Published in final edited form as:

Heart Rhythm. 2012 October ; 9(10): 1594–1602. doi:10.1016/j.hrthm.2012.06.036.

Intracardiac J-point elevation before the onset of polymorphic ventricular tachycardia and ventricular fibrillation in patients with an implantable cardioverter-defibrillator

Larisa G. Tereshchenko, MD, PhD¹, Aaron McCabe, PhD², Lichy Han, BS³, Sanjoli Sur³, Timothy Huang³, Joseph E. Marine, MD¹, Alan Cheng, MD¹, David D. Spragg, MD¹, Sunil Sinha, MD¹, Hugh Calkins, MD¹, Kenneth Stein, MD², Gordon F. Tomaselli, MD¹, and Ronald D. Berger, MD, PhD¹

¹The Division of Cardiology, Department of Medicine, Johns Hopkins Hospital, Baltimore, MD

²Boston Scientific, St. Paul, MN

³Whiting School of Engineering, The Johns Hopkins University, Baltimore, MD

Abstract

Background—The clinical importance of the J-point elevation on ECG is controversial.

Objective—Study intracardiac J-point amplitude before ventricular arrhythmia.

Methods—Baseline 12-lead ECGs and far-field (FF) right ventricular (RV) intracardiac ICD electrograms (EGMs) were recorded at rest in 494 patients [mean age 60.4±13.1; 360 (72.9%) men] with structural heart disease [278 (56.3%) ischemic cardiomyopathy] who received primary [463 (93.9%) patients] or secondary prevention ICD. Ten-second intracardiac FF EGMs before the onset of arrhythmia were compared with the baseline. The J-point amplitude was measured on the baseline 12-lead surface ECG and the intracardiac FF EGM. The relative J-point amplitude was calculated as the ratio of J-point amplitude to peak-to-peak R-wave.

Results—The paired *t*-test showed that the relative intracardiac J-point amplitude was significantly higher before polymorphic ventricular tachycardia (PVT)/ventricular fibrillation (VF) onset (0.28±0.08 vs. -0.19±0.39; *p*=0.012) than at baseline. In a mixed-effects logistic regression model, adjusted for multiple episodes per patient, each 10% increase in relative J-point amplitude increased the odds of having VT/VF by 13% [OR 1.13 (95% CI 1.07–1.19); *P*<0.0001] and increased the odds of having PVT/VF by 27% [OR 1.27 (95% CI 1.11–1.46); *P*=0.001].

Conclusion—The relative intracardiac J-point amplitude is augmented immediately before the onset of PVT/VF in patients with structural heart disease.

© 2012 The Heart Rhythm Society. Published by Elsevier Inc. All rights reserved.

Correspondence to Larisa G. Tereshchenko, MD, Carnegie 568, 600 N. Wolfe St., Baltimore, MD 21287. lteresh1@jhmi.edu. Phone: 410-502-2796; Fax: 410-614-8039.

Study Registration Identification Numbers: NCT00733590, NCT00916435

Potential Conflict of Interest: Dr. McCabe and Dr. Stein are employees of Boston Scientific.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Keywords

electrocardiography; implantable cardioverter-defibrillator; ventricular arrhythmia; J point elevation; intracardiac electrogram

Case reports,¹ case series,² and case-control-studies³ have shown an association between idiopathic VF and J-point elevation on the surface ECG. In particular, J-point elevation in the inferior ECG leads was shown to be a marker of VT/VF risk in patients with coronary artery disease⁴ and a marker of sudden death⁵ and cardiovascular mortality in the general population.^{6,7} However, other large population studies^{8,9} have failed to find an association between J-point elevation and cardiovascular mortality, and the topic remains controversial. Clinical experience of the benign nature of the familiar early repolarization phenomenon on surface ECG has led to debate over the significance of this finding.¹⁰

Little is known about J-point amplitude behavior immediately before the onset of VT/VF. Rare observations of augmented J-wave immediately before VF onset suggested a cause-effect relationship^{11,12}. Understandably, it would be difficult to conduct a study of J-point amplitude on the surface ECG before the onset of VF. The intracardiac FF EGM of ICD is similar to surface ECG and has been shown to be useful for QRS-morphology-based rhythm recognition¹³ detection of ST-segment depression,¹⁴ T-wave alternans,¹⁵ and QT variability.¹⁶ However, correlation between surface ECG and intracardiac J-point amplitude has not been previously studied, nor has intracardiac J-point amplitude immediately before VT/VF onset in ICD patients been explored.

To address these knowledge gaps, we conducted a study of intracardiac J-point in patients with structural heart disease and an ICD, implanted for primary or secondary prevention of SCD.

Methods

The study protocol was approved by the Johns Hopkins University and the Washington University Human Studies Committees, and all patients gave written informed consent before entering the study.

Study Population

We prospectively devised the design of this study as an ancillary study of two ongoing prospective observational VT/VF risk stratification cohort studies of patients with structural heart disease and systolic dysfunction: the ICD-EGM study (NCT00916435)¹⁷ and the PROSE-ICD study (NCT00733590).^{18,19} Our study included patients with standard indications for primary or secondary prevention ICD or CRT-D and with implanted transvenous Boston-Scientific ICD or CRT-D devices and integrated bipolar ICD leads.

