Perspective

Maze permutations during minimally invasive mitral valve surgery

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Surgical ablation for atrial fibrillation is most frequently done in the concomitant setting, and most commonly with mitral valve surgery. Minimally invasive surgical techniques for the treatment of atrial fibrillation have developed contemporaneously with techniques for minimally invasive mitral valve surgery. As in traditional surgery for atrial fibrillation, there are many different permutations of ablations for the less invasive approaches. Lesion sets can vary from simple pulmonary vein isolation (PVI) to full bi-atrial lesions that completely reproduce the traditional cut-and-sew Cox Maze III procedure with variable efficacy in restoring sinus rhythm. Additionally, treatment of the atrial appendage can be done through minimally invasive approaches without any ablation at all in an attempt to mitigate the risk of stroke. Finally, hybrid procedures combining minimally invasive surgery and catheter-based ablation are being developed that might augment surgical treatment of atrial fibrillation at the time of minimally invasive mitral valve repair. These various permutations and their results are reviewed.

Keywords: Atrial fibrillation; mitral valve surgery; minimally invasive; ablation

Submitted Aug 25, 2015. Accepted for publication Sep 21, 2015.
doi: 10.3978/j.issn.2225-319X.2015.09.07
View this article at: http://dx.doi.org/10.3978/j.issn.2225-319X.2015.09.07

Introduction

Atrial fibrillation is the most common arrhythmia, with a prevalence of 1-2% and an increasing prevalence in recent studies (1,2). It remains a significant healthcare burden, and is independently associated with increased morbidity from stroke and increased mortality (3). Atrial fibrillation is a common comorbidity of patients with mitral valve disease, present in over a third of all patients referred for mitral valve surgery. Evidence continues to accumulate demonstrating benefit in quality of life, increased freedom from stroke, and decreased mortality in patients that are in sinus rhythm after mitral valve surgery (4). As a result, clinical practice guidelines from multiple cardiology and cardiac surgical societies recommend concomitant treatment of atrial fibrillation at the time of mitral valve surgery (5,6).

Surgical techniques and technologies for minimally invasive treatment of mitral valve disease and atrial fibrillation have significant overlap. As techniques and experience with minimally invasive mitral valve repair have developed, so has experience with minimally invasive ablation of atrial fibrillation. Accordingly, the minimally invasive treatment of mitral valve disease represents a prime opportunity to improve the quality of life, freedom from stroke, and decrease the mortality of patients with atrial fibrillation. As in traditional sternotomy approaches to atrial fibrillation surgery, there are a variety of treatment options during minimally invasive surgery, with differing efficacies and degrees of complexity. These can be divided into three broad categories: treatment of the left atrial appendage alone, pulmonary vein isolation (PVI) alone, and a full Cox-Maze lesion set. Recently, hybrid approaches to atrial fibrillation combining minimally invasive surgical techniques with catheter ablation have been developed. Although these techniques are not typically combined with concomitant valve surgery, they might be applied in the concomitant setting in future studies, and merit discussion.

Left atrial appendage

In the spectrum of possible treatments for atrial fibrillation, treatment of the left atrial appendage represents a least

invasive adjunct to minimally invasive mitral valve surgery.

The significance of the left atrial appendage and the risk of stroke is well documented (7). Minimally invasive exclusion or amputation of the left atrial appendage was developed prior to catheter-based treatment of the left atrial appendage and has been in practice since the initial efforts to make the Cox Maze procedure less invasive. Wolf and colleagues described bilateral thoracoscopic PVI with surgical stapler excision of the left atrial appendage in 2005 (8). Initial experience in the open setting was with surgical stapling or oversewing (9). Surgical clips were subsequently developed to address the risk of staple misfire and subsequent complications related to bleeding from a friable, incompletely controlled left atrial appendage stump. The initial experience with the AtriClip, a surgical clip, demonstrated high efficacy in excluding blood flow to the left atrial appendage and minimal extra risk to the patient during concomitant operative procedures (10). Although this trial did not demonstrate a reduction in stroke, subsequent trials in the interventional cardiology literature have demonstrated at least non-inferiority of LAA occlusion when compared to warfarin therapy, the standard in treating non-valvular atrial fibrillation (11).

