Role of catheter ablation in patients with ischemic ventricular tachycardia: From basic to clinical practice

Ting-Yung Chang\textsuperscript{a,b,c,1}, Chin-Yu Lin\textsuperscript{a,b,c}, Fa-Po Chung\textsuperscript{a,b,c}, Yenn-Jiang Lin\textsuperscript{a,b,c}, Shih-Lin Chang\textsuperscript{a,b,c}, Li-Wei Lo\textsuperscript{a,b,c}, Yu-Feng Hu\textsuperscript{a,b,c}, Shih-Ann Chen\textsuperscript{a,b,c}

\textsuperscript{1}Heart Rhythm Center, Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; \textsuperscript{2}Division of Cardiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; \textsuperscript{3}Institute of Clinical Medicine, and Cardiovascular Research Institute, National Yang-Ming University, Taipei, Taiwan, ROC

Abstract. Catheter ablation provides a therapeutic option for decreasing episodes of ventricular tachycardia in patients with coronary artery disease. Clinical studies show improvement with catheter ablation in reducing arrhythmia recurrence and therapy from implantable defibrillators, but not in decreasing mortality. Ablation can be an important tool for patients with electrical storm. Overall, complication rates of catheter ablation are acceptable, but recurrence rates are still significant. Advances in mapping and ablation technologies could be expected to improve the success rates and reduce the mortality.

Keywords: Ablation; Myocardial ischemia; Ventricular tachycardia

1. INTRODUCTION

Ventricular tachycardia (VT) and ventricular fibrillation (VF) are common causes of mortality in patients with coronary artery disease. Implantable cardioverter defibrillators (ICD) have been shown to reduce mortality from VT or VF in patients with a history of myocardial infarction and a poor ejection fraction.\textsuperscript{1} Notwithstanding, recurrence of VT and ICD therapies still contribute to an increase in morbidity and mortality.\textsuperscript{2,3} A previous systematic review and meta-analysis of randomized controlled trials revealed that amiodarone might increase the risk of death in patients with an ICD.\textsuperscript{4} Thus, with advance of ablation technologies and techniques, catheter ablation has become an acceptable option in the management of VT. In this review, we discuss the advance of VT ablation with a focus on patients with underlying ischemic heart disease. We also review the basics of VT ablation, the evidence behind the procedure, and future directions in the field.

2. INCIDENCE AND PREVALENCE OF ISCHEMIC VENTRICULAR ARRHYTHMIA

The estimated incidence per 100,000 population of sudden cardiac death (SCD) was 52.5 in Asia, 86.4 in Europe, 98.1 in North America, and 112.9 in Australia.\textsuperscript{5} During an acute myocardial infarction (AMI), the reported incidence of sustained VT or VF is about 10%.\textsuperscript{6} More than 80% of VT or VF happened within the first 48 hours after AMI. For those who had AMI, VT or VF would result in a high in-hospital mortality rate of 27%.\textsuperscript{7} ICD could reduce the risk of SCD by terminating VT episodes in patients with prior AMI. However, recurrent VT develops in up to 60% of patients after an episode of spontaneous sustained VT.\textsuperscript{8} In East Asia, one study reported that ischemic VT accounted for 21.9% in those substrate VT referred for catheter ablation.\textsuperscript{9} In patients with a depressed left ventricular ejection fraction (LVEF) after AMI who received an implantable loop recorder, the incidence of sustained VT was about 3% during a follow-up of 2 years. Thus current guideline recommends ICD implantation for patients with LVEF of 35% or less that is due to ischemic heart disease who are at least 40 days post-MI and at least 90 days after revascularization and for patients with nonsustained VT due to prior MI, LVEF of 40% or less and inducible sustained VT or VF at electrophysiological study.\textsuperscript{10}

