A review of current surgical treatment of patients with atrial fibrillation

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Surgical therapy for patients with atrial fibrillation has undergone significant advances over the past 30 years. The Cox Maze III technique is currently the gold standard of care for these patients. However, Maze IV, a less complex procedure using alternative energy sources, is rapidly replacing the Cox Maze III in clinical practice. The use of alternative energy sources such as cryothermy and radiofrequency eliminates some of the "cut and sew" lesions of the Maze III, resulting in an easier and faster procedure with less morbidity. Video-assisted technology and hybrid procedures have further ushered in the future of surgical therapy. This article presents the latest surgical therapeutic options for patients with atrial fibrillation. The history of these procedures is presented, followed by a discussion of modern-era techniques, including concomitant ablation and standalone (also referred to as "lone") procedures. Finally, the article explores breaking developments and future directions for the surgical treatment of patients with atrial fibrillation.

As the most common sustained cardiac arrhythmia (1), atrial fibrillation (AF) currently affects over 5 million Americans (2) and is projected to affect 12 million Americans by 2050 (1). Adults aged ≥40 years have an approximately 1 in 4 lifetime risk of developing AF (3). Problems associated with AF are threefold: rapid ventricular response, resulting in decreased cardiac output and occasionally tachycardia-mediated cardiomyopathy; loss of the atrial transport function, which variably may result in decreased cardiac output; and stasis with clot formation and thromboembolism. AF is a known risk factor for stroke, heart failure, and premature death (4). In fact, AF confers a 5-fold increase in the risk of stroke (5, 6), causing 15% of the strokes in the United States (7). A study of over 4600 patients revealed an increased mortality risk within the first 4 months of an AF diagnosis compared with the general population (hazard ratio, 9.62; $P < 0.0001$) (4). This condition, therefore, has warranted much research over the past few decades. Procedural development has focused on less invasive techniques with lower morbidity.

This article highlights the current surgical therapy options for patients with AF. The history of surgery for AF is presented, followed by a discussion of modern-era techniques, including concomitant ablation procedures and standalone (also referred to as "lone") surgical therapy. Finally, the article explores hybrid techniques and future directions for the surgical treatment of patients with AF.

THE EVOLUTION OF SURGICAL TREATMENT FOR ATRIAL FIBRILLATION

The first major surgical breakthrough in AF therapy was observed in 1980, when the left atrial isolation technique was reported (8). With AF isolated in the left atrium, the rest of the heart could be restored to normal sinus rhythm (NSR) as a result of this surgery. However, reduced cardiac output and the risk of systemic thromboemboli persisted because of the remaining AF. Two years later, Scheinman and colleagues developed His bundle ablation to control the irregular rapid ventricular response attendant to AF (9). Patients undergoing this procedure required a permanent ventricular pacemaker. The surgery conferred an improvement only in the AF-related irregular and rapid heart rate. It did not manage the loss of the atrial kick or the risk for the development of thromboemboli (8).

The Guiraudon corridor technique, an open-heart surgery that regulated the heart rate and reduced the need for a permanent pacemaker, was pioneered in 1985 (8). Despite such advances, neither side of the heart was in atrioventricular synchrony, thromboembolism risk remained high, and both atria remained in fibrillation after the surgery. The aforementioned His bundle ablation procedure yielded comparable physiologic outcomes without requiring open-heart surgery.

The following year, an atrial transection procedure, involving pulmonary vein isolation (PVI) and incisions in the atria, was performed on a patient for the first time (8, 10). With this patient's heart having remained in NSR for 5 months, Cox et al established that AF could be corrected with surgical alteration of the atria.

Cox and colleagues went on to formulate the cut-and-sew maze technique (11). First performed on a patient in 1987 (11),

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this Cox maze technique comprises several atrial incisions that form a set of scars that obstruct all potential points of reentry (12). Although efficacious, this Maze I procedure resulted in occasional left atrial dysfunction and the frequent inability to generate adequate sinus tachycardia in response to maximal exercise (8). Maze II, the next step in the evolution of the cut-and-sew procedure, excluded the sinus node incision in the high lateral right atrium. Also, in order to enhance intraatrial conduction, the left atrium dome transverse atriotomy was relocated to the posterior. Complete transection of the superior vena cava was required as a result of such modification, however.

