

Surgical Approaches for Atrial Fibrillation

Adam E. Saltman, MD, PhD^{a,*}, A. Marc Gillinov, MD^b

KEYWORDS

- Atrial fibrillation • Ablation • Left atrial appendage
- Mitral valve disease • Maze procedure

Although it long has been recognized that atrial fibrillation (AF) is common in patients presenting for mitral valve surgery and other forms of cardiac surgery, ablation of AF in such patients has recently become more popular. This change in surgical practice is attributable to new data clarifying the pathogenesis and dangers of untreated AF along with the development of new ablation technologies that facilitate ablation. For cardiac surgery patients presenting with AF, surgeons now offer a more complete operation that corrects the structural heart disease and the AF simultaneously. In addition, surgeons are rapidly developing easier and more sophisticated, minimally invasive, epicardial, beating-heart approaches for stand-alone AF ablation. The purposes of this review are to (1) review the rationale for surgical ablation of AF in cardiac surgery patients, (2) describe the classic maze procedure and its results, (3) detail new approaches to surgical ablation of AF, (4) emphasize the importance of management of the left atrial (LA) appendage, and (5) consider challenges and future directions in the ablation of AF in cardiac surgery patients.

RATIONALE FOR SURGICAL ABLATION

Atrial Fibrillation Prevalence

Because AF is particularly common in patients who have mitral valve dysfunction, most studies examining concomitant ablation—and surgical ablation in general—focus on this group. AF is present in up to 50% of patients undergoing mitral valve surgery and in 1% to 6% of patients

presenting for coronary artery bypass grafting or aortic valve surgery.^{1–4} As in the general population, the prevalence of AF in patients who have mitral valve disease increases with increasing patient age. In patients who have mitral valve dysfunction, AF is a marker of advanced cardiovascular disease and often is associated with the onset or exacerbation of heart failure.⁵ Compared with patients who have mitral valve dysfunction who do not have AF, those who have AF have higher New York Heart Association functional class, more severe left ventricular dysfunction, and greater left atrial size.^{4,6–9}

Risks of Atrial Fibrillation

AF is associated with increased mortality and morbidity in patients who have mitral valve dysfunction and coronary artery bypass graft. In patients who have degenerative mitral valve disease, AF is an independent risk factor for cardiac mortality and morbidity.^{1–4} In patients undergoing mitral valve surgery, persistence of postoperative AF is a marker and a risk factor for increased mortality;^{10,11} in addition, AF is associated with morbidity that includes stroke, other thromboembolism, and anticoagulant-related hemorrhage. In some patients, AF causes symptomatic tachycardia, reduced cardiac output, and tachycardia-induced cardiomyopathy. This is deleterious particularly in patients who have structural heart disease and reduced cardiac output. For these reasons, the presence of AF should be included in planning the operative strategy for cardiac surgery patients,

A version of this article originally appeared in *Medical Clinics of North America*, volume 92, issue 1.

This work was supported by the Atrial Fibrillation Innovation Center, a Third Frontier Project Funded by the State of Ohio.

^a Cardiothoracic Surgery Research, Maimonides Medical Center, 4802 10th Avenue, Brooklyn, NY 11219, USA

^b Atrial Fibrillation Center, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH, USA

* Corresponding author. Division of Cardiothoracic Surgery, Maimonides Medical Center, 4802 10th Avenue, Brooklyn, NY 11219.

E-mail address: USAadamsaltman@mac.com (A.E. Saltman).

Cardiol Clin 27 (2009) 179–188

doi:10.1016/j.ccl.2008.09.012

0733-8651/08/\$ – see front matter © 2009 Elsevier Inc. All rights reserved.

noting that the risk associated with the added rhythm treatment is low.^{12,13}

The onset of AF is a relative indication for mitral valve surgery in those who have known mitral valve dysfunction.² And once AF appears, it is uncommon for mitral valve surgery alone to restore sinus rhythm.⁶⁻⁸ When AF has been present for 3 months or less, particularly if it is paroxysmal, lone mitral valve surgery may convert as many as 80% of patients,^{6,7} but when the duration of preoperative AF exceeds 6 months, 70% to 80% of patients remain in AF if they do not undergo rhythm correction.^{6,7} Therefore, ablation should be added to a mitral valve procedure in any patient who has had AF for more than 6 months or in whom AF is persistent or permanent. Such procedures, performed on this patient group, uniformly have enjoyed high success in restoring sinus rhythm and improving cardiac function.^{14,15}

Atrial Fibrillation Mechanisms and the Implications for Surgical Ablation

The clinical presentation of AF varies widely among individuals. The current treatment guidelines account for this somewhat by classifying AF as paroxysmal, persistent, or permanent.¹⁶ Even though the pathogenesis of all types remains incompletely understood, there is agreement that patients who have persistent and permanent AF most likely have a more complex pathophysiology. Unfortunately, among those who have coexistent mitral valve disease, permanent AF is the most common form.^{17,18} It is, therefore, not surprising that there is little consensus concerning which ablation strategy to use at the time of surgery, so procedural details and techniques vary widely.

Endocardial electrophysiologic mapping has demonstrated that the pulmonary veins and posterior left atrium are critical anatomic sites in humans who have isolated AF.^{19,20} Mapping studies performed during concomitant heart surgery also support the importance of the left atrium as the driving chamber in patients who have mitral valve disease.²¹⁻²⁶ Often, regular and repetitive rapid activation can be identified in the posterior left atrium in the regions of the pulmonary vein orifices and LA appendage,²¹⁻²⁵ however, some patients manifest dominant right atrial focal or re-entrant activation.²¹

These findings emphasize the need for an individualized approach to each patient. But until real-time, intraoperative mapping becomes routine,²⁶ a more-or-less constant, all-encompassing anatomic approach based on empiric results is reasonable. Over the past 5 to 10 years, this line of attack has become the foundation for

catheter-based AF ablation; tracking down and destroying individual AF triggers has given way to the complete encirclement of the pulmonary veins and posterior left atrial wall.²⁷⁻³¹ A left atrial procedure that includes a box-like lesion around all four pulmonary veins and a lesion to the mitral annulus seems to eliminate AF in 70% to 90% of patients who have mitral valve regurgitation.^{25,32-35} The addition of right atrial lesions in these patients likely confers some benefit with little additional risk.^{36,37} Specific omission of a right atrial isthmus lesion, however, leaves some patients at risk for typical atrial flutter and others at risk for continued AF.³⁸ Therefore, because right-sided lesions can be created quickly and safely, AF ablation in cardiac surgery patients almost always should include a biatrial lesion set.