3. MECHANISM OF VENTRICULAR ARRHYTHMIA IN ACUTE AND CHRONIC MYOCARDIAL ISCHEMIA

Acute myocardial ischemia affects the electrophysiological properties of myocardium profoundly, resulting in changes in ion currents, resting membrane potential, and action potential. All these lead to alterations in conduction velocity, automaticity, and refractoriness, which give rise to the occurrence of ventricular arrhythmias. Within minutes after acute occlusion of coronary artery, frequent VT and VF could happen and from 30 to 90 minutes after myocardial infarction, the burden of VT and VF was greatly diminished.\textsuperscript{11} Four hours after AMI, a delayed phase of spontaneous ventricular arrhythmia may occur and these arrhythmias include premature ventricular contractions, accelerated idioventricular rhythms, and VT. Mechanisms include automaticity in surviving Purkinje fibers, which pave the way for re-entry, that is...
facilitated by both triggered activity due to delayed afterdepolarizations and unidirectional conduction block.\textsuperscript{12} During the healing phase, the heterogeneous process of collagen deposition and myocyte resorption leads to islands of surviving myocardium in healed region.\textsuperscript{13} Besides, structural remodeling after AMI also involves deposition of adipose tissue in the infarcted myocardium. A previous report showed that myocardial fatty replacement 3 weeks after AMI in sheep resulted in reduced conduction velocity and decreased bipolar voltage.\textsuperscript{14} The presence of inducible VT in animals after AMI was correlated with larger adipose deposition and slower conduction velocity in the border regions of infarcts.

One month after AMI, transmembrane potential characteristics of myocardium surviving in infarcted zones almost recover. Notwithstanding, effective conduction velocity may still be slow, owing to structural changes in the infarct scars. Electrically inactive scar tissue forms a region around which re-entrant circuits can develop. Channels of viable but poorly coupled cardiomyocytes within the border zones between scar and healthy myocardium form the slowly conducting pathway of re-entrant circuits, which allow recovery of excitability of the remaining myocardium during tachycardia.\textsuperscript{15}

4. MAPPING AND ABLATION STRATEGIES

Although antiarrhythmic drugs (AADs) with ICD implantation is currently the standard of treatment for the management of VT, it is vital to remember that both treatments cannot cure ventricular arrhythmias. Long-term AAD use may be necessary to achieve suppression of VT, but severe side effects should be taken into consideration, especially in patients with multiple comorbidities, such as pulmonary, renal, or hepatic diseases. Current guideline recommends catheter ablation for patients with prior myocardial infarction and recurrent episodes of symptomatic sustained VT who present with VT or VF and have failed, or are intolerant of AADs.\textsuperscript{10}

In recent decades, there has been a growing role for catheter-based ablation both in the acute and long-term management of VT.\textsuperscript{16} This growth is partly due to significant improvement in the knowledge of the pathological basis of arrhythmias, as well as the continued evolution in technologies to identify and ablate the origin of VT (Fig. 1). Nowadays, radiofrequency is the most common energy source for VT ablation. A 3.5- or 4-mm irrigated-tip catheter is considered to create deeper lesions in case of intramural or epicardial circuits.

The general approach to catheter ablation of VT consists of the characterization of clinical VTs, delineation of the proarrhythmic substrate, and ablation of the arrhythmogenic tissue. Cardiac magnetic resonance imaging (CMR) has become an important tool and has been recognized as the gold standard for imaging of the cardiac substrate.\textsuperscript{13} CMR could assess morphology and function, visualization of fibrotic myocardium based on measurement of the signal intensity of late gadolinium enhancement (Fig. 2), and could be integrated into electroanatomic mapping system to facilitate ablation procedure.\textsuperscript{18}

Identification of the initiation and perpetuation of ventricular reentry is crucial during mapping of the VT isthmuses. Visualizing the critical components of the VT circuits can facilitate to terminate the VTs through limited ablation. The basic flowchart of VT ablation in our laboratory was shown in Fig. 3.
For hemodynamically-tolerable VT, the localization of the critical isthmuses relies on both activation and entrainment mapping. Pacing from the mapping catheter at a cycle-length of 20 to 30 milliseconds faster than the tachycardia cycle length was needed when entrainment mapping was performed. The VT isthmuses was confirmed once the following criteria are achieved: (1) concealed fusion of all 12-lead ECG during entrainment, (2) the postspacing interval within 30 milliseconds of the VT cycle length, (3) the stimulus-to-electrogram interval was within 20 milliseconds of the electrogram-QRS interval following entrainment, and (4) the local electrogram to QRS interval was between 30% and 70% of the VT cycle length. Notwithstanding these above criteria, there are still several pitfalls during the entrainment pacing and sometimes interpretation of the results could be challenging.

