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High atrioventricular phase index on near-field intracardiac electrogram is associated with risk of ventricular arrhythmia

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Abstract The purposes of this study were to characterize and quantify concordance between consecutive atrial and ventricular activation time points through analysis of phases and to explore its association with outcomes in patients with implantable cardioverter-defibrillator (ICD). Patients with structural heart disease and dual-chamber ICDs underwent 5 min baseline right ventricular (V) near-field and atrial (A) electrogram (EGM) recording. The cross-dependencies of phase dynamics of the changes in consecutive A (AA′) and V (VV′) were quantified and the AV phase dependency index was determined. In Cox regression analysis, a high AV phase index (in the highest quartile, >0.259) was significantly associated with higher risk of ventricular tachyarrhythmias (HR 2.84; 95% CI 1.05–7.67; $P = 0.04$). In conclusion, in ICD patients with structural heart disease, high sinus AV phase dependency index on EGM is associated with the risk of ventricular arrhythmia.

Keywords: Symbolic dynamics; Sympathetic; Phase dependency; Atrial; Ventricular

Introduction

Implantable cardioverter–defibrillators (ICDs) are widely used in eligible patients to prevent sudden cardiac death (SCD). Despite effective termination of ventricular tachycardia (VT)/ventricular fibrillation (VF), the occurrence of VT/VF is associated with increased mortality and heart failure hospitalizations in ICD patients [1]. Timely (within 1–3 months window) prediction of sustained VT/VF [2] might trigger timely adjustment in patients′ management and therefore, prevent appropriate, but undesirable ICD therapies, and improve patients outcomes. It is important to identify novel risk markers of VT/VF in ICD patients, which would help to develop robust risk score of VT/VF events in the future.

We recently showed that increased percentage of near-field (NF) right ventricular (RV) intracardiac electrogram (EGM) VV′ alternans (i.e. short-long-short, or long-short-long sequences of VV′ intervals) was associated with increased mortality in ICD patients [3]. However, it is unknown whether VV′ alternans appearance is mainly driven by the sinus node, or if atrioventricular (AV) node contributes to it. No prior studies have analyzed the phase dependency between atrial AA′ intervals (measured on atrial EGM) and VV′ intervals (measured on NF RV EGM, and the prognostic value of this measure. The purpose of this study was to characterize the dependency between phase changes of atrial and ventricular activation intervals in patients with implanted ICD and to determine their association with sustained VT/VF events with appropriate ICD therapies.

Methods

We analyzed data collected for the ICD-EGMs study (NCT00916435) [4]. The study conformed to principles outlined in the Declaration of Helsinki and was approved by the Johns Hopkins University and Washington University Human Studies Committees. All participants provided written informed consent.

Study population

Inclusion and exclusion in the ICD-EGMs study have been previously described [4]. For this study, we included only study participants with implanted dual-chamber ICD. Participants with implanted single-chamber ICD, or cardiac resynchronization device (CDR) have been excluded. We further excluded patients if they had more than 15% of non-sinus beats on baseline EGM or were paced either from right atrium or ventricle more than 5% during the preceding 3 months. In addition, we excluded patients if no EGM

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recording in sinus rhythm was available for analysis. Only sinus rhythm EGM recordings were analyzed in this study.

Atrial and ventricular EGM analysis

Intracardiac EGMs have been recorded during regular office visit, as previously described [4]. Only non-paced recordings in sinus rhythm were included in this study. For our analysis, we selected 50 consecutive sinus beats. Atrial (A) and ventricular (V) NF RV EGM peaks were detected as the dominant deflections in the EGM recordings as previously described [3], using custom Matlab software (MathWorks, Natick, MA, USA) and were visually scanned. AA′ and VV′ intervals were measured between consecutive A or V EGM dominant deflections, respectively. AV′ interval was measured as the interval between each A and V EGM dominant deflection. Joint symbolic dynamics (JSD) was used to measure AA′, VV′ and AV′ changes. Applied equations are described in the online supplement [5]. Symbolic dynamics is an approach that involves coarse-graining of observed time series into sequences of symbols, providing significant patterns for quantification of system dynamics [6–8].

Fig. 1(A) and (B) shows the atrial and ventricular electrograms and their corresponding sequence of symbols generated from AA′ and VV′ intervals. Symbolic patterns were generated using three successive symbols and were grouped into three families [9]: 1) V0: no variations between consecutive symbols; 2) V1: two consecutive symbols are similar while the remaining is different; and 3) V2: all consecutive symbols are different. (See Fig. 2).

In order to quantify A–V dependencies, we computed the directionality index rather than calculating percentage of dependency using JSD. Phase is defined as the fractional part of a cycle, measured from an arbitrary origin, through which the time has advanced, and is often expressed as an angle.

