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Surgical Management of Atrial Fibrillation

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1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia in adults and a major burden of morbidity and mortality in cardiovascular patients (1). The major sequelae are cardiovascular and include heart failure and thromboembolic events, primarily stroke. The prevalence of AF is 0.4-1% in the overall population which rises with age to approximately 15% in those patients 70 years and older (2). The incidence of AF is rising due in part to the increase in the aging population, increase in those living with structural cardiovascular pathology and more frequent diagnosis from the use of ambulatory monitoring devices. Overall, AF affects more than 2.5 million adult in the US and 200,000 to 250,000 in Canada (Heart and Stroke Foundation of Canada statistics; http://www.heartandstroke.com). Overall, this represents a considerable burden of illness in vulnerable populations such as the elderly and those with congestive heart failure.

The Framingham Study found that development of chronic AF was associated with a two-fold increase in mortality from cardiovascular disease (2). Furthermore, AF was an independent risk factor for mortality in this population (3). The risk of stroke with persistent AF is 8% per year and 2% per year with warfarin. This is balanced with a bleeding risk of 2% per year while on warfarin at an INR of 2-3 (4). Of 5070 patients in the Framingham Study followed for 34 years, a two-fold increase in stroke events were found with AF with higher rates in those with heart failure (5). The attributable risk of stroke increases with age from 1.5% for the youngest cohort (50-59 years) to 23.5% for the oldest cohort (80-89 years).

AF is defined based on the clinical presentation, relevant patient characteristics and any associated cardiac pathology. There is considerable variation in the descriptors for types of atrial fibrillation. These include acute, chronic, long-standing, sustained, recurrent, and so forth. The Society of Thoracic Surgeons (STS) has published reporting guidelines to facilitate consistency in reporting which include classification of AF as paroxysmal, persistent and permanent; duration of arrhythmia and patient burden (percentage of overall time in AF) as well as previous interventions and relevant patient characteristics such as association with cardiac pathology (6). The European Society of Cardiology differs in that for AF lasting greater than 1 year, patients undergoing a rhythm control strategy have longstanding persistent AF whereas patients who have accepted the arrhythmia and are not therefore treated with rhythm control therapy have permanent AF. Table 1 provides the descriptors and definitions of AF utilized in this chapter.

AF Subtypes	Definition
Paroxysmal*	>2 episodes, duration < 7 days, spontaneous termination
Persistent*	> 7 days or requires cardioversion
Longstanding Persistent	>1 year with rhythm control treatment; failed or no cardioversion
Permanent	> 1 year without rhythm control treatment
Primary / Lone	Not associated with cardiac pathology, usually MR
Secondary / Concomitant	Associated with cardiac pathology
Post-Operative	Post-cardiac surgery, usually transient

MR, mitral regurgitation
* Characterized by the most frequent presentation

Table 1. Definition of AF Subtypes

Electrophysiologically, AF is characterized by irregular and uncoordinated atrial activation caused by macro re-entry circuits in left and right atria. In paroxysmal AF, 90% of micro re-entry circuits or triggers exist in close proximity to the pulmonary veins (in the context of mildly dilated atria) which trigger large macro-reentrant circuits (7). This is the basis for pulmonary vein isolation (PVI). There is however evidence for extrapulmonary vein sites for initiation of AF which include superior vena cava (8), ligament of Marshall (9), left atrial (LA) posterior wall (10,11), coronary sinus, crista terminalis, interatrial septum, and LA appendage (LAA) (12). An important caveat is that most mapping studies have been performed in lone AF cases and may not be reflective of concomitant AF, particularly in atria with significant structural alterations. Atrial fibrillation may be conceptualized as a spectrum of severity. Paroxysmal AF resulting from macro reentry circuits in the absence of major tissue remodeling. If untreated, this may progress to persistent and then permanent AF with substrate alterations associated with atrial structural remodeling (Figure 1). These later stages of AF may not be sufficiently addressed with PVI and may require a more extensive procedure, to be discussed in later sections.

Patients with concomitant AF may have associated mitral pathology and possibly other valvulopathy as well as coronary disease. This is relevant as the atrial tissue is rendered susceptible to AF secondary to atrial stretch or damage, resulting in loss of myocardium and replacement fibrosis (13). The ultimate end result is electrical remodeling and shortened refractory periods (14). In fact, left atrial size may be utilized as a surrogate marker for atrial remodeling. There also exists some evidence for a role of proinflammatory signaling as seen with active valvular or coronary disease and/or dysfunction of sinoatrial and atrioventricular nodes in AF development (15).

Medical management of AF is based on rate or rhythm control as well as anticoagulation for stroke prevention. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial, a 4060 patient multicentered randomized controlled trial demonstrated no survival difference between rate and rhythm control at 3.5 years, although rate control was associated with fewer adverse events (16). Anticoagulation has been traditionally accomplished with warfarin (INR 2-3) for stroke prophylaxis but is associated with bleeding events. More recently, anticoagulation with the direct thrombin inhibitor dabigatran has shown similar stroke prevention rates with lower bleeding events and without the need for INR monitoring (17).