Another strategy easily applied during minimally invasive mitral surgery is oversewing of the left atrial appendage from inside the heart. Meticulous technique is of utmost importance when using this approach, as long-term durability of left atrial appendage exclusion is extremely variable among surgeons, even within clinical trials performed to evaluate the benefit of treating the left atrial appendage during concomitant surgery (12). Moreover, an incompletely ligated appendage may lead to increased thromboembolic events (13).

Pulmonary vein isolation (PVI)

PVI with minimally invasive techniques has been an available treatment modality for surgeons for at least a decade. Typically, a bipolar radiofrequency clamp is used to isolate the left and right pulmonary veins separately. The first reports of this technique described a bilateral thoracoscopic approach, interestingly on patients placed in the left lateral decubitus position without intraoperative repositioning (8). These techniques can be done off-pump, and as such, could be integrated into a minimally invasive mitral operation in the period of time before going on bypass.

Results have been mixed with PVI alone. Short-term success is achievable, but few reports of long-term, greater than 1 year, efficacy have been reported. Freedom from atrial fibrillation after thoracoscopic PVI is between 60% and 75% at 6 months to one year, and greater success is reported largely in patients with paroxysmal atrial fibrillation (14,15). The results are much worse in patients with greater burden of atrial fibrillation. At 5 years, the success rate drops to 28% in patients with persistent or long-standing persistent atrial fibrillation (14).

Adjunctive procedures have included left atrial appendage occlusion or excision as already discussed and targeted ablation of ganglionated plexi (GP) felt to be involved in vagal innervation of the heart. No randomized trial has been performed to evaluate the added benefit of this additional ablation, and long-term results are not reported with PVI and GP ablation. There is laboratory evidence that ablation of GP may yield changes in electrophysiology in the short term, but re-innervation of the heart often occurs, negating the effect of GP ablation, as short as 30 days postoperatively (16). Furthermore, in a multicenter retrospective review of 519 patients undergoing the Cox Maze IV, the addition of GP ablation made no difference in the freedom from atrial fibrillation after a median follow up of 36.7 months (17). Thus, GP ablation is only routinely applied at a few centers with mixed results, and has not improved the results of PVI.

Cox maze procedure

There is greater experience with the full Cox-Maze lesion set, in both traditional approaches and recently with minimally invasive approaches. The Cox Maze procedure was originally developed in 1987 by Dr. James Cox at Washington University in Saint Louis. It involved a set of incisions designed to create lines of conduction block on the atrium in a pattern such that the reentrant circuits thought to be responsible for AF would be disrupted while leaving a pathway for normal sinus conduction (18). At the turn of the century, several technologies evolved to replace these incisions with lines of ablation, simplifying the procedure and increasing the use of the Cox Maze procedure. Due to the ease of use of these ablative technologies, mainly cryoablation and bipolar, clamp-based radiofrequency energy, adaptation of these techniques to minimally invasive techniques was inevitable.

There is growing experience with the Cox Maze procedure in the minimally invasive setting. The Washington University group utilizes both radiofrequency clamps and cryoablation to perform the ablation-based Cox-Maze IV with excellent results. This group reported

their experience in the midterm in 2014, demonstrating equivalent efficacy with a minimally invasive technique and traditional sternotomy approach, with a 74% freedom from atrial arrhythmias off antiarrhythmic drugs at two years of follow up (19). Half of this population had a concomitant mitral valve procedure. Dr. Ad and colleagues use mainly cryothermy alone, but also combine cryothermy and RF ablation. In their experience with minimally invasive techniques, albeit in lone AF, they achieve 80% freedom from atrial arrhythmias at 3 years of follow up (20). This group, when reporting the sum total of their experience including concomitant mitral procedures and minimally invasive techniques, achieve similar two-year rates of success, at 80% (21). These two groups have the largest experience with minimally invasive Cox Maze procedures.

The success rate at other centers is similar, at least in small numbers and in early follow up. Park *et al*. reported 87% success for a group of 47 patients at two years following minimally invasive mitral surgery with biatrial cryoablation (22). The group at the University of Maryland included a small cohort of patients with a minimally invasive approach in their study of cryoablation-assisted Cox Maze procedures in the concomitant setting, demonstrating 76% freedom from atrial fibrillation at one year (23). Particularly noteworthy in all these series is the high proportion of patients with long-standing persistent atrial fibrillation. It is thought that the full Cox Maze lesion set is the most effective in treating this difficult patient population.

