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How To Achieve Durable Pulmonary Vein Antral Isolation?

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Abstract

The inability to achieve durable pulmonary vein isolation (PVI) remains a major limitation to catheter ablation for the treatment of atrial fibrillation (AF), potentially resulting in AF recurrence. In this review, we discuss the research performed investigating methods to improve lesion permanence for the goal of durable PVI. Investigations evaluating procedural techniques, various catheters utilized, adjunctive pharmacologic therapy, and novel energy sources designed to improve ablation lesion permanence are discussed.

Introduction

Catheter ablation to treat atrial fibrillation (AF) has evolved dramatically over the past decade. It is currently considered first line therapy in patients with paroxysmal AF refractory to an anti-arrhythmic medication.[1] A common target during AF ablation is the wide area around the pulmonary veins (PV), the so-called "antrum". Although clinically successful AF ablation has been reported without pulmonary vein isolation (PVI),[2-5] the Task Force recommends in the 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of AF[1] that "ablation strategies that target the PVs and/or PV antrum are the cornerstone for most AF ablation procedures and that complete electrical isolation of all PVs should be the goal". Despite advancement in PVI techniques, recurrence rate of AF remains significant with recurrence rates at 1 year after a single radiofrequency (RF) ablation procedure for paroxysmal AF approximately around 20%–30% and even higher rates of recurrence for persistent AF.[6] Some of those recurrences may be due to pulmonary vein reconnection. PV reconnection generally result from anatomical gaps in the ablation lines or from failure to create permanent transmural lesions.[7] While acute PV isolation is obtained in the vast majority of patients, there is a significant rate of subsequent PV reconnection, up to 80%[8,9] presumably due to the resolution of swelling and inflammation after ablation. In addition to PV trigger elimination, PVI also suppresses AF by eliminating the substrate located in the PV antrum area, as demonstrated by the better efficacy of antral PVI compared to ostial PVI.[10] The objective of this review is to discuss the tools available to minimize antral PV reconnection.

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Catheter Contact

The majority of AF recurrences (54%) originate from reconnection of previously isolated PVs, suggesting the importance of delivering durable ablation lesions in decreasing recurrence rate.[11] Optimal catheter contact is a critical factor in ensuring durable PV lesions. Good catheter-tissue contact allows optimal energy coupling to tissue and less energy dissipation into the circu-lating blood pool.

Effective Ablation With First Lesion

Poor contact leads to ineffective lesions as well as local edema and inflammation. This inflam-matory process may render tissue resistant to further ablation. After RF delivery, swelling and inflammation typically occurs immediately, resulting in thickening of the left atrial wall.[12] Further ablation in this area may therefore become ineffective. Furthermore, the resolution of the edema after the procedure may result in recovery of conduction in myocardial cells that had tem-porarily disabled by the edema. This was demonstrated in a recent MRI study where the high burden of atrial tissue edema immediately after ablation increased the odds of arrhythmia recur-rence compared to patients with true atrial necrosis (effective lesions).[13] Therefore, delivering effective transmural lesions during the first ablation at a given location may be critical in ensuring long-term success.

Use Of Sheaths

Efficient catheter contact can be facilitated through the use of non-steerable and steerable sheaths that allow easy maneuverability, access and contact to target sites. Piorkowski et al compared the use of steerable sheaths with the use of non-steerable sheaths during

AF ablations in a prospective randomized trial.[14] Although the rate of acute PV isolation and total RF application time did not differ between both groups, single procedure success was significantly higher in patients treated with a steerable sheath (76% vs. 53% at 6 months). The difference persisted at 12 months (75.7% success) after a single AF catheter ablation procedure using steerable sheath.[15] Therefore the utilization of a steerable sheath may help to improve the maneuverability of the ablation catheter, catheter stability and, tissue contact. This could potentially reduce recurrence through the enhancement of lesion continuity and transmurality.