One observational multicenter study showed that 38% of patients with prior AMI had both mappable and unmappable VT and 31% of those had only unmappable VT. In such situations, mapping and ablation of substrate or late potential during sinus rhythm would be taken into consideration for patients with unmappable VT. By now, numerus strategies have been described: core isolation, ablation of late potentials or local abnormal ventricular activity (LAVA), scar homogenization, scar dechanneling, decrement-evoked potential mapping with extra stimulus, and simultaneous amplitude frequency electrogram transformation (SAFE-T) map. However, current substrate-based methods assume that the substrate for VT circuit within the healed myocardium is simply structural, neglecting the functional electrophysiological properties responsible for initiation and perpetuation of re-entry.

Tung R. introduced the isochronal late activation mapping to display ventricular activation during sinus rhythm. The authors found that successful ablation sites for VT were not associated with latest late potentials identified during sinus rhythm. Targeting the slowest conduction regions would be a novel method for ablation of VT.

With the progress of technology, the newer high-dense electroanatomic mapping system could provide a sufficient resolution to identify those areas vulnerable for re-entry. Recently, Anter et al. showed a novel method to specifically identify the VT isthmus during sinus rhythm in the ischemic swine model. The authors found that steep activation gradient with conduction velocity slowing 68.6% in the VT critical zone, which served as anchors for multiple configurations and cycle lengths of VT. This new physiological approach may pave the way for focused ablation to the critical arrhythmogenic substrate.

The noninducibility of VT by programmed stimulation was wildly adapted as procedure endpoint, but previous study showed that VT recurrence could be observed in 29% of patients with noninducibility of VT during index procedure. Additional procedure endpoints, such as elimination of all late potentials or LAVAs, were then introduced and the results showed significant reduction of VT recurrence and improvement of cardiac survival. Nevertheless, more studies would be needed to develop reliable procedure endpoints for ablation of ischemic VT.

### 5. EPICARDIALABLATION

Epicardial ablation has become an important ablation strategy, although proximity of major coronary arteries or the phrenic...
nerve to critical sites may preclude adequate energy delivery. In patients with ischemic heart disease, epicardial ablation is usually performed after failure of endocardial ablation. Hayashi et al. showed that the presence of the critical epicardial substrate responsible for VT could be demonstrated in at least 14% of patients with ICM. The majority of epicardial critical ablation sites were distributed opposite to the endocardial bipolar scar area and catheter ablation was effective in achieving long-term arrhythmia control. One recent systemic review and meta-analysis showed that a combined endocardial-epicardial ablation was associated with a lower risk of VT recurrence and subsequent mortality than endocardial only VT ablation in patients with scar-related VT. However, procedural complications were higher with the endocardial-epicardial approach.

6. PROPHYLACTIC MECHANICAL HEMODYNAMIC SUPPORT DURING ABLATION

On account of complex substrate, depressed systolic function, and concomitant comorbidities, catheter ablation of VT might result in significant morbidity and mortality. Santangeli et al. indicated that acute hemodynamic decompensation (AHD) happened in 11% of patients undergoing catheter ablation of scar-related VT and is still related to increased risk of mortality over follow-up.

The PAINESD risk score has been developed in an observational study including 193 consecutive patients undergoing catheter ablation of VT in the setting of structural heart disease. The PAINESD risk score included age, diabetes, ischemic cardiomyopathy (ICM), reduced LVEF, chronic obstructive pulmonary disease, presentation with VT storm, and New York Heart Association (NYHA) functional class III/IV. An additional variable that was also found to be associated with increased risk of AHD was the use of general anesthesia.

