Perspective

Management of refractory atrial fibrillation post surgical ablation

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Over the past two decades, invasive techniques to treat atrial fibrillation (AF) including catheter-based and surgical procedures have evolved along with our understanding of the pathophysiology of this arrhythmia. Surgical treatment of AF may be performed on patients undergoing cardiac surgery for other reasons (concomitant surgical ablation) or as a stand-alone procedure. Advances in technology and technique have made surgical intervention for AF more widespread. Despite improvements in outcome of both catheter-based and surgical treatment for AF, recurrence of atrial arrhythmias following initial invasive therapy may occur.Atrial arrhythmias may occur early or late in the post-operative course after surgical ablation. Early arrhythmias are generally treated with prompt electrical cardioversion with or without antiarrhythmic therapy and do not necessarily represent treatment failure. The mechanism of persistent or late occurring atrial arrhythmias is complex, and these arrhythmias may be resistant to antiarrhythmic drug therapy. The characterization and management of recurrent atrial arrhythmias following surgical ablation of AF are discussed below.

Keywords: Refractory atrial fibrillation (AF); surgical ablation; catheter ablation; post-surgery arrhythmias

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Introduction

Atrial fibrillation (AF) is the most common cardiac rhythm disturbance, and its incidence continues to increase (1,2). In patients undergoing cardiac surgery, AF is even more common than in the general population, because coronary artery disease and valvular heart disease are risk factors for the development of AF (3,4). AF is associated with significant morbidity, including increased risk of stroke, heart failure and death. Furthermore, AF may be highly symptomatic and have a significant impact on quality of life. Over the past two decades, invasive techniques to treat AF, including catheter-based and surgical procedures, have evolved along with our understanding of the pathophysiology of this arrhythmia. Surgical treatment of AF may be performed on patients undergoing cardiac surgery for other reasons (concomitant surgical ablation) or as a stand-alone procedure. Advances in technology and technique have made surgical intervention for AF more widespread. In an analysis of the Society of Thoracic Surgeons National Cardiac Database by 2006, 40.2% of patients with AF undergoing cardiac surgery had

concomitant AF surgery, and that number has certainly increased over the ensuing years (5). Despite advances in both catheter-based and surgical treatment for AF, recurrence of atrial arrhythmias following initial invasive therapy may occur. The characterization and management of recurrent atrial arrhythmia following surgical ablation of AF are discussed below.

Early recurrence of atrial arrhythmia

Frequency and significance

Early post-operative arrhythmias are common following surgical AF ablation, and occur in 43-59% of patients, even when routinely treated postoperatively with antiarrhythmic agents. More than 90% of these arrhythmias will occur within the first ten post-operative days but can occur up to three months after surgery (6-8). The most common arrhythmias are AF and atrial flutter, with atrial tachycardia occurring less frequently (8). Early arrhythmia may represent early reconnection or recovered conduction across lines of electrical block. However, other mechanisms may play a role, including inflammation resulting from atrial injury or pericarditis.

Most early arrhythmias are transient or resolve within the first month and do not represent treatment failure per se. Nonetheless, the early recurrence of atrial arrhythmia after surgical ablation is a risk factor for longer term recurrence as was demonstrated in a study by Maroto *et al.*, in which 106 patients underwent concomitant surgical ablation for AF. In this series, early recurrence of atrial arrhythmia was defined as occurring during the post-operative stay and was an independent risk factor for late recurrence, conferring a hazard ratio of 3.45, which is consistent with the effect seen in other series using contemporary surgical techniques (6,7).

Management

There is evidence that early treatment with electrical cardioversion of atrial arrhythmias after catheter ablation of AF may improve the long-term outcome (9). The use of antiarrhythmic agents routinely in the first few months following an ablation procedure is routine practice and is effective in preventing early recurrence of arrhythmia. However, the effectiveness of early antiarrhythmic therapy on long-term recurrence of atrial arrhythmia is less clear (10). For patients who undergo catheter ablation and were on antiarrhythmic drugs, this is continued if tolerated during the post-procedural period to prevent early recurrence of arrhythmia. It is reasonable to extrapolate the data from catheter ablation to surgical ablation and use a similar treatment strategy in the early post-operative period. Early atrial arrhythmias should be treated in a timely manner with direct current cardioversion, with or without the adjunct of an antiarrhythmic agent.