THE MAZE PROCEDURE

The Cox maze III operation, or maze procedure, is the gold standard for surgical treatment of AF. It is the most effective curative therapy for AF yet devised for any type of AF and for patients who have or who do not have concomitant cardiac disease.³⁹⁻⁴¹ In the maze procedure, multiple left and right atrial incisions and cryolesions are placed to isolate triggers and interrupt multiple re-entrant circuits (Fig. 1). The maze procedure includes en bloc isolation of the pulmonary veins and posterior left atrium along with excision of the LA appendage; these maneuvers are critical to the efficacy of the procedure in the restoration

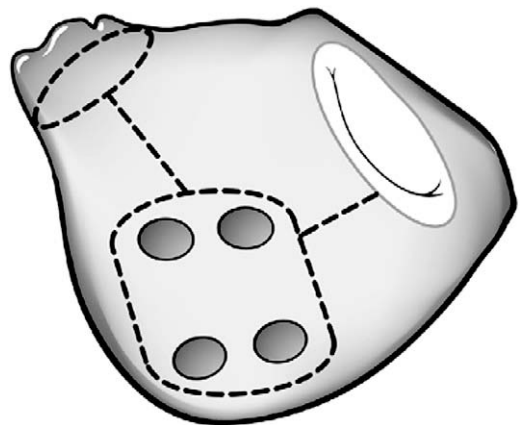


Fig. 1. Left atrial lesion set of the maze procedure. Small circles represent pulmonary vein orifices and white oval represents the mitral valve. Dashed lines represent surgical incisions. (Reprinted from The Cleveland Clinic Center for Medical Art & Photography © Copyright 2007. All rights reserved; with permission.)

of sinus rhythm and in the reduction of thromboembolic risk.

Although the maze procedure is a complex operation that adds cardiopulmonary bypass and cardiac arrest time, experienced surgeons have performed the classic operation in large numbers of patients having concomitant cardiac surgery.^{1-3,6,41} The addition of a maze procedure does not increase operative mortality or morbidity;⁴²⁻⁴⁴ however, it carries with it a 5% to 10% risk for implantation of a permanent pacemaker.⁴⁵ This happens most commonly in patients who have pre-existing sinus node dysfunction or in those undergoing multivalve surgery. Recent data demonstrate that the maze procedure has equivalent long-term efficacy at establishing sinus rhythm in patients undergoing lone operations and concomitant procedures; successful restoration of sinus rhythm has been achieved in 70% to 96% of patients.⁴²⁻⁴⁴

Early postoperative AF is common after a maze procedure, usually abating by 3 months.⁴²⁻⁴⁴ This also is true of catheter-based procedures and should not be confused with a relapse of the presenting disease, although it may be a predictor of long-term outcomes.⁴⁶ Although the pathogenesis of failure over the long term is unclear, several risk factors have been identified: increasing left atrial diameter, longer duration of preoperative AF, and advanced patient age all increase the late prevalence of AF.⁴⁷⁻⁵⁰ Thus, 5 years after a concomitant maze procedure, the predicted prevalence of AF is only 5% in patients who have mitral valve regurgitation who have a 4-cm left atrium; in contrast, the predicted prevalence is 15% in similar patients who have a 6-cm left atrium.⁵¹ Others have identified similar risk factors for AF after the maze procedure, suggesting the possibility that earlier operation and left atrial size reduction in those who have left atrial enlargement (>6 cm) might improve results.⁵¹⁻⁵³

The temporal pattern of AF (paroxysmal, persistent, or permanent) does not seem to have an impact on the results of the maze procedure.⁴⁴ Similarly, in patients who have mitral valve dysfunction, the cause does not influence results, and there is general agreement that the maze procedure is effective in patients who have rheumatic or degenerative disease.^{54,55} Even in patients who have rheumatic disease, biatrial contraction usually is restored.⁵⁴

Beyond restoring sinus rhythm, the maze procedure is associated with additional important clinical benefits in patients who have mitral valve disease. Recent data suggest that restoration of sinus rhythm improves survival in this group,¹⁰ and the risks for stroke, other thromboembolism,

and anticoagulant-related hemorrhage likewise are reduced.^{10,11,56,57} The reduced risk for late stroke after a maze procedure deserves particular emphasis. In the largest series focusing on this outcome, Cox and colleagues⁵⁷ noted a single late stroke at a mean follow-up of 5 years in 300 patients who had a classic maze procedure. This remarkable late freedom from late stroke likely is attributable to restoration of sinus rhythm in the majority of patients and to excision of the LA appendage, an integral component of the maze procedure.

These results confirm the safety of the maze procedure, its efficacy at restoring sinus rhythm, and the resulting clinical benefits, most notably the virtual elimination of late strokes. Despite these excellent results, the maze procedure has been underused, and today it is almost obsolete. Most surgeons are reluctant to add a maze procedure to the operative course of patients who are having mitral valve surgery or other cardiac surgery. With recent advances in the understanding of the pathogenesis of AF and development of new ablation technologies, however, surgeons increasingly are likely to ablate AF using simpler techniques that require only a few minutes of operative time.