Recording of intracardiac ICD far-field electrograms

All implanted devices were programmed to store 10-second EGMs before spontaneous events. Programming of the device for arrhythmia detection was based on the clinical evaluation of the attending electrophysiologist. Intracardiac FF EGMs were recorded as the difference of potentials between the distal coil of the integrated bipolar ICD lead, implanted in the right ventricular (RV) apex, and the ICD pulse generator. Study participants had been implanted with Boston Scientific devices: either current generation TELIGEN[®] ICD/COGNIS[®] CRT-D or older generations devices (CONFIENT[®] ICD, VITALITY[®] ICD, VENTAK[®] PRIZM[®] ICD, LIVIAN[®] CRT-D, CONTAK RENEWAL[®] CRT-D). Settings of the device amplifier differ between these two generations of devices. FF EGMs in

TELIGEN® ICD/COGNIS® CRT-D devices are stored with 200 Hz sampling frequency and 15.625 $\mu\text{V/bit}$ amplitude resolution. FF EGMs in older generation devices are stored with the same sampling frequency, but variable amplitude resolution. The stored FF EGM signal was filtered using a band-pass filter of 3–60 Hz.

Baseline EGMs—In the ICD-EGM study, baseline FF EGM was recorded for 5 minutes in sinus rhythm at rest during the routine office visit 1 week after device implantation and thereafter at every subsequent follow-up office visit. One-lead (lead II) surface ECG was recorded simultaneously with EGMs via the Boston Scientific Latitude Programmer using the NI USB-9215A portable data acquisition system (National Instruments, Austin, TX) with 1000 Hz sampling frequency. In the PROSE-ICD study, baseline FF EGM was recorded for 3 minutes in sinus rhythm at implantation procedure (after disappearance of local injury current²⁰, but before defibrillation threshold testing¹⁷), and was stored in the memory of the device. The device was interrogated at least once a year during regular follow-up visits, and all stored events were extracted as save-to-disk data. EGMs were converted into an analyzable digital format using proprietary Boston Scientific custom software and further analyzed using a customized MATLAB (MathWorks, Inc., Natick, MA) software application.

Pre-onset EGMs—All ICD interrogation data were classified by an independent endpoint adjudication committee. Spontaneous ventricular arrhythmia events were categorized as (1) MMVT and (2) PVT, or VF, and were defined as previously described.¹⁹ For our analysis, we considered only ventricular arrhythmia events with appropriate ICD therapies (shock or antitachycardia pacing). Length of arrhythmia and average cycle length of arrhythmia were measured.

Pre-onset FF EGMs, recorded by the device if storage was triggered by anything other than ventricular arrhythmia (treated or untreated supraventricular arrhythmia, sinus tachycardia, T-wave oversensing), were included in the category of SVT events.

Simultaneous recording of the surface ECG and FF EGM at baseline permitted verification of sinus beat morphology. Ventricular-paced beats, distorted beats of undetermined origin, and ectopic beats were excluded. At least 2 sequential sinus beats were required for episode to be analyzed. Episodes with ventricular bigeminy were excluded. Measured parameters were averaged across all analyzed beats.

Relative intracardiac J-point amplitude on far-field EGM

The intracardiac J-point on FF EGM was automatically detected as the end of the intracardiac QRS complex (Figure 1) by application of an algorithm, initially developed by Zong et al,²¹ for analysis of the surface ECG. The amplitude of the intracardiac J point and the peak-to-peak FF EGM R-wave amplitude (p-p R) were measured, and the relative intracardiac J-point amplitude was calculated as the ratio of J-point amplitude to p-p R, a unitless measurement. Only the unitless metrics could be compared in our study because of the inconsistent settings of the amplifiers in the two generations of Boston-Scientific devices. The relative intracardiac J-point amplitude was measured on FF EGM at baseline and immediately before any spontaneous event.

J-point amplitude on surface 12-lead ECG

Baseline digital 12-lead ECG was recorded in PROSE-ICD patients at rest a few hours before device implantation. ECGs were digitally downloaded from the GE Marquette MUSE system (GE Medical Systems, Milwaukee, WI). The J-point amplitude on each ECG lead was measured automatically by the Magellan ECG Research Workstation Software (GE

Healthcare, Wauwatosa, WI). The results of the automated analysis were manually verified by investigators (T.H., L.G.T.) to confirm a correct J-point amplitude assessment. Baseline ECGs of ICD-EGM study participants were recorded by a GE Marquette unit (GE Medical Systems, Milwaukee, WI), saved as an image file, and then magnified for manual measurements. The J-point amplitude was measured by two investigators with an interobserver agreement of 95%. Significant J-point elevation was diagnosed²² if the elevation of the QRS-ST junction (J-point) measuring at least 0.1 mV from baseline was detected in at least two leads, either lateral (I, aVL, V5, V6) or inferior (II, III, aVF).

