Non-Reentrant Ventricular Arrhythmias In Patients With Structural Heart Disease Unrelated To Abnormal Myocardial Substrate

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BACKGROUND Ventricular arrhythmias in the absence of structural heart disease are commonly referred to as "idiopathic." Patients with structural heart disease have ventricular arrhythmias with the same mechanisms and sites of origin as idiopathic ventricular arrhythmias, but the prevalence of such arrhythmias is not well defined.

OBJECTIVES To identify the prevalence of non-reentrant ventricular arrhythmias unrelated to abnormal myocardial substrate in patients with structural heart disease and to compare these arrhythmias to ventricular arrhythmias in patients with structurally normal hearts.

METHODS Of 249 consecutive patients referred for ablation of ventricular arrhythmias, 97 patients had non-reentrant arrhythmias unrelated to underlying structural heart disease. Fifty-five patients had structurally normal hearts, and 42 had underlying structural heart disease.

RESULTS Compared with patients with structurally normal hearts, patients with structural heart disease were more likely to have non-reentrant ventricular arrhythmias unrelated to underlying abnormal myocardial substrate originating from the aortic cusps and left ventricular outflow tract whereas patients without structural heart disease more often had arrhythmias originating from the right ventricular outflow tract. There was a significant increase in the average left ventricular ejection fraction after ablation in patients with structural heart disease.

CONCLUSION Non-reentrant ventricular arrhythmias unrelated to abnormal myocardial substrate are common in patients with structural heart disease, and sites of origin differ from those seen in patients with structurally normal hearts. When managing structural heart disease in patients with ventricular arrhythmias, a focus on arrhythmia mechanism, origin, and relationship to underlying myocardial substrate may have important implications for future treatment options and patient outcomes.

KEYWORDS Idiopathic ventricular tachycardia; Outflow tract tachycardia; Premature ventricular contractions; Structural heart disease; Coronary artery disease; Myocardial infarction; Cardiomyopathy; Left ventricular dysfunction; Tachycardia-mediated cardiomyopathy

ABBREVIATIONS **EP** = electrophysiology/electrophysiological; **CMR** = cardiac magnetic resonance; **ICD** = implantable cardioverter-defibrillator; **ILVT** = idiopathic left ventricular tachycardia; **LGE** = late gadolinium enhancement; **LV** = left ventricle/ventricular; **LVEF** = left ventricular ejection fraction; **PVC** = premature ventricular contraction; **RV** = right ventricle/ventricular; **RVOT** = right ventricular outflow tract; **UTAS** = unrelated to abnormal substrate; **VT** = ventricular tachycardia

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Introduction

Ventricular tachycardia (VT) is most commonly seen in patients with underlying structural heart disease where myocardial fibrosis provides the substrate for reentry.[1] Patients with structural heart disease and reentrant monomorphic VT are at an increased risk of sudden cardiac death.[2,3] A minority of patients referred for the evaluation of VT will have no identifiable structural heart disease,[4–6] and these patients generally have a more benign prognosis.[7–10] Historically, VT in the absence of underlying structural heart disease has been referred to as "idiopathic." Most commonly, these arrhythmias are due to a triggered mechanism and frequently originate from the right and left ventricular outflow tracts and aortic cusps but may also originate from other sites including the fascicles or valve rings.[11–14]

Although the literature on triggered outflow tract tachycardias focuses on patients with structurally normal hearts, patients with structural heart disease also manifest non-reentrant ventricular arrhythmias, which are often unrelated to their abnormal myocardial substrate. In such patients, these arrhythmias may have a more benign clinical course and a more robust response to treatment as compared to reentrant VT. With this in mind, we should focus on arrhythmogenic mechanism, which is of utmost importance when assessing a patient with structural heart disease and ventricular arrhythmias.

Triggered outflow tract tachycardias in patients with structurally normal hearts is well studied in the literature,

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but the prevalence of these arrhythmias in patients with underlying structural heart disease has not been well defined. In this study, we sought to identify the prevalence, clinical characteristics, and responses to treatment of non-reentrant ventricular arrhythmias unrelated to any abnormal myocardial substrate in patients with structural heart disease and to compare these arrhythmias with those observed in patients without structural heart disease.

