

Challenges in the diagnosis and management of idiopathic ventricular fibrillation



Jonathan Lipton, MD, PhD,^{*} George J. Klein, MD,[†] Raymond W. Sy, MBBS, PhD^{*‡}

From the ^{*}Department of Cardiology, Royal Prince Alfred Hospital, Camperdown, NSW, Australia, [†]University of Western Ontario, London, Ontario, Canada, and [‡]Sydney Medical School, University of Sydney, Sydney, NSW, Australia.

Introduction

The management of idiopathic ventricular fibrillation is challenging. While the exact underlying mechanism remains elusive, the Purkinje system appears to be critically involved in many cases. Medical therapy is largely empirical and ablation may be required in patients with drug-refractory arrhythmia. However, targets for ablation may be difficult to identify when the spontaneous arrhythmia occurs infrequently. In this setting, 12-lead Holter monitoring is extremely useful in identifying a potential target for mapping and ablation prior to the electrophysiology study.

Case report

A 40-year-old woman presented with recurrent syncope without warning that occurred at rest. Her medical history and family history were unremarkable. Resting 12-lead ECG showed sinus rhythm with an RsR' in lead V₂, normal QT interval, and, specifically, no suggestion of Brugada pattern or arrhythmogenic right ventricular cardiomyopathy (Figure 1). Early repolarization was not observed at any point. Echocardiography and cardiac magnetic resonance imaging were normal. Exercise testing and flecainide challenge were unremarkable.

During admission to the hospital, 2 short episodes of nonsustained ventricular tachycardia (VT) were recorded (Figure 2). The coupling interval of the initiating premature ventricular complex (PVC) was approximately 280–300 ms, and the overall burden of PVCs was low (< 10 in 24 hours).

Electrophysiologic study (EPS) was performed. Baseline intervals were normal, as were anterograde and retrograde conduction. Spontaneous PVCs were not observed. Atrial and ventricular burst pacing were performed and repeated

after administration of isoprenaline (5 µg/min) without arrhythmia induction. Up to 4 ventricular extrastimuli from the right ventricular apex to 10 ms above the refractory period failed to induce arrhythmia.

With a presumptive diagnosis of idiopathic polymorphic VT, a defibrillator was implanted, and quinidine therapy was commenced (10 mg/kg/d). The decision to implant a defibrillator was extremely challenging and was reached only after extensive consultation with electrophysiology colleagues and in-depth discussions with the patient and her family. The presence of recurrent syncope, the relative short coupling interval of the initiating PVC, and the short cycle length of the polymorphic VT influenced the decision.

Three months later, the patient presented after another episode of syncope. Interrogation of her implantable cardiac defibrillator (ICD) revealed sustained polymorphic VT degenerating into ventricular fibrillation (VF), which was treated successfully with a shock (Figure 3A). Several other episodes of nonsustained polymorphic VT also were observed.

The patient had been compliant with quinidine therapy, and atenolol 25 mg twice daily was added. Four weeks later, she complained of lightheadedness while she was taking her children to school. Interrogation of the device showed some reduction in resting heart rate after initiation of beta-blocker treatment but more frequent episodes of VT (Figure 3B).

Twelve-lead Holter monitoring (SEER 12-channel Holter ECG Digital Recorder; GE Medical Systems, Milwaukee, WI) was performed with the limb lead electrodes placed in a Mason-Likar configuration on the torso and the precordial leads in a standard position. Holter monitoring revealed several episodes of nonsustained polymorphic VT initiated by stereotypical PVC with a narrow QRS, qR pattern in lead V₁, and left superior axis (Figure 4C).

The patient was admitted to the hospital. Quinidine and atenolol were discontinued, and EPS was repeated 5 days later.

Multipolar recording catheters were placed in the coronary sinus, His-bundle position, and right ventricle. Care was taken to position the surface ECG electrodes in the same position as the Holter monitor. Using a retroaortic approach, a decapolar catheter and roving ablation catheter were placed against the left ventricular septum to map Purkinje potentials

KEYWORDS Ventricular fibrillation; Purkinje; Ablation; Sudden death; Holter
ABBREVIATIONS EPS = electrophysiologic study; ICD = implantable cardiac defibrillator; LV = left ventricle; PVC = premature ventricular complex; VF = ventricular fibrillation; VT = ventricular tachycardia (Heart Rhythm Case Reports 2015;1:269–274)

Address reprint requests and correspondence: Dr. Raymond W. Sy, Department of Cardiology, Royal Prince Alfred Hospital, Missenden Road, Camperdown, NSW 2050, Australia. E-mail address: raymond.sy01@gmail.com.