Previously, Baratto et al. reported favorable outcomes with use of extracorporeal membrane oxygenation (ECMO) in 64 patients (45% ICM; mean LVEF = 27%) undergoing VT ablation. Conversely, poorer outcomes with ECMO were reported in another study (21 patients, 90% ICM; mean LVEF = 21.1%). It is important to know that the latter study use ECMO as “rescue” therapy after development of AHD, whereas ECMO use was prophyactic in 92% of patients in the Baratto et al study. A similar discrepancy in outcomes could be observed in studies of percutaneous ventricular assist devices (PVADs). One study showed rise of periprocedural mortality from 4.2% with prophylactic PVAD use to 58.3% with “rescue” indication. These findings point out the importance to ensure that high-risk, potentially unstable patients are identified and appropriately triaged to prophylactic mechanical circulatory support before VT ablation.

7. OUTCOMES OF CATHETER ABLATION IN ISCHEMIC VENTRICULAR TACHYCARDIA

Previous randomized controlled trials (RCTs) of catheter ablation in ICD patients with ICM and VT, such as substrate mapping and ablation in sinus rhythm to halt ventricular tachycardia (SMASH-VT) or ventricular tachycardia ablation in coronary heart disease (VTACH) study, have shown that catheter ablation could prolong time to recurrence of VT, and resulted in fewer appropriate ICD interventions. However, the Substrate Modification Study (SMS) trial failed to demonstrate that catheter ablation could prolong the time to first VT/VF recurrence, but could reduce the total number of ICD interventions (50%). The details of RCTs are summarized in Table.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>Sample size</th>
<th>Inclusion criteria of VA</th>
<th>Control group</th>
<th>Ablation strategy</th>
<th>Conclusions</th>
</tr>
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<tbody>
<tr>
<td>SMASH-VT trial</td>
<td>2007</td>
<td>Ablation: 64</td>
<td>VT, VF; Syncope with inducible VT in EPS; single appropriate ICD shock, not using class I or III AADs</td>
<td>ICD and medical management without class I or III AADs</td>
<td>Substrate modification in SR</td>
<td>VT ablation and ICD implantation was associated with fewer appropriate ICD interventions.</td>
</tr>
<tr>
<td>VTACH trial</td>
<td>2010</td>
<td>Ablation: 52</td>
<td>Stable clinical VT. Incessant VT and bundle-brunch re-entry tachycardia were excluded.</td>
<td>ICD implantation and medical management, including AADs.</td>
<td>Ablation of clinical VT or substrate modification in SR in case of unstable hemodynamics.</td>
<td>VT ablation before ICD implantation seemed to prolong time to recurrence of VT, and had fewer appropriate ICD interventions, and fewer admissions for cardiac reasons.</td>
</tr>
<tr>
<td>CALYPSO pilot trial</td>
<td>2015</td>
<td>Ablation: 13</td>
<td>ICD interventions for monomorphic VT. Incessant VT was excluded.</td>
<td>ICD with AADs</td>
<td>Ablation of clinical VT or substrate modification in SR in case of unstable hemodynamics.</td>
<td>Screen failures: (1) 44% patients were on AADs. (2) 11% VT were due to reversible causes and 20% VT were incessant.</td>
</tr>
<tr>
<td>VANISH trial</td>
<td>2016</td>
<td>Ablation: 132</td>
<td>ICD interventions for VT during treatment of class I or III AADs.</td>
<td>ICD with escalating AADs (amiodarone or amiodarone plus mexiletine)</td>
<td>Substrate modification in SR or ablation during stable VT.</td>
<td>VT ablation had lower rates of primary outcome that was driven by trends toward reductions in rates of appropriate shocks and episodes of VT storm. (The primary outcome was a composite of death, VT storm, or appropriate ICD shock.)</td>
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<tr>
<td>SMS trial</td>
<td>2017</td>
<td>Ablation: 54</td>
<td>Unstable spontaneous VT, or cardiac arrest, or syncope with unstable VT inducible at the baseline EPS.</td>
<td>ICD Implantation</td>
<td>Ablation of clinical VT or substrate modification in SR in case of unstable hemodynamics.</td>
<td>VT ablation before ICD implantation did not prolong time to recurrence of VT/VF but could reduce the total number of ICD Interventions (&gt;50%).</td>
</tr>
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AAD = antiarrhythmic drug; EPS = electrophysiological study; ICD = implantable cardioverter–defibrillator; SR = sinus rhythm; VF = ventricular fibrillation; VT = ventricular tachycardia.
In the Heart Center of Leipzig VT (HELP-VT) study, which prospectively analyzed outcomes after catheter ablation of VT in patients with nonischemic dilated cardiomyopathy compared with ICM, 164 (72%) patients with ICM (mean LVEF = 32%) were enrolled. Noninducibility of any clinical and nonclinical VT could be achieved in 77.4% of ICM patients, and after 1-year follow-up, VT-free survival in patients with ICM was 57%.