The cut-and-sew maze technique then continued to progress. Maze III placed the septal incision posterior to the superior vena cava orifice, enabling enhanced exposure of the left atrium (8). This procedure enhanced long-term atrial transport and sinus node function, diminished the need for a pacemaker, lessened the recurrence of arrhythmia, and increased the occurrence of postsurgery NSR, all while being more technically manageable than previous maze iterations.

In 1999, Cox et al modified Maze III into a minimally invasive approach using a 7-cm right submammary incision (11). At that time, two patients underwent the surgery without cardiopulmonary bypass. Cox and colleagues as well as the Cleveland Clinic and the Mayo Clinic have illustrated the safety and efficacy of Maze III, with mortality rates of ≤1.4%, a 1.2% long-term failure rate, 90.4% of the patients being in NSR 3 years after surgery, and 3.2% to 15% needing new pacemakers (11, 13–15). Maze III is currently the gold standard of surgical therapy for patients with AF (16).

FROM MAZE III TO MAZE IV AND RADIOFREQUENCY ABLATION

The conventional Cox Maze III procedure entailed multiple atrial incisions, which were associated with increased morbidity and complexity. Thus, the procedure was not commonly implemented. Widespread acceptance occurred only after advances in enabling technology yielded multiple energy sources that could be utilized to create lines of transmural necrosis, thereby replacing surgical incisions. This modified technique, Maze IV, employed a connecting lesion rather than the initial box lesion and isolated pulmonary veins bilaterally (8). Damiano et al innovated much of this procedure using bipolar radiofrequency (AtriCure, Inc.; Cincinnati, OH) and revealed that when performed with alternative energy sources, its efficacy equaled that of the traditional cut-and-sew maze approach (17). This group demonstrated that a box lesion yielded greater overall freedom from AF recurrence than did a single connecting lesion at 1 month (87% vs. 69%; $P = 0.015$) and 3 months (96% vs. 85%; $P = 0.028$) (18). Also, antiarrhythmic drug usage was lower in the Maze IV box lesion group compared with the single connection lesion group at 3 months (35% vs. 58%; $P = 0.018$) and 6 months (15% vs. 44%; $P = 0.002$). Furthermore, Weimar and colleagues studied 112 patients who underwent the Maze III procedure and 100 patients who underwent the Maze IV procedure (19). Median cardiopulmonary bypass time was significantly reduced with Maze IV compared with Maze III (129 minutes vs. 163 minutes; $P < 0.001$), as was mean aortic cross-clamp time (39 minutes vs. 90 minutes; $P < 0.001$). Maze IV also produced significantly lower major complication rates ($P = 0.003$). Freedom from AF was comparable between the two groups (90% [95% CI, 81–95] for Maze IV vs. 96% [95% CI, 86–98] for Maze III).

The maze procedure has flourished as a result of the discovery of alternative energy sources. Several treatments utilizing these energy sources were developed after Haïssaguerre and colleagues' landmark finding that pulmonary veins are the major source of the early potential factors that cause paroxysmal AF (recurrent AF ending spontaneously ≤7 days) and that they respond to radiofrequency ablation (8, 20). Besides bipolar and unipolar radiofrequency and cryoablation, other energy sources that have been integrated into maze with varying levels of success include laser, microwave, and high-frequency ultrasound energy. Laser energy has been discontinued due to its inability to produce transmural lesions (21). Also, high-intensity focused ultrasound has not met safety criteria for treatment of patients with AF (22). Microwave energy is unsuccessful in PVI or long-term prevention of AF, as determined by Pruitt and colleagues in 2007 (23); therefore, its clinical use was virtually abolished, and it was then withdrawn from the market. Only radiofrequency and cryoablation have proven to be effective, efficient, and safe.

One objective in the utilization of radiofrequency energy is to increase resistive heating and reduce conductive heating in order to deepen the lesion penetration. Conductive heating restricts penetration by creating surface char. Some surgical devices minimize this conductive heating by using saline irrigation to cool the surface. Other devices utilize bipolar directional "pens" wherein the energy flows between the two poles of the pen. These pens may be irrigated for cooling or not. The directional nature of these pens also allows the surgeon to create scar tissue without causing collateral damage (12). Bipolar radiofrequency is the most commonly used energy source for minimally invasive surgical AF ablation (24). A 99.5% overall procedural success rate (procedure completion without conversion to cardiopulmonary bypass or median sternotomy) was revealed in a review of minimally invasive surgical AF ablation series using totally thoracoscopic bipolar radiofrequency (24). Conversely, unipolar radiofrequency energy may produce less reliable transmural lesions (12). One variant of unipolar radiofrequency energy attempts to increase tissue contact by utilizing suction-assisted attachment to the atrium to ensure ablation line continuity. However, in animal studies, this did not prove efficacious (25).