KEY TEACHING POINTS

- Twelve-lead Holter monitoring may allow identification of a potential target for ablation in cases of idiopathic ventricular fibrillation (VF), especially in patients with a low arrhythmia burden.
- Purkinje-related arrhythmias can manifest as both monomorphic and polymorphic ventricular tachyarrhythmias in patients with normal hearts as well as in patients with structural heart disease or channelopathy.
- Purkinje-related polymorphic ventricular tachycardia and VF may not respond to beta-blockade or flecainide therapy but may be amenable to catheter ablation.

suggested by the morphology of the initiating PVC on Holter monitoring. The catheter positions in the left anterior oblique view are shown in Figure 5. The intracardiac electrograms in sinus rhythm are shown in Figure 6A. Presystolic Purkinje potentials were recorded during sinus rhythm with proximal-to-distal activation on the septally placed left ventricular (LV) catheters (indicated by the arrow; activation from proximal to distal LV catheter).

PVCs were not observed in the baseline state or during isoprenaline infusion. After right ventricular burst pacing, nonsustained polymorphic VT was observed on 2 occasions over a 60-minute period. The morphology of the initiating PVC was very similar to the PVC previously documented on Holter monitoring (Figure 4).

Intracardiac electrograms recorded during an episode of polymorphic VT are shown in Figure 6. Purkinje potentials preceded the initiating PVC as well as both diastolic and presystolic Purkinje potentials during tachycardia, with variation in the duration from Purkinje potential to QRS onset. On beats 1 and 4, there also appeared to be a

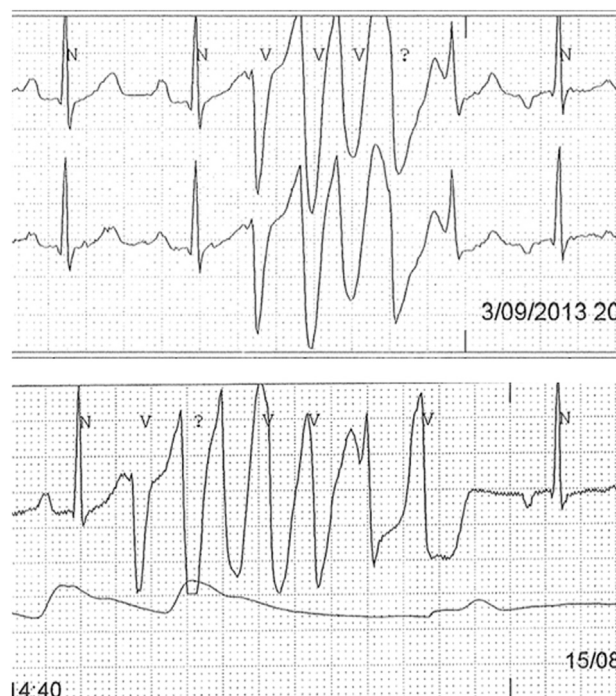


Figure 2 Telemetry recordings demonstrating nonsustained episodes of polymorphic ventricular tachycardia. Both episodes are initiated by a short coupled (280–300 ms) premature ventricular beat.

proximal-to-distal activation sequence of the presystolic potentials.

Radiofrequency ablation (irrigated, 35 W) was performed in the mid-LV septum at the site of earliest presystolic Purkinje potential during the initiating PVC. During ablation, there were ventricular ectopic beats, presumably related to automaticity from the Purkinje system. There was apparent loss of local Purkinje potentials at the ablation site, but the delay in the occurrence of the local ventricular electrogram was minimal (<10 ms). Diastolic potentials were not observed during sinus rhythm at the ablation site. Ablation was empirically extended in a linear fashion over 2–3cm, perpendicular to the long axis of the left

