Radiofrequency Ablation Strategies for Intramural Ventricular Arrhythmias

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ABSTRACT: Catheter ablation is an established treatment strategy for ventricular arrhythmias. However, the presence of intramural substrate poses challenges with mapping and delivery of radiofrequency energy, limiting overall success of catheter ablation. Advances over the past decade have improved our understanding of intramural substrate and paved the way for innovative treatment approaches. Modifications in catheter ablation techniques and development of novel ablation technologies have led to improved clinical outcomes for patients with ventricular arrhythmias. In this review, we explore mapping techniques to identify intramural substrate and describe available radiofrequency energy delivery techniques that can improve overall success rates of catheter ablation.

INTRODUCTION

Treatment of ventricular arrhythmias (VAs) has evolved tremendously over the past 2 decades, with rapid advances in catheter ablation techniques and available technologies.[1] While tools to target the endo- and epicardial surfaces of the ventricle have allowed successful therapy, the presence of arrhythmic substrates located in the midmyocardial regions poses an enormous clinical challenge. In particular, intramural substrate presents challenges to both electrical mapping and delivery of radiofrequency energy,[2] and it is estimated that between 10% to 15% of VAs have an intramural origin.[3] In this review, we summarize the current mapping techniques to detect the presence of intramural substrate and site of origin and discuss specific approaches for effective catheter ablation of these difficult sites.

IDENTIFYING AND MAPPING INTRAMURAL VAs AND SUBSTRATE

Preprocedural imaging with cardiac magnetic resonance can often identify midmyocardial delayed enhancement that corresponds to intramural abnormal substrate.[4] In the presence of cardiac implantable devices, however, the accuracy of preprocedural imaging to define an abnormal substrate is suboptimal due to the presence of device-related imaging artifacts that may significantly affect imaging quality.

Intraprocedural analysis of the bipolar and unipolar voltage characteristics from surface contact mapping is an established method to characterize the myocardial substrate on the endocardial and epicardial surfaces.[5] Even so, current techniques using electrogram voltage are unable to reliably identify residual excitable substrate in the midmyocardial layer, which can potentially contribute to ventricular tachycardia (VT) circuits. Indeed, although unipolar voltage abnormalities in the presence of normal bipolar voltage invariably suggest the presence of far-field substrate remote from the recording electrode, its reliability to distinguish midmyocardial from epicardial far-field substrate is undefined.[6] Pacing techniques that require two recording catheters from either side of the suspected intramural substrate and that rely on the measurement of the transmural activation gradient, such as the transseptal conduction time in patients with midmyocardial septal substrate, have been proposed to identify dense intramural substrate.[7]

More recently, analysis of unipolar electrograms derived from a needle-tip catheter has identified intramural excitable substrate also in the presence of endocardial scar. In an elegant study, Qian et al. analyzed electrogram recordings from 659 intramural sites within the left ventricle and found that endocardial unipolar voltage was significantly higher in sites with deep intramural excitable substrate compared with transmural scar.[8] In addition, unipolar electrograms recorded from the tip of the needle ablation catheter showed a higher median voltage in sites with intramural excitable substrate. On spectral analysis of the electrograms, a power frequency integral > 0.77 mV^2/s was associated with a 90% sensitivity to detect intramural substrate.

Thus far, the only approach that has been reproducibly demonstrated to allow for direct intramural layer recording is by accessing septal coronary arterial or venous tributaries.[9] From a practical perspective and to enhance safety, most operators prefer septal venous perforator mapping; this is accomplished by accessing the anterior interventricular vein and its septal perforating branches and deploying a multipolar catheter or a partially insulated wire to record and pace within the intramural septal space. Additional mapping with recording of near-field bipolar signals within the intramural substrate can be achieved using small-caliber recording catheters that can be advanced into the septal perforator branches (Figure 1). Direct intramural recording has been particularly helpful to guide ablation since conventional multisite surface mapping is insufficient and occasionally misleading due to the presence of preferential conduction. In these cases, conventional surface activation and pace mapping may fail to identify an "early" site, often with broad areas of slightly presystolic activation,[10] and poor surface ECG matches with pace mapping. When an early intramural site of origin is recorded, radiofrequency (RF) energy is applied from anatomical vantage points that are closer to the earliest intramural recording site, as determined by orthogonal fluoroscopy, 3-dimensional mapping, and/or intracardiac echocardiography.[9,10] However, clinical studies evaluating the benefit of this "anatomical" ablation approach using conventional RF energy have reported suboptimal results, likely due to the inability of standard RF energy to reach the deep intramural sites of origin when applied to the mappable endo- or epicardial surface.