Late or persistent recurrence

Reports of the long-term efficacy of the surgical treatment of AF vary widely but have been reported to be as high as 97.5%. However, initial reports of success following the procedure did not use rigorous means to detect post-operative atrial arrhythmias, with many using only questionnaires or single ECGs. The impact of monitoring on the reported success of the procedure can be substantial. Hanke *et al*. followed 45 patients who underwent surgical ablation of AF, with the implantation of loop recorder at the time of surgery. Each patient also underwent 24-hour Holter monitoring at three-month intervals. In this study, even a relatively rigorous follow up protocol proved to have a low sensitivity and negative predictive value for detecting recurrent arrhythmias at 12 months (0.60 and 0.64 respectively) (11).

Determinants of recurrence

The determinants of recurrent atrial arrhythmia following surgical treatment of AF have been examined in several studies. In general, larger LA, advanced age and longer duration of AF were associated with a lower success rate (6,12). While it is important to understand the risk of recurrence when undertaking the procedure as well as when discussing outcomes with patients, some risk factors are not readily modifiable. However, procedural aspects of surgical ablation have an important impact on the recurrence of atrial arrhythmia post-operatively, as well as implications for their treatment.

A full discussion of surgical techniques for the treatment of AF is beyond the scope of this article; however, there are a few important points worth reviewing. The mainstay of surgical and ablative techniques for the treatment of AF involves the destruction of myocardial tissue, creating lines of electrical block which can interrupt propagation of arrhythmia and/or modify the electrical substrate that results in AF. Earlier surgical techniques employed a "cut and sew" method to achieve electrical block, with a goal of interrupting macro-reentrant circuits as in the

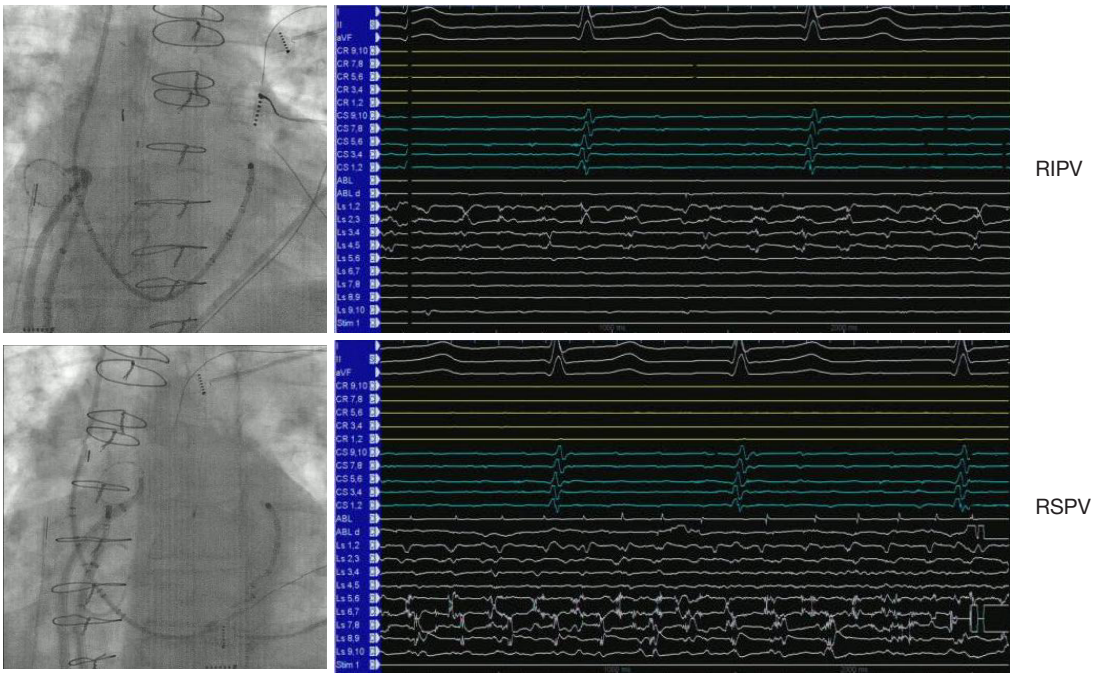

Figure 1 Fluoroscopy images and intracardiac electrograms of patients with late recurrent atrial fibrillation (AF) following surgical ablation. The images clearly show as all pulmonary veins (PVs) and the posterior wall are not electrically isolated and are re-connected.