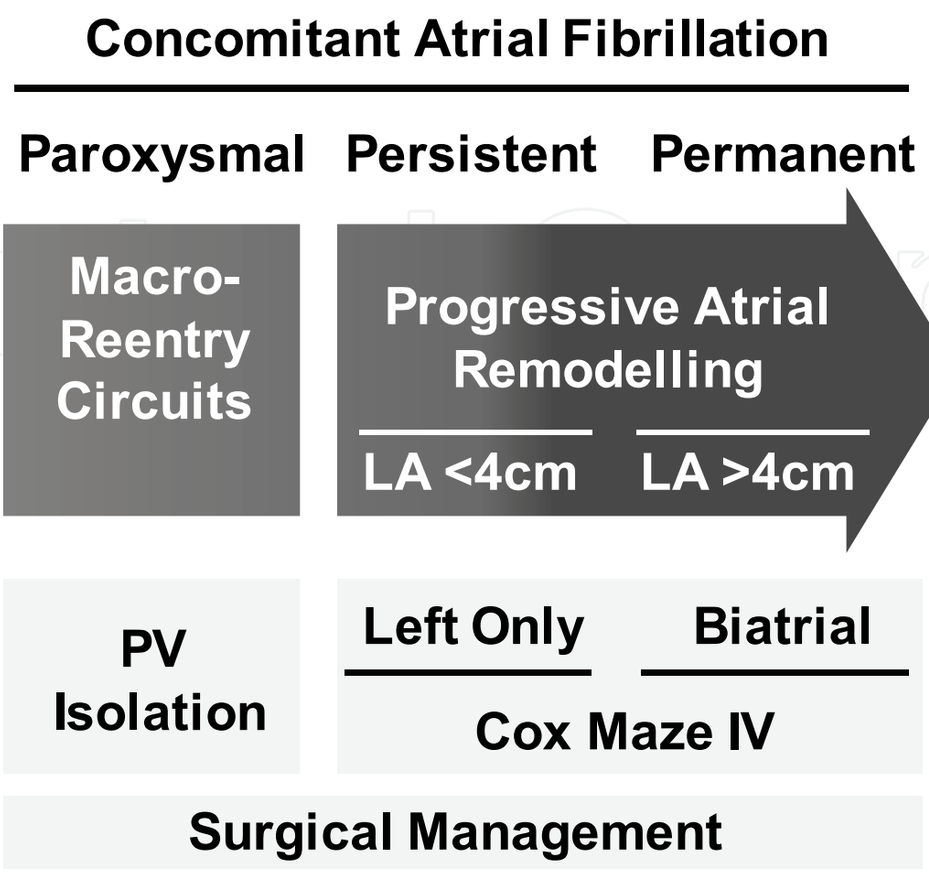


Fig. 1. Pathophysiology and surgical management of concomitant AF. Atrial fibrillation may be described clinically as paroxysmal, persistent or permanent, which is associated with macro reentry circuits plus progressive left atrial remodeling. Surgical management of paroxysmal AF may be limited to pulmonary vein isolation, but more chronic AF types require left-only or complete Maze IV lesion sets.

Another rhythm control strategy is interventional. Generally patients with lone AF who are refractory to medical management are initially considered for catheter ablation. This is best suited for patients with paroxysmal AF where pulmonary vein isolation (PVI) alone may address the ectopic foci. In patients with longstanding persistent or permanent AF, due to atrial substrate alterations, linear and ECG-guided extra pulmonary vein ablation may be necessary but even with these adjuncts, the success of less likely. The major limitation of this technology is inconsistent outcomes due to procedural failure and AF recurrence. For patients with paroxysmal AF, success is approximately 66% after a single procedure (18). Percutaneous LAA closure is also possible as an adjunct to ablation.

Several devices have been developed and tested for percutaneous LAA closure for thromboembolic prevention. In the prospective, randomized controlled trial PROTECT-AF, the WATCHMAN LAA closure device (Atritech, Plymouth, MN) was found to be non-inferior to warfarin alone for the composite endpoint of stroke, cardiovascular death, and systemic embolism (3.0 vs. 4.9/100 patient years) but hemorrhagic stroke was lower in the intervention group (19). There were, however, risk of procedural complications including

pericardial effusions and stroke, likely due to air embolism, and less commonly device embolization. Other devices used for percutaneous LAA closure include the PLAATO (Percutaneous LAA Transcatheter Occlusion) membrane-covered self-expandable nitinol cage system and the Amplatzer Septal Occluder (20,21).

2. Surgical management of atrial fibrillation

The underlying basis for surgical management of atrial fibrillation is *targeted synthesis of scar tissue which does not conduct electrical impulses*. We will consider surgical management of patients with primary or lone AF and those with concomitant valvular or coronary disease who are undergoing surgery and are being considered for adjunctive AF surgery.

