Magnetic Resonance Imaging-Confirmed Ablative Debulking of the Left Atrial Posterior Wall and Septum for Treatment of Persistent Atrial Fibrillation: Rationale and Initial Experience

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LA Debulking for Atrial Fibrillation. ***Introduction:*** **Though pulmonary vein (PV) isolation has been widely adopted for treatment of atrial fibrillation (AF), recurrence rates remain unacceptably high with persistent and longstanding AF. As evidence emerges for non-PV substrate changes in the pathogenesis of AF, more extensive ablation strategies need further study.**

Methods: **We modified our PV antrum isolation procedure to include abatement of posterior and septal wall potentials. We also employed recently described image-processing techniques using delayed-enhancement (DE) MRI to characterize tissue injury patterns 3 months after ablation, to assess whether each PV was encircled with scar, and to assess the impact of these parameters on procedural success.**

Results: **118 consecutive patients underwent debulking procedure and completed follow-up, of which 86 underwent DE-MRI. The total left atrial (LA) radiofrequency delivery correlated with percent LA scarring by DE-MRI ($r = 0.6$, $P < 0.001$). Based on DE patterns, complete encirclement was seen in only 131 of 335 PVs (39.1%). As expected, Cox regression analysis showed a significant relationship between the number of veins encircled by delayed enhancement and clinical success (hazard ratio of 0.62, $P = 0.015$). Also, progressive quartile increases in postablation posterior and septal wall scarring reduced recurrences rates with a HR of 0.65, $P = 0.022$ and 0.66, $P = 0.026$, respectively.**

Conclusion: **Pathologic remodeling in the septal and posterior walls of the LA helps form the pathogenic substrate for AF, and these early results suggest that more aggressive treatment of these regions appears to correlate with improved ablation outcomes. Noninvasive imaging to characterize tissue changes after ablation may prove essential to stratifying recurrence risk.** *(J Cardiovasc Electrophysiol, Vol. 21, pp. 126-132, February 2010)*

atrial fibrillation, radiofrequency ablation, debulking, magnetic resonance imaging, delayed enhancement, complex fractionated electrograms

Introduction

In the past decade, significant progress has been made in understanding some of the underlying mechanisms that promote the occurrence of atrial fibrillation (AF) and underlie its persistence.[1] Nevertheless, due to the modest outcomes associated with the initially proposed focal ablation approach in patients with persistent or longstanding persistent phenotypes, various modifications have led to more extensive left atrial (LA) ablation, shifting the targeted area from the pulmonary vei-ostia to the PV antrum or left atrial-PV junction.[2,3] These new suggested strategies are still associated with a 20–50% failure rate.[4-7]

Even among practitioners who employ the PV antral isolation strategy, there remains great variance as to where radiofrequency is delivered relative to PV ostia. One reason for this variance is that the anatomical border of the pulmonary vein PV antrum is often ill-defined. Also, debate remains as to the extent lesion sets should include the posterior and septal walls. But there is emerging support for the notion that more inclusive ablation regions offer better procedural outcomes.[6-9]

We thus proposed modification of the PV antrum electrical isolation procedure to include ablation of posterior and septal wall potentials, to improve outcomes associated with the procedure by more completely modifying the tissue substrate underlying atrial fibrillation. For the purpose of the study, we modified the PV antrum isolation approach by extending the posterior lesion set of the antrum to target the

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whole LA posterior wall in addition to extending the anterior part of the right-sided antral lesion set to include the LA septum.

To further test the premise that comprehensive substrate modification would improve ablative outcomes, we modified our recently described image-processing techniques using cardiac delayed-enhancement (DE) MRI to not only quantify the total scar formation after ablation, but also to characterize the distribution of tissue injury after ablation to assess the impact of this distribution on procedural success.