Cox Maze procedure and its modifications (13). Since then, our understanding of the pathogenesis of AF has evolved considerably. Two decades ago, Haïssaguerre and colleagues demonstrated the importance of electrically active tissue in the pulmonary veins in the pathophysiology of AF. Furthermore, they demonstrated that targeting these triggers or electrically isolating the veins could successfully treat the arrhythmia (14-16). Isolation of the pulmonary veins and adjacent structures, including the pulmonary vein antra and posterior wall, has become the mainstay of the catheter-based treatment of paroxysmal AF and an important part of the treatment of persistent and long-standing persistent AF. In persistent and long-standing persistent AF, ablation of the pulmonary veins alone without further identification of triggers or modification of the atrial substrate is inadequate to prevent a high rate of recurrence (17).

In the modified Cox Maze III procedure, the "cut and sew" lines created result in the isolation of the pulmonary veins and the posterior wall. This along with the other linear lesions has no doubt contributed to the high success rate of the procedure. Contemporary techniques which have decreased the length and complexity of the procedures by using various energy sources to create linear lines of ablation include radiofrequency (RF) energy, cryoablation and high-intensity ultrasound. Furthermore, modifications were made to the original lesion sets, resulting in decreased procedure times and less collateral damage to the conduction system. Even in the "cut and sew" procedure, inadequate isolation or recovery of conduction appears to be a common cause of recurrence of atrial arrhythmias (especially AF) (18). Additional linear lesions play an important role in the surgical treatment of AF, and the mechanism of recurrent atrial arrhythmia as discussed below. However, regardless of the lesion set or energy source used, confirmation of the electrical isolation or conduction block across a line should be an essential component of the procedure. Recovery of conduction or failure to achieve block at the time of surgery in our experience has been a major factor of recurrence of atrial arrhythmias following surgery (*Figure 1*).

Mechanisms of recurrence and the role of catheter ablation

Surgical technique has a significant impact on both the mechanism and the frequency of recurrent atrial arrhythmia after surgical ablation. In one series, Wazni *et al*. evaluated 23 patients with atrial arrhythmias refractory to antiarrhythmic drugs, who had a "cut and sew" Maze procedure. Each

patient underwent electrophysiologic study (EPS) (18) and more than one third of these patients had recurrent AF secondary to recovered conduction around the lines encircling the pulmonary veins. The remaining patients had atrial flutters or atrial tachycardias. Macro-reentry was an important cause of recurrence, with 4 of the 23 patients having right atrial incisional flutters. Six patients had left atrial flutters which were mapped to the mitral annulus and the right pulmonary veins. The remaining patients were found to have focal atrial tachycardia originating primarily from the coronary sinus (CS). Of this group, 22 were treated with catheter ablation and 19 remained arrhythmia-free off antiarrhythmic agents at one year.

Reconnection of the pulmonary veins is frequently responsible for the recurrence of AF following surgical ablation (*Figure 1*). While the source of more organized atrial arrhythmias is diverse, gaps in ablation lines appear to play an important role as well. Magnano *et al*. examined 20 patients with organized atrial arrhythmias following surgical AF ablation (19). In this series, a variety of energy sources were used, including microwave, RF, cryoablation and laser. Most patients had only left atrial lesion sets, which included left atrial appendage exclusion along with a single encirclement of all four pulmonary veins, thereby also isolating the posterior wall. In a subset of patients, right atrial lesions including a cavo-tricuspid isthmus (CTI) line and a line from the superior vena cava (SVC) to the inferior vena cava (IVC) were performed. Nearly half of the patients had more than one mechanism of tachycardia. Most arrhythmias were macro-reentrant (flutters) with about one third being typical right-sided atrial flutter. The most common pattern of macro-reentry involved an area of slow conduction in close proximity to the scar lines in the posterior wall. There were two reentry circuits utilizing the isthmus between the left inferior pulmonary vein and the mitral annulus, occurring in patients in whom a line of ablation had been attempted at this site. Often this may occur due to residual conduction in the muscular sleeve of the CS. These patterns of recurrence suggest that arrhythmias were the result of breaks in the ablation lines. Importantly, reentry involving the scar line resulting from left atrial appendage occlusion was also noted. In our experience, the left atrial appendage and the CS are important sources of arrhythmogenesis following surgical ablation. While appendage exclusion is an important benefit of the surgical approach, even with exclusion, arrhythmias can occur at the site of the stump. We therefore believe that during the surgical procedure, before appendage exclusion/ligation, proximal electrical isolation of this structure should be performed. *Figure 2* shows a case of a patient where during surgery, the left atrial appendage was closed with a dedicated device. During endocardial ablation, isolation of the left atrial appendage stump was necessary to achieve long-term freedom from atrial arrhythmias (20) (*Figure 2*).