When performed by experienced hands, the Cox Maze produces excellent rates of freedom from AF in the minimally invasive setting. Surgeons must be careful and complete when performing a Cox Maze on their patients. The definition of a surgical Maze ablation procedure is very specific. The Heart Rhythm Society consensus statement defines it as an ablation procedure that includes right-sided lesions, including the tricuspid isthmus, and left-sided lesions that include isolation of the posterior left atrium and pulmonary veins with a line to the mitral valve, the mitral isthmus. Additionally, the left atrial appendage must be addressed (5). When these principles are followed, the concomitant ablation of AF can effectively restore sinus rhythm.

Left atrial lesion sets

A large proportion of surgical ablation for atrial fibrillation performed by cardiac surgeons does not involve a full bi-atrial Cox Maze lesion set. Instead, a left lesion set is used. Many surgeons leave out the right atrial lesions, believing that this limits the rate of post-maze permanent pacemaker insertion; however, this has never been demonstrated in a randomized, control trial. Furthermore, a meta-analysis in 2006 by Ad *et al.* concluded that bi-atrial lesion sets offered higher efficacy (24). Despite this, left-sided lesion sets are common, and the literature is replete with case series since 2006 examining their effectiveness. With current technologies and techniques, these lesion sets can be readily applied at the time of concomitant mitral valve surgery without the need to open the right atrium.

The results with isolated left atrial lesion sets are variable, but good short-term results can be achieved. In a small study utilizing monopolar radiofrequency, Oueida and colleagues demonstrated 88.5% rate of sinus rhythm at one year after concomitant mitral valve surgery in 52 patients (25). Sternik and colleagues reported 85% freedom from atrial fibrillation and antiarrhythmic drugs at 2 years in a series of 53 patients, 61% of who had concomitant mitral surgery (26). Phan and colleagues performed a meta-analysis of all randomized, controlled trials of surgical ablation during mitral valve surgery in 2014 (27). Only nine total trials were identified, and almost half of these trials reported the results of left atrial lesion sets alone. The success rate overall was 76% at one year but ranged from 44% to 95% in the trials involving only left-sided lesion sets.

Similarly, the exact lesions of a left-sided lesion set vary from study to study. Starting from PVI, most authors currently create a box around the posterior left atrium and include a line to the mitral annulus, across the mitral isthmus to prevent left-sided atrial flutter (25,26,28). Another common addition is a line of ablation to the base of a ligated or excised left atrial appendage (29). A common theme is the necessity to isolate a box of posterior left atrial tissue to include the pulmonary veins and an ablation across the mitral isthmus to prevent left-sided flutter.

Left atrial volume reduction

Increased left atrial size is a known risk factor for recurrent atrial fibrillation (30). Because of this, some groups have proposed left atrial reduction as part of the surgical treatment of atrial fibrillation. With an open left atrium at the time of mitral surgery, it is relatively easy to excise atrial tissue at the time of surgery. In a relatively large study out of Thailand, a single surgeon performing concomitant Maze procedures at the time of mitral valve surgery demonstrated greater freedom from atrial fibrillation after left atrial reduction (4). In this study, overall freedom from

AF was 79.4% at 5 years, with a rate of 88% if postoperative left atrial size was ≤50 mm and only 44% if >50 mm. Remarkably, patients with rheumatic disease comprised a large fraction of the patients in this study.

Hybrid ablation

Hybrid ablation represents a natural evolution in the minimally invasive approach to atrial fibrillation. Developed to avoid cardiopulmonary bypass and aortic cross-clamping, hybrid ablation procedures typically involve a surgical PVI with bipolar radiofrequency clamps via a thoracoscopic approach followed by endocardial, catheter-based ablation to create additional lines of ablation. These can be used to complete the box isolation of the posterior left atrium, ablate the mitral isthmus to prevent left-sided flutter, and even to create right-sided lesions. This is an important advantage for surgeons unwilling to open the right atrium during minimally invasive mitral valve surgery, as right-sided atrial flutter was found to be the mode of failure in over 20% of such cases in a mapping study of patients who had undergone surgical AF ablation (31).