Patient Selection

Patients referred to our center for management of persistent or longstanding AF were considered for this procedure if: (1) AF was symptomatic and refractory to initial antiarrhythmic drug therapies, or (2) contractile dysfunction coexistent with recalcitrant tachycardia. During this consecutive enrollment, 2 cases were also included with asymptomatic persistent AF where the need for secondary prevention of AF-related cardioembolic events conflicted with relative contraindications to long-term anticoagulation. During this early experience, all AF ablations by the authors were performed to include septal and posterior wall debulking.

ICE-Guided PV Antral Isolation

The principal components of PV antral isolation, as performed by the authors, have been described previously.[3] We here provide a brief summary of this approach.

Prior to arrival, oral anticoagulation (INR >2) was administered for >3 weeks. Since local electrograms during AF often show temporally unstable high-frequency signals related to disorganized propagation and collision of wavefronts generated remote from the site of interest,[10] we preferred substrate mapping in sinus rhythm, and thus attempted DC cardioversions in all patients in AF on arrival to the laboratory.

A right atrial/coronary sinus recording catheter was introduced via right internal jugular vein. Prior to septal puncture, we administered bolus heparin to achieve a target ACT between 350 seconds and 400 seconds. Double transseptal puncture was then performed using intracardiac echocardiographic (ICE) and fluoroscopic guidance, with preference for posterior septal punctures. A 10-pole (6-mm spacing) Lasso mapping catheter (Biosense-Webster Inc., Diamond Bar, CA, USA) was advanced through the first transseptal sheath, and a 3.5-mm-tip, Thermocool-irrigated ablation catheter (Biosense-Webster Inc.) was advanced through the second.

Electroanatomic preablation mapping was then performed using CARTO, and used throughout the case for catheter navigation relative to anatomic landmarks, and for ablation lesion tracking. Initial ablation efforts targeted PV potentials within the antra. Using ICE and fluoroscopic guidance, the Lasso catheter was positioned such that the PV ostial margin bisected the circular Lasso (see Fig. 1). RF was delivered for 15 seconds at each antral Lasso position with PV potentials, using 50 W and 50°C (30 mL/min open irrigation). RF delivery was interrupted if the impedance rose suddenly, or if a burst in microbubble density was seen by ICE.[11] If PV potentials were not eliminated after the initial 15-second lesion at a target, the RF catheter was nonetheless advanced to the next target, and persistent electrograms were later retreated after several minutes of cooling. This process was repeated until all PV antra were circumferentially treated and all antral PV potentials eliminated.

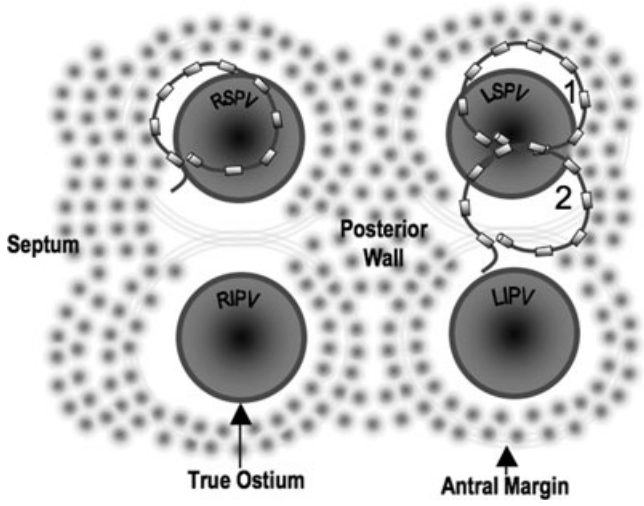

Figure 1. *The use of circular mapping catheter to target sites external to the pulmonary vein ostium. In Lasso position "1," the lasso is bisected by the margin of the left superior pulmonary vein (LSPV) ostium, and the outermost electrodes are targeted for ablation (sparing internal lasso points as these lie within the pulmonary vein). Once local electrogram abatement is achieved, the Lasso is serially repositioned and ablated to achieve this anatomic lesion set.*