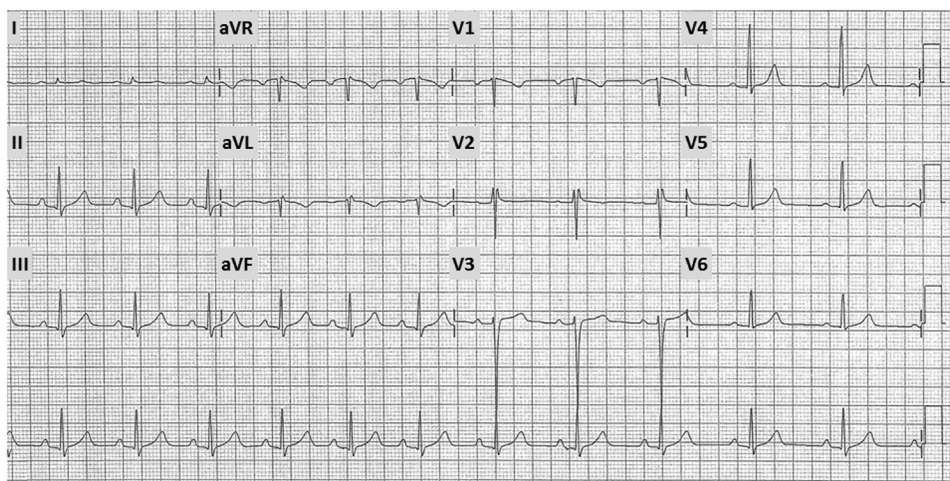


Figure 1 Baseline 12-lead electrocardiogram.

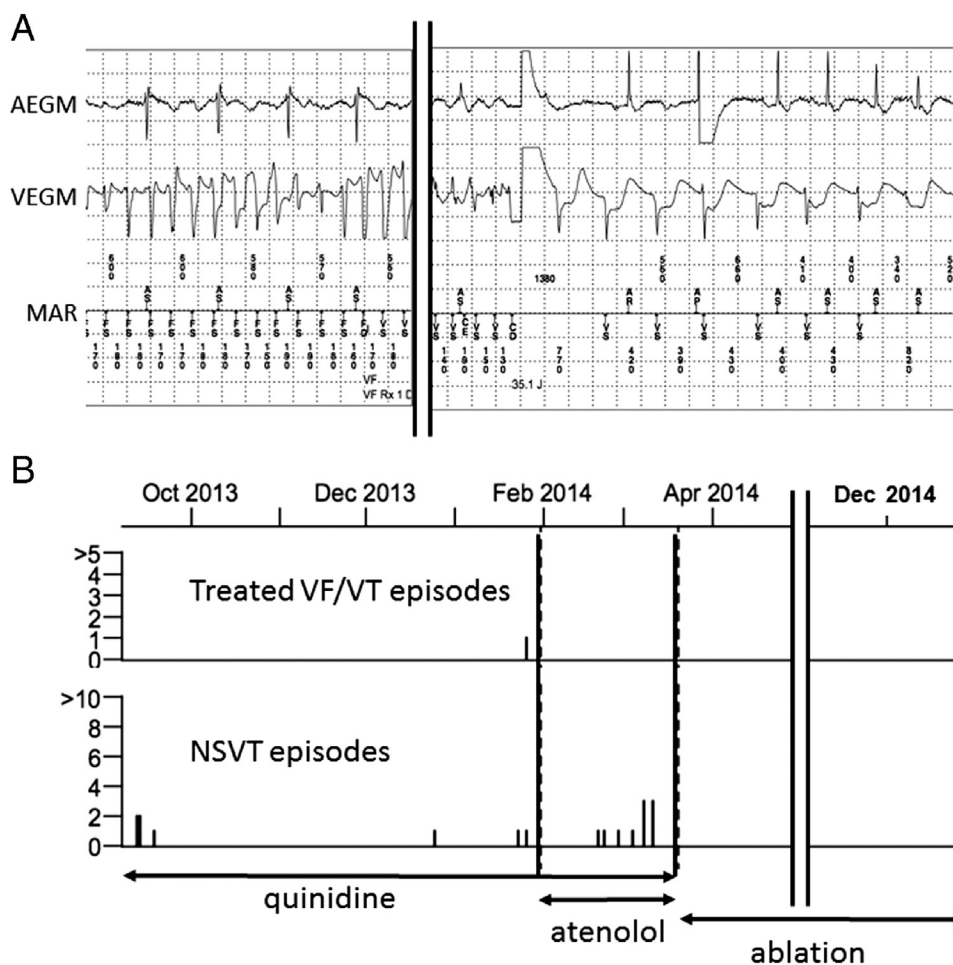


Figure 3 A: Printout of the implantable cardiac defibrillator (ICD) during syncope. Ventricular fibrillation is detected and successfully treated with a shock. B: Incidence of VF/VT episodes detected and treated by the ICD under medical treatment and after ablation. AEGM = atrial electrocardiogram; MAR = marker channel; NSVT = nonsustained ventricular tachycardia; VEGM = right ventricular tip-to-ring electrocardiogram; VF = ventricular fibrillation; VT = ventricular tachycardia.

ventricle, with the aim of expanding the lesion in the area of interest. Care was taken to avoid more proximal ablation near the His bundle or bifurcation of the left anterior and posterior fascicles. No spontaneous PVCs were observed after ablation, and tachycardia was non-inducible. Mitral valve function was unaffected by ablation. The patient has been arrhythmia-free for 9 months without medical therapy.