Others have attempted to better characterize organized atrial arrhythmias that occur following surgical ablation. McElderry *et al*. report similar findings in a series of 143 consecutive patients who underwent Cox Maze III operations using a combination of surgical incisions and cryo- or RF ablation to create lines between the SVC and IVC, CTI, encirclement of all four pulmonary veins, as well as lines to connect the mitral annulus and atrial appendage stump to the encircled posterior wall (21). Twenty-two patients developed sustained regular atrial arrhythmias. Macro-reentry was the predominant mechanism of regular tachycardias and was often related to persistent conduction through regions that were targeted for ablation, or at the gap of a surgical incision as it joined an anatomic boundary. Importantly, these authors identified the CS as an important area where there is commonly incompletely ablated tissue sustaining arrhythmia. All of the regular tachycardias identified were mapped at EPS and were successfully treated with RF ablation.

Findings appear similar in those patients undergoing minimally invasive surgical ablation. Zeng *et al*. describe a series of 130 patients who underwent minimally invasive surgery with a bipolar RF clamp to isolate the pulmonary veins (22). Additionally, the left atrial appendage was excised and the ligament of Marshall was divided. The pattern of recurrence appears similar in those patients who undergo minimally invasive surgery. Twenty-seven patients had recurrent atrial arrhythmias and eight patients had persistent arrhythmia despite cardioversion and antiarrhythmic drugs. Among these eight patients, AF recurred in half and resulted from gaps in the ablation lines, which occurred even among those patients who had intraoperative testing of conduction block. The remainder had left atrial flutters and tachycardias involving the mitral valve annulus, the base of the appendage stump, and other areas from within the left atrium. All eight patients were successfully ablated with no recurrence of arrhythmia off antiarrhythmic drugs. Taken together, these results illustrate the importance of creating durable lesion sets at the time of surgical ablation. Electrophysiologic testing at the time of surgery is the only reliable means by which block can be