Posterior Wall Ablation

Attention was then turned to the posterior wall. The Lasso catheter was again used to identify high-frequency potentials between left- and right-sided antra. Caution was given to the proximity of the RF catheter to the esophagus, as seen on ICE. When RF was delivered to tissue directly apposing the esophagus, we attempted "light" catheter-tissue contact, as determined by preserved responsiveness of the catheter tip position relative to fixed fluoroscopic landmarks during the cardiac cycle. Fluoroscopy was used more liberally in this region to further ensure that catheter manipulation resulted in tip advancement, and attention was paid to avoiding any lesion durations in excess of 15 seconds. With these precautions in mind, RF energy settings were not modified from those described above. Given the reduction in prescribed lesion duration, a second pass was usually required to achieve voltage abatement in this region. Although this strategy is vulnerable to tissue edema limiting the transmurality of lesions, previous work suggests esophageal injury is lessened by capping the lesion times.[11]

Along the posterior wall, there were fewer anatomic features to which the Lasso catheter position could be anchored. It was therefore crucial that a second trained operator be present to maintain the Lasso position relative to ICE and fluoroscopic landmarks as RF was being delivered. Achieving this stability often required subtle catheter torsion to counter the displacing force being applied by the RF catheter.

For septal debulking, the Lasso was first positioned to bisect the septal margin of the right-sided PV ostia, and the anterior half of the Lasso electrodes was targeted for ablation. Often, achieving a stable ablation catheter position at these targets required that a loop be formed with the catheter in

the LA. Both inferoseptal and anteroseptal segments were targeted, and ablation was continued until the myocardial stripe between the septal aspect of the right-sided pulmonary veins and the fossa ovalis was debulked.

In our experience, it is not uncommon to see the recovery of PV potentials in regions where electrical silence had been achieved earlier in the case. Therefore, after posterior and septal debulking was performed, we repeated a thorough survey of all antral, posterior, and septal targets. When all antral PV potentials were thought to be eliminated, a recording was made with the Lasso catheter engaged in the PV to confirm entrance block. Furthermore, a voltage map was constructed of the postablation left atrium to ensure no gaps remained in the lesion set (see Fig. 2).

Postablation Care and Follow-Up

Conservative protamine dosing was used to achieve an ACT less than 150 seconds prior to pulling sheaths. Full-dose heparin and oral coumadin were started the evening after the procedure with a goal INR of 2–3. If no evidence of complications was seen, patients were discharged the following day with a 60-day event monitor (with both automated and patient-triggered detections). The heparin bridge was not continued after discharge. Given the deleterious effect of atrial dysrhythmias on atrial remodeling, we attempted to maximize the time spent in sinus rhythm during the 90-day blanking period. If AF or atrial flutter was seen during the blanking period, a temporary course of antiarrhythmic drugs was prescribed, with preference for drugs used by the patient prior to ablation, and cardioversions were performed when these rhythms sustained.

Patients were scheduled for clinic follow-up at months 3, 6, and 12 after ablation, with Holter monitors performed prior to each of these visits. We asked patients to contact us if they experienced any symptoms consistent with their arrhythmia. If no AF episodes were seen by 6 months, coumadin was stopped and replaced with aspirin, 325 mg daily by mouth, unless there existed an increased risk of stroke or other anticoagulation indications.

Noninvasive Assessment of Left Atrial Tissue Changes Postablation

We recently described novel techniques to use cardiac MRI data to image LA tissue changes postablation.[12] As previously reported, the intensity of delayed enhancement signal induced by radiofrequency ablation is very high relative to that seen in any preablation images, and thus clearly represents ablation-induced changes. It is therefore likely that, as expected with delayed enhancement techniques, these imaging changes represent increased fibrosis. Though future work is needed to prove this histologic correlation, we refer to these marked increases in delayed enhancement signal as reflecting "scar" for purposes of this manuscript.

For this study, we employed techniques similar to those previously described to generate atrial tissue scar images, and then further processed these images to characterize PV encirclement and segmental scar distributions. DE cardiac MRI scans were obtained at 3 months postablation. After segmentation of the LA myocardium, 3D reconstruction was performed and grayscale images were reassigned color values using bimodal color-lookup-tables (CLUT) to improve the graphical distinction between enhanced and nonenhanced tissue voxels. Using blood-pool-based 3D geometries as reference, the PV ostia were manually identified on the tissue images.