Filtering of ECG Signal Experiment

As it was stored in the ICD memory, the FF EGM signal underwent filtering. In order to quantify the influence of signal filtering on the J-point amplitude on surface ECG, we performed a filtering experiment. Surface ECGs of three patients with significant J-point elevation were subjected to filtering with the same settings as the FF EGM signal (i.e., bandpass 3–60 Hz). The J-point amplitude was measured on the filtered (3–60 Hz) ECG and the original ECG signal (high-pass 0.05 Hz). Bland-Altman analysis²³ was performed to determine agreement.

Statistical Analysis

Our results are presented as mean $\pm$ standard deviation (SD) for normally distributed variables. The independent samples *t*-test was used to compare continuous variables, and the Pearson chi-square test was used to compare categorical variables. A paired *t*-test was used to compare baseline FF EGMs parameters with pre-onset EGMs, and pre-SVT-onset EGMs with pre-ventricular arrhythmia-onset EGMs. Linear regression analysis was performed to determine whether the J-point amplitude on surface ECG (independent variable) determined the intracardiac J-point amplitude on FF EGM (dependent variable). Linear regression analysis was performed separately for inferior, lateral, infero-lateral, and anterior ECG leads, and for all ECG leads together. Multilevel mixed-effects logistic regression, adjusted for multiple events in the same patient, was used to determine the predictive value of the relative J-point amplitude. Mixed models contained both fixed effects (intracardiac relative J-point amplitude) and random effects of the grouping structure of the data (multiple events of the same patient). A *P*-value of <0.05 was considered significant. We used STATA 12 (StataCorp LP, College Station, Texas) with *gllamm* (generalized linear latent and mixed models) function²⁴ for calculations.

Results

Study population

The study population was 494 patients, 130 (26.3%) of whom were enrolled in the ICD-EGMs study and 364 (73.7%) of whom were enrolled in the PROSE-ICD study. Clinical characteristics of the patients are presented in Table 1. During the mean follow-up of 3.4 ± 1.9 years, 58 patients (3.7% per person-year of follow-up) experienced VT/VF with appropriate ICD therapies. MMVT events were detected in 46 patients (9.3%), and PVT/VF events were detected in 12 patients (2.43%). Two patients had both MMVT and PVT/VF events. SVT events were detected in 25 patients (5.1%) in isolation, and an additional 16 patients had both MMVT and SVT events. There was no overlap between the PVT/VF and SVT patient sets (Figure 2). Patients with PVT/VF had lower left ventricular ejection fraction, and ischemic cardiomyopathy patients with PVT/VF events were less likely to be revascularized than other subgroups (Table 1). We observed no other differences in clinical variables.

Figure 2 is a study flow chart. Of 1386 events extracted from the memories of 83 patients' ICDs, 1022 were excluded due to ventricular pacing or frequent ventricular ectopy before the onset of a VT/VF event, or aborted without ICD therapy VT/VF events, and 364 events were analyzed. There were 213 episodes of MMVT with a cycle length of 326 ± 60 ms, 70 episodes of PVT/VF with a cycle length of 258 ± 73 ms, and 81 episodes of SVT with a cycle length of 418 ± 130 ms. On average 148 ± 75 beats were analyzed at baseline, 6 ± 3 beats before VT/VF event onset, and 6 ± 4 beats before SVT event onset.

Baseline relative intracardiac J-point amplitude, and J-point amplitude on surface ECG

The baseline relative intracardiac FF EGM J-point amplitude did not differ significantly between patients who sustained VT/VF during follow-up and those who did not (-0.095 ± 0.237 vs. -0.145 ± 0.889 ; $p=0.468$). A positive relative intracardiac J-point amplitude 0.005 was found in 52 (10.5%) patients at baseline, who had a significantly higher rate of VT/VF events during follow-up than did patients with an isoelectric or negative J-point (intracardiac J-point amplitude < 0.005) [23.1% vs. 10.0% , $P=0.047$].

We found significant J-point elevation on inferior ECG leads in 16 (3.24%) patients, on lateral leads in 22 (4.45%) patients, and on both inferior and lateral leads in 5 (1.0%) patients. Although there was a trend toward more frequent VT/VF among patients with baseline J-point elevation on surface ECG, the difference did not reach statistical significance.

To investigate correlations between J-point amplitude on surface ECG and on FF EGM, we performed linear regression analysis only on PROSE-ICD study data. We took this step to diminish bias in measurements due to the dynamic nature of the J-point amplitude. Only one patient had significant J-point elevation on both the surface ECG and the FF EGM, and there was no correlation between the baseline relative intracardiac J-point amplitude and the relative J-point amplitude on surface ECG (Figure 3).

Surface ECG and intracardiac J-point amplitude did not differ significantly among clinical subgroups (Table 2). At baseline in patients with subsequent PVT/VF there was weak negative correlation between heart rate and relative J-point amplitude ($r = -0.134$; $P=0.03$). Interestingly, in patients with subsequent SVT there was positive correlation ($r=0.327$; $P=0.02$). There were no significant correlations between relative J-point amplitude and heart rate immediately before arrhythmia onset.