NEW APPROACHES TO SURGICAL ABLATION OF ATRIAL FIBRILLATION

Lesion Sets

Like recent approaches to catheter-based ablation, newer surgical techniques for AF ablation create lines of conduction block in the left atrium.⁵⁸⁻⁶⁰ Because the left atrium is open during mitral valve procedures, precise creation of lesions is possible. A variety of lesion sets have been used to ablate AF in patients who have mitral valve disease. Most include pulmonary vein isolation, excision or exclusion of the LA appendage, and linear left atrial connecting lesions.⁵⁸⁻⁶² The pulmonary veins may be isolated with a box-like lesion, as in the maze procedure, or with separate right- and left-sided ovals around the pulmonary veins. With the advantage of direct vision, surgeons easily can create a lesion from the left pulmonary veins to the mitral annulus; this lesion improves results, particularly in patients who have permanent AF and mitral valve disease.⁶³ In patients who have left atrial enlargement (>6 cm), the authors recommend left atrial reduction, as this may increase restoration of sinus rhythm.

The issue concerning the creation of biatrial lesions (more closely mimicking the Cox maze III set) versus creating left atrial lesions alone remains contentious. It is easier and faster to create a more limited lesion set; yet recent data indicate that

patients undergoing right and left atrial treatment have a better long-term result at maintaining sinus rhythm.³⁷ Through the judicious selection of a technology or multiple technologies, it is becoming possible to create right-sided lesions without opening the right atrium or prolonging cardiopulmonary bypass time or aortic cross-clamp time. In this manner, the largest number of patients can be treated in the most efficacious and safest fashion.

Surgical Ablation for Lone Atrial Fibrillation

When considering the number of patients presenting to operating rooms with AF in combination with coronary or valvular disease, even if all undergo concomitant ablation, it is unlikely that more than 40,000 patients would be treated annually. This is a small fraction of the total number of people suffering from this disease. A much larger patient population, therefore, could benefit from stand-alone AF ablation. It is difficult, however, to justify using cardiopulmonary bypass and cardioplegic arrest, especially through a sternotomy, to open the heart for the surgical treatment of lone AF: witness the relatively poor adoption of the maze procedure over the past 20 years despite its established safety and efficacy.

To bring an effective therapy to the largest number of patients, therefore, there has been recent activity directed toward developing an epicardial approach to ablation that can be performed on a beating heart, preferably through small access incisions or ports. Such an approach should be able to overcome the disadvantages associated with the traditional Cox maze operation (significant morbidity, lengthy operative time, and extended recuperation) and the endocardial, catheter-based techniques (indirect visualization, ablation within a flowing blood pool, and inability to manage the LA appendage).

The first report of such a minimally invasive, epicardial ablation performed on a beating heart appeared in 2003.⁶⁴ Since then, three main, less invasive surgical technologies have been developed and used for the ablation of lone AF: robotics,⁶⁵ thoracoscopy (endoscopy),^{66–68} and minithoracotomies.^{69,70} Each has its own advantages and disadvantages but all provide physicians with access to the entire atrial epicardium of a beating heart, whereupon lesions can be placed with precision and immediate visual feedback. Pulmonary vein isolation, for example, is easily accomplished in this manner, and LA appendage management is straightforward.

It is not possible to state conclusively which approach or which ablative technology used in

a minimally invasive setting provides superior results. The numbers of patients treated are small and there are technologic hurdles to be overcome (mitral annular and tricuspid isthmus lesion creation, for example). Refinements in approach and technology are progressing rapidly and new tools and methods are becoming available.

A Review of the Available Energy Sources

The classic lesion creation method is cutting and sewing tissue. Once the healing process is complete, there remains a scar composed mostly of collagen and little cellular material. It is not electrically conductive and the lesion is, by definition, transmural. The goal of any energy source, therefore, is to create a similar scar by exposing tissue to extremes of temperature, inducing thermal injury, coagulation necrosis, and healing.

To produce such an irreversible injury, the tissue must be heated to 50°C or frozen to –60°C.^{71,72} The quantity of tissue injured usually is directly proportional to the duration of time for which it is held at either temperature. The various energy sources differ mainly in the method by which they transfer energy to the tissue and how deeply that energy is conducted into the tissue. Heat-based energy sources include radiofrequency, laser, microwave, and high-intensity focused ultrasound. Cold-based sources include argon and nitrous oxide gases. As of 2008, all these devices are Food and Drug Administration–labeled for the ablation of soft tissues or cardiac tissue but not for treatment of AF. The specific treatment of AF is considered, therefore, off-label use.

Despite clearly different energy forms and application methods, when applied to the left-atrial endocardium of the arrested heart there seems to be little difference in safety or efficacy among the devices.⁷³ For example, surveying the use of the dry, unipolar radiofrequency probe (Cobra, ESTECH, San Ramon, California) in more than 1100 patients, Khargi and colleagues⁷³ found that it was effective at freeing patients from AF between 42% and 92% of the time. But there are several complications attributed to the use of the probe, the most worrisome being esophageal injuries, resulting in death 60% of the time.^{74,75} Adverse events can occur with any technology when applied incorrectly,⁷⁶ but as more experience is gained and safer methods of ablation developed (eg, placing a cold, wet sponge between the posterior wall of the left atrium and the esophagus or shielding the probe in nonconducting sheaths), these injuries have become a rarity.

THE LEFT ATRIAL APPENDAGE

Between 60% and 90% of stroke-causing emboli in patients who have AF originate in the LA appendage,⁷⁷⁻⁷⁹ giving it the moniker, “our most lethal human attachment.”^{80,81} Therefore, excision or exclusion of the LA appendage is a critical component of operations to treat AF; as discussed previously, this may explain in part the exceedingly low risk for stroke after the maze procedure. Ligation of the LA appendage in patients who have mitral valve regurgitation and who have AF reduces the late risk for thromboembolic events even if patients do not have intraoperative ablation.⁷³

Surgical technique has an impact on results of LA appendage ligation, with incomplete ligation increasing the risk for thromboembolism.^{82,83} Currently used techniques include exclusion by suture ligation or noncutting stapler and excision with suture closure or stapling.⁸³ The authors currently favor surgical excision of the appendage with standard cut-and-sew techniques as complete elimination with minimal cul-de-sac formation is most likely. Development of devices designed specifically for management of the LA appendage will facilitate this procedure. Published preclinical experience with several new LA appendage management devices is promising, and clinical trials are anticipated in the near future (Figs. 2 and 3).⁸⁴⁻⁸⁷

CHALLENGES AND FUTURE DIRECTIONS

One of the most significant obstacles facing the widespread adoption of surgical AF ablation is lack of data. Large, controlled studies describing well-defined patient populations, detailed techniques, and outcomes are missing from the literature. Electrophysiologic colleagues are addressing

this need and studies are underway. The advances necessary to improve AF ablation in cardiac surgery patients, therefore, must include (1) uniform definitions and methodology for reporting results, (2) improved technology to facilitate the ablation procedure and its intraoperative assessment, and (3) refinement of minimally invasive procedures.

