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Coupling Interval Variability Differentiates Ventricular Ectopic Complexes Arising in the Aortic Sinus of Valsalva and Great Cardiac Vein From Other Sources

Mechanistic And Arrhythmic Risk Implications

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Objectives The objective of this study was to determine whether premature ventricular contractions (PVCs) arising from the aortic sinuses of Valsalva (SOV) and great cardiac vein (GCV) have coupling interval (CI) characteristics that differentiate them from other ectopic foci.

Background PVCs occur at relatively fixed CI from the preceding normal QRS complex in most patients. However, we observed patients with PVCs originating in unusual areas (SOV and GCV) in whom the PVC CI was highly variable. We hypothesized that PVCs from these areas occur seemingly randomly because of the lack of electrotonic effects of the surrounding myocardium.

Methods Seventy-three consecutive patients referred for PVC ablation were assessed. Twelve consecutive PVC CIs were recorded. The ΔCI (maximum − minimum CI) was measured.

Results We studied 73 patients (age 50 ± 16 years, 47% male). The PVC origin was right ventricular (RV) in 29 (40%), left ventricular (LV) in 17 (23%), SOV in 21 (29%), and GCV in 6 (8%). There was a significant difference between the mean ΔCI of RV/LV PVCs compared with SOV/GCV PVCs (33 ± 15 ms vs. 116 ± 52 ms, $p < 0.0001$). A ΔCI of >60 ms demonstrated a sensitivity of 89%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 94%. Cardiac events were more common in the SOV/GCV group versus the RV/LV group (7 of 27 [26%] vs. 2 of 46 [4%], $p < 0.02$).

Conclusions ΔCI is more pronounced in PVCs originating from the SOV or GCV. A ΔCI of 60 ms helps discriminate the origin of PVCs before diagnostic electrophysiological study and may be associated with increased frequency of cardiac events. (J Am Coll Cardiol 2014;63:2151–8) © 2014 by the American College of Cardiology Foundation

Idiopathic premature ventricular complexes (PVCs) are generally considered benign and are often treated conservatively. However, sustained ventricular tachycardia (VT), symptomatic PVCs resistant to medical therapy, and PVCs thought to contribute to an underlying cardiomyopathy are often treated with radiofrequency ablation (RFA). Noninvasive mapping criteria based on 12-lead electrocardiogram (ECG) characteristics can help with procedural planning and guide mapping if RFA is needed (1–13). However, PVCs with a V_3 precordial ECG transition are difficult to localize and can be of right ventricular outflow tract (RVOT) or left ventricular outflow tract origin (14).

The reportedly benign nature of outflow idiopathic PVCs has been disputed by some (15). There is reasonable evidence that a small proportion of these cases may be higher risk for R-on-T phenomena and sudden cardiac death (SCD). However, limited data exist to help the clinician risk stratify on the basis of PVC characteristics.

PVCs occur at relatively fixed coupling intervals (CIs) from the preceding normal QRS complex in most patients. However, we observed some patients with PVCs originating in unusual areas (aortic sinuses of Valsalva [SOV], great

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Abbreviations and Acronyms

ΔCI = coupling interval
CI = coupling interval
ECG = electrocardiogram
GCV = great cardiac vein
LV = left ventricle/ventricular
PVC = premature ventricular complexes
Q = quartile
RFA = radiofrequency ablation
RV = right ventricle/ventricular
RVOT = right ventricular outflow tract
SCD = sudden cardiac death
SOV = sinus of Valsalva
VT = ventricular tachycardia

cardiac vein [GCV]) in whom the PVC CI was highly variable. We hypothesized that PVCs from these areas could occur seemingly randomly because of the lack of restraining electrotonic coupling effects of the surrounding myocardium. We also hypothesized that this variable CI characteristic might be a valuable diagnostic tool as well as provide further insights into the functional behavior of these PVCs and possible cardiac event risk associated with a given PVC origin.

Methods

Consecutive cases of idiopathic PVCs that were mapped and ablated were assessed. Only cases with PVCs with a frequency of >10/min were studied. However, the majority had a pattern of bigeminy or trigeminy. Cases with rare PVCs or only nonsustained or sustained VT were excluded, as were cases of fascicular PVC/VT. Patients with cardiomyopathy were excluded if the PVCs were thought to be secondary to the underlying cardiomyopathy. Cases of cardiomyopathy thought secondary to a high burden of PVCs were included as long as alternative etiologies of cardiomyopathy such as severe obstructive coronary artery or significant valvular disease were ruled out. Approval for enrollment into the study was obtained from the respective institutional review boards.