Of patients with lone AF, those that failed one or more attempts at catheter ablation or those who prefer surgery based on superior published outcomes, are considered for surgical management. Lee et al (22) reviewed AF surgery and correctly identified that patients with lone AF are generally unwilling to undergo sternotomy to address AF alone. In such patients, a minimally-invasive approach to AF surgery offers a reasonable alternative. These approaches include PVI, minimally-invasive Cox-Maze IV procedure or beating heart epicardial ablation, all through a right thoracotomy.

More commonly, approximately half of patients with mitral valve disease have reported some degree of AF (23). The presence of AF increases mortality post-MV surgery. The cut-and-sew maze, also known as the Cox-maze III procedure, has been the gold standard AF surgical technique for sinus restoration (24). However, due to the morbidity of cut-and-sew atrial lesions including those related to bleeding and increased CPB and cross-clamp times, most centers opt for the use of alternative energy sources. For paroxysmal AF without significant atrial enlargement, PVI alone may be a reasonable adjunctive procedure. For patients with persistent or permanent AF, the full Maze IV lesion set offers highest chance of success at sinus restoration. Although other modified lesions sets such as the Cox Mini-Maze and left only-Maze procedure and others have been introduced, we will limit our discussion to the full Maze lesion set (25-27).

2.1 Surgical techniques

Ultimately the success of sinus restoration is dependent on the type and duration of AF, patient-specific and anatomical factors, and the successful creation of a transmural lesion set. Furthermore, for adjunctive procedures, the added surgical morbidity and mortality related to increased time on CPB and increased complications must be taken into consideration. All patients considered for AF surgery should have a careful assessment of their symptoms as well as transthoracic echocardiography for comprehensive assessment of left and right atrial anatomy.

2.1.1 Maze procedure

In 1987, Dr. Cox introduced the maze procedure and subsequently reported outcomes on the first seven patients who were free of AF (28). However, the original maze procedure was complicated by an inability to generate tachycardic response during exercise, left atrial dysfunction as well as surgical complexity and resulting long bypass and cross clamp times (29). Since that time, the maze has undergone several iterations. As mentioned, the Cox Maze III is the gold standard for AF surgery. The Cox-maze III procedure is associated with a higher incidence of sinus restoration, improved sinus node

function, fewer pacemaker requirements and improved atrial function compared with its predecessors. Importantly the Cox-Maze III has proven robust effectiveness in the setting of paroxysmal, persistent or permanent AF (30). Although this procedure has not been widely adopted, it is important to appreciate the lesion set which forms the basis of the Cox Maze IV procedure.

The Cox Maze III procedure is generally performed as an adjunct to a mitral procedure. The left-sided lesion set is performed at the time of MV repair/replacement via the left atriotomy, then the right-sided lesion set is performed on the beating heart at the time of patient rewarming. Briefly, the complete lesion set for the Maze III may be performed as follows: The LA is entered via the inter-atrial groove. 1) PVI is performed to prevent the macro-reentry circuits originating from the PVs. To accomplish this, the left atriotomy is extended in a circumferential fashion, until all pulmonary veins are encircled and the left atrium completely detached from its base. 2) Then the LAA is isolated to block re-entry circuits at its base. The LAA is excised and the remaining defect incorporated into the atriotomy closure. 3) The mitral line and coronary sinus (CS) lesion are created to block conduction originating from mitral orifice and the CS, respectively. The PV encircling incision is joined to the mitral annulus at its postero-medial aspect and the CS is spot cryoablated. 4) On the right side, the intercaval lesion circuits originate from the SVC and IVC. To block these circuits, the longitudinal atriotomy is fashioned along the free wall of the right atrium extending from the tricuspid annulus (atrioventricular groove) to the left atriotomy incision. 5) The right atrial counter lesion blocks signals originating from the RAA. A second incision is fashioned along the free wall of the RAA, once again originating at the level of the tricuspid annulus, however extending only partially along the wall of the atrium. The resulting island provides a conduction 'corridor' through which normal stimuli can travel. 6) The T-lesion blocks RA flutter waves and reentry circuits (31). The right atrial isthmus incision is created, once again, using cryoablation.

In cases of concomitant and continuous AF with normal RA size and no evidence of flutter waves, as the source is likely the LA, some groups have suggested that a left-only Maze may be sufficient. This would avoid a more complex operation with incision into the RA. However, the RA isthmus has been identified as a source of atrial flutter. As such, atrial flutter post-left Maze may necessitate additional right atrial catheter ablation (32). If the RA dimension is abnormal, the RA may support two of more macro reentrant circuits and a full Maze lesion set is recommended. Furthermore, a full Maze lesion set is recommended in cases where atrial flutter is present or when the RA is already opened.