Surface ECG filtering experiment results

Bandpass filtering (3–60 Hz) of the ECG signal did not change the absolute J-point amplitude (Figure 4A), but significantly attenuated relative J-point amplitude (Figure 4B). Bland-Altman analysis²³ (Figure 4C) showed a modest agreement between the regular signal (high-pass filter 0.05 Hz) and the filtered (bandpass 3–60 Hz) ECG relative J-point amplitude (Bias -0.057 [-0.160 ; 0.055]). Importantly, non-filtered and filtered relative J-point amplitude significantly correlated (Pearson's $r = 0.60$; $P<0.0001$; Figure 4D).

Pre-onset relative J-wave amplitude

Figure 5 illustrates data recorded in a patient who experienced PVT during follow-up. There was no J-point elevation on the baseline surface ECG (Figure 5D), but there was a small J-wave on baseline FF EGM (Figure 5A) and a dramatically enlarged J-wave immediately before the onset of PVT (Figure 5B). We observed characteristic changes in T-wave morphology before PVT/VF events. Intracardiac FF EGM T-wave is biphasic as it represents a filtered signal. Although the typical baseline FF EGM T-wave morphology is characterized by first negative and second positive phases (Figure 1, Figure 5A), the T-wave

immediately before the onset of PVT was frequently (in 65.7%) characterized by the first positive phase, but second negative phase (Figure 5B). As compared with baseline, changes in T-wave morphology and augmented intracardiac J-wave were observed before the onset of PVT events. Relative intracardiac J-point elevation > 0.005 was seen before 58 out of 70 (82.9%) PVT/VF events. In contrast, a predominantly negative or isoelectric J-point was observed before the onset of MMVT and SVT events. Relative intracardiac J-point elevation > 0.005 was seen before 108 out of 213 MMVT events (50.7%), before 57 out of 81 SVT events, and before 67 out of 308 baseline recordings (21.8%).

In paired analysis (Table 3) relative intracardiac J-point amplitude was significantly greater before MMVT and PVT/VF than before the baseline and SVT events, but no significant differences in these parameters were observed when comparing baseline to pre-SVT events. There was a trend toward more frequently observed elevated intracardiac J-point amplitude before PVT/VF in post-MI patients with ischemic cardiomyopathy, as compared to patients with non-ischemic cardiomyopathy [5/7 Post-MI patients (71%) vs. 1/5 NICM patients (20%), $P=0.08$].

Mixed-effects logistic regression

In a mixed-effects logistic regression model, adjusted for multiple episodes per patient, each 10% increase in relative J-point amplitude increases the odds of having VT/VF by 13% [OR 1.13 (95% CI 1.07–1.19); $P<0.0001$] and increases the odds of having PVT/VF by 27% [OR 1.27 (95% CI 1.11–1.46); $P=0.001$].

Discussion

To the best of our knowledge, this is the first study of intracardiac J-point amplitude in ICD patients with structural heart disease. We found a significant increase in positive intracardiac J-point amplitude immediately before the onset of PVT/VF, but not the onset of MMVT or SVT.

Augmentation of intracardiac J-point amplitude immediately before PVT/VF

Antzelevitch et al., in a series of fundamental studies²⁵ using an arterially perfused canine ventricular wedge preparation, showed that an outward shift in repolarizing current due to either a decrease in depolarizing currents (I_{Na} , I_{Ca}) or an increase in repolarizing currents (I_{to} , I_{K-ATP} , or I_{K-Ach} , or other outward currents) can result in J-point elevation with prominent J-waves or ST-segment elevation shown on ECG. Prominent I_{to} and an outward shift of current can cause a smaller action potential amplitude during phase 1, because of which the L-type Ca-current fails to activate, resulting in loss of the dome and shortening of the action potential. Heterogeneous shortening of the action potential results in *phase 2 reentry*. Importantly, Antzelevitch and coauthors depicted a universal mechanism underlying the development of *phase 2 reentry* in various clinical scenarios (acute myocardial ischemia and myocardial infarction, Brugada syndrome, idiopathic VF with J-point elevation on surface ECG).²⁶ Our results support the universality of enhanced I_{to} and the *phase 2 reentry* mechanism of PVT/VF. For our group of patients with structural heart disease, in paired analysis we found a prominent augmented J-wave immediately before PVT/VF (Figure 5B). After adjustment for multiple episodes per patient, in a mixed-effects logistic regression model the relative intracardiac J-point amplitude was a strong predictor of PVT/VF. Interestingly, prominent J-waves before the onset of PVT/VF have been found in patients with isoelectric or even negative intracardiac J-point amplitude at baseline (Table 3). We made another interesting observation: the appearance of the intracardiac T wave immediately before PVT/VF (“+/-” biphasic T wave) differed from that of the “-/+” biphasic baseline T-wave.