Viewing each PV en fos, 2 independent judges then determined whether complete encirclement was present (with a third judge to settle any disagreements). The overall scar percent was calculated as the percentage of voxels with delayed enhancement within the entire LA tissue volume. Also, to describe the posterior and septal wall scar burdens, these portions of the LA tissue reconstruction were manually segmented, subtracting the insertion points of the pulmonary veins, and percentages of voxels showing delayed enhancement were again calculated.

Results

The population reported here included 76 males (mean age 64 years) and 42 females (mean age 72 years). The mean ejection fraction was 52%, range 20–70%. All patients had persistent or longstanding AF. Procedural parameters were as follows (mean $\pm$ SD): fluoroscopy time $= 96 \pm 26$ minutes, total RF delivery $= 50 \pm 13$ minutes, time in left atrium $= 174 \pm 46$ minutes, and total procedure time $= 240 \pm 52$ minutes.

Noninvasive Assessment of Postablation Tissue Changes

CLUT images were available on 86 patients (sample images are shown in Fig. 3). There was a wide range of scar burdens seen, ranging from 5% to 33% of total LA myocardium, mean 16%. As expected, there was a highly significant correlation between the total LA RF delivery time and the overall scar percent as quantified by DE-MRI ($r = 0.6$, $P < 0.001$).

At 3 months postablation, complete encirclement was seen in 131 of 335 PVA (39.1%). Complete scarring of all 4 PVA was seen in 9 patients (10.5%), scarring of 3 PVA in 11 patients (12.8%), and scarring of 2 PVA was seen in 17 patients (19.8). Twenty-nine patients (33.7%) exhibited complete scarring in 1 PVA, while 20 patients (23.3%) exhibited scarring in 0 PVA. As shown in Figure 3, Kaplan-Meier analysis suggested a progressive improvement in procedural outcomes when more PVA were encircled. To assess the univariate effect of the number of veins encircled on the clinical success (using survival time data), we performed Cox regression. This revealed a hazard ratio of 0.62, $P = 0.015$ (that is, for each additional vein that was encircled, the recurrence rate dropped a relative 38%).

Posterior wall scar burden, as assessed by cardiac MRI, was the strongest predictor of ablation success (for example, see images, Fig. 4). Progressive increases in postablation posterior wall scarring, when assessed by quartile with Cox regression, reduced recurrences rates with a hazard ratio of 0.65, $P = 0.022$, commonly interpreted to suggest each quartile increase in PW scar reduces the risk of recurrence by 35%. However, the advantage was driven mainly by the advantage seen in the highest quartile of scar percent (>57% scar). (see Kaplan-Meier curve, Fig. 4) Higher levels of septal scarring also improved ablation outcomes (hazard ratio of 0.66, $P = 0.026$).