Discussion

Clinical characteristics

We describe a case of idiopathic polymorphic VT likely related to reentry in the left posterior fascicular network. The clinical characteristics of the arrhythmia were as follows. Arrhythmia occurred in a middle-aged subject in the absence of demonstrable structural heart disease or channelopathy. Polymorphic VT occurred at rest and was unresponsive to empirical quinidine and beta-blocker therapy, the latter possibly associated with an increased frequency of arrhythmia. Spontaneous arrhythmia occurred very infrequently, was not provokable by adrenergic stimulation, and was

inconsistently induced with pacing. The case was challenging because of the paucity of clinical arrhythmia. It highlights the use of 12-lead Holter monitoring during periods of increased symptoms.¹ The observation of initiating monomorphic short-coupled PVCs was critical in identifying the left posterior fascicular network as the likely culprit. This allowed targeted mapping of the arrhythmia during the repeat EPS.

Mechanistic considerations

Gelatinous fibers in the ventricular subendocardium were first described by Purkinje² in 1885. The function of the Purkinje fibers as part of the conduction system was subsequently assessed by Tawara³ in 1905. Polymorphic VT was reported by Zipes et al⁴ in 1979. Belhassen et al⁵ found that verapamil was effective in suppressing ventricular arrhythmias related to the Purkinje system. The presence of Purkinje fiber potentials and successful ablation at the site of these potentials in this patient group were described in 1993 by Nakagawa et al.⁶

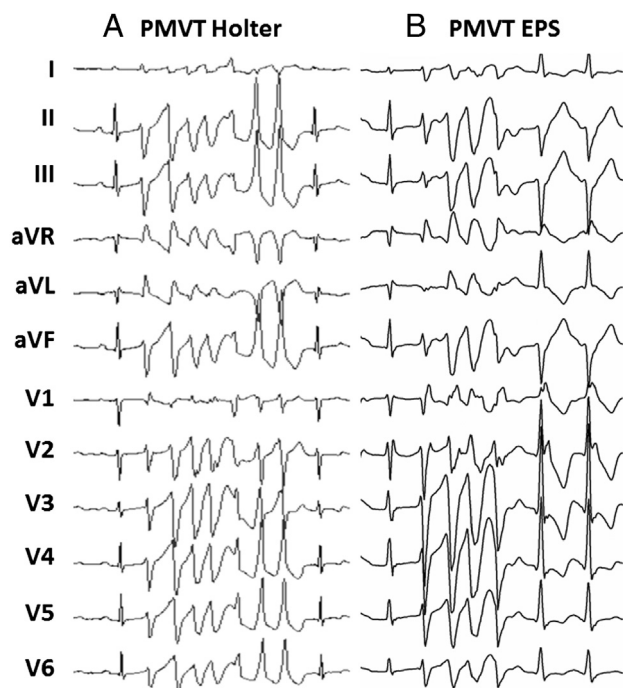


Figure 4 Polymorphic ventricular tachycardia (PMVT) preceded by a short coupled premature ventricular beat with a narrow QRS complex, qR pattern in lead V₁, and left superior axis. Morphology is nearly identical in the initiating beat recorded on Holter monitoring (A) and during electrophysiologic study (EPS) (B).

VT related to the Purkinje system can be classified as monomorphic or polymorphic (Table 1). The mechanism of monomorphic VT is eclectic but generally believed to be due to either reentry using the fascicles and/or bundle branches and/or myocardium, or possibly focal automaticity of Purkinje tissue. These are potentially treatable by ablation.