In 2004, the Cox-maze IV was introduced which replaced most surgical incisions with alternative energy sources (33). This has significantly shortened cross-clamp times compared with the Cox-maze III (41min vs 93 min) with comparable short term freedom from AF (34). The lesion set of the Cox Maze IV is shown in Figure 2. On the left, the PVs are isolated and two linear ablation lines are used to create a box lesion. Voeller et al (35) found that a box lesion around all four PVs which completely isolates the posterior LA wall led to greater mid-term freedom from AF as opposed to isolation in pairs. The LAA is surgically removed but if performed through a right thoracotomy, the LAA is oversewn from the inside. The mitral line is created and the CS is cryoablated. On the right the intercaval lesion is created. Through the right atriotomy the counter lesion and T-lesion are created.

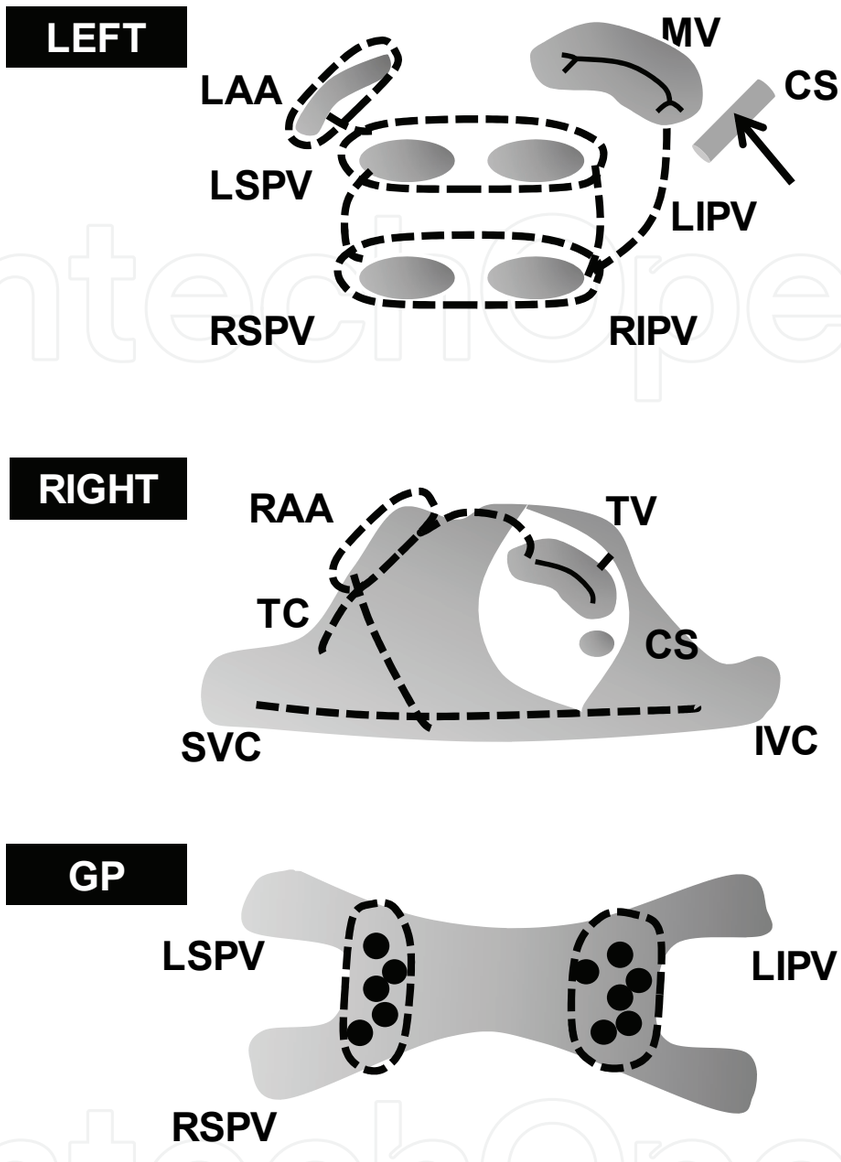


Fig. 2. Illustration of lesion sets for Cox-Maze IV and GP ablation. We illustrate left and right Maze IV lesions (dotted lines) as well as foci for GP (black circles) ablation.

There are several alternative energy sources for the Cox Maze IV at different stages of development and clinical evaluation (Table 2). The major problem with such devices is the challenge of reliably creating a transmural lesion due to loss of energy to circulating blood creating a 'heat sink'. The most commonly utilized ablation devices today are based on bipolar radiofrequency (RF) which addresses this challenge by focusing energy only in tissues between the jaws of the device, thereby eliminating surrounding blood. Radiofrequency can be delivered dry or saline-irrigated, the later may be more likely to deliver a transmural lesion by cooling the surface thereby creating a lesion of greater depth, however esophageal injury is a risk (36). With the use of any alternative energy source, it is important to use some confirmatory technique to ensure establishment of exit block.