Reporting Results

Standard terminology and methodology for reporting results has been absent from the cardiac surgery literature, and current reporting is haphazard and rightly subject to criticism.⁸⁸⁻⁹⁰ Although there are guidelines for categorizing the clinical pattern of AF, these are applied inconsistently. Techniques for postablation rhythm assessment vary, with no generally accepted standard. Technologies for long-term and continuous rhythm monitoring are becoming available but they are costly and not yet convenient. Data obtained with such systems could be analyzed in uniform fashions to determine (1) absolute freedom from AF, (2) changes in the AF burden for individual patients, and (3) prevalence of AF in treated populations.⁸⁸⁻⁹⁰

Ablation Technology and Intraoperative Assessment

Current surgical ablation technology has several limitations. No single ablation device can create all of the maze lesions from the epicardial aspect.^{91,92} When working from the endocardium, collateral tissue injury is possible. In addition, because real-time mapping is not yet available, the exact ablation procedure cannot yet be tailored to each patient's particular electrophysiologic

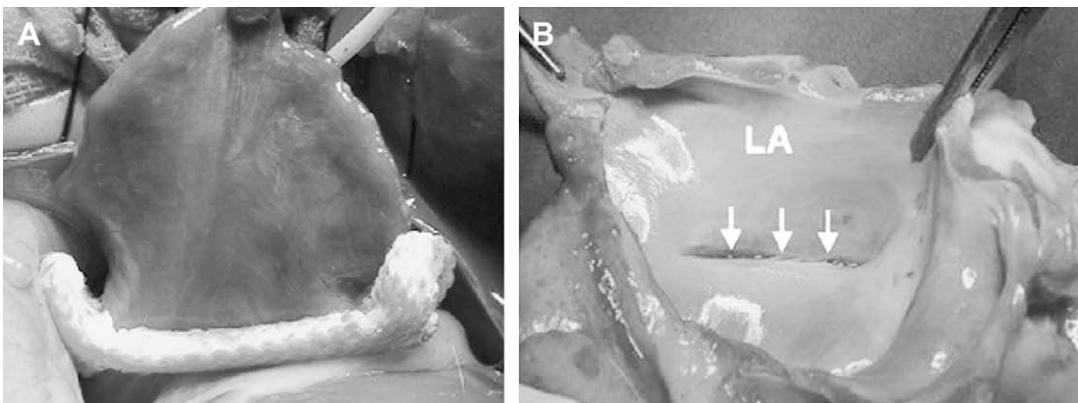


Fig. 2. LA appendage exclusion with a specially designed, cloth-covered clip. (A) Epicardial view of the clip placed on the canine LA appendage. (B) Endocardial view of the excluded appendage orifice 90 days after clip application. Arrows indicate residual LA appendage ostium.

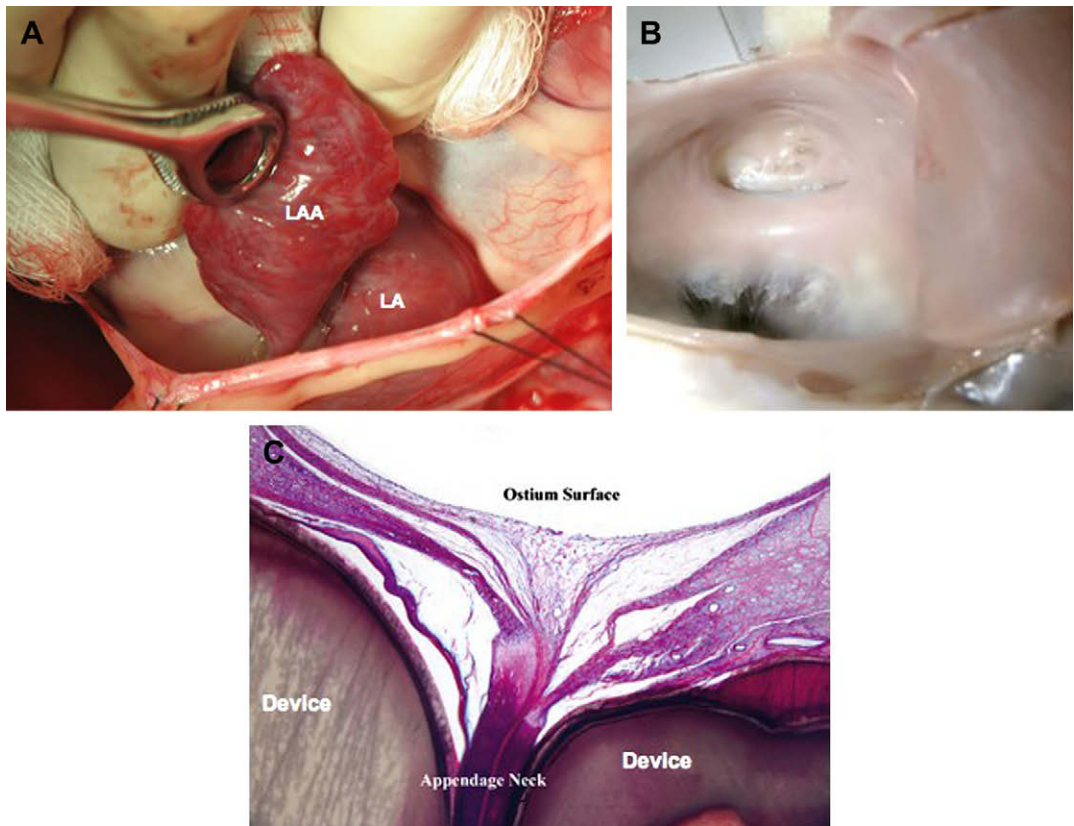


Fig. 3. LA appendage exclusion with a specially designed transmural fixation device. (A) Epicardial view of the clip placed on the canine LA appendage (LAA). (B) Endocardial view of the excluded appendage orifice 30 days after clip application. (C) Photomicrograph of a section taken transversely across the appendage orifice, showing complete endothelialization of the orifice without thrombus.