VF is of unknown mechanism but is thought to be perpetuated by reentry or spiral waves throughout the myocardium. Purkinje fiber involvement in VF initiation has been demonstrated in Brugada syndrome, long QT syndrome, amyloidosis, chronic myocarditis, cardiomyopathies, and catecholaminergic polymorphic VT. Leenhardt et al⁷ described the involvement of the Purkinje system in VF initiated by short-coupled premature beats in normal hearts. Why these triggers cause VF in some individuals and not others is unclear. Other potential “triggers” of idiopathic VF have been described in the right and left ventricular outflow tracts, pulmonary artery, and papillary muscle.^{1,8,9}

It has been postulated that the mechanism of the short-coupled variant of Purkinje-related polymorphic VT/VF depends on calcium overload in the Purkinje tissue and defective “gating” in the Purkinje system. Calcium overload in Purkinje tissue results in delayed potentials, leading to reentry in the Purkinje network due to defective gate function.¹⁰ Abnormal dispersion in the refractory period of the Purkinje network allows signals from the myocardium to reenter the system and result in a reentrant tachycardia.¹¹

Ablation of the culprit Purkinje fibers as a treatment strategy was described in 2002 by Haissaguerre et al,^{12,13}

who targeted the earliest Purkinje signals relative to the QRS during the premature beats. A short (<10-ms duration) sharp potential preceding a larger ventricular electrogram during sinus rhythm and ectopic beats (by 11 and 36 ms, respectively) suggested a Purkinje signal, whereas the absence of such a signal at the site of earliest activation suggested an origin from ventricular muscle.¹³ Bänsch et al¹⁴ described suppression of VF in patients after myocardial infarction by ablation of Purkinje signals preceding premature ventricular beats. They observed Purkinje potentials preceding ventricular activation in sinus rhythm by 23–26 ms and preceding the premature beats by 126–160 ms. Targeting ablation to these signals resulted in suppression of VF.

Absence of spontaneous PVCs and noninducibility of VT are clinical end-points of ablation, but these are not always practical as demonstrated in the present case. Surrogate end-points include the abolition of local Purkinje potentials and a slight delay in the occurrence of the local ventricular electrogram at the site of ablation during sinus rhythm.¹³ The demonstration of diastolic Purkinje potentials indicating intra-Purkinje conduction block is another potential end-point.^{15,16} Moreover, it is unknown whether clinical success may be enhanced by additional “substrate modification” within the neighboring Purkinje network to address multiple foci or local reentry.¹ However, more extensive ablation may increase the possibility of collateral injury to the conduction system (especially with more proximal ablation) as well as injury to the mitral valve apparatus.

Clinical observations suggest that the mechanism of Purkinje system–initiated VF can display characteristics of both triggered activity and reentry.¹⁷ Rapid polymorphic VTs may be induced by a ventricular premature beat with short coupling intervals as well as atrial burst pacing. Arrhythmias may be suppressed by verapamil, suggesting

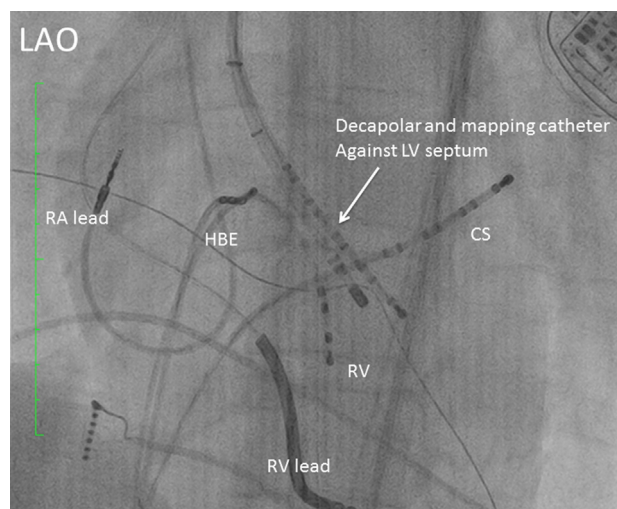


Figure 5 Left anterior oblique (LAO) projection of catheter positions during mapping of Purkinje potentials. The mapping catheter and decapolar catheter are positioned using a retroaortic approach on the left septum. The dual-chamber implanted defibrillator and leads are visible. CS = coronary sinus; HBE = His-bundle electrode; LV = left ventricle; RA = right atrium; RV = right ventricle.