Intracardiac FF EGM was shown to be a sensitive and specific marker of ST-segment elevation due to acute ruptured plaque and thrombotic occlusion of coronary vessels, conditions confirmed by angiography and intravascular ultrasonography.¹⁴ We cannot rule out acute ischemia as one of the mechanisms of PVT/VF in our study as patients who developed PVT/VF during follow-up had a significantly lower baseline rate of revascularization procedures (Table 1). Occurrence of J-point elevation and J-waves on surface ECG as a marker of VF risk during acute ischemia has been described.^{27,28}

Comparison of J-point amplitude on surface ECG and intracardiac FF EGM

After the seminal clinical observation of Haissaguerre et al,³ which showed increased prevalence of J-point elevation in patients with idiopathic VF, the link between the experimental findings of J-point elevation obtained from a canine ventricular wedge preparation and the increased J-point amplitude on clinical 12-lead ECG has been established. However, unlike the experimental wedge preparation, 12-lead ECG reflects the electrical activity of the whole heart and the multiple factors that might influence J-point amplitude on the surface ECG. This might be the primary reason for the conflicting results of population studies of J-point elevation seen on surface ECG. In a community-based general population study of more than 10,000 middle-aged subjects, J-point elevation on the inferior ECG leads was associated with an increased risk of cardiovascular mortality.⁶ Inferior J-point elevation was a marker of VT/VF risk in a population of patients with coronary artery disease.⁴ The MONICA/KORA case-cohort study showed an increased risk of cardiac mortality in individuals with inferior J-point elevation.⁷ The population-based Atherosclerosis Risk in Communities (ARIC) study of more than 15,000 participants showed that J-point elevation ≥ 0.1 mV in any lead was associated with an increased risk of SCD in whites and women, but not in blacks or men²⁹. However, a study of about 2000 subjects undergoing health examinations⁹ and a recent large study of about 30,000 ambulatory ECGs⁸ did not confirm an association between J-point elevation and cardiovascular mortality.

The results of our study might help to explain this discrepancy. Although we clearly demonstrated an elevated J-point amplitude before PVT/VF onset, we did not observe significant correlation between intracardiac and surface ECG J-point amplitudes (Figure 3). We showed that a mere difference in filter settings between surface ECG and FF EGM does not explain absence of correlation (Figure 4). This outcome might be because (1) the vector of the FF EGM does not correspond to the vector of any of the 12 surface ECG leads and (2) apart from prominent I_{to} , other factors can contribute to the occurrence of J-point elevation.

Resolution volume and axis of FF EGM lead—Indeed, the vector of the intracardiac FF EGM is different from any of the vectors of the 12 surface ECG leads. In our study we used a coil-can FF EGM configuration, which is known to have the highest lead resolution volume and encompasses up to 70% of the ventricular myocardium.³⁰ Some, but not all regions of the heart (right ventricle, inter-ventricular septum, apex, mid-inferior and mid-lateral left ventricular wall) are well represented on FF RV coil-can EGM.³⁰

An alternative hypothesis of J-point elevation origin was never previously explored. Besides the *functional hypothesis* of J-wave origin (due to prominent I_{to}),³¹ other factors, not necessarily associated with the risk of PVT/VF, can contribute to the occurrence of J-point elevation on surface ECG. Here we propose a *structural hypothesis* of J-wave origin, the first idea of which was conceived by Boineau² in 2007. We speculate that particular features of left ventricular anatomy (e.g., prominent ventricular trabeculation, additional papillary muscles, local noncompaction, invagination of Purkinje fibers) can be responsible for J-point elevation. Although cases of false tendon-related PVT have been described,³²

accessory papillary muscles and false tendons are generally viewed as benign findings. Autopsy studies of normal human hearts reported a 55%–68% prevalence rate of prominent left ventricular trabeculations and false tendons³³. Recently Nakagawa et al³⁴ reported high incidence of J-waves on ECG in subjects with false tendon, detected by echocardiography. We speculate that such peculiar structural features without abnormally high I_{to} could be responsible for benign J-point elevation on 12 leads ECG.⁸ Interestingly, we observed that at baseline heart rate positively correlates with relative J-point amplitude in patients with subsequent SVT, but negatively correlates in patients with subsequent PVT/VF, which indirectly confirms 2 different mechanisms of J-point elevation.

Importantly, in our study of patients with structural heart disease, elevated J-point amplitude on baseline surface ECG did not have the characteristic pattern of an early repolarization ECG. Instead, it signified areas of likely transmural scar with a left ventricular aneurysm or prominent left ventricular dilatation and multiple scars.

Limitations

VT/VF detection cutoff was programmed at the discretion of the attending electrophysiologist and varied significantly. However, categorization of VT/VF events was based on cycle length and QRS morphology. Separate analysis of MMVT, PVT and VF events diminished risk of biased analysis.

The duration of the pre-onset EGMs was short and therefore may have limited the accuracy of the intracardiac EGM measurements before VT/VF events. Furthermore, we do not know the timeline of intracardiac J-point amplitude changes before VT/VF onset, as only 10 seconds immediately before VT/VF onset was available for analysis.

While we were very careful in interpreting origin of analyzed beats, the fact that surface ECG immediately before the onset of arrhythmia was not available for analysis leaves a chance for detected changes in EGM morphology due to different beat origins, rather than due to true change in morphology of sinus beats.

Threshold of novel VT/VF predictors was not defined *a priori*. This is the first observation of intracardiac J-point and its predictive value. Independent validation of predictive accuracy of the intracardiac J-point in another prospective study cohort is warranted.

Importantly, our study population consisted of patients with structural heart disease and primary or secondary prevention ICD, both ischemic and non-ischemic cardiomyopathy. The behavior of the intracardiac J-point and the intracardiac $\int QT$ ratio in a population of patients with idiopathic VF and secondary prevention ICD is unknown.