characteristics. Many of these problems are not unique to surgeons and their instruments but are shared by the electrophysiologists and are among the foremost challenges facing the device industry today. It is safe to say, however, that the next generation of ablation tools, capable of measuring impulse conduction and lesion effectiveness in real time, will greatly improve results and permit for the first time a tailored and more effective approach.

Minimally Invasive Approaches

Although most valve surgeries are performed via the median sternotomy, it is now possible to perform minimally invasive procedures and achieve excellent results with less morbidity and mortality.^{93–96} Ablative procedures—stand alone and concomitant—also are being done through these small right thoracotomies or partial upper sternotomies with a variety of technologies.^{97–107} They are technically challenging, however, as minimally invasive or keyhole approaches remain

hampered by difficult access to the posterior left atrium and LA appendage. Additional refinements in exposure, manipulation, ablation technology, and lesion assessment are necessary to facilitate the widespread application of minimally invasive cardiac surgery with ablation.

SUMMARY

AF is common in patients presenting for cardiac surgery. Left untreated, AF increases morbidity and jeopardizes survival. Recent data demonstrate that AF ablation improves outcomes in these patients. Therefore, virtually all cardiac surgery patients who present with AF should receive a concomitant AF ablation procedure. The cut-and-sew maze procedure is obsolete, replaced by operations that use alternate energy sources to create lines of conduction block rapidly with little risk for bleeding. Minimally invasive cardiac surgery for AF ablation now is possible. Continued progress will facilitate tailored ablation approaches for individual patients and improve

results. Development of new devices to facilitate minimally invasive exclusion of the LA appendage may offer a new alternative to patients who have AF and are at risk for stroke.

REFERENCES

- Cox JL. Intraoperative options for treating atrial fibrillation associated with mitral valve disease. *J Thorac Cardiovasc Surg* 2001;122:212–5.
- Ad N, Cox JL. Combined mitral valve surgery and the Maze III procedure. *Semin Thorac Cardiovasc Surg* 2002;14:206–9.
- Grigioni F, Avierinos JF, Ling LH. Atrial fibrillation complicating the course of degenerative mitral regurgitation: determinants and long-term outcome. *J Am Coll Cardiol* 2002;40:84–92.
- Quader MA, McCarthy PM, Gillinov AM, et al. Does preoperative atrial fibrillation reduce survival after coronary artery bypass grafting? *Ann Thorac Surg* 2004;77:1514–22.
- Kareti KR, Chiong JR, Hsu SS, et al. Congestive heart failure and atrial fibrillation: rhythm versus rate control. *J Card Fail* 2005;11(3):164–72.
- Obadia JF, el Farra M, Bastien OH. Outcome of atrial fibrillation after mitral valve repair. *J Thorac Cardiovasc Surg* 1997;114:179–85.
- Chua YL, Schaff HV, Orsulak TA. Outcome of mitral valve repair in patients with preoperative atrial fibrillation. Should the maze procedure be combined with mitral valvuloplasty? *J Thorac Cardiovasc Surg* 1994;107:408–15.
- Lim E, Barlow CW, Hosseinpour AR, et al. Influence of atrial fibrillation on outcome following mitral valve repair. *Circulation* 2001;104:159–163.
- Jessurun ER, van Hemel NM, Kelder JC. Mitral valve surgery and atrial fibrillation: is atrial fibrillation surgery also needed? *Eur J Cardiothorac Surg* 2000;17:530–7.
- Bando K, Kasegawa H, Okada Y. The impact of pre- and postoperative atrial fibrillation on outcome after mitral valvuloplasty for nonischemic mitral regurgitation. *J Thorac Cardiovasc Surg* 2005;129:1032–40.
- Bando K, Kobayashi J, Kosakai Y. Impact of Cox maze procedure on outcome in patients with atrial fibrillation and mitral valve disease. *J Thorac Cardiovasc Surg* 2002;124:575–83.
- Molloy TA. Midterm clinical experience with microwave surgical ablation of atrial fibrillation. *Ann Thorac Surg* 2005;79(6):2115–8.
- Ngaage DL, Schaff HV, Mullany CJ, et al. Influence of preoperative atrial fibrillation on late results of mitral repair: is concomitant ablation justified? *Ann Thorac Surg* 2007;84(2):434–42 [discussion 442–33].
- Hematpour K, Steinberg JS. Treatment of atrial fibrillation in hypertrophic cardiomyopathy. *Anadolu Kardiyol Derg* 2006;(6 Suppl 2):44–8.
- Stulak JM, Schaff HV, Dearani JA, et al. Restoration of sinus rhythm by the Maze procedure halts progression of tricuspid regurgitation after mitral surgery. *Ann Thorac Surg* 2008;86(1):40–4 [discussion 44–5].
- Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 guidelines for the management of patients with atrial fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation* 2006;114(7):e257–354.
- Wu T-J, Kerwin WF, Hwang C. Atrial fibrillation: focal activity, re-entry, or both? *Heart Rhythm* 2004;1:117–20.
- Savelieva I, Camm J. Update on atrial fibrillation: part I. *Clin Cardiol* 2008;31(2):55–62.
- Haissaguerre M, Jais P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339(10):659–66.
- Todd DM, Skanes AC, Guiraudon G, et al. Role of the posterior left atrium and pulmonary veins in human lone atrial fibrillation: electrophysiological and pathological data from patients undergoing atrial fibrillation surgery. *Circulation* 2003;108(25):3108–14.
- Nitta T, Ishii Y, Miyagi Y. Concurrent multiple left atrial focal activations with fibrillatory conduction and right atrial focal or reentrant activation as the mechanism in atrial fibrillation. *J Thorac Cardiovasc Surg* 2004;127:770–8.
- Yamauchi S, Ogasawara H, Saji Y. Efficacy of intraoperative mapping to optimize the surgical ablation of atrial fibrillation in cardiac surgery. *Ann Thorac Surg* 2002;74:450–7.
- Harada A, Konishi T, Fukata M. Intraoperative map guided operation for atrial fibrillation due to mitral valve disease. *Ann Thorac Surg* 2000;69:446–50.
- Harada A, Sasake K, Fukushima T, et al. Atrial activation during chronic atrial fibrillation in patients with isolated mitral valve disease. *Ann Thorac Surg* 1996;61:104–12.
- Sueda T, Imai K, Ishii O. Efficacy of pulmonary vein isolation for the elimination of chronic atrial fibrillation in cardiac valvular surgery. *Ann Thorac Surg* 2001;71:1189–93.
- Schuessler RB. Do we need a map to get through the maze? *J Thorac Cardiovasc Surg* 2004;127:627–8.