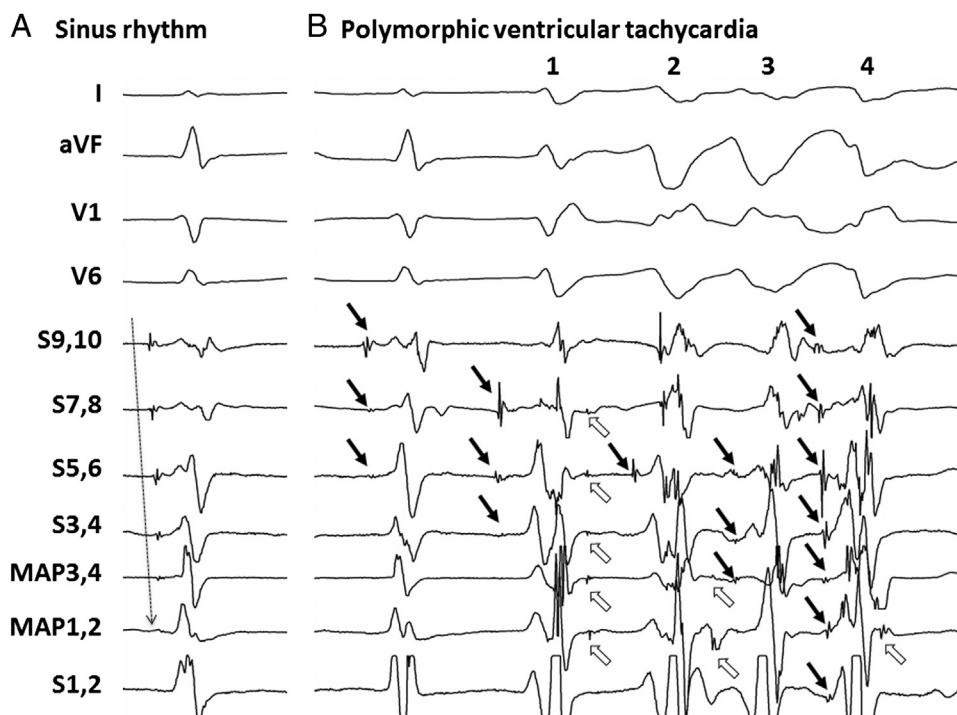


Figure 6 Intracardiac electrocardiograms. **A:** Arrow highlights the proximal-to-distal activation of presystolic Purkinje potentials along the septum in sinus rhythm. **B:** Episode of polymorphic ventricular tachycardia. Black arrows indicate presystolic Purkinje potentials. White arrows indicate diastolic Purkinje potentials. S9,10 were located at the proximal left ventricular septum. MAP indicates signals from the ablation catheter, which was positioned parallel to the decapolar catheter.

triggered activity within the Purkinje system. Alternatively, the observation that VF suppression may occur after ablation from within the Purkinje system but not at the site with the earliest ventricular signal may suggest a reentrant circuit involving the Purkinje system.¹

Quinidine has been found to be effective in suppressing VF in patients with Brugada syndrome and idiopathic VF.¹⁸ However, the patient in the current report continued to experience arrhythmias despite empirical quinidine therapy. Verapamil has also been used to suppress idiopathic ventricular tachyarrhythmia.^{5,7} However, neither medical

therapy nor catheter ablation provides absolute protection from sudden death.^{7,19} For example, Knecht et al¹⁹ reported a recurrence rate of 18% in 38 patients who underwent apparently successful ablation for idiopathic VF. This finding would argue for ICD placement in these individuals regardless of the apparent success of ablation and/or medical therapy.

Practical considerations

Practical lessons from the present case include the need for repeated evaluation at times of increased arrhythmia burden because of the stochastic nature of this specific arrhythmia. Twelve-lead Holter monitoring may be extremely useful in identifying a potential target for mapping and ablation before the electrophysiologic procedure. Management may involve a combination of medical therapy (probably with verapamil), ablation where feasible, and ICD implantation.

Table 1 Categories of Purkinje system arrhythmias

Monomorphic VT	Polymorphic VT/VF
I. Verapamil-sensitive left fascicular VT	I. Idiopathic VF
II. Purkinje fiber-mediated VT postinfarct	II. VF in ischemic heart disease
III. Bundle branch/interfascicular reentrant VT	III. Associated with structural heart disease
	A. Myocarditis
	B. Amyloidosis
	C. Nonischemic cardiomyopathy
	D. Aortic valve disease
IV. Focal Purkinje VT	IV. Associated with channelopathy (long QT syndrome, Brugada syndrome)

VF = ventricular fibrillation; VT = ventricular tachycardia. Adapted from Nogami.¹⁵

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