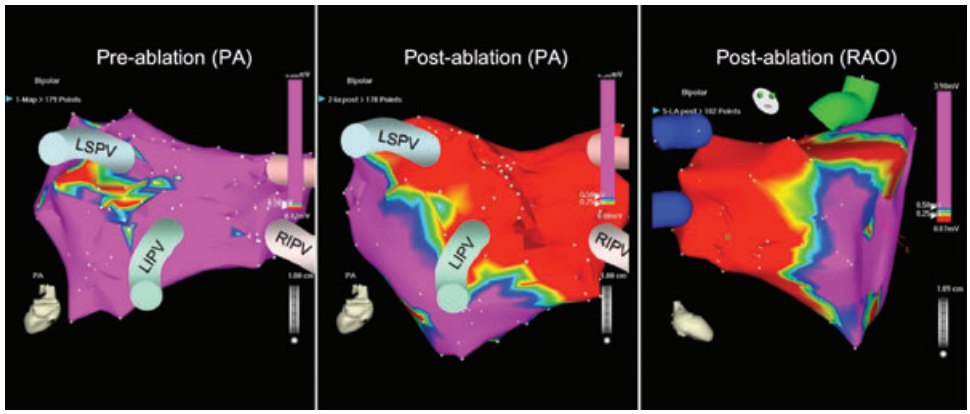

Figure 2. *Voltage map of left atrium before and after ablation procedure. The color red represents scar (<0.25 mV) and violet represents viable endocardium (>0.5 mV). Normal voltage was present prior to ablation (left). The entire posterior wall and all 4 pulmonary vein antra have been replaced with scar by the ablation procedure (middle), as was the posterior interatrial septum briding the right-sided pulmonary veins and the fossa ovalis, as seen in the RAO projection (right).*

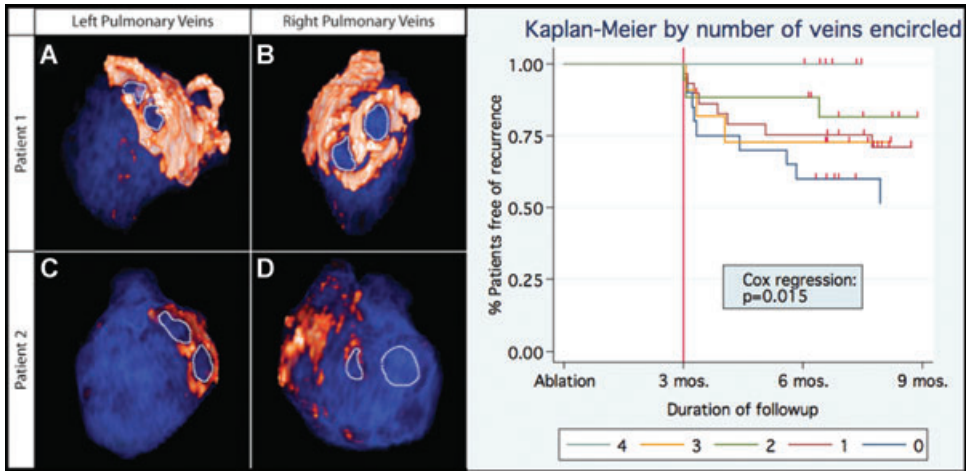

Figure 3. *Delayed-enhancement (DE) cardiac MRI. These color maps of 3D reconstructions of DE-MRI slices allows visualization of scar distribution imparted by the debulking procedure, and assessment of whether the pulmonary vein ostia are completely encircled. Panels A and B show left- and right-sided PV ostia, respectively, from a patient whose vein ostia were deemed encircled. Panels C and D show a patient for whom only the left inferior ostium was completely treated by the procedure. Panel E shows the Kaplan-Meier curves for patients with 0–4 PVs encircled, showing a progressive improvement in outcomes when more veins are encircled.*

Clinical Outcomes and Complications

We defined procedural success by the absence of any documented atrial flutter or fibrillation exceeding 1 minute in duration, excepting a 3-month "blanking period" after ablation. After a mean follow-up of 360 days, 69.5% of all patients demonstrated no evidence of sustained AF or flutter. The Kaplan-Meier curves depicting these rates of recurrence are shown in Figure 5. Of note, there is a continued gradual failure rate during the first year without an apparent plateau. However, among the 78 patients whose follow-up exceeded 1 year (mean follow-up 509 days), the success rate only fell to 65.4%.

No esophageal complications nor cardioembolic complications were seen in this small series. No hemodynamically significant PV stenoses have been diagnosed in this population. Two patients presented to the emergency room the day after discharge with shortness of breath attributed to pulmonary edema, and both responded to diuresis. One major left groin hematoma was seen, but did not require surgical intervention. One patient experienced cardiac perforation and tamponade requiring pericardiocentesis.

Discussion

The principal findings reported here are that (1) an ablation strategy that adds posterior and septal wall electrical debulking to PV antral isolation is feasible; (2) that noninvasive assessment of PV antral encirclement by DE-MRI methods stratifies clinical outcomes postablation and reproves the notion that increased posterior and septal scar burdens postablation improve ablation outcomes; and (3) early experience with this technique applied to a population with persistent and longstanding AF phenotypes was encouraging with regard to procedural parameters and clinical results.