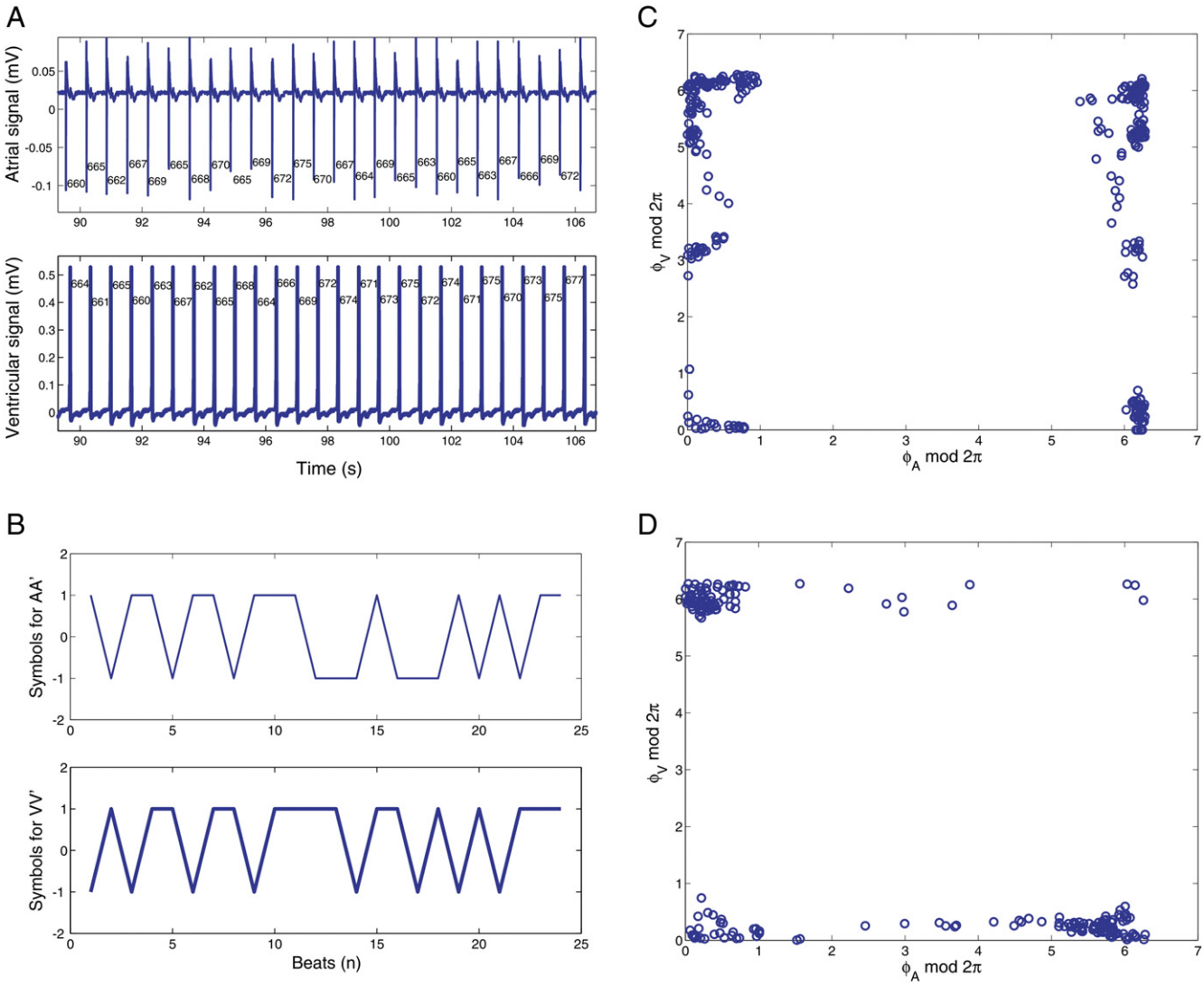

Fig. 1. Illustration of symbolic dynamics and phase dependency of atrial and ventricular electrograms (EGM). A, Selected beats of simultaneous atrial and ventricular EGM recordings with the corresponding intervals in ms shown in-between the beats. B, Plot of symbolic sequences of AA′ and VV′ intervals calculated from atrial and ventricular EGMs as described in the methods section. During the first 11 beats AA′ is driving VV′ while VV′ is driving AA′ from beat 17 to 24. C, Phase plot indicating the influence of phase of VV′ on phase of AA′ (as increments can be observed in φ_V while φ_A shows no changes). D, Similar phase plot as panel C, showing that the phase of AA′ is influenced by VV′ phases.