Antiarrhythmic medications were discontinued at least 48 h before the procedure as per protocol at the participating institutions. Surface ECG leads from the diagnostic electrophysiological study were analyzed using electronic calipers at a 100 mm/s sweep speed. Only monomorphic PVCs were studied. The first available period in the diagnostic study during which 12 consecutive PVCs were available for analysis was assessed. The interval from the initial Q- or R-wave of the preceding sinus beat to the beginning of the subsequent PVC beat was measured in milliseconds. The difference in milliseconds between the maximum and minimum CI (ΔCI) was calculated. The first 12 consecutive PVCs were chosen for analysis to limit the effect of procedural sedation later in the study as well as to maximize the clinical utility of any findings, which could potentially translate to evaluation, not only from the diagnostic electrophysiological study, but also from a 12-lead ECG or rhythm strip obtained in a cardiology office or from an outpatient ambulatory ECG monitor.

A standard diagnostic electrophysiological study was then performed using several percutaneously placed multielectrode catheters. If needed, isoproterenol infusion was used to increase the frequency of PVCs. Mapping of the PVC origin was performed targeting the earliest site of activation compared with the onset of the surface PVC QRS complex, after which RFA was attempted using standard or irrigated radiofrequency energy after excluding an unacceptable proximity to a major coronary artery (e.g., epicardial mapping at the left ventricular [LV] base). In most cases, advanced mapping systems such as CARTO version 3.0 (Biosense-Webster, Diamond Bar, California) or NavX version 3.0 (St. Jude Medical, Minneapolis, Minnesota) were used to facilitate mapping.

Continuous variables were expressed as mean ± SD, and comparison between 2 groups was analyzed using the Student *t* test. Categorical variables were analyzed using the Fisher exact test. Given the heterogeneity of variance in ΔCI, Welch's *t* test was used to compare groups. A receiver-operating characteristic curve was constructed and Youden's Index applied to determine the optimal cutoff for ΔCI as a diagnostic test.

Results

We studied 73 patients (age 50 ± 16 years, 47% male) (Table 1). The PVC origin was right ventricle (RV) in 29 (40%), LV in 17 (23%), SOV in 21 (29%), and GCV in 6 (8%). Of the RV PVCs, 22 (76%) were from the RVOT with the remainder from the RV body (3 septal, 2 basal inferior, and 2 inferoseptal). Of the LV PVCs, 2 were from the aortomitral continuity, 5 from the anterior wall (2 endocardial and 3 epicardial), 5 from the inferior wall, 3 from the lateral wall, and 1 from the septal wall. Of the SOV PVCs, 1 (5%) originated from the right SOV, 16 (76%) originated from the left SOV, and 4 (19%) originated from the left and right junction. The index PVC was successfully ablated in 68 of 73 (93%) of all cases and in 68 of 69 (99%) of cases in which ablation was attempted. Ablation was deferred because of location near a coronary artery in 4 of 73 (5%).

When baseline characteristics were compared on the basis of the location of PVC origin, there was no difference in age (47 ± 18 years vs. 52 ± 15 years, $p = 0.25$), sex (56% male vs. 41% male, $p = 0.46$), baseline ejection fraction (47 ± 12% vs. 50 ± 11%, $p = 0.31$), or baseline PVC burden on ambulatory ECG monitor (24.3 ± 10.5% vs. 23.5 ± 11.4%, $p = 0.83$) in the SOV/GCV groups versus the RV/LV group, respectively. There was no difference in the proportion of patients taking beta-blockers (63% vs. 70%, $p = 0.61$), calcium channel blockers (11% vs. 7%, $p = 0.66$), or standard antiarrhythmic medications (15% vs. 26%, $p = 0.36$) before the procedure.

Pre-procedure syncope, cardiac arrest, or documented polymorphic VT were more common in the SOV/GCV group versus the RV/LV group (7 of 27 [26%] vs. 2 of 46 [4%], $p < 0.02$). In the SOV/GCV group, there were 3 SCDs, 1 documented polymorphic VT, and 3 syncopal episodes, whereas in the RV/LV group, there was 1 syncopal