Acknowledgments

Financial Support: This study was supported by Boston Scientific as an Investigator-initiated Research Project (awarded to Dr. Tereshchenko), NIH HL R01 091062 (Gordon Tomaselli), Donald W. Reynolds Foundation (Gordon Tomaselli).

Abbreviations

VF	ventricular fibrillation
VT	ventricular tachycardia
FF	far-field
EGM	electrogram

ICD	implantable cardioverter-defibrillator
SCD	sudden cardiac death
CRT-D	cardiac resynchronization therapy defibrillator
MMVT	monomorphic ventricular tachycardia
PVT	polymorphic ventricular tachycardia
SVT	supraventricular tachycardia
SD	standard deviation
NYHA	New York Heart Association

Reference List

- Shinohara T, Takahashi N, Saikawa T, Yoshimatsu H. Characterization of J wave in a patient with idiopathic ventricular fibrillation. *Heart Rhythm*. 2006; 3:1082–1084. [PubMed: 16945806]
- Boineau JP. The early repolarization variant--normal or a marker of heart disease in certain subjects. *J Electrocardiol*. 2007; 40:3–6.
- Haissaguerre M, Derval N, Sacher F, et al. Sudden cardiac arrest associated with early repolarization. *N Engl J Med*. 2008; 358:2016–2023. [PubMed: 18463377]
- Patel RB, Ng J, Reddy V, et al. Early repolarization associated with ventricular arrhythmias in patients with chronic coronary artery disease. *Circ Arrhythm Electrophysiol*. 2010; 3:489–495. [PubMed: 20657030]
- Haruta D, Matsuo K, Tsuneto A, et al. Incidence and prognostic value of early repolarization pattern in the 12-lead electrocardiogram. *Circulation*. 2011; 123:2931–2937. [PubMed: 21646495]
- Tikkanen JT, Anttonen O, Junttila MJ, et al. Long-term outcome associated with early repolarization on electrocardiography. *N Engl J Med*. 2009; 361:2529–2537. [PubMed: 19917913]
- Sinner MF, Reinhard W, Muller M, et al. Association of early repolarization pattern on ECG with risk of cardiac and all-cause mortality: a population-based prospective cohort study (MONICA/KORA). *PLoS Med*. 2010; 7:e1000314. [PubMed: 20668657]
- Uberoi A, Jain NA, Perez M, et al. Early repolarization in an ambulatory clinical population. *Circulation*. 2011; 124:2208–2214. [PubMed: 21986288]
- Klatsky AL, Oehm R, Cooper RA, Udaltsova N, Armstrong MA. The early repolarization normal variant electrocardiogram: correlates and consequences. *Am J Med*. 2003; 115:171–177. [PubMed: 12935822]
- Surawicz B, MacFarlane PW. Inappropriate and confusing electrocardiographic terms: J-wave syndromes and early repolarization. *J Am Coll Cardiol*. 2011; 57:1584–1586. [PubMed: 21474037]
- Kawata H, Noda T, Yamada Y, et al. Effect of sodium-channel blockade on early repolarization in inferior/lateral leads in patients with idiopathic ventricular fibrillation and Brugada syndrome. *Heart Rhythm*. 2012; 9:77–83. [PubMed: 21855521]
- Kitazawa H, Wakasugi T, Sugimoto T, Yamamoto K, Yoshii S, Aizawa Y. Evolving J waves Prior to Ventricular Fibrillation Postoperative Coronary Bypass. *Intern Med*. 2011; 50:2337–2340. [PubMed: 22001461]
- Gold MR, Ahmad S, Browne K, Berg KC, Thackeray L, Berger RD. Prospective comparison of discrimination algorithms to prevent inappropriate ICD therapy: Primary results of the Rhythm ID Going Head to Head Trial. *Heart Rhythm*. 2012; 9:370–377. [PubMed: 21978966]
- Fischell TA, Fischell DR, Avezum A, et al. Initial clinical results using intracardiac electrogram monitoring to detect and alert patients during coronary plaque rupture and ischemia. *J Am Coll Cardiol*. 2010; 56:1089–1098. [PubMed: 20863952]
- Swerdlow C, Chow T, Das M, et al. Intracardiac electrogram T-wave alternans/variability increases before spontaneous ventricular tachyarrhythmias in implantable cardioverter-defibrillator

