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Review

Catheter ablation for ventricular tachyarrhythmia in patients with channelopathies

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ABSTRACT

Drug treatment and/or implantable cardioverter defibrillator (ICD) implantation are the most widely accepted first-line therapies for channelopathic patients who have recurrent syncope, sustained ventricular tachycardia (VT), or documented ventricular fibrillation (VF), or are survivors of cardiac arrest. In recent years, there have been significant advances in mapping techniques and ablation technology, coupled with better understanding of the mechanisms of ventricular tachyarrhythmia in channelopathies. Catheter ablation has provided important insights into the role of the Purkinje network and the right ventricular outflow tract in the initiation and perpetuation of VT/VF, and has evolved as a promising treatment modality for ventricular tachyarrhythmia even in channelopathies. When patients are exposed to a high risk of sudden cardiac death or deterioration of their quality of life due to episodes of tachycardia and frequent ICD discharges, catheter ablation may be an effective treatment option to reduce the risk of sudden cardiac death and decrease the frequency of cardiac events. In this review, we summarize the current understanding of catheter ablation for VT/VF in patients with channelopathies including Brugada syndrome, idiopathic VF, long QT syndrome, and catecholaminergic polymorphic VT.

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1. Introduction

A channelopathy (also termed a primary electrical disorder) is defined as an inherited syndrome caused by mutations in genes encoding for ion channels, their subunits, or their associated proteins [1]. Drug therapy and implantable cardioverter defibrillator (ICD) implantation are generally used as first-line therapies for the treatment and prevention of sudden cardiac death (SCD) in channelopathy patients [1]. However, recent advances in mapping techniques and ablation technology allow us to perform ablation therapy more safely and effectively for the treatment of ventricular tachycardia (VT) and ventricular fibrillation (VF), even in channelopathies. A recent consensus report recommended that catheter ablation of VT or a triggering focus of VF should be considered as a class IIa indication in patients with VT/VF storm when adequate operator experience is available, although, presumably,

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this recommendation also includes VT/VF in patients with structural heart disease [1]. According to the European Heart Rhythm Association Survey, catheter ablation for tachyarrhythmia is currently undertaken in 5–10% of recurrent cases with channelopathies such as Brugada syndrome (BrS) and long QT syndrome (LQTS) [2]. However, the long-term effectiveness of catheter ablation for VT/VF remains to be precisely elucidated as no randomized data on the effect of catheter ablation on arrhythmic events has been collected. In this article, we summarize the clinical reports on catheter ablation for the treatment of VT/VF in channelopathic patients in Table 1 and describe the current understanding of this field.

2. Brugada syndrome

BrS is characterized by coved-type or saddleback-type ST-segment elevation in the right precordial leads of the standard electrocardiogram (ECG) or high intercostal ECG. It is associated with an increased risk of SCD due to VF [3]. Approximately 15–30% of BrS cases are attributed to mutations in *SCN5A*, and a further 10–20% of BrS cases are attributed to mutations in other genes [4,5]. ICD implantation is recommended in patients with a diagnosis of BrS who are survivors of a cardiac arrest and/or have documented VF or spontaneous sustained VT with or without syncope. Isoproterenol and quinidine are also useful for the treatment of electrical storm in BrS patients. Experimental studies have shown that heterogeneous loss of the action potential dome occurs at the right ventricular (RV) epicardial sites, resulting in a marked dispersion of repolarization which underlies the development of local re-excitation via a mechanism termed phase 2 reentry in BrS [6]. Phase 2 reentrant ventricular extrasystole can trigger polymorphic VT/VF. Therefore, the elimination of trigger ventricular premature contractions (VPCs) might suppress VT/VF.

Haïssaguerre et al. reported the electrophysiological properties and effects of catheter ablation in three symptomatic patients with BrS [7], with one patient exhibiting a familial *SCN5A* deletion mutation (2850delT). Monomorphic VPCs originating from the RV outflow tract (RVOT) were observed in all patients, with monomorphic VPCs with left bundle-branch block (LBBB) and superior axis in one patient. RVOT triggers were eliminated by radiofrequency (RF) energy applications at the earliest site (25 and 40 ms before QRS onset), and VF inducibility was modified after ablation in two patients. In the third patient, RF energy application could ablate the VPCs originating from the anterior RV Purkinje network, thus rendered the VF non-inducible. During a mean follow-up period of 7 ± 6 months, there was no evidence of recurrence of syncope, VF, or SCD in any of the patients.

