Advances in Surgical Treatment of Atrial Fibrillation

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Abstract—Atrial fibrillation (AF) is the most common sustained arrhythmia. It is associated with increased risks of death and stroke; most strokes in AF patients are thought to arise from thrombi in the left atrial appendage. Surgical ablation of AF includes excision of the left atrial appendage and is an effective means of treating this arrhythmia, with the classic Maze procedure curing AF in $>$90% of patients and virtually eliminating the risk of late stroke. A complex but safe operation, the Maze procedure has been applied by relatively few surgeons. However, recent advances in the understanding of the pathogenesis of AF and development of new ablation technologies enable surgeons to perform pulmonary vein ablation, create linear left atrial lesions, and remove the left atrial appendage rapidly and safely. Lesions are created under direct vision, minimizing the risk of damage to the pulmonary veins and adjacent mediastinal structures. The majority of surgical ablation procedures have been performed in conjunction with mitral valve surgery, with the combination of mitral valve repair and cure of AF enabling patients to avoid lifelong anticoagulation. Recently developed surgical instrumentation now enables thoracoscopic and keyhole approaches, facilitating extension of epicardial AF ablation and excision of the left atrial appendage to patients with isolated AF and no other indication for cardiac surgery. In addition, novel devices designed specifically for minimally invasive epicardial exclusion of the left atrial appendage will broaden the range of treatment options for patients with AF, possibly eliminating the need for anticoagulation in selected patients. (Stroke. 2007;38[part 2]:618-623.)

Key Words: ablation ■ atrial fibrillation ■ stroke

Atrial fibrillation (AF) currently affects $\approx$2.4 million Americans; this number is expected to increase to $>$5.6 million by 2050.1 The prevalence of AF increases with increasing patient age, and recent data from the Framingham Heart Study suggest that the lifetime risks for development of AF are 1 in 4 for men and women aged $\geq$40 years.2 This epidemic has a growing impact on the healthcare system and a multibillion dollar cost. The clinical consequences of AF are well documented. AF is associated with reduced life expectancy and increases the risk of stroke 5-fold, accounting for $\approx$15% of all strokes nationally.3-8 These AF-related strokes are a major challenge and a focus of several clinical trials investigating strategies for primary and secondary prevention.9 Currently, antithrombotic therapy is the mainstay for stroke prevention in AF patients.

Although there is currently some consensus concerning pharmacological strategies for stroke prevention in AF patients, choice of therapy for the heart rhythm is controversial and evolving.9,10 Available antiarrhythmic therapies inconsistently restore sinus rhythm and are associated with complications. In fact, the risks associated with antiarrhythmic drug therapy may counterbalance the potential benefit of restoration of sinus rhythm.9,10 These observations, coupled with increased understanding of the pathogenesis of AF, have resulted in the development of interventional strategies to restore sinus rhythm. Both catheter-based and surgical approaches have demonstrated effectiveness in this regard. Developed by Dr James Cox, the classic Maze procedure is the predicate operation for ablation of AF; long-term data suggest that the Maze procedure eliminates AF in $>$90% of patients.11-14 Despite these unmatched results, the complexity and time associated with the Maze procedure have prevented widespread application by surgeons.

Recently, however, there has been increased interest in direct surgical ablation of AF, fueled by technological advances and demonstration that the pulmonary veins and left atrium are the drivers of AF in most patients.15 New ablation technologies enable surgeons to perform pulmonary vein isolation, create strategically placed, linear left atrial lesions, and excise the left atrial appendage rapidly and safely.16-23 Alternate energy sources used to create lines of conduction block and replace surgical incisions of the Maze procedure include radiofrequency, microwave, ultrasound, cryothermy, and laser.16-25 Applied primarily in patients with valvular heart disease, procedures in which these ablation technologies are used add 15 to 20 minutes to operative time and cure AF in $\approx$80% of patients. In addition, recent adaptation of these new ablation technologies for thoracoscopic and keyhole approaches now enables AF ablation in patients with lone AF, and early results of these procedures are promising.

In this report, we will (1) review surgical technique and results of the Maze procedure, (2) describe new approaches for surgical AF ablation, (3) summarize current strategies for...
surgical AF ablation in patients with valvular heart disease and in those with isolated AF, and (4) discuss the development of technology for minimally invasive epicardial ligation of the left atrial appendage.