Methods

Study population

Two hundred forty-nine consecutive patients with frequent monomorphic premature ventricular contractions (PVCs) and/or VTs referred to our electrophysiology (EP) laboratory for PVC and/or VT ablation between August 2004 and April 2011 were identified retrospectively and screened for inclusion in the study. A total of 309 discrete ablation procedures were performed in this patient population between the aforementioned dates. Of the 249 patients identified, 50 had more than 1 ablation procedure performed. For each PVC and/or VT identified during an EP study, the site of arrhythmia origin as well as the tachycardia mechanism was defined. The identification of multiple PVCs and/or VTs in a single patient during an EP study was common. Focal non-reentrant ventricular arrhythmias unrelated to abnormal myocardial substrate were identified for inclusion in the study. For the purposes of this study, these arrhythmias will be referred to as non-reentrant ventricular arrhythmias unrelated to abnormal substrate (UTAS). Patients with at least 1 non-reentrant arrhythmia UTAS were then classified on the basis of the presence or absence of underlying structural heart disease identified previously or at the time of the EP study. These 2 groups were then used for subsequent analyses.

Identification of arrhythmias unrelated to underlying structural heart disease

Ventricular arrhythmias were classified into either of the 2 primary mechanisms of arrhythmogenesis: (1) abnormal impulse generation, including triggered activity and enhanced automaticity, and (2) abnormal impulse conduction leading to reentry. Reentrant arrhythmias were defined by their mode of initiation, response to entrainment maneuvers, resetting characteristics, and appearance on electroanatomic activation mapping. Triggered and automatic arrhythmias were identified by their onset and offset; their response to isoproterenol, adenosine, and carotid sinus massage; as well as their response to overdrive pacing maneuvers. A definitive arrhythmia mechanism could not be defined for all ventricular arrhythmias. Of note, a small number of idiopathic left ventricular tachycardias (ILVTs) were identified during the study period. Although ILVT probably more closely resembles non-reentrant ventricular arrhythmias than scar-mediated reentrant VTs in its clinical characteristics and response to treatment, it has a distinctly different arrhythmogenic mechanism from the majority of non-reentrant ventricular arrhythmias identified in this study, which were generally triggered outflow tract tachycardias. Given its unique mechanism and the small number of cases encountered, these cases were excluded.

Sites of origin were assessed on the basis of electroanatomic activation mapping as well as pace mapping. They were then compared to known areas of abnormal myocardial substrate identified by fixed perfusion defects on nuclear imaging, wall motion abnormalities on echocardiogram or cardiac magnetic resonance (CMR), late gadolinium enhancement (LGE) on CMR, or voltage mapping at the time of the EP study. Voltage maps were generated during sinus rhythm, and a voltage cutoff of <1.5 mV was used to define an area of abnormal myocardium. Of note, in our experience, certain areas of the ventricles such as the annuli commonly have areas of low voltage on electroanatomic mapping, even in patients with structurally normal hearts. For this reason, areas of low voltage were not considered abnormal unless they were also associated with fractionated electrograms.

All VTs with a reentrant mechanism and those PVCs and/or VTs associated with an abnormal myocardial substrate were excluded. Ventricular arrhythmias that had a non-reentrant mechanism and that originated from an area distinct from any identifiable abnormal myocardial substrate, termed non-reentrant ventricular arrhythmias UTAS, were included in subsequent analyses.

Definition of structural heart disease

After identifying all patients with non-reentrant ventricular arrhythmias UTAS, patients were divided into 2 groups on the basis of the presence or absence of underlying structural heart disease. Structural heart disease was defined as a left ventricular ejection fraction (LVEF) $<50\%$ at the time of the initial EP study, which failed to normalize after ablation. Patients with a low LVEF that totally normalized after ablation of arrhythmia were included in the structurally normal heart category if they had no other known cardiac disease ($n = 5$). Patients with a normal LVEF ($>50\%$) were also evaluated for the presence of other structural heart diseases, including arrhythmogenic right ventricular cardiomyopathy, hypertrophic cardiomyopathy, cardiac sarcoid, severe valvular stenosis, and/or regurgitation; the presence of LGE on CMR; or low-voltage areas on electroanatomic mapping. If any of the above were present, these patients were included in the structural heart disease group. All patients with decreased LVEFs were then further classified according to their underlying substrate, including presence of coronary artery disease on the basis of coronary angiography or nuclear perfusion imaging and history of myocardial infarction on the basis of the presence of Q waves on 12-lead electrocardiogram, fixed nuclear perfusion defects, or previous documentation when other information was unavailable.

Statistical analysis

Continuous variables are expressed as mean $\pm$ SD and categorical variables as a number (percentage). The Student *t*