Energy Source	Advantage	Disadvantage
High Intensity Frequency Ultrasound	Focused lesion Minimal 'heat sink'	Fixed penetration depth
Unipolar RF	May be irrigated/non-irrigated	Significant 'heat sink'
Bipolar RF	Energy focused between clamps - Minimal 'heat sink'	Costly
Microwave*		Significant 'heat sink' Inconsistent lesion
Cryoablation	Less damage to adjacent critical tissue Reusable probe	Slower Questionable transmurality
Laser*		Significant 'heat sink' Inconsistent lesion

*No longer in clinical use

Table 2. Alternative Energy Devices for Maze IV

2.1.2 Pulmonary vein isolation

The identification of AF triggers adjacent to the PVs is the rationale for PVI (7). This can be performed successfully by a sternotomy, a thoracotomy or completely thoracoscopically. A minimally-invasive procedure via bilateral minithoracotomies for paroxysmal AF is associated with 80.8% freedom from AF at 1 year (37). Thoracoscopic bilateral PVI and LAA exclusion has also been described for treatment of lone AF refractory to cathether ablation (38,39). For patients with concomitant, paroxysmal AF, PVI may be performed using a bipolar RF device to create two lesions separately encircling left and right pulmonary veins for patients undergoing MV repair or replacement, AVR or CABG.

2.1.3 Ganglion ablation

Electrophysiological studies have found that ectopic impulses originating from the autonomic ganglionic plexus (GP) in epicardial fat adjacent to the atria-PV interface to be a source of arrhythmias (7, 40). To address this, GP ablation may be performed as an adjunct to Maze procedure (Figure 2). A prospective randomized trial of 67 patients demonstrated improved freedom from AF with the addition of GP ablation to catheter-based PVI (85.3% vs 60.6% freedom from AF) at 4.3 months follow up (41). Similarly, comparison of patients of GP ablation with Maze vs. a case-matched control Maze cohort found significantly higher freedom from AF at 1 year (90% versus 50%)(42).

2.1.4 Atrial plasty

A subset of patients with AF is those with giant LA (GLA), defined as LA diameter > 65mm. This may occur as a primary defect in the LA wall or secondary to mitral valve pathology, Rheumatic or otherwise. Major complications of GLA include compression of bronchopulmonary and left ventricle, post-operative low output syndrome and respiratory complications. Furthermore, LA enlargement exacerbates macro re-entrant circuits and is a risk factor for thromboembolic disease. Left atrial size was found to be a significant predictor for stroke and death in the Framingham Heart Study (43). Furthermore, GLA (70 vs 58mm, LA diameter) was associated with failure to restore sinus rhythm following Maze procedure at the time of MV surgery (44). Several studies have demonstrated that addition of left atrial plication

to mitral valve surgery improved restoration of sinus rhythm compared to mitral valve surgery alone (45, 46). However, others have shown greater than 50% recurrent arrhythmias in patients post-Cox Maze IV with LA size greater than 8cm even with a LA plasty (47).
The surgical approaches for LA plasty include excision of either inferior or inferior and superior walls as well as the autotransplant approach. An added advantage of these techniques is excellent exposure of the mitral valve to facilitate replacement or repair. The classical wall plication targets the inferior LA wall and has since been modified to a para-annular and superior approach (48). The biatrial reduction plasty when utilized with Maze IV during valvular surgery has demonstrated effective sinus restoration (49). In the combined superior-transseptal approach, the interatrial septum is opened at the fossa ovarium and extended to the inferior limbus and towards the LA appendage (50). The inferior wall can then be plicated from the LAA to the posteromedial aspect of the mitral valve using several interrupted sutures and reinforced with an over-and-over stitch. More recently, spiral resection has been proposed which extends a superior-transseptal left atriotomy in the direction of the left atrial appendage, to the inferior wall and then to the right atrial free wall (51). This approach is associated with an extensive suture line with increased bleeding risk but has the advantage of placation of the LA, RA and interatrial septum. Reef imbricate technique used as an adjunct to maze and MV surgery was associated with significant LA size reduction and sinus restoration in patients with LA enlargement and GLA, respectively (52). A 'half-moon' continuous reef imbricate sutureline suture is placed between the left and right PVs and circumferentially around the left atriotomy.
LA size reduction for GLA is associated with lower mitral valve surgical mortality, likely due to reduction in compression effects, low output syndrome, thromboembolic complications and restoration of sinus rhythm (48, 53). Whether reduction in LA size for patients with GLA undergoing mitral valve surgery in the absence of AF reduces the incidence of new onset AF is unknown. We generally do not perform reduction plasty in the absence of AF as LA size may undergo positive remodeling with relief of LA volume load.

2.2 Adverse effects

There has been no significant additive operative mortality with concomitant Maze procedures for patients undergoing coronary or valvular surgery (54). The reported risks of the Maze procedure include bleeding and blood transfusion, need for permanent pacemaker (PPM), impaired left atrial transport and rarely atrioesophageal fistula (54). Sinus node dysfunction immediately post-Maze is often reversible but if there is no recovery within 7-10 days, PPM implantation should be considered. The overall incidence of sinus node dysfunction requiring PPM is approximately 3-4%. It is unlikely that Maze lesion sets cause direct harm to the sinoatrial node and more likely that successful ablation of AF uncovers a sick sinus requiring pacing (55). Importantly, atrial transport may become impaired as scar tissue does not contribute to atrial contractility and as portions of atrial tissue may still fibrillate, depending on the location of the lesion sets.