**The Maze Procedure**

The Cox-Maze III operation, or Maze procedure, is the gold standard for surgical treatment of AF. In fact, it is the most effective curative therapy for AF yet devised, and these facts must be considered when new ablative approaches to AF are developed. Cox and colleagues designed the procedure on the basis of early experimental and clinical evidence concerning the pathophysiology of AF. To improve results and simplify the operation, they modified the procedure twice, culminating in the Cox-Maze III.

In the Maze procedure, right and left atrial incisions and cryolesions are constructed to interrupt the multiple, disorganized reentrant circuits that characterize AF (Figure 1). In addition, these lesions direct the sinus impulse from the sinoatrial node to the atrioventricular node along a specified route. Multiple “blind alleys” off this main conduction pathway (the Maze analogy) allow coordinated electric activation of the atrial myocardium. Key components of the Maze procedure include isolation of the pulmonary veins and excision of the left atrial appendage. These features are maintained in most of the newer operations designed to ablate AF.

Although the Maze procedure can be completed minimally invasively through a small chest wall incision, the operation requires cardiopulmonary bypass and cardiac arrest. In experienced hands, the Maze procedure requires 45 to 60 minutes of cardiopulmonary bypass and cardiac arrest. The operation may be performed alone or in conjunction with other cardiac surgical procedures, such as mitral valve repair or coronary artery bypass grafting.

Cox and colleagues have reported the largest series of patients undergoing the Maze procedure. Among 346 patients, operative mortality was 2%. Reported AF cure rate was 99%, and only 2% required long-term postoperative antiarrhythmic medication. Successful ablation of AF was unaffected by presence of mitral valve disease, left atrial size, and type of AF (paroxysmal, persistent, or permanent). Temporary postoperative AF was common, occurring in 38% of patients. This transient postoperative AF was attributed to a shortened atrial refractory period in the perioperative period, and its occurrence did not diminish long-term results. Fifteen percent of patients required new pacemakers after surgery, and this was generally necessary in patients with underlying sinus node dysfunction. Despite multiple right and left atrial incisions, right atrial transport function was demonstrated in 98% and left atrial transport in 93%. Perhaps most importantly, in addition to restoring sinus rhythm, the Maze procedure virtually eliminated the risk of stroke or other thromboembolism.

Other centers have documented excellent results with the Maze procedure, with restoration of sinus rhythm in 75% to 95% of patients, low risk of late stroke, and very low operative morbidity and mortality. In recent series, the need for a new pacemaker has decreased to 5% to 10%. These results confirm the safety of the Maze procedure, its efficacy at restoring sinus rhythm, and the prevention of late strokes. Despite these findings, the Maze procedure has been relatively underused. Today, few patients are referred for a surgical Maze procedure for lone AF, and, even in patients requiring cardiac surgery for other reasons, surgeons are reluctant to add a Maze procedure. The perceived surgical complexity and magnitude of the operation account for these trends.

**New Approaches for Surgical AF Ablation**

The development of new surgical approaches to AF has been predicated on 2 factors: (1) recognition that the pulmonary veins and left atrium are critical to the initiation and maintenance of AF and (2) development of ablation technologies that use alternate energy sources to facilitate rapid and safe creation of lines of conduction block under direct vision.

Whereas the Maze procedure was designed to interrupt the multiple macroreentrant circuits that characterize AF, new approaches are more precisely anatomically focused. There is general agreement that AF requires a substrate and a trigger and that these substrates and triggers are usually located in the pulmonary veins and left atrium. Haissaguerre and colleagues demonstrated that paroxysmal AF originates from ectopic beats in the pulmonary veins in 94% of cases. This likely relates to the anatomic transition from pulmonary vein endothelium to left atrial endocardium; at this juncture, 2 types of tissue with different electric properties are juxtaposed, and this may potentiate development of AF. In addition, autonomic nerves in these regions may contribute to the pathogenesis of AF. Catheter ablation of the posterior left atrium, including the antra surrounding the pulmonary veins, has proven effective at ablating both paroxysmal and permanent AF. These data suggest that modification of the left atrial substrate, in combination with pulmonary vein isolation, is an effective therapy for all forms of AF.
On the basis of these advances in understanding of the pathophysiology of AF, a variety of new ablation tools have been developed to facilitate surgical ablation of AF. These probes and catheters rely on alternate energy sources to create long, continuous, linear lesions that block conduction. Energy sources that have been used clinically include radiofrequency, laser, ultrasound, microwave, and cryothermy. Radiofrequency, laser, ultrasound, and microwave are heat-based energy sources that create lines of conduction block through thermal injury. Each of these modalities can be used for minimizing invasive epicardial ablation. A microwave catheter (AFx, Inc, Freemont, Calif) has been used to perform off-pump thoracoscopic AF ablation. Recently developed ultrasound (Epicor, Inc, Sunnyvale, Calif) and laser-based probes (Edwards Lifesciences, LLC, Irvine, Calif) have been designed specifically for thoracoscopic AF ablation.