27. Pappone C, Santinelli V, Manguso F, et al. Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation. *Circulation* 2004;109(3):327–34.
28. Oral H, Scharf C, Chugh A, et al. Catheter ablation for paroxysmal atrial fibrillation: segmental pulmonary vein ostial ablation versus left atrial ablation. *Circulation* 2003;108(19):2355–60.
29. Marrouche NF, Dresing T, Cole C, et al. Circular mapping and ablation of the pulmonary vein for treatment of atrial fibrillation: impact of different catheter technologies. *J Am Coll Cardiol*. 2002;40(3):464–74.
30. Markowitz SM. Ablation of atrial fibrillation: patient selection, technique, and outcome. *Curr Cardiol Rep* 2008;10(5):360–6.
31. Yamada T, McElderry HT, Doppalapudi H, et al. Catheter ablation of focal triggers and drivers of atrial fibrillation. *J Electrocardiol* 2008;41(2):138–43.
32. Kondo N, Takahashi K, Minakawa M. Left atrial maze procedure: a useful addition to other corrective operations. *Ann Thorac Surg* 2003;75:1490–4.
33. Gaita F, Gallotti R, Calo L. Limited posterior left atrial cryoablation in patients with chronic atrial fibrillation undergoing valvular heart surgery. *J Am Coll Cardiol* 2000;36:159–66.
34. Tuinenburg AE, van Gelder IC, Tieleman R. Mini-maze suffices as adjunct to mitral valve surgery in patients with preoperative atrial fibrillation. *J Cardiovasc Electrophysiol* 2000;11:960–7.
35. Kalil RAK, Lima GG, Leiria TLL, et al. Simple surgical isolation of pulmonary veins for treating secondary atrial fibrillation in mitral valve disease. *Ann Thorac Surg* 2002;73(4):1169–73.
36. Deneke T, Khargi K, Grewe PH, et al. Left atrial versus bi-atrial Maze operation using intraoperatively cooled-tip radiofrequency ablation in patients undergoing open-heart surgery: safety and efficacy. *J Am Coll Cardiol* 2002;39(10):1644–50.
37. Barnett SD, Ad N. Surgical ablation as treatment for the elimination of atrial fibrillation: a meta-analysis. *J Thorac Cardiovasc Surg* 2006;131(5):1029–35.
38. Usui A, Inden Y, Mizutani S. Repetitive atrial flutter as a complication of the left-sided simple maze procedure. *Ann Thorac Surg* 2002;73:1457–9.
39. Cox JL, Schuessler RB, Boineau JP. The development of the Maze procedure for the treatment of atrial fibrillation. *Semin Thorac Cardiovasc Surg* 2000;12(1):2–14.
40. McCarthy PM, Gillinov AM, Castle L, et al. The Cox-Maze procedure: the Cleveland Clinic experience. *Semin Thorac Cardiovasc Surg* 2000;12(1):25–9.
41. Schaff HV, Dearani JA, Daly RC, et al. Cox-Maze procedure for atrial fibrillation: Mayo Clinic experience. *Semin Thorac Cardiovasc Surg* 2000;12(1):30–7.
42. Prasad SM, Maniar HS, Camillo CJ, et al. The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. *J Thorac Cardiovasc Surg* 2003;126(6):1822–8.
43. Gillinov AM. Ablation of atrial fibrillation in mitral valve surgery. *Curr Opin Cardiol* 2005;20:107–14.
44. Gillinov AM, Sirak JH, Blackstone EH. The Cox maze procedure in mitral valve disease: predictors of recurrent atrial fibrillation. *J Thorac Cardiovasc Surg* 2005;130:1653–60.
45. Reston JT, Shuhaiber JH. Meta-analysis of clinical outcomes of maze-related surgical procedures for medically refractory atrial fibrillation. *Eur J Cardiothorac Surg* 2005;28(5):724–30.
46. Richter B, Gwechenberger M, Socas A, et al. Frequency of recurrence of atrial fibrillation within 48 hours after ablation and its impact on long-term outcome. *Am J Cardiol* 2008;101(6):843–7.
47. Scherer M, Dzemali O, Aybek T. Impact of left atrial size reduction on chronic atrial fibrillation in mitral valve surgery. *J Heart Valve Dis* 2003;12:469–74.
48. Gaynor SL, Schuessler RB, Bailey MS, et al. Surgical treatment of atrial fibrillation: predictors of late recurrence. *J Thorac Cardiovasc Surg* 2005;129(1):104–11.
49. Isobe F, Kawashima Y. The outcome and indications of the Cox maze III procedure for chronic atrial fibrillation with mitral valve disease. *J Thorac Cardiovasc Surg* 1998;116:220–7.
50. Kosakai Y, Kawaguchi AT, Isobe F, et al. Modified maze procedure for patients with atrial fibrillation undergoing simultaneous open heart surgery. *Circulation* 1995;92(9 Suppl):II359–64.
51. Chen MC, Chang JP, Guo GB, et al. Atrial size reduction as a predictor of the success of radiofrequency maze procedure for chronic atrial fibrillation in patients undergoing concomitant valvular surgery. *J Cardiovasc Electrophysiol* 2001;12(8):867–74.
52. Kim YH, Lee SC, Her AY, et al. Preoperative left atrial volume index is a predictor of successful sinus rhythm restoration and maintenance after the maze operation. *J Thorac Cardiovasc Surg* 2007;134(2):448–53.
53. Marui A, Nishina T, Tambara K, et al. A novel atrial volume reduction technique to enhance the Cox maze procedure: initial results. *J Thorac Cardiovasc Surg* 2006;132(5):1047–53.
54. Lee JW, Park NH, Choo SJ. Surgical outcome of the maze procedure for atrial fibrillation in mitral valve disease: rheumatic versus degenerative. *Ann Thorac Surg* 2003;75:57–61.
55. Jatene MB, Marcial MB, Tarasoutchi F. Influence of the maze procedure on the treatment of rheumatic atrial fibrillation - evaluation of rhythm control and