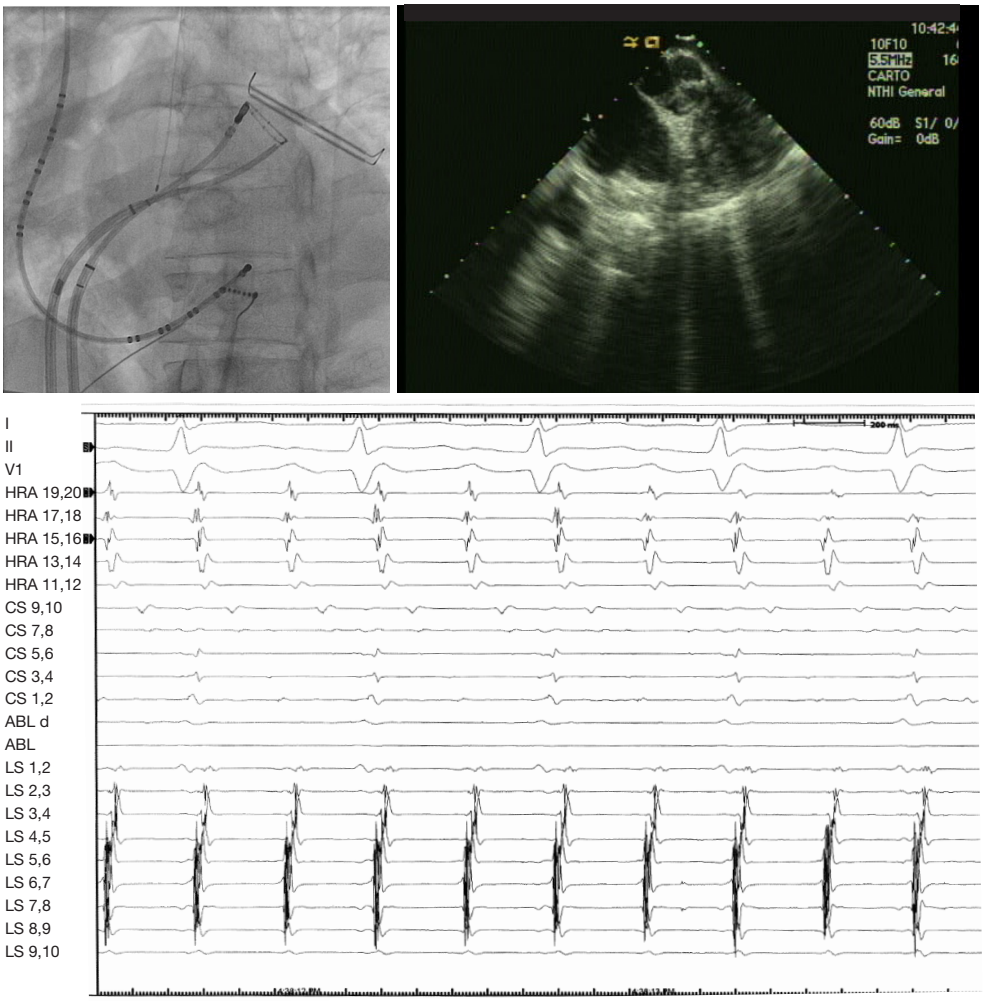

Figure 2 LAA stump (ICE and FLUORO) in a patient who underwent surgical atrial fibrillation (AF) ablation and placement of a LAA clip. The intracardiac electrograms show a tachycardia from the LAA. The circular mapping catheter is placed at the level of the LAA stump.

assured; however, even when this is performed, recovery of conduction may occur.

Management of late or persistent arrhythmia

Antiarrhythmic agents may be useful in the treatment of arrhythmias that persist or occur late after surgical ablation. However, at least among patients undergoing catheter ablation, antiarrhythmic drugs do not appear to be an effective long-term strategy compared to a repeat procedure. In a study of 154 patients who had recurrence of atrial arrhythmia after catheter ablation of paroxysmal AF, Pokushalov *et al*. randomized patients to repeat ablation versus antiarrhythmic therapy. Those who were randomized to repeat ablation demonstrated a significant decrease in the progression of the arrhythmia (79% versus 25%) as documented at three years by means of an implantable loop recorder (23). While the patient population of those undergoing catheter ablation differs from those undergoing surgical ablation, data support the safety and efficacy of EPS and ablation for the successful diagnosis and treatment of arrhythmias following surgical ablation, as discussed above and in other series (24). This is particularly true among patients in whom atrial flutter or atrial tachycardia recurs, where these arrhythmias are generally able to be mapped and successfully ablated. Thus, in patients with symptomatic late or persistent recurrence of arrhythmias following surgical ablation, it would be reasonable to

attempt cardioversion or management with antiarrhythmic agents. However in patients with recurrent organized atrial arrhythmias, catheter ablation should be considered.

In the absence of pulmonary vein reconnection, an atypical atrial flutter reflects the presence of a non-pulmonary vein trigger which needs to be identified. In this respect, the most common locations are either the CS or the left atrial appendage or both. If patients experience focal tachycardias, ablation of this arrhythmia could be sufficient to achieve long-term freedom from atrial arrhythmias. However, additional potential triggers should always be excluded with a high dose of isoproterenol challenge.

Conclusions

Surgical ablation for AF performed concomitantly to cardiac surgery or as a stand-alone procedure can be highly effective in the treatment of arrhythmias. Despite advances in technology and technique, recurrent atrial arrhythmias following the procedure may occur. Early recurrence tends to occur within the first ten days after surgery and does not necessarily indicate long-term failure. Early recurrence should be managed with timely cardioversion with or without the addition of antiarrhythmic drugs.

AF, atrial flutter, or atrial tachycardia may be persistent after surgery or recur late. The mechanisms of these arrhythmias are variable but frequently involve gaps, recovered conduction, or incompletely ablated tissue along ablation lines created at the time of surgery. Successful isolation of the pulmonary veins appears to be critical in preventing recurrence of AF and many focal and macro-reentry tachycardias following surgical ablation. The mitral annulus, including the musculature of the CS, atrial incision sites, as well as the stump of the left atrial appendage following exclusion are also common sites of recurrence. Intraoperative electrophysiologic testing is the best method to ensure complete block along ablation lines at the time of surgery in order to prevent recurrence. The use of antiarrhythmic agents can be considered in patients with recurrent arrhythmia following surgical ablation; however, EPS and catheter ablation is safe and effective for the diagnosis and treatment of persistent or late recurring arrhythmias after surgical ablation for AF.

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