Surgeons have used these alternate energy sources to create a variety of left atrial lesions sets, ranging from wide pulmonary vein isolation with excision of the left atrial appendage to a lesion set that resembles that of the Maze procedure (Figure 2).16,21 The lesion from the right pulmonary veins to the mitral annulus may be particularly important in the prevention of postprocedure left atrial flutter.30 The addition of right atrial lesions may increase freedom from recurrent AF and atrial flutter, but their importance is controversial.37,38 However, creation of a right atrial isthmus lesion to reduce occurrence of atrial flutter is simple and safe, and we currently favor its incorporation at the time of surgical ablation.

Because the surgeon has the advantages of (1) direct visualization of cardiac structures and (2) catheters that facilitate rapid creation of transmural lesions, there is great interest in ablating AF in patients presenting for other cardiac surgical procedures. Completion of left atrial lesion sets requires only 10 to 20 minutes. This amount of time contrasts with the 1 hour required to perform the Maze procedure. In addition, because incisions are replaced by heat- or cryo-based lesions, the risk of bleeding is virtually eliminated when alternate energy sources are used.

Although approaches vary somewhat, results are similar with a variety of different lesion sets and energy sources. AF is ablated in 70% to 80% of patients having concomitant heart surgery.21,23,38 Thus far, most treated patients have had organic heart disease and have received a mitral valve procedure in addition to AF ablation. For them, results with alternate energy sources fall just short of those reported for the classic Maze procedure.14,26,27

After surgical ablation, perioperative AF is common, occurring in ~50% of patients.21 Although 30% to 40% of patients leave the hospital in AF, many return to sinus rhythm over the ensuing 3 months.23 Thus, discharge in AF is not an indication of procedure failure.39 Factors that influence procedure success include larger left atrial size, longer duration of AF, and choice of lesion set in permanent AF.40,41

The development of new techniques and operations for surgical treatment of AF has caused a change in cardiac surgical practice. At the Cleveland Clinic, our current policy is to perform ablation in almost all patients coming to the operating room with preexisting AF. In 2005 we performed 400 operations for AF. Eighty-six percent were in patients requiring cardiac surgery for concomitant valvular heart disease. This approach is particularly beneficial in patients having mitral valve repair because successful valve repair and AF ablation leave the patient with his native valve and free of the need for long-term anticoagulation.

Fifty-seven percent of these patients had perioperative AF; however, by 1 year postoperatively, 84% were free of AF. Given the high incidence of perioperative AF, a strategy that includes 3 months of routine postoperative antiarrhythmic therapy and anticoagulation in all patients is recommended. Because heart rhythm varies in the first 3 months after surgery, we recommend aggressive attempts to restore sinus rhythm during this time frame when patients develop AF or atrial flutter. Heart rhythm generally stabilizes by 6 months after surgery. In this cohort, no patient had a late stroke. Finally, new pacemakers were required in 4%, and, as with the classic Maze procedure, this was generally attributable to underlying sinus node dysfunction or heart block.