- clinical outcome in a comparative study. *Eur J Cardiothorac Surg* 2000;17:117–24.
56. Handa N, Schaff HV, Morris JJ. Outcome of valve repair and the Cox maze procedure for mitral regurgitation and associated atrial fibrillation. *J Thorac Cardiovasc Surg* 1999;118:628–35.
 57. Cox JL, Ad N, Palazzo T. Impact of the maze procedure on the stroke rate in patients with atrial fibrillation. *J Thorac Cardiovasc Surg* 1999;118:833–40.
 58. Gillinov AM, Blackstone EH, McCarthy PM. Atrial fibrillation: current surgical options and their assessment. *Ann Thorac Surg* 2002;74(6):2210–7.
 59. Gillinov AM, McCarthy PM. Advances in the surgical treatment of atrial fibrillation. *Cardiol Clin* 2004;22:147–57.
 60. Gillinov AM, McCarthy PM, Marrouche N, et al. Contemporary surgical treatment for atrial fibrillation. *Pacing Clin Electrophysiol* 2003;26(7 Pt 2):1641–4.
 61. Raman J, Ishikawa S, Storer MM. Surgical radiofrequency ablation of both atria for atrial fibrillation: results of a multicenter trial. *J Thorac Cardiovasc Surg* 2003;126:1357–66.
 62. Sie HT, Beukema WP, Elvan A. Long-term results of irrigated radiofrequency modified maze procedure in 200 patients with concomitant cardiac surgery: six years experience. *Ann Thorac Surg* 2004;77:512–6.
 63. Luria DM, Nemecek J, Etheridge SP. Intra-atrial conduction block along the mitral valve annulus during accessory pathway ablation: evidence for a left atrial "isthmus". *J Cardiovasc Electrophysiol* 2001;12:744–9.
 64. Saltman AE, Rosenthal LS, Francalancia NA, et al. A completely endoscopic approach to microwave ablation for atrial fibrillation. *Heart Surg Forum* 2003;6(3):E38–41.
 65. Reade CC, Johnson JO, Bolotin G, et al. Combining robotic mitral valve repair and microwave atrial fibrillation ablation: techniques and initial results. *Ann Thorac Surg* 2005;79(2):480–4.
 66. Salenger R, Lahey SJ, Saltman AE. The completely endoscopic treatment of atrial fibrillation: report on the first 14 patients with early results. *Heart Surg Forum* 2004;7(6):E555–8.
 67. Pruitt JC, Lazzara RR, Dworkin GH, et al. Totally endoscopic ablation of lone atrial fibrillation: initial clinical experience. *Ann Thorac Surg* 2006;81(4):1325–30 [discussion 1330–21].
 68. Bisleri G, Manzato A, Argenziano M, et al. Thoracoscopic epicardial pulmonary vein ablation for lone paroxysmal atrial fibrillation. *Europace* 2005;7(2):145–8.
 69. Wolf RK, Schneeberger EW, Osterday R, et al. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. *J Thorac Cardiovasc Surg* 2005;130(3):797–802.
 70. Cox JL, Ad N. The importance of cryoablation of the coronary sinus during the Maze procedure. *Semin Thorac Cardiovasc Surg* 2000;12:20–4.
 71. Nath S, Lynch C 3rd, Whyne JG, et al. Cellular electrophysiological effects of hyperthermia on isolated guinea pig papillary muscle. Implications for catheter ablation. *Circulation* 1993;88(4):1826–31.
 72. Lustgarten DL, Keane D, Ruskin J. Cryothermal ablation: mechanism of tissue injury and current experience in the treatment of tachyarrhythmias. *Prog Cardiovasc Dis* 1999;41(6):481–98.
 73. Khargi K, Hutten BA, Lemke B, et al. Surgical treatment of atrial fibrillation; a systematic review. *Eur J Cardiothorac Surg* 2005;27(2):258–65.
 74. Gillinov AM, Pettersson G, Rice TW. Esophageal injury during radiofrequency ablation for atrial fibrillation. *J Thorac Cardiovasc Surg* 2001;122(6):1239–40.
 75. Doll N, Borger MA, Fabricius A, et al. Esophageal perforation during left atrial radiofrequency ablation: is the risk too high? *J Thorac Cardiovasc Surg* 2003;125(4):836–42.
 76. Manasse E, Medici D, Ghiselli S, et al. Left main coronary arterial lesion after microwave epicardial ablation. *Ann Thorac Surg* 2003;76(1):276–7.
 77. Ohara K, Hirai T, Fukuda N, et al. Relation of left atrial blood stasis to clinical risk factors in atrial fibrillation. *Int J Cardiol* 2008.
 78. Mobius-Winkler S, Schuler GC, Sick PB. Interventional treatments for stroke prevention in atrial fibrillation with emphasis upon the WATCHMAN device. *Curr Opin Neurol* 2008;21(1):64–9.
 79. Hur J, Kim YJ, Nam JE, et al. Thrombus in the left atrial appendage in stroke patients: detection with cardiac CT angiography—A preliminary report. *Radiology* 2008;249:81–7.
 80. Johnson WD, Ganjoo AK, Stone CD. The left atrial appendage: our most lethal human attachment! Surgical implications. *Eur J Cardiothorac Surg* 2000;17:718–22.
 81. Garcia-Fernandez MA, Perez-David E, Quiles J. Role of left atrial appendage obliteration in stroke reduction in patients with mitral valve prosthesis: a transesophageal echocardiographic study. *J Am Coll Cardiol* 2003;42:1253–8.
 82. Rosenzweig BP, Katz E, Kort S. Thromboembolus from a ligated left atrial appendage. *J Am Soc Echocardiogr* 2001;14:396–8.
 83. Gillinov AM, Pettersson G, Cosgrove DM. Stapled excision of the left atrial appendage. *J Thorac Cardiovasc Surg* 2004;129:679–80.
 84. Kamohara K, Fukamachi K, Ootaki Y. A novel device for left atrial appendage exclusion. *J Thorac Cardiovasc Surg* 2005;130:1639–44.