2.3 Post-operative management

All patients should be monitored by telemetry post-operatively for the duration of hospital admission. Also, all patients, regardless of freedom from AF immediate post-operatively, should continue on oral anticoagulation until comprehensive cardiology assessment at 3 and 6 months time. It is not uncommon for patients to be in AF acutely post-operatively as atrial scar formation takes time to develop and thus success or failure of AF surgery should be

assessed at follow-up clinic 3-6 mo post-operatively. If patients are in sinus rhythm at this time, as assessed by the absence of symptoms, ECG or 24 hour Holter monitor, then oral anticoagulation is discontinued. All patients require routine cardiology follow-up to monitor for AF recurrence.

3. Clinical evidence for surgical management of atrial fibrillation

3.1 Sinus restoration

Most evidence for the efficacy of Maze procedures are for concomitant AF during repair or replacement of mitral valve. Several observational studies strongly suggests that surgical intervention is beneficial for return to sinus rhythm (54,56,57). The original Maze III cohort reported by Dr. Cox's group showed 95.9% and 97.5% freedom from AF at 5.4 years performed in lone and concomitant AF, respectfully (54). In another report and perhaps more importantly, the stroke rate in this cohort was 0.1% per year over 11.5 years of follow-up (56). As the authors mention, this is likely the result of 1) sinus restoration, 2) preservation of atrial transport function and 3) removal or obliteration of the LAA. A single center trial comparing patients undergoing mitral valve replacement or repair demonstrated improved conversion to sinus rhythm with concurrent modified radiofrequency maze ablation versus medical treatment (75% vs 39%) at 1 year follow-up (57). Damiano et al (47) recently report 89% freedom success with the Maze IV at 1 year. This outcome is notable in that the results are comparable to those of the Maze III and they utilized a strict definition of success as freedom from AF, A flutter or atrial tachycardia as determined by ECG or 24h Holter monitor and disuse of arrhythmia medications. The predictors of late AF recurrence following with Maze IV were enlarged LA, failure to isolated the posterior LA and presence of early tachyarrhythmias (47). Other groups have recapitulated these results demonstrating similar conversions to sinus rhythm and lowered stroke rates.

Six randomized controlled trials (RCTs) have been performed using various Maze procedures which have all demonstrated higher sinus restoration compared with no maze. The first RCT in 2001 randomized 30 patients with concomitant AF to demonstrate sinus restoration with saline-irrigated-cooled-tip-radiofrequency ablation (SICTRA) or MV surgery alone (58). In 2003, 35 patients who underwent either MV repair with Maze III or MV repair alone (2.5:1 ratio) at one year follow-up demonstrated 92% vs 20% freedom from AF (59). In another study, sixty-seven patients randomized to either adjuvant port-access irrigated radiofrequency Maze procedure demonstrated favorable freedom from AF at 1 year (93.6% vs 9.4%)(60) compared with mitral rahe surgry alone. Another RCT demonstrated that PVI and Maze both demonstrated similar improvements in sinus restoration in patients with mitral valve disease compared with MV surgery alone (61). Yet another RCT in 70 patients with Rheumatic heart disease demonstrated an improvement in sinus restoration (79.4% vs 26.9%) with SICTRA procedure (62). The largest trial included 160 patients in India undergoing surgery for rheumatic valve disease with maze III, left maze, PV isolation or no AF surgery who experienced 62.5%, 57.5%, 67.5% and 20% return to sinus rhythm, respectively (63). Although these clinical trials are relatively small single center experiences with short-term follow up times, they demonstrate a consistent improvement in sinus rhythm restoration regardless of the underlying MV pathology and procedure used including maze III, Left Maze, Maze with alternative energy sources and PVI. Importantly, no clinical trial has yet demonstrated survival benefit with a Maze procedure. Clearly, a large multicenter RCT with long term follow up is necessary to conclusively demonstrate freedom from AF and survival benefit. Regarding survival

benefit, considering that medical therapy leading to sinus restoration has not demonstrated improved survival, it may not be surprising if surgery for AF does not show this (22).

Two meta-analyses have been performed to date. The first is a meta-analysis of 69 studies, mostly retrospective, included 5885 patients with persistent, concomitant AF report that Maze III was associated with greater freedom from AF at 1-3 years and that biatrial Maze III was more effective than Left Maze III (92.0-87.1% vs 86.1-73.4% range over 1-3 years) (64). However, no significant differences were found in survival between surgical approaches compared to control groups. Forty-two percent of studies were small (<50 patients), only 19% included control populations and most data was extrapolated from Kaplan-Meier plots. The authors made no attempt to screen studies but rather to perform a comprehensive examination of the current literature. Another meta-analysis of four RCT and six retrospective studies demonstrate weak evidence in support of a reduction in stroke but an increase in need for PPM following the Maze procedure (65).