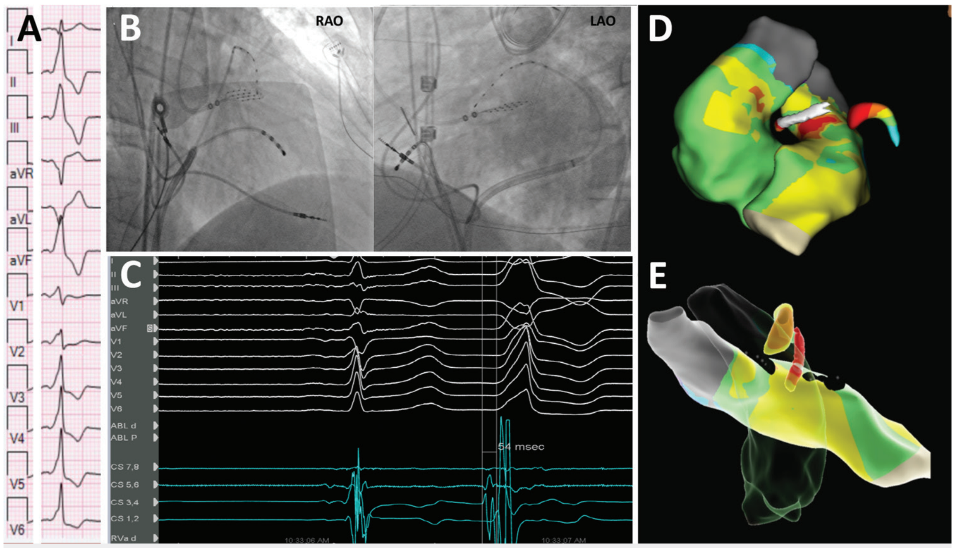

Figure 1.
(A) 12-lead morphology of the clinical premature ventricular contraction (PVC) showing the right bundle left inferior axis. (B) Fluoroscopic views of the mapping catheter in the first septal perforator branch. (C) Earliest activation in the septal catheter preceding the PVC QRS onset by 54 ms. (D) Activation map showing earliest activation within the septal venous perforator (white). (E) Ablation lesions (black) placed anatomically proximal to the earliest activation with successful elimination of the premature ventricular contraction.

ALTERNATIVE RF ABLATION STRATEGIES FOR INTRAMURAL VAs

Several alternative bail-out RF ablation (RFA) approaches have been suggested to increase the ablation success for intramural VAs when conventional RFA fails.

Simultaneous Unipolar Ablation

Simultaneous unipolar RFA involves delivery of RF from two catheter tips on either side of an area of interest. Depending on the site of intramural substrate, sites of ablation can be modified using anatomical landmarks to encompass most of the tissue of interest. In preclinical studies, this strategy has been reported to result in larger lesion size and depth.[11] Yamada et al. demonstrated the safety of this approach in targeting intramural foci in the left ventricular outflow tract.[12] In fact, the utility of this approach in targeting intramural foci in nonischemic cardiomyopathy has been demonstrated. For this technique, two open-irrigated ablation catheters are used with a power of 30 to 50 W titrated to at least a 10% impedance drop (recorded at each RF generator). In a study of 6 patients with nonischemic cardiomyopathy and deep septal substrate, this approach led to a VT-free survival in two-thirds after failure of sequential unipolar ablation.[13] Simultaneous unipolar ablation allows for independent titration of power from each RF generator, accounting for catheter contact and local impedance variations, and such may offer some advantages over bipolar ablation (Figure 2).

Bipolar Ablation

Bipolar RFA refers to the delivery of RF energy between two catheter tips with active ablation from one of the ablation catheters, referred to as the active catheter (Figure 3). This technique delivers focused energy to the return catheter that is positioned opposite of the area of interest, leading to increased current density within the targeted region.[14,15] The return catheter can be incorporated in the mapping system and visualized on the electroanatomic map during ablation. In animal models, bipolar ablation has been shown to produce different lesion characteristics with increased lesion depth and volume compared to simultaneous unipolar ablation.[16] Clinically, bipolar ablation has been efficacious in treating refractory arrhythmias from the outflow tracts, LV summit, and interventricular septum.[17] For typical ablation of septal VAs, the catheters are positioned at the sites of earliest activation and opposite of the interventricular septum. To target deep substrate from the LV summit, the return electrode is usually placed within the distal coronary venous system or the most septal aspect of the anterior right ventricular outflow tract (Figure 3). Bipolar ablation using two generators allows monitoring of impedance and temperature in each separate catheter, probably increasing the safety of this approach compared to simultaneous unipolar ablation.