85. Kamohara K, Fukamachi K, Ootaki Y, et al. Evaluation of a novel device for left atrial appendage exclusion: the second-generation atrial exclusion device. *J Thorac Cardiovasc Surg* 2006;132(2):340–6.
86. Salzberg SP, Gillinov AM, Anyanwu A, et al. Surgical left atrial appendage occlusion: evaluation of a novel device with magnetic resonance imaging. *Eur J Cardiothorac Surg* 2008;34:766–70.
87. Saltman AE, Virmani R, Mohan A. Development and testing of a novel device for left atrial appendage occlusion. Kos, Greece: International Society for Cardiothoracic Surgery; 2008.
88. Pacifico A, Henry PD. Ablation for atrial fibrillation: are cures really achieved? *J Am Coll Cardiol* 2004;43:1940–2.
89. Gillinov AM, McCarthy PM, Blackstone EH. Surgical ablation of atrial fibrillation with bipolar radiofrequency. *J Thorac Cardiovasc Surg* 2004;129:1322–9.
90. Shemin RJ, Cox JL, Gillinov AM, et al. Guidelines for reporting data and outcomes for the surgical treatment of atrial fibrillation. *Ann Thorac Surg* 2007;83(3):1225–30.
91. Gillinov AM, Saltman AE. Ablation of atrial fibrillation with concomitant cardiac surgery. *Semin Thorac Cardiovasc Surg* 2007;19(1):25–32.
92. Gillinov AM. Advances in surgical treatment of atrial fibrillation. *Stroke* 2007;38(Suppl 2):618–23.
93. Loulmet DF, Patel NC, Jennings JM, et al. Less invasive intracardiac surgery performed without aortic clamping. *Ann Thorac Surg* 2008;85(5):1551–5.
94. Umakanthan R, Leacche M, Petracek MR, et al. Safety of minimally invasive mitral valve surgery without aortic cross-clamp. *Ann Thorac Surg* 2008;85(5):1544–9 [discussion 1549–50].
95. Greco E, Zaballos JM, Alvarez L, et al. Video-assisted mitral surgery through a micro-access: a safe and reliable reality in the current era. *J Heart Valve Dis* 2008;17(1):48–53.
96. Mohamed KS. Minimally invasive right posterior minithoracotomy for open-heart procedures. *Asian Cardiovasc Thorac Ann* 2007;15(6):468–71.
97. Doll N, Kiaii BB, Fabricius AM, et al. Intraoperative left atrial ablation (for atrial fibrillation) using a new argon cryocatheter: early clinical experience. *Ann Thorac Surg* 2003;76(5):1711–5.
98. Mohr FW, Fabricius AM, Falk V, et al. Curative treatment of atrial fibrillation with intraoperative radiofrequency ablation: Short-term and midterm results. *J Thorac Cardiovasc Surg* 2002;123(5):919–27.
99. Edgerton JR, Edgerton ZJ, Weaver T, et al. Minimally invasive pulmonary vein isolation and partial autonomic denervation for surgical treatment of atrial fibrillation. *Ann Thorac Surg* 2008;86(1):35–8 [discussion 39].
100. Wolf RK. Minimally invasive surgical treatment of atrial fibrillation. *Semin Thorac Cardiovasc Surg* 2007;19(4):311–8.
101. Matsutani N, Takase B, Ozeki Y, et al. Minimally invasive cardiothoracic surgery for atrial fibrillation: a combined Japan-US experience. *Circ J* 2008;72(3):434–6.
102. Pruitt JC, Lazzara RR, Ebra G. Minimally invasive surgical ablation of atrial fibrillation: the thoracoscopic box lesion approach. *J Interv Card Electrophysiol* 2007;20(3):83–7.
103. Gillinov AM, Saltman AE. Surgical approaches for atrial fibrillation. *Med Clin North Am* 2008;92(1):203–15, xii.
104. Gillinov AM, Svensson LG. Ablation of atrial fibrillation with minimally invasive mitral surgery. *Ann Thorac Surg* 2007;84(3):1041–2.
105. Moten SC, Rodriguez E, Cook RC, et al. New ablation techniques for atrial fibrillation and the minimally invasive cryo-maze procedure in patients with lone atrial fibrillation. *Heart Lung Circ* 2007;(16 Suppl 3):S88–93.
106. Suwalski P, Suwalski G, Wilimski R, et al. Minimally invasive off-pump video-assisted endoscopic surgical pulmonary vein isolation using bipolar radiofrequency ablation—preliminary report. *Kardiologia Pol* 2007;65(4):370–4 [discussion 375–6].
107. Saltman AE. Minimally invasive surgery for atrial fibrillation. *Semin Thorac Cardiovasc Surg* 2007;19(1):33–8.