As mentioned, GLA is seen in a significant proportion of patients with AF. Several studies have demonstrated that addition of left atrial plication to mitral valve surgery improved restoration of sinus rhythm compared to mitral valve surgery alone (45, 46). Left atrial size reduction (69 to 55mm) was associated with a significant improvement in sinus restoration at 3 years compared with those that had mitral valve surgery and RF ablation alone (45). Furthermore, LA size reduction at the time of maze procedure improves outcomes. On the other hand, Choo et al (66) demonstrated similar sinus conversion rates comparing patients with GLA vs non-GLA (67.4 vs 61.1mm, LA diameter) undergoing mitral surgery and maze. Interestingly, another report from the same group found that patients under 50 had significantly better 5-year freedom from AF than those older than 50 (87.1% vs 77.3%, respectively) (67). These differences may be attributed, at least in part, to the somewhat arbitrary cut-off of GLA on the spectrum of LA enlargement.

Compared with surgical outcomes, cathether-based ablation has inferior short term outcomes and longterm results are pending. Catheter-based RF ablation may be used for paroxysmal and persistent AF with overall mid-term rates of sinus restoration of approximately 50-80% (68-70). More recently, Weerasooriya et al (71) present single center results demonstrating 5-year freedom from arrhythmia recurrence of 29% with one procedure and 63% with repeat ablation. Consistent with these clinical outcomes, Niv et al (72) demonstrated that 95% of pulmonary veins tested post-catheter ablation at the time of subsequent Maze III/IV were not electrically-isolated. We recommend that catheter ablation be best suited for younger patients with new onset (<6 months) paroxysmal lone AF. This may be combined with percutaneous device closure of LAA which has proven non-inferior to anticoagulation for stroke prevention but as mentioned, initially associated with complications including pericardial effusion, bleeding and device embolization (73-75).

There are several important considerations with respect to outcomes. When evaluating outcomes, it is important to clearly define the patient selection, choice of lesion set, energy source utilized and the use of a confirmatory technique for successful creation of a transmural lesion. Success or failure of AF surgery should be assessed following a blanking period of 3-6 months needed for scar tissue to develop. An important issue is the definition and measurement of procedural success. Early studies utilized mailed questionnaire or telephone interviews to determine if patients had symptoms or clinical events. A more accurate determination is ECG or 24-hour Holter monitor. More recently, the HRS/EHRA/ECAS consensus statement proposed a more stringent definition of success as the following: 1) freedom from AF, atrial fibrillation and atrial tachycardia lasting >30seconds and 2) off Vaughan-Williams class I and III anti-arrhythmic medications (76). Finally, much evidence has come from high-volume expert centers. It is clear that patient

selection is key as is the surgical skill and knowledge of anatomy for comprehensive completion of a complete ablation set. It is unclear whether the outcomes in real-world practice at lower volume centers can mimic these results.

3.2 Areas of uncertainty

It is unclear whether patients with lone AF, should undergo percutaneous ablation or minimally invasive surgical ablation. As mentioned, the midterm outcome with catheter ablation is approximately 50-60% with repeat procedures. On the other hand, Weimar et al (77) demonstrated 90% freedom from AF and 84% freedom from AF off antiarrhythmic medication at 24 months. Even with video-assisted, thoracoscopic PVI and LAA exclusion procedure alone, Wang et al (2011) found improved freedom from AF compared to percutaneous ablation at 1-3.9 year follow up (74.7% vs. 59.0%). Yet another option which requires evaluation is off-pump, epicardial ablation for lone AF (78). Ultimately, the patient will have to balance the need for repeat intervention with catheter ablation vs. the upfront risk associated with surgery.

It remains a challenge to identify those patient subsets for which AF surgery is unlikely to be beneficial. These include patients with paper thin LA, calcified walls, cardiothoracic ratio > 70% and a LA diameter > 80 mm (79). With regards to AF characteristics, low amplitude fibrillatory waves and longstanding AF (> 6 months) are associated with poor rates of sinus restoration. In addition, although the risk associated with the Maze procedure may be low, appropriate judgment must be exercised in selecting the most appropriate patients for this procedure. In very elderly or high risk patients, the potential benefits of a successful Maze procedure are unlikely to outweigh the risks of atriotomy and a longer bypass time.

The importance of parasympathetic ganglion ablation to AF pathogenesis and whether such should be addressed is yet unclear. Ganglia plexi are located in epicardial fat pads in close proximity to the left and right PV antrum. The rationale for GP ablation is based on early basic studies which identified efferent parasympathetic and sympathetic processes in the GPs and implicated their involvement in triggering and sustaining AF (80,81). Ablation targets can be identified by vagal response to high-frequency stimulation. However, the additional benefit of adjunctive GP ablation to Maze procedure and the patient subset that is likely to benefit are not known.