Rationale for an Extended Lesion Set

AF ablation was historically inspired by the success of the surgical Maze procedure, which prompted attempts at Maze-like radiofrequency lesion sets. The initial recognition of AF triggers within the pulmonary veins provided a specific target for ablation strategies that held promise to reduce the need for extensive lesion sets and to thereby possibly reduce complications. However, both recurrence and complication rates were high with the prototype focal ablation strategies

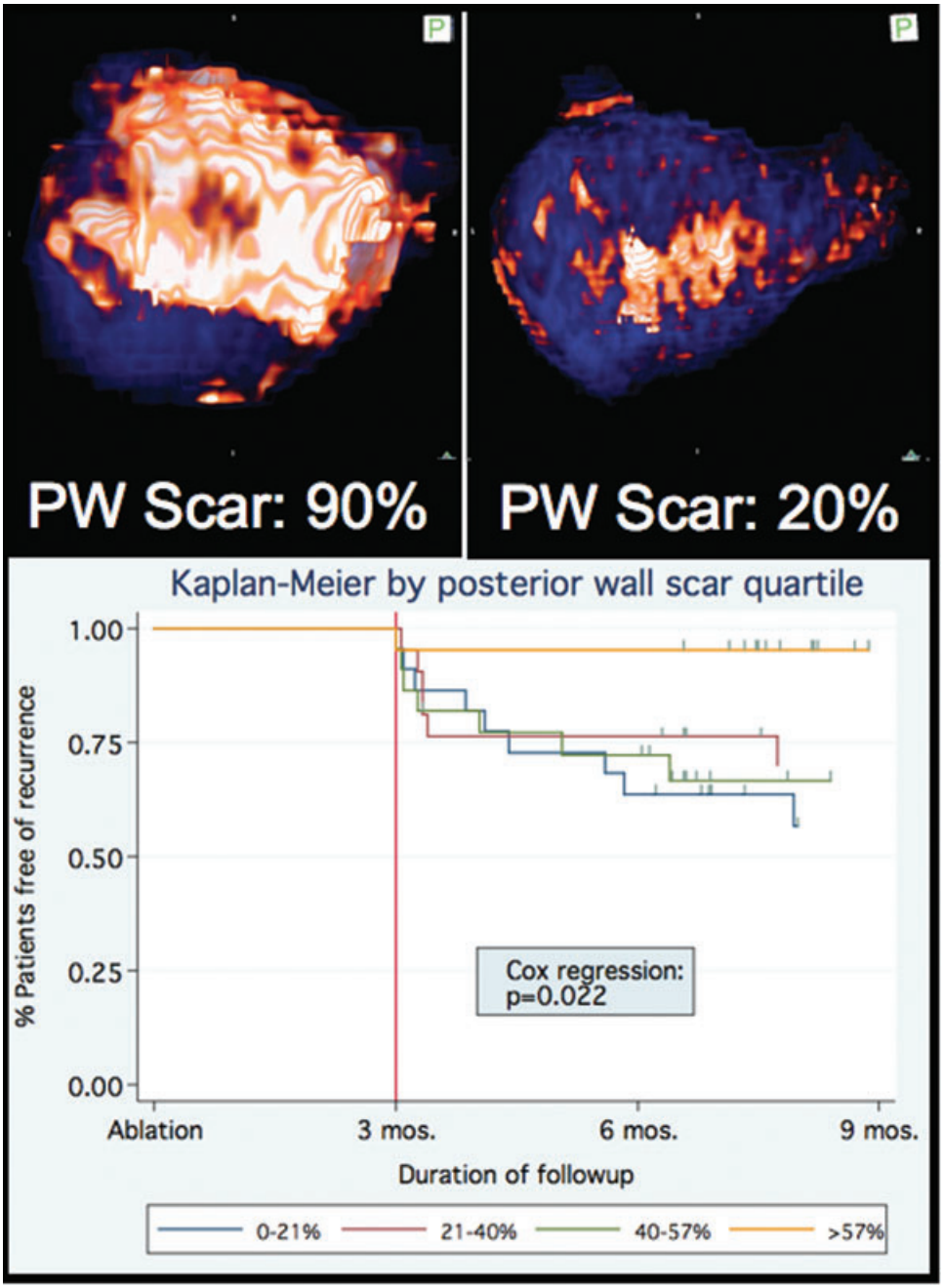

Figure 4. *Posterior wall scar quantitation. These example posteroanterior (PA) projections of 3D reconstructions of DE- MR images of the left atrium allow quantitation of scar distribution within the posterior wall.*

and contemporary work has now returned to more extensive lesion sets that avoid ablation within the PVs.[13] However, much debate remains as to the optimal lesion set.

LA posterior and septal walls play essential roles in harboring and maintaining atrial arrhythmias and their triggers.[14,15] The LA posterior wall seems to be the central site of interest for many physiologic AF ablation targets like dominant frequency (DF) sites,[16] complex fractionated electrograms (CFAE),[17] ganglionic plexi,[18] and fibrillatory activity.[19] There exist 2 main strategies for modifying these features of the AF substrate. One strategy is to localize and focally treat these regions of interest. However, focal strategies have met with disappointing clinical results, particularly in longstanding persistent atrial fibrillation.[16,20]

