or atrial fibrillation within the last 3 months, recent history of unstable angina unless treated by coronary intervention, history of New York Heart Association class III/IV heart failure, ejection fraction <20%, anticipated unavailability for 1 week follow-up at the study center.

In all patients, the right ventricular lead was positioned in the right ventricular apex. Clinical data including demographics, medical history, and echocardiographic left ventricular ejection fraction (LVEF) measurements (measured within 6 months before the study) were obtained from electronic medical records.

Pacing and recording protocol

Baseline electrocardiographic (ECG) recordings were performed in AAI and DDD mode with a short AV delay at a rate 10% faster than sinus on the day of implantation. Care was taken to achieve a stable and equivalent heart rate in both pacing modes while avoiding superimposition of the atrial pacing spike/P wave on the preceding T wave in the AAI mode and complete capture of the ventricle in the DDD mode. At least a 2-minute equilibration time at the pacing cycle length was allowed before recordings. After the baseline recording was complete, the devices were programmed in the DDD mode with a short paced and sensed AV delay (100 to 120 ms) and lower rate as clinically indicated (typically 60 beats/min). In 1 week, the follow-up recordings were conducted in the reverse order (first DDD and then AAI modes at the heart rate equal to baseline recording).

ECG recording and analysis

Twelve-lead ECGs were recorded using an MAC 5000 electrocardiograph (GE Marquette, Milwaukee, Wisconsin) with a 0.16- to 40-Hz filter and were stored digitally on a floppy disk at a sample rate of 500 Hz. The signals were extracted using Magellan ECG Research Workstation Software version 1.1 (GE Marquette) and analyzed using Visual ECG software (NewCardio, Inc., Santa Clara, California). Visual ECG calculates Frank leads X, Y, and Z from the standard 12-lead ECG input using the inverse Dower formula,[14] creates a vectorcardiogram (VCG), and provides tools for 3-dimensional vector loop analysis. Mean square QRST complex was reconstructed using the formula: $\sqrt{X^2+Y^2+Z^2}$ and used to calculate the following parameters: QRS and QT durations, maximal QRS and T-vector magnitudes; QRS and T areas; QRS and T vector magnitudes at half area. Several derivatives were calculated: maximal QRS/T magnitude ratio; QRS/T area ratio; QRS – T area difference. Additional parameters were calculated from the VCG: ventricular gradient; azimuth, and elevation for maximal QRS and T vectors and points corresponding to half-areas of QRS and T waves of the mean square QRST complex; 3 dimensional QRS-T angle, and CM angle, representing the 3-dimensional angle between T-vector direction in AAI mode and paced QRS vector in DDD mode. Elevation (θ) was defined as the angle between the vector and the vertical axis (Y) with zero pointing in the caudal direction and 180° pointing in the cranial direction.[15,16] Azimuth (φ) was defined as the angle in the transverse plane (X-Z plane) with zero pointing to the left (positive X axis), forward motion from 0° to 180°, and backward motion 0° to −180° (Figure 1). CM magnitude was calculated as the T-vector peak displacement (TPD), a 3-dimensional distance between the peaks of T vectors at baseline and after 7 days of DDD pacing as described previously[17] in both AAI and DDD pacing modes.

Statistics

Time-dependent changes of continuous-scale variables were analyzed by the paired samples *t*-test or Wilcoxon signed ranks test if distributions significantly departed from normal. Linear regression analysis and independent samples *t*-test were used to estimate the effects of clinical and VCG variables on CM magnitude (SPSS version 14.0, SPSS, Inc., Chicago, Illinois). Circular data were analyzed using the Watson-Williams test (Oriana 2.0, KCS, Inc. Agnlesey, UK). Values of $P < .05$ were considered significant. Data are presented as mean ± SD. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the article as written.

Results

Baseline patient characteristics are presented in Table 1. All patients completed the 7-day pacing protocol with no complications. As expected, at 7 days after switching from DDD to AAI pacing, deep T-wave inversions were evident in the inferior and precordial leads (Figure 2A) with the T vector during AAI pacing approaching the direction of the QRS vector during DDD pacing (Figure 3). Comparison of ECGs during DDD pacing showed that on Day 7 there

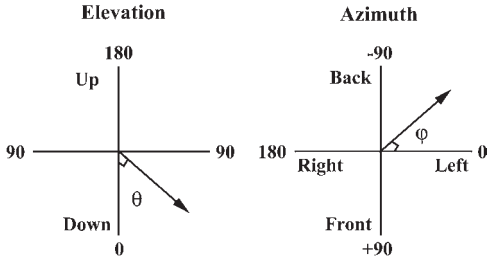

Figure 1 Definitions of elevation and azimuth. Elevation (θ) is the angle between the vector and the vertical (Y) axis with 0° corresponding to the caudal and 180° to the cranial direction. Azimuth (φ) is the angle between the vector and X axis in the transverse plane with 0° corresponding to the left, forward direction to 180° and backward direction to −180°.