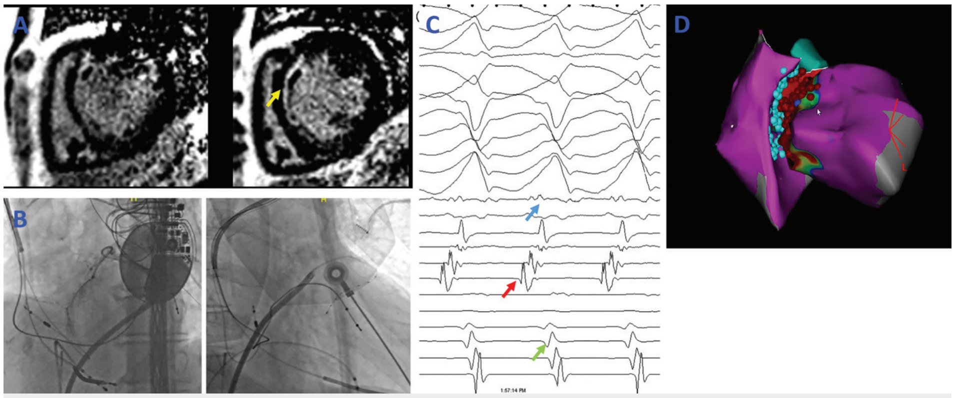

Figure 2.
(A) Cardiac magnetic resonance imaging showing midmyocardial delayed enhancement. (B) Left anterior oblique view of selective coronary venogram of the first septal perforator, and right anterior oblique view of a multipolar catheter in the septal perforator. (C) Activation during ventricular tachycardia showing earliest activation within the septum (red arrow), compared with the left ventricular (LV) endocardium (blue arrow) and LV epicardium (green arrow). (D) Final ablation lesion set following sequential unipolar ablation of the septum from the right and left ventricles.

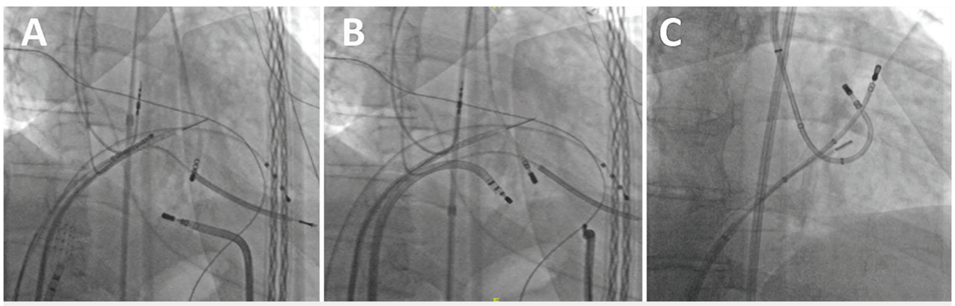

Figure 3.
Fluoroscopic views of ablation catheter for bipolar ablation targeting different anatomical substrates. (A) Ablation catheters in the left ventricular (LV) endocardium and epicardium. (B) Ablation catheters in the LV endocardium and middle cardiac vein. (C) Ablation catheters between the pulmonic cusp and left coronary cusp to target LV summit.

Although bipolar RFA offers the advantage of focused energy delivery between two catheter tips, the amount of energy that can be safely delivered may be greatly limited in the presence of a significant impedance mismatch between the two catheters. In addition, power cannot be titrated individually in each catheter. It is also important to emphasize that collateral damage can be generated for any structure anatomically positioned between the catheters, such as the conduction system and coronary arteries. Recently, Igarashi et al. reported their multicenter experience of using bipolar RFA to target intramural substrate refractory to sequential unipolar ablation in 18 patients with nonischemic cardiomyopathy, with half of the patients having a septal substrate for VAs.[18] Acute success was achieved in 89%, while 44% had recurrent VAs within 1 year. There were three procedural complications including steam pop, complete atrioventricular block, and injury to the left anterior descending artery. Similar safety concerns have also been noted in the multicenter bipolar VT study that was halted due to a higher-than-expected rate of adverse events.[19] More recently, Della Bella et al. reported outcomes of bipolar ablation in 21 patients with nonischemic cardiomyopathy presenting with drug refractory ventricular tachycardia. Interestingly, patients in whom septal substrate was targeted with bipolar ablation had significantly higher freedom from recurrent VT compared to those with nonseptal substrate, with no acute procedural complications of septal bipolar ablation.[20] These data point toward use of this technique in specialized centers with experience in this technology.