**Current Indications and Strategies for Surgical AF Ablation**

A variety of treatment options are available for patients with AF. These include anticoagulation with rate control, antiarrhythmic drug therapy, atrioventricular node ablation with pacemaker placement, catheter-based ablation, and surgical ablation. The pathogenesis of AF and patient symptoms and profiles vary widely; these factors prevent development of global recommendations for a standard treatment in all patients. However, surgical ablation is likely to have an increasing role in AF treatment for a variety of reasons.
Surgical treatment of AF has a long track record of success; the Maze procedure is an extremely effective treatment for AF.\textsuperscript{30,42} The surgeon has the advantage of direct visualization of the left atrium and pulmonary veins, either from the epicardial or endocardial surface of the heart, and this factor, coupled with new ablation technology, enables rapid and safe ablation. Because the surgeon can see the cardiac structures, ablation lines can be placed safely on the left atrial cuffs adjacent to the pulmonary vein orifices, thereby avoiding the dreaded complication of pulmonary vein stenosis. Epicardial ablation eliminates the risk of esophageal injury. With surgical approaches, the left atrial appendage is excised, and this is likely important in decreasing the risk of late stroke. Finally, the simplicity of these techniques makes them generally applicable; all cardiac surgeons can now ablate AF. In current clinical practice, almost all patients with AF who present for cardiac surgery should have both AF ablation and the intended cardiac procedure.

Using this experience as a springboard, surgeons have developed epicardially based, minimally invasive, and thoracoscopic approaches to offer rapid and safe AF ablation to patients with lone AF—those patients without structural heart disease that would necessitate other cardiac surgical procedures. Pulmonary vein isolation and excision of the left atrial appendage can be performed with the use of a minimally invasive “keyhole approach” or thoracoscopically; neither approach requires cardiopulmonary bypass.\textsuperscript{33,44} These minimally invasive procedures enable wide, circumferential pulmonary vein isolation, either with a single “box” lesion or separate oval-shaped ablations on the right and left. Procedure times are generally 2 to 4 hours, and median length of hospital stay is 3 days. Early results, obtained primarily in patients with paroxysmal AF, demonstrate 80% to 90% freedom from AF 6 months after ablation. With continued experience and further advances in instrumentation, procedure time is expected to fall to <2 hours, and hospital length of stay is expected to decline to a single day. Application of these minimally invasive, thoracoscopic, and keyhole procedures will offer the potential for cure of AF, with improved quality of life and freedom from anticoagulation and antiarrhythmic medications in large numbers of patients.

Future Directions: The Left Atrial Appendage

Currently, there is great interest in development and assessment of endocardial and epicardial procedures for exclusion of the left atrial appendage.\textsuperscript{45,46} It is widely believed that formation and embolism of left atrial appendage thrombi are responsible for the increased risk of stroke in AF patients.\textsuperscript{4,47,48} Each year, $\approx$60 000 Americans with AF experience strokes; these strokes are often large and devastating, emphasizing the need for primary prevention. In AF patients, clinical evidence demonstrates that warfarin inhibits formation of atrial appendage thrombi and reduces cardioembolic strokes, and aspirin prevents smaller, noncardioembolic strokes. On the basis of data from the Stroke Prevention in Atrial Fibrillation trials, one third of AF patients are at high risk for stroke and should be treated with warfarin.\textsuperscript{4} Despite these observations and recommendations, warfarin is underprescribed in AF patients. Furthermore, many patients cannot or will not take warfarin. Therefore, interventional therapies that specifically address the left atrial appendage in AF patients are being investigated as potential alternatives to warfarin therapy.

Excision or exclusion of the left atrial appendage is currently performed during surgical ablation of AF and is recommended in American College of Cardiology/American Heart Association guidelines for patients undergoing mitral valve surgery. However, standard surgical exclusion by suture closure is incomplete in 30% of cases, and stapled closure or excision has been associated with bleeding complications.\textsuperscript{46,49} Thus, there is a need for new surgical approaches to the left atrial appendage. Several devices for epicardial exclusion of the left atrial appendage are under development (Figure 3). Preclinical studies suggest that epicardial exclusion of the left atrial appendage is rapid and safe and has the advantage of avoiding placement of a foreign body in the fibrillating atrium. Preclinical studies with a simple left atrial appendage clip confirm complete exclusion of the left atrial appendage from the body of the left atrium and long-term safety of the implant (Figure 3).\textsuperscript{50} This and other new technologies for minimally invasive epicardial ablation of the left atrial appendage will soon be available for clinical use. Clinical trials are being designed to test the hypothesis that epicardial, device-based exclusion of the left atrial appendage will reduce the risks of stroke and other thromboembolism in patients with AF. Should this hypothesis prove correct, physicians will be able to offer a new strategy for primary or secondary stroke prevention in AF patients.

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