The other strategy is to surround these regions with circumferential ablation lesions. This approach is well known to achieve acute electrical isolation of these regions, and often achieves acute success in terminating and preventing AF. Although circumferential ablation strategies may alter the interface between the principal fibrillatory substrate and the remaining left atrium, it is unclear how these strategies permanently modify the substrate since restoration of conduction across circumferential lesion sets is more the rule than the exception.[21] Furthermore, there is debate as to whether clinical success depends on persistence of PV isolation. On one hand, several studies have shown that recurrences are more likely when lasting PV isolation is not achieved.[7,22–25] However, other studies have shown similar rates of electrical

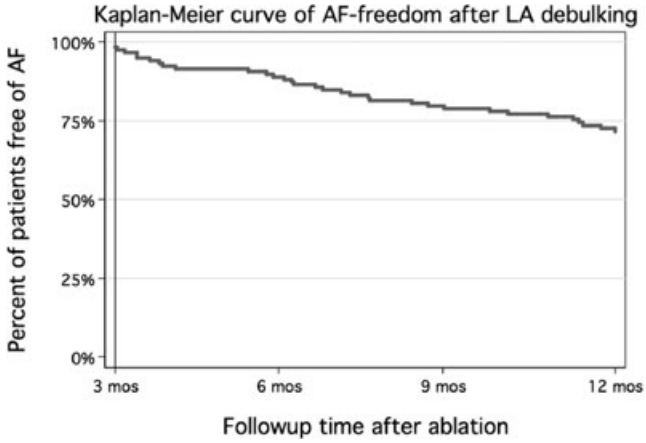

Figure 5. *Kaplan-Meier curve of overall procedural outcomes. The percentage of patients at risk who demonstrated no episodes of atrial fibrillation or flutter (1 minute or greater) is plotted versus time after the 3-month blanking period.*

venoatrial reconnection among patients without recurrences as those with recurrences.[26,27] It is likely that the differing conclusions of these studies arise in part from differences in ablation technique, but this debate highlights that PV isolation is not likely to be the only electrophysiologic endpoint of importance.