Low Ionic Irrigant Ablation

Open irrigation during RFA actively cools the electrode tip to allow higher power delivery to the tissue. However, normal saline (NS) used for irrigation conducts an electrical current with low impedance, which results in RF energy being preferentially dispersed away from the relatively higher impedance interface between the targeted tissue and the ablation electrode. Lower ionic concentration could partially prevent this phenomenon, thereby increasing the amount of RF energy delivered at the tissue–electrode interface. Preclinical models have shown that use of half normal saline (HNS) creates a larger ablation lesion size compared to NS irrigation. Based on the same principle, use of nonionic dextrose water has been shown to produce even larger lesions than HNS.[21,22]

Given the encouraging results in preclinical studies, use of HNS ablation as a bail-out strategy when conventional irrigated RF fails has been clinically evaluated. In a prospective multicenter study, Nguyen et al. reported the outcomes of HNS irrigant ablation performed in 94 patients with ventricular arrhythmias refractory to conventional NS irrigation.[23] Most anatomical sites that warranted use of HNS ablation included thicker ventricular structures, such as the papillary muscle and the interventricular septum. Acute procedural success was 83% at 1 year after HNS ablation, with arrhythmia-free survival of 89.4%. About half of these patients had septal substrate, and 5% of patients ultimately received bipolar ablation using HNS. Changing the ionic content of the irrigant is simple and does not require additional equipment. However, more recent studies evaluating the biophysics of this technique have not fully replicated the larger lesion sizes previously reported, especially when low-flow irrigant ablation catheters were used. In a swine model, Tschabrunn et al. reported no difference in lesion size but a higher incidence of steam pops with HNS compared to NS.[24] While these conflicting results need further investigation, particularly with regard to the modulatory effect of different irrigation rates, HNS ablation remains a potential alternative to target intramural substrate when conventional RF fails.

Needle Ablation

Radiofrequency energy delivery to intramural substrate remains a major obstacle to successful ablation. Lesion penetration from the endocardial and epicardial surface of the left ventricle rarely extends beyond 6 to 7 mm, even with use of long-duration lesions. To improve access to intramural substrates, a needle infusion ablation catheter has been developed with an 8F catheter and dome (tip) electrode. Through the dome electrode, a 27-gauge needle with an incorporated thermocouple can be extended up to 1 cm depending on the target tissue thickness.[25] Once an endocardial site for ablation has been identified, the needle catheter is advanced under fluoroscopic visualization and confirmed by contrast injection. In addition, the intramural region stained by contrast extravasation approximately delineates the extent of the lesion. Following this, the needle is irrigated with NS during RF energy delivery. Pacing through the needle can then be performed to identify areas of viability in intramural substrate and analyze the effect of RF.[26] In a multicenter study of 31 patients with VT refractory to conventional RFA, Stevenson et al. reported a 48% success rate with the needle ablation catheter at approximately 1 year follow-up.[27] This approach was relatively safe, with only one case of intramural dissection and tamponade that resolved with percutaneous drainage. Other complications noted in the study, such as heart block with septal ablation and pulmonary embolism, were unrelated to the specific technology used.

CONCLUSION

Ventricular arrhythmias with an intramural origin remain a major clinical challenge with limited options for mapping and effective ablation. The last few years have witnessed significant advances in mapping techniques and expanded our understanding of the intramural substrates associated with VAs. Conventional RFA strategies are greatly limited in these cases, mostly due to limited access to the intramural space. Alternative RFA approaches have been proposed and implemented with variable success. While these techniques and approaches require further investigation, preliminary results from clinical studies are encouraging.

KEY POINTS

- Intramural substrate is being increasingly recognized as a source of ventricular arrhythmias and presents a clinical challenge to effective catheter ablation.
- Preprocedural imaging can aid identification of intramural substrate and facilitate procedural planning.
- Modifications to energy delivery such as simultaneous unipolar ablation, bipolar ablation, and using low ionic irrigants can help improve lesion delivery and durability of ablation when targeting intramural substrate.

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