Use Of Intracardiac Echocardiogram (ICE)

ICE allows real-time visualization of the anatomic structures and their relationship to ablation catheter. ICE can thus be used to verify adequate catheter contact. In animal model comparing the use of ICE to fluoroscopy, ICE guidance resulted in higher percentage of successful applica-tions (P=0.02) and mean achieved temperature (P=0.004).[16] Another study demonstrated a significant correlation between utility of ICE to evaluate tissue contact and lesion size. It was shown that ICE can be used to improve the percentage of applications with good contact.[17] Furthermore, ICE has demonstrated the presence of significant catheter 'sliding' despite apparent stability based on electrogram assessment.[18] However, one of the limitations of ICE is the dif-ficulty to maintain clear and stable images during the entire ablation lesion.

Use Of Electroanatomical Mapping Systems

There is no absolute need for an electroanatomical mapping (EAM) system to guide PVI. How-ever, the addition of EAM may help to reduce fluoroscopy exposure and help define certain complex areas in the LA, such as the ridge between left superior pulmonary vein and left atrial appendage, a common area of poor stability, and therefore potential site of reconnection. One study that compared fluoroscopy alone versus image integration in EAM guided PVI even found a higher procedural success rate after a mean follow-up of 14 months in the group of patients that received ablation guided by EAM.[19]

Ablation Catheter Choice

Surface cooling technology with saline used in irrigated catheters during energy delivery reduces heating at the point of highest current density where excessive temperatures would usually pro-duce a significant rise in impedance.[20] These irrigated catheters can deliver higher energy to tissue when compared to standard 4mm tip ablation catheters resulting in larger and deeper le-sions. RF ablation performed using irrigated tip catheter has been shown to result in lower symp-tomatic AF recurrence compared to 4m tip ablation catheter.[21] A novel porous tipped irriga-tion catheter (ThermoCool SF Biosense-Webster, Diamond Bar, CA, USA and Therapy Cool Flex, St.Jude Medical) is now available as an alternative to the conventional 6 pores irrigation catheter. The porous irrigation catheter was able to achieve PVI with a significant decrease in the procedure and total RF time; however, a clinical benefit has not been demonstrated at this stage.[22]

Alternative Energies To RF For PVI

Several sources of energy alternative to RF have been developed. Cryoballoon (CB) ablation is a recently introduced technique to isolate the PVs in patients with AF. Recurrence rate of PVI in patients with paroxysmal and persistent AF has not been shown to be better than RF ablation.[23, 24] According to a worldwide survey,[25] RF remained the dominant form of energy used.

Laser balloon technology seems an effective tool for endocardial ablation, resulting in electrical isolation and transmurality. Laser ablation PVI using a fiberoptic balloon catheter was tested in a porcine model showing its ability to achieve PVI in a reliable, reproducible and persistent man-ner. A study tested the utility of this technology in humans through a multicenter study.[26] In 56 patients, 98% of PV's were acutely isolated, and most importantly, 86% of PV's remained isolated in 52 patients that returned for PV remapping. Interestingly, 62% of patient remapped had all 4 veins chronically isolated, suggesting the effectiveness of this therapy for chronic lesion formation.[27] Another recent study compared 2 balloon catheter technologies: laser versus CB, showing that 99% of PV's can be isolated with a single balloon catheter, however no difference in AF free survival was appreciated between the two technologies.[28] Further studies are needed to investigate the efficacy of laser balloon in reducing AF recurrence.