The efficacy of a hybrid approach has not been well established. Some groups are able to achieve high rates of success, but others have not. In one series, largely comprised of patients with paroxysmal atrial fibrillation, patients had only a 52% freedom from AF off antiarrhythmics at one year compared to 87.5% for the patients who had a traditional cut-and-sew maze in the same study (32). In contrast, two studies from Europe, where experience is greater with hybrid treatment, have demonstrated as high as 91% freedom from AF, off antiarrhythmic drugs (33,34). In experienced hands, and with appropriate patient selection, this minimally invasive modality is an attractive alternative to traditional surgical ablation.

As an adjunct to minimally invasive mitral valve surgery, the hybrid approach is not the intuitive choice initially. With an open atrium and arrested heart, it makes little sense to leave ablation to a catheter for creating left atrial lines. The techniques and approach of the hybrid operators, however, could be used to maximally treat mitral valve patients with concomitant AF. Some centers in Europe have a staged hybrid approach where a minimally invasive surgical PVI is performed followed by an interval catheter-based ablation (34). This approach could easily be adapted to increase the success of concomitant surgical ablation, especially if limited lesion sets are performed at the time of surgery where there might be concerns of extra morbidity due to prolonged cross clamp times in high-risk patients and where there may be limited exposure due to minimally invasive access. Although not specifically called a hybrid approach, a German electrophysiology group ablated a group of patients with failed surgical ablation postoperatively. In these patients who had failed surgical ablation, this group was able to reverse the failure and achieved 87% freedom from atrial fibrillation at a mean follow-up of 18 months after catheter ablation (31). A hybrid approach might be necessary to completely treat patients with complex atrial fibrillation and mitral valve disease.

Conclusions

Concomitant surgical treatment of atrial fibrillation can range in complexity from simple left atrial appendage ligation to the full Cox Maze lesion set. These options have varying difficulty and differing efficacy, but represent a wide range of choices available to the minimally invasive mitral surgeon to help patients with atrial fibrillation. Results are probably better in the surgical literature with a full biatrial lesion set, and Dr. James Cox himself supports this (35). Results with left atrial lesion sets can also be good in the short term. With the advent of hybrid ablation techniques and technology, an initial PVI could be performed in the operating room, for example in a high-risk surgical patient where aortic cross clamp time should be minimized. Subsequent catheter-based intervention could then be used to achieve higher rates of freedom from AF such as those achieved in early hybrid series. This requires that the surgeon and electrophysiologist and cardiologist work with a common goal of treating both the mitral valve disease and atrial fibrillation with equal fervor.

Minimally invasive mitral valve surgery represents a prime opportunity for cardiac surgeons to intervene in a meaningful way on a common disease with great associated comorbidity. Although randomized controlled studies demonstrating mortality benefit from concomitant ablation of atrial fibrillation have not been reported, ongoing follow-up of randomized trials may demonstrate this in the future. However, the benefits for patient quality of life, symptoms, and stroke have been repeatedly demonstrated in retrospective follow up of patients undergoing concomitant mitral valve surgery (36-38). With an open left atrium, a mandatory aspect of mitral valve surgery, performing a full Cox-Maze procedure seems like a natural adjunct. Despite this, the rate of concomitant ablation of atrial fibrillation is low. In an analysis of the Society of Thoracic Surgeons (STS) database, Ad and colleagues noted a downward trend in the percentage of patients receiving a concomitant ablation,

despite the increased proportion of patients presenting for cardiac surgery with atrial fibrillation between 2005 and 2010 (39). Forty percent of patients undergoing isolated mitral valve surgery in 2010 who had atrial fibrillation had no attempt at surgical ablation. In an earlier study of the STS database, Gammie and colleagues found no increase in operative mortality when a concomitant ablation was added, even after propensity matching for operative risk (40). Thus, there should be no hesitation when a cardiothoracic surgeon is presented with a mitral valve patient who also has atrial fibrillation. The opportunity to address this highly morbid condition should not be lost.

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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Cite this article as: Lee AM. Maze permutations during minimally invasive mitral valve surgery. Ann Cardiothorac Surg 2015;4(5):463-468. doi: 10.3978/j.issn.2225-319X.2015.09.07