- patients: a prospective, multi-center study. *Circulation*. 2011; 123:1052–1060. [PubMed: 21357826]
16. Tereshchenko LG, Fetits BJ, Domitrovich PP, Lindsay BD, Berger RD. Prediction of Ventricular Tachyarrhythmias by Intracardiac Repolarization Variability Analysis. *Circulation: Arrhythmia and Electrophysiology*. 2009; 2:276–284. [PubMed: 19808478]
 17. Tereshchenko LG, Faddis MN, Fetits BJ, Zelik KE, Efimov IR, Berger RD. Transient local injury current in right ventricular electrogram after implantable cardioverter-defibrillator shock predicts heart failure progression. *J Am Coll Cardiol*. 2009; 54:822–828. [PubMed: 19695461]
 18. Tereshchenko LG, Cheng A, Fetits BJ, et al. A new electrocardiogram marker to identify patients at low risk for ventricular tachyarrhythmias: sum magnitude of the absolute QRST integral. *J Electrocardiol*. 2011; 44:208–216. [PubMed: 21093871]
 19. Tereshchenko LG, Han L, Cheng A, et al. Beat-to-beat three-dimensional ECG variability predicts ventricular arrhythmia in ICD recipients. *Heart Rhythm*. 2010; 7:1606–1613. [PubMed: 20816873]
 20. Saxonhouse SJ, Conti JB, Curtis AB. Current of injury predicts adequate active lead fixation in permanent pacemaker/defibrillation leads. *J Am Coll Cardiol*. 2005; 45:412–417. [PubMed: 15680721]
 21. Zong W, Moody GB, Jiang D. A robust open-source algorithm to detect onset and duration of QRS complexes. *Comput Cardiol*. 2003; 33:737–740.
 22. Corrado D, Pelliccia A, Heidbuchel H, et al. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. *Eur Heart J*. 2010; 31:243–259. [PubMed: 19933514]
 23. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986; 1:307–310. [PubMed: 2868172]
 24. Rabe-Hesketh S, Skrondal A, Gjessing HK. Biometrical modeling of twin and family data using standard mixed model software. *Biometrics*. 2008; 64:280–288. [PubMed: 17484777]
 25. Antzelevitch C, Sicouri S, Litovsky SH, et al. Heterogeneity within the ventricular wall. Electrophysiology and pharmacology of epicardial, endocardial, and M cells. *Circ Res*. 1991; 69:1427–1449. [PubMed: 1659499]
 26. Antzelevitch C, Yan GX. J wave syndromes. *Heart Rhythm*. 2010; 7:549–558. [PubMed: 20153265]
 27. Shinde R, Shinde S, Makhale C, et al. Occurrence of “J waves” in 12-lead ECG as a marker of acute ischemia and their cellular basis. *Pacing Clin Electrophysiol*. 2007; 30:817–819. [PubMed: 17547622]
 28. Jastrzebski M, Kukla P. Ischemic J wave: novel risk marker for ventricular fibrillation? *Heart Rhythm*. 2009; 6:829–835. [PubMed: 19467513]
 29. Olson KA, Viera AJ, Soliman EZ, Crow RS, Rosamond WD. Long-term prognosis associated with J-point elevation in a large middle-aged biracial cohort: the ARIC study. *Eur Heart J*. 2011; 32:3098–3106. [PubMed: 21785106]
 30. Requena-Carrion J, Vaisanen J, Alonso-Atienza F, Garcia-Alberola A, Ramos-Lopez FJ, Rojo-Alvarez JL. Sensitivity and spatial resolution of transvenous leads in implantable cardioverter defibrillator. *IEEE Trans Biomed Eng*. 2009; 56:2773–2781. [PubMed: 19643701]
 31. Yan GX, Antzelevitch C. Cellular basis for the electrocardiographic J wave. *Circulation*. 1996; 93:372–379. [PubMed: 8548912]
 32. Betsuyaku T, Muto H, Sugiyama E, Minoshima A, Sato M. False Tendon-Related Polymorphic Ventricular Tachycardia. *Pacing Clin Electrophysiol*. 2011
 33. Boyd MT, Seward JB, Tajik AJ, Edwards WD. Frequency and location of prominent left ventricular trabeculations at autopsy in 474 normal human hearts: implications for evaluation of mural thrombi by two-dimensional echocardiography. *J Am Coll Cardiol*. 1987; 9:323–326. [PubMed: 3805522]
 34. Nakagawa M, Ezaki K, Miyazaki H, et al. Electrocardiographic characteristics of patients with false tendon: Possible association of false tendon with J waves. *Heart Rhythm*. 2012; 9:782–788. [PubMed: 22209947]

Figure 1. Representative example of FF EGM in sinus rhythm. J-point amplitude is negative. T-wave is biphasic with first negative and second positive deflection. J-point is marked as a circle.

Figure 2.
Flow diagram showing the distribution of spontaneous events in study participants.
NSVT=non-sustained ventricular tachycardia

Figure 3. Scatterplots of baseline relative intracardiac FF EGM J-point amplitude by relative J-point amplitudes on 12 ECG leads.

Figure 4. Results of filtering experiment

A. Comparison of J-point elevation presentation on inferior ECG leads (II, III, aVF). Blue-color ECG represents surface ECG signal with applied 0.05 Hz high-pass filter. Red-color ECG represents the same ECG signal with applied bandpass filtering set to 3–60 Hz. **B.** Line plot of paired comparison of non-filtered and filtered 12 lead ECG. Relative J-point amplitude on each out of 12 ECG leads of 3 study subjects is plotted separately. **C.** Bland-Altman plot of difference vs. average value for each out of 12 lead ECG pair filtered vs. non-filtered signal. **D.** Correlation between non-filtered and filtered 12 lead ECG.

Figure 5.