The multicenter Ventricular Tachycardia Ablation versus Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease (VANISH) trial prospectively compared outcomes of escalating doses of amiodarone and/or mexiletine with catheter ablation. The results showed lower rate of the primary outcome (death, VT storm, or appropriate ICD shock) in the catheter ablation group.

The International VT Ablation Center Collaborative group study enrolled more than 2000 patients with structural heart disease undergoing catheter ablation. In the subset of patients with postinfarction VT and severe ventricular dysfunction (EF ≤ 30%), catheter ablation provided significant reduction in transplant-free mortality (83% vs 59%) in those without recurrent VT across all NYHA functional classes.

The factors that predict recurrent VT after catheter ablation have also been shown in several multicenter studies. Recurrent VT was related to a history of multiple AMI, larger scar revealed by electroanatomic mapping, more numbers of induced VTs, and failure to achieve noninducibility of VT after the ablation procedures.

8. NEW APPROACH AND TECHNOLOGIES FOR ABLATION

The efficacy of catheter ablation is limited by the presence of deep circuits, often intramural, unreachable with standard techniques. For these challenging circumstances, multiple new approaches are under investigation, such as bipolar radiofrequency ablation, transcoronary ethanol injection, intramural needle ablation, and noninvasive stereotactic radioablation. Despite the fact that cooled tip radiofrequency catheters and contact force monitoring have improved lesion formation, deep intramural target still remains a problem. Bipolar radiofrequency energy between two separate ablation catheters placed on the septum from both side of ventricle has proven to be effective in preliminary studies.

Transcoronary ethanol injection is an alternative approach that has been used in the setting of malignant refractory VT when standard approaches fail. Important considerations include coronary anatomy (artery or vein), risk of atrioventricular block, and risk of hemodynamic deterioration due to the loss of normal myocardium.

Needle ablation catheter for the creation of deeper intramural lesions show promising results in early human studies where standard catheter ablation techniques have failed. In the ovine model, irrigated needle ablation is associated with more frequent, larger, deeper, and more often transmural lesions compared with conventional irrigated ablation.

Recently, Robinson et al11 reported the results of prospective phase II/I trial of noninvasive cardiac radioablation in adults with treatment-refractory episodes of VT (57.9% ICM). Reduction was observed for both implantable cardioverter-defibrillator shocks and antitachycardia pacing. VT episodes burden were reduced in 17/18 evaluable patients (94%). The frequency of VT episodes burden was reduced by 75% in 89% of patients. Overall survival was 89% at 6 months and 72% at 12 months. Close collaboration between radiation oncologists and cardiac electrophysiologists is vital to achieve high levels of ablation accuracy.

In conclusion, the catheter ablation for VT associated with ICM could be challenging and requires a comprehensive evaluation and a multidisciplinary approach. Even though catheter ablation can significantly reduce VT recurrences, it should translate into an improved quality of life and should be considered early in the management of these patients. However, it is important to recognize that the rate of VT recurrence remains significant and depends on electroanatomic characteristics of the substrate. Technological advances in mapping and ablation are expected to further improve success rates.

REFERENCES


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