Indeed, linear ablations may in fact work by focal substrate modification as much as by achieving electrical isolation. In fact, the only study of long-term linear isolation to include a control population without clinical recurrences suggested that lasting electrical isolation did not correlate with procedural success.[27] Furthermore, additional studies have observed that AF can recur even when lasting PV isolation is achieved, highlighting the importance of other pathophysiologic substrates that are untreated with PV isolation alone.[7,24,28]

That factors extrinsic to the PVs play a potentially important role in the AF substrate is further corroborated by the improvement in ablation outcomes offered by wide-area circumferential ablation when compared to segmental PV isolation.[5] Furthermore, there appears to be additional and cumulative benefit from ablation of the LA roof, mitral isthmus, and other features of the LA in some patients.[29] This may in part be due to the common presence of ganglionated plexi well outside the margins of a typical circumferential ablation lesion set.[30] Although recent randomized clinical trial data have suggested a lack of incremental benefit with ablation targeting CFAE on the posterior wall and other tissues outside the PV antra,[31] this trial used single-pass ablation with low maximum power settings, and their reported outcomes differ substantially from those previously reported by multiple investigators using electrogram-guided ablation strategies.[32]

Postablation Tissue Imaging: Proof of Concept

Two key observations can be made from our early results from postablation tissue imaging. The first is the marked variability among this population, in the degree of tissue changes seen 3 months postablation. It is unclear, as yet, which patient characteristics or procedural parameters are most impacting on this variability. Second, of course, is the clear correlation between the degree of tissue change and the long-term procedural success. Although we present these findings as support for a more extensive substrate modification strategy, the results also point to a role for intraoperative tissue imaging in future ablation laboratories. If information regarding immediate postablation substrate changes could be provided to the ablationist, perhaps on-the-go procedural changes could be implemented to avoid reductions in procedural success.

Safety of Posterior Wall Ablation

Clearly, enthusiasm for more aggressive posterior wall ablation is tempered by concern for esophageal injury, and the minimization of patient risk remains a primary concern. But measures other than posterior wall avoidance can be taken to lessen the risk of esophageal complications. Previous work has demonstrated, by endoscopy, a substantial reduction in esophageal injury using irrigated tip catheter technology[11] compared to nonirrigated technology. Furthermore, by using ICE guidance to precisely visualize the posterior wall-esophageal apposition during ablation of posterior wall targets,[3] RF lesion durations can be reduced when the risk of esophageal injury is heightened.

The electrogram and anatomy-guided substrate modification strategy we propose no longer depends on a single line of block and comprises a more all-inclusive lesion to lessen the chances of untreated critical substrates. It is also plausible that by broadening the target region for ablation therapy, this ablation strategy is less dependent on a single line of transmurality. This redundancy eliminates the need to be highly aggressive with energy delivery within narrow spatial confines, and may explain why no esophageal complications have been seen with the debulking approach. Our initial results challenge the assumption that the risk/benefit ratio of AF ablation is improved by minimizing posterior wall energy delivery where many electrophysiologic stigmata of AF are found. Though further study is needed to confirm the safety of this strategy, our early experience suggests that the potential benefits of complete posterior wall abatement can be achieved with an acceptable risk of esophageal complications.

Limitations

This study is nonrandomized, and is therefore not designed to definitively compare procedural outcomes and complication rates to other methods. However, these data provide a novel look at the effect of posterior wall substrate modification on ablation outcomes, and provide compelling evidential support for the debulking strategy and justification for future randomized study. Also, as mentioned above, DE-MRI changes seen postablation likely represent increased myocardial fibrosis akin to that seen in ventricular myocardium, but histologic confirmation of these changes awaits further study. Also, the duration of follow-up is short, and recurrence patterns may be different with future follow-up. Though collection of longer follow-up is underway, these short-term clinical outcomes are encouraging, and already there exists distinct outcome differences when grouped by MRI-based substrate characterization.

Conclusion

Pathologic remodeling in the septal and posterior walls of the left atrium help form the substrate that underlies the initiation and maintenance of atrial fibrillation. We report here our initial experience with adding posterior and septal electrical

abatement to the previously described PV antral isolation procedure. These new procedural elements are feasible for experienced operators, appear to not impose increased risk, and offer promising clinical success rates that corroborate their postulated benefit for ablation efficacy. Novel tissue imaging techniques using DE-MRI allow segmental quantification of postablation tissue changes, and these early results suggest that more aggressive septal and posterior wall modification improves ablation outcomes. This ablation technique deserves further study in a prospective, controlled fashion.

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