The optimal energy source for maze IV is yet unclear. Cryoablation has the advantage that it enables safe creation of the isthmus lesion as use of RF poses a risk of injury to vascular structures such as circumflex coronary artery. All unipolar devices including laser, microwave, unipolar RF and HIFU are limited as blood is not excluded from the interface thereby dissipating heat, thus negatively impacting transmurality, termed the 'heat sink effect' (82). Due to inconsistency in creation of transmural lesion sets, early energy sources such as microwave and laser have largely been discontinued.

4. Guidelines

In 2010, three major guideline revisions were released by the European Society of Cardiology (ESC)(83), by a joint committee of the American College of Cardiology Foundation (ACCF)/American Heart Association (AHA)/Heart Rhythm Society (HRS) and the Canadian Cardiovascular Society (CCS). Then in 2011, focused revisions were released by the American College of Cardiology Foundation (ACCF)/American Heart Association (AHA)/Heart Rhythm Society (HRS) in their respective journals (84). The CCS published their guidelines in 2011 and here we will focus on those that pertain to surgical management (85).

By in large, the recommendations of surgical management of atrial fibrillation are comparable. Bearing in mind that the data does not demonstrate a survival benefit for adjuvant ablation, the rationale for surgery include symptom relief, prevention of thromboembolism, preservation of atrial contraction and support of ventricular function in the setting of CHF. For symptomatic AF, the guidelines suggest a class IIa indication for adjuvant surgical ablation with two exceptions: the ACCF/AHA/HRS suggest a class I indication for paroxysmal AF and the CCS suggest a class I indication for AF with mitral valve disease. The ESC gives a class IIb and CCS suggest a conditional recommendation for surgical management of lone AF.

The guidelines suggest that for patients with recurrent, paroxysmal AF who fail medical management, PV isolation or LA substrate modification may be considered. For patients with persistent AF with symptoms who fail or do not tolerate medical management, LA ablation, the maze and AV nodal ablation and pacing may be considered. AF surgery is indicated for lone AF in patients who 1) prefer surgical management, 2) failed or have a contraindication to catheter ablation or 3) failed (developed thrombus) or have a contraindication to anticoagulation.

5. Summary in points

1. The gold standard surgical treatment for AF is the complete biatrial Cox-Maze lesion set
2. The indications for atrial fibrillation surgery are the following:
   a. Recommendation for patients who i) prefer surgical management, ii) failed or have a contraindication to catheter ablation or iii) failed or have a contraindication to anticoagulation
   b. Recommendation for concomitant AF during a mitral valve procedure
   c. Conditional recommendation for lone AF
3. Randomized controlled trials have consistently demonstrated that surgery for concomitant AF offer improved sinus restoration with very low additive risk.
4. Atrial fibrillation surgery does not offer survival benefit.
5. For lone AF, catheter ablation is currently the preferred technique but minimally-invasive Maze or PVI offers improved freedom from AF with a cosmetically-acceptable incision.
6. Adjunctive procedures to a Maze are ganglia plexus ablation and left atrial plasty. The additive benefit of such still requires careful evaluation.

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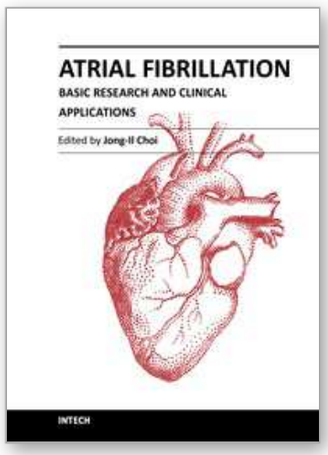
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Atrial Fibrillation - Basic Research and Clinical Applications

Edited by Prof. Jong-Il Choi

ISBN 978-953-307-399-6
Hard cover, 414 pages
Publisher InTech
Published online 11, January, 2012
Published in print edition January, 2012

Atrial Fibrillation-Basic Research and Clinical Applications is designed to provide a comprehensive review and to introduce outstanding and novel researches. This book contains 22 polished chapters and consists of five sections: 1. Basic mechanisms of initiation and maintenance of atrial fibrillation and its pathophysiology, 2. Mapping of atrial fibrillation and novel methods of signal detection. 3. Clinical prognostic predictors of atrial fibrillation and remodeling, 4. Systemic reviews of catheter-based/surgical treatment and novel targets for treatment of atrial fibrillation and 5. Atrial fibrillation in specific conditions and its complications. Each chapter updates the knowledge of atrial fibrillation, providing state-of-the art for not only scientists and clinicians who are interested in electrophysiology, but also general cardiologists.

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Bobby Yanagawa, Khaled D. Algarni and Gideon Cohen (2012). Surgical Management of Atrial Fibrillation, Atrial Fibrillation - Basic Research and Clinical Applications, Prof. Jong-Il Choi (Ed.), ISBN: 978-953-307-399-6, InTech, Available from: http://www.intechopen.com/books/atrial-fibrillation-basic-research-and-clinical-applications/surgical-management-of-atrial-fibrillation

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