Impedance Monitoring

Decrease in impedance during RF application occurs as a result of tissue heating. Data has specifically shown that increased tissue contact is associated with a higher initial impedance drop during an RF application.[29] An initial drop in impedance using standard irrigation catheter is a good indicator of adequate tissue contact during PVI.[30]

Contact Force Sensing

Contact force sensing is a novel technology used to assess the degree of catheter contact during ablation through the use of a sensor at the distal tip of the ablation catheter. In the multi-center TOCCATA trial[31] average contact force during ablation was an important determinant of clinical recurrence of AF. A mean contact force >20 g predicted indeed the best outcomes (80% freedom from AF recurrence over 12 months), whereas 100% of patients with mean contact force <10 g had evidence of AF recurrence during the follow-up period. In a prospective case control study[32] the efficiency of contact force sensing in reducing AF recurrence was demonstrated. PV reconnection occurred in 21% of patients when the operator was blinded to contact force sensing while it occurred in only 4% of patients in which the operator was not blinded (p=0.001). In addition, catheter contact was shown to be higher when contact force sensing was utilized (p=0.002).[33] Therefore, contact force monitoring during PVI is a promising tool that may allow optimal lesions delivery with less PV reconnection and potentially less AF recurrence.

Pharmacological Methods

Ineffective ablation lesions may lead to reversible injury with a temporary loss of PV connection immediately post-ablation, with a potential to recover when the acute inflammation and swelling resolves. The identification of dormant tissue that has been rendered unexcitable by "stunning" or edema is a significant challenge that may potentially increase risk of AF recurrence. The de-tection of such "dormant conduction" during the initial ablation procedure may therefore help identify PVs that have a potential to reconnect after the index procedure, and targeted ablation at these sites may reduce the risk of recurrent AF. In animal model RF induced thermal injury resulted in reversible or irreversible (depending on the degree of injury) cardiomyocyte membrane depolarization, leading to sodium channel (INa) inactivation and loss of cellular excitability.[34]

Adenosine has been purported to uncover dormant conduction. The mechanism by which adeno-sine uncovers dormant conduction

was elucidated in an in vivo study in canine model.[35] Fol-lowing ablation, adenosine selectively hyperpolarizes PV cells by increasing inward rectifier po-tassium current (IKAdo), thereby restoring excitability of inactivated voltage- dependent INa and reestablishing conduction in dormant PVs.[35] Adenosine was shown to be clinically useful in identifying PV reconnection in multiple studies as well as cavotricuspid isthmus reconnection.[36] An early study (2004) reported that adenosine induced reconnection in 25% of PVs imme-diately after successful isolation.[37] Tritto et al further demonstrated that delivering additional RF lesions at electrical gap sites elicited by adenosine definitively eliminated recovery of PV re-connection in all cases.[38] Subsequent studies have also shown that AF recurrence after PV isolation could be reduced by delivering additional ablation lesions to eliminate adenosine in-duced dormant PV conduction.[39,40,41,42] Other studies[43,44] did not confirm the usefulness of adenosine in AF recurrence after PVI, thereby fueling a need for a randomized trial. The Adenosine Following Pulmonary Vein Isolation to Target Dormant Conduction Elimination (ADVICE) study is an ongoing randomized clinical trial assessing the impact of adenosine-guided PVI in preventing AF recurrences compared to conventional PVI.[45]

Another drug that has been used to reveal dormant PV triggers after PVI is the B-adrenergic stimulant, Isoproterenol.[41,46,47] Although it has a similar mechanistic effect to adenosine in hyperpolarizing resting membrane potential of PV cells and, thus, restoring excitability and con-duction,[39] it is considered to be inferior to adenosine[41] for the purpose of transient PV re-connection . Isoproterenol on the other hand has been shown to be useful particularly for PV ca-rina triggers and non PV triggers.[47,48] A recent study demonstrated that the use of adenosine and isoproterenol guided ablation may be useful in decreasing AF recurrence.[48]

Therefore, the utilization of pharmacological provocative testing serves as a valuable tool during AF ablation, by identifying PVs that may reconnect, by potentially accelerating PV reconnection and revealing various non-PV triggers.

Conclusions:

Durable antral PVI isolation can potentially be enhanced by optimizing catheter tissue contact and the utilization of drugs to guide additional ablation lesions. There is no convincing evidence at this stage that other sources of energy are superior to radiofrequency ablation.

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