Representative example of an FF EGM and a surface ECG recorded in the study patient with a spontaneous sustained polymorphic ventricular tachycardia (PVT) event during follow-up: **A.** Baseline FF EGM in sinus rhythm. Small J-wave is visible. **B.** FF EGM immediately before (PVT). J-wave is dramatically enlarged. **C.** FF EGM recorded during this whole spontaneous PVT event, treated with ICD shock. **D.** Baseline surface 12-lead ECG of the same patient before ICD implantation.

Table 1

Clinical characteristics of patients with and without arrhythmia events

Characteristic	No arrhythmia N=411	SVT N=25	MMVT N=46	PVT/VF N=12	P
Age $\pm$ SD, y	60.4 $\pm$ 13.1	60.4 $\pm$ 15.3	61.1 $\pm$ 12.4	58.5 $\pm$ 13.9	0.673
Male, n (%)	297 (72.3)	20 (80.0)	34 (73.9)	9 (75.0)	0.856
Ischemic CM, n (%)	237 (57.7)	12 (48.0)	22 (47.8)	7 (58.3)	0.499
History of revascularization, n (%) ^a	163 (68.8 ^a)	7 (63.6 ^a)	15 (71.4 ^a)	1 (14.3 ^a)	0.024
History of hypertension, n (%)	247 (60.1)	18 (72.0)	25 (54.1)	6 (50.0)	0.456
History of atrial fibrillation, n (%)	102 (24.9)	12 (48.0)	14 (30.4)	4 (33.3)	0.070
Baseline LVEF $\pm$ SD, %	24.2 $\pm$ 10.3	26.6 $\pm$ 14.7	26.7 $\pm$ 12.5	22.8 $\pm$ 12.7	0.017
NYHA class III-IV, n (%)	181 (44.2)	11 (44.0)	12 (26.1)	4 (33.3)	0.269
Bundle branch block, n (%)	128 (31.1)	4 (16.0)	9 (19.6)	3 (25.0)	0.103
Beta blockers, n (%) ^b	337 (92.5 ^b)	22 (91.7 ^b)	36 (81.2 ^b)	10 (90.9 ^b)	0.423
Amiodarone, n (%) ^b	39 (17.7 ^b)	5 (25.0 ^b)	9 (27.3 ^b)	4 (40.0 ^b)	0.199
Statins, n (%) ^b	266 (81.1 ^b)	15 (68.2 ^b)	33 (78.6 ^b)	6 (60.0 ^b)	0.202

^a As a percentage of ischemic cardiomyopathy cases.^b As a percentage of non-missing cases.

SD=standard deviation; CM=cardiomyopathy; LVEF=left ventricular ejection fraction; SVT=supraventricular tachycardia; VF=ventricular fibrillation; PVT=polymorphic ventricular tachycardia; MMVT=monomorphic ventricular tachycardia; NYHA=New York Heart Association.

Table 2

Baseline intracardiac J-point amplitude, by demographics and clinical characteristics

Variable	Categories (n)	Baseline heart rate, bpm	Baseline intracardiac relative J amplitude	Baseline JPE on inferior or lateral ECG leads, n (%)
Age	70y (361)	78±17	-0.08±0.12	22 (6)
	>70y (133)	72±14	-0.07±0.08	15 (11.5)
P		0.003	0.543	0.120
Gender	Male (360)	75±16	-0.08±0.10	25 (7)
	Female (134)	80±16	-0.08±0.14	12 (9)
P		0.063	0.669	0.543
NYHA class	I+II (285)	75±17	-0.08±0.11	20 (7)
	III+IV (209)	78±15	-0.08±0.12	16 (8)
P		0.064	0.815	0.925
Diabetes mellitus	Yes (123)	77±17	-0.08±0.09	9 (7)
	No (371)	76±14	-0.08±0.12	26 (7)
P		0.643	0.679	0.808
Bundle branch block	Yes (148)	78±20	-0.09±0.13	12 (13)
	No (346)	76±14	-0.07±0.10	9 (5)
P		0.491	0.244	0.010
B-blocker	On BB (456)	74±15	-0.08±0.11	32 (7)
	No BB (38)	75±16	-0.06±0.08	5 (13)
P		0.494	0.510	0.416
Amiodarone	On Amio (57)	71±16	-0.08±0.09	4 (6)
	No Amio (437)	79±16	-0.11±0.14	39 (9)
P		0.025	0.219	0.645

JPE=J-point elevation

Table 3

Paired comparison of relative J-point amplitude

Event categories (n)	Relative J-point amplitude
Baseline EGM (152)	-0.10 ± 0.21
VT/VF event onset (152)	-0.01 ± 0.08
P-value	<0.0001
Baseline EGM (51)	-0.02 ± 0.15
SVT event onset (51)	0.01 ± 0.07
P-value	0.139
SVT event onset (76)	-0.01 ± 0.05
VT/VF event onset (76)	0.01 ± 0.07
P-value	0.0048
Baseline EGM (140)	-0.09 ± 0.14
MMVT onset (140)	-0.02 ± 0.08
P-value	<0.0001
Baseline EGM (34)	-0.19 ± 0.39
PVT/VF onset (34)	0.28 ± 0.08
P-value	0.0116