Nademanee et al. reported nine symptomatic patients with BrS who experienced VF and underwent electrophysiological study and catheter ablation [8]. The patients exhibited abnormal epicardial electrograms characterized by fragmented electrograms with a relatively low voltage (< 1 mV), prolonged duration, and fractionated late potentials exclusively localized over the anterior aspect of the RVOT epicardium. Catheter ablation over these abnormal areas at the epicardial sites of the anterior aspect of the RVOT rendered the VT/VF non-inducible in seven of nine patients (78%) and normalized the Brugada ECG pattern in eight patients (89%). After a mean follow-up of 20 ± 6 months, eight of nine patients (89%) had no recurrence of VF episodes, and there were no shocks from the ICD. Amiodarone was resumed at 100 mg daily in only one patient with VF recurrence after ablation, and there were no VT/VF recurrences up to 33 months after the ablation. Thus, RVOT was suggested to be an important target for catheter ablation, as an originating site of trigger VPCs and as an arrhythmogenic substrate of VF in BrS [9–11].

3. Idiopathic ventricular fibrillation

Idiopathic ventricular fibrillation (IVF) is generally diagnosed by exclusion of apparent structural heart disease, identifiable genetic syndromes, and any other potential causes of VF [12]. Thus, IVF may not strictly be categorized as a channelopathy. The gold standard treatment for either primary or secondary prevention of SCD is the insertion of an ICD. Recent progress in understanding the mechanism of IVF strongly suggests that the Purkinje network [13–17] and the RVOT [15,18] play a pivotal role in both the initiation and perpetuation of VF.

PVCs originating from the RVOT occasionally trigger VF although these are generally considered to be benign. Noda et al reported on 16 patients who showed spontaneous VF and/or polymorphic VTs initiated by VPCs arising from the RVOT [17]. The optimal ablation site was determined by the earliest local activation site during the spontaneous target VPC and/or by pace mapping. Eventually, catheter ablation with a mean of 9 ± 4 RF energy applications was successful in 13 of 16 patients and partially successful in three patients. During programmed ventricular stimulation after ablation, nonsustained polymorphic VT was induced in two patients and VF in one patient who underwent ICD implantation. During a mean-follow-up period of 54 ± 39 months, there were no episodes of syncope, VF, or SCD (four patients received a β-blocker).

The short-coupled variant of torsades de pointes (TdP) is defined as a syndrome in which VF is exhibited secondary to a short-coupled VPC (with coupling interval < 300 ms) without obvious heart disease or QT prolongation [19]. The VPCs triggering VF may arise from the Purkinje network rather than RVOT or the working myocardium. Haïssaguerre et al summarized a cohort of 27 patients diagnosed as having IVF (without structural heart disease, QT prolongation, or a Brugada-like ECG) who underwent catheter ablation [15]. In this study, VPCs originated from the Purkinje networks in 23 patients (LV septum in 10, anterior RV in nine, both in four), and from the RVOT in four patients, and the former had a shorter coupling interval initiating VF or polymorphic VT than the latter (280 ± 26 vs 355 ± 30 ms). The interval from the Purkinje potential to the following myocardial activation varied from 10 to 150 ms during premature beat but was 11 ± 5 ms during sinus rhythm. After ablation for VPCs, 24 patients (89%) without drug therapy had no VF recurrence during a 24 ± 28 months follow-up period.

The long-term prognosis of patients with IVF after catheter ablation was reported in a multicenter study [20]. VPCs originated from the right ($n=16$), the left ($n=14$), or both ($n=3$) Purkinje systems, and from the myocardium ($n=5$) (including the RVOT [$n=4$]). After ablation, seven (18%) of the 38 patients (21 men, age 42 ± 13 years) experienced VF recurrence during a median postprocedural follow-up period of 63 months. Five of these seven patients underwent repeat ablation and had no subsequent recurrence of VF or documented VPCs for 28 months. The number of significant events (confirmed VF or aborted SCD) was reduced from 4 (interquartile range 3–9) before ablation to 0 (interquartile range 0–4) after ablation ($p < 0.01$). Taken together, short-coupled VPCs triggering VF originate predominantly from the Purkinje system and the RVOT, and catheter ablation for the triggers is feasible and is associated with long-term freedom from VF recurrence in patients with IVF.

Early repolarization (ER) is characterized by elevation of the QRS-ST junction (J point) and QRS notching or slurring (J wave) in multiple leads, especially the inferior and/or left precordial leads. Although this finding has been considered to be a benign ECG manifestation, Haïssaguerre et al reported that the ER pattern was found in 31% (64/206) of IVF patients compared to 5% (21/412) of matched control subjects [21]. An ER pattern in the inferior or inferolateral leads has been