Another form of energy used in the surgical treatment of patients with AF, cryoablation, freezes tissue, creating a scar via a bimodal process of tissue necrosis (12). Cryoablation usually requires emptying the heart on cardiopulmonary bypass because the immense heat sink of circulating intracavitary blood can absorb the energy, rendering a complete freeze of the endocardial tissue difficult or even impossible. It is therefore ineffective on the full, beating heart. A study of 63 patients undergoing concomitant cardiac procedures including cryoablation for AF yielded an 88.5% rate of freedom from AF at 1 year (26). Cryothermy is also not directional and may allow for collateral damage if not used with care.

CONCOMITANT SURGICAL ABLATION

Studies have shown that patients who undergo surgery for cardiac conditions other than AF but who have preoperative AF are at high risk for late morbidity, stroke, and reduced survival (27–29). Quader et al found that, in patients with preoperative AF undergoing coronary artery bypass grafting (CABG), 10-year survival was reduced by 24% compared with patients without AF (27). Ngaage and colleagues studied patients undergoing aortic valve replacement and determined that patients with preoperative AF had a significantly higher probability of later rhythm-associated interventions ($P = 0.0002$), congestive heart failure ($P = 0.005$), and stroke ($P = 0.005$) than did patients without AF (28). In another study, these authors demonstrated that preoperative AF was associated with a higher operative mortality rate (2% vs. 0; $P = 0.05$) as well as increased late cardiac events and stroke (63% vs. 31%; $P < 0.0001$) (29).

In light of such data, surgical AF ablation that is performed concomitantly with at least one other previously planned cardiac surgery is recommended by the International Society of Minimally Invasive Cardiothoracic Surgery consensus panel (30). Concomitant surgical ablation reduces the risks of stroke and thromboemboli, improves ejection fraction, increases NSR incidence, and improves long-term survival and exercise tolerance for patients with persistent AF (lasting >7 days, or lasting <7 days but necessitating cardioversion) and permanent AF (ongoing, long-term, refractory AF). Also, the current Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society expert consensus statement on catheter and surgical ablation of AF calls for all patients with AF undergoing other cardiac procedures to be considered for ablation if the risks of adding this procedure are small, the procedure is executed by an experienced surgeon, and there is adequate probability of success (16).

Studies, including several randomized controlled trials, have demonstrated that concomitant radiofrequency AF ablation is successful in restoring and maintaining NSR (31–35). Doukas et al revealed rates of return of NSR of 44.4% for patients undergoing concomitant AF ablation compared with 4.5% for patients undergoing mitral valve surgery without AF ablation ($P < 0.001$) (33). However, they performed only left atrial lesions, not the full maze lesion set. Similarly, Abreu Filho and colleagues demonstrated that 79.4% of patients having concomitant AF ablation experienced a return of NSR compared with 26.9% of patients having mitral valve surgery and no AF ablation ($P = 0.001$) (32). Chevalier et al reported 12-month postoperative NSR rates of 57% for patients undergoing concomitant AF ablation and 4% for those who had only mitral valve surgery ($P = 0.004$) (34). Finally, von Oppell et al conducted a study in which 75% of the patients receiving mitral valve surgery plus AF ablation were in NSR at 12-month follow-up compared with 39% of the patients who had only mitral valve repair ($P = 0.03$) (35). Gammie et al conducted a retrospective review of over 67,000 patients in the Society of Thoracic Surgeons National Cardiac Database who underwent cardiac procedures between 2004 and 2006 (36). For the 6231 patients who underwent surgery for AF and mitral valve repair, the risks were not significantly different for death (odds ratio [OR], 1.00 [95% CI, 0.83, 1.20]; $P = 0.975$), any reoperation (OR, 0.98 [95% CI, 0.87, 1.12]; $P = 0.802$), renal failure/dialysis (OR, 1.03 [95% CI, 0.88, 1.21]; $P = 0.689$), postoperative length of stay ≥14 days (OR, 1.00 [95% CI, 0.88, 1.13]; $P = 0.949$), or prolonged ventilation (OR, 0.98 [95% CI, 0.88, 1.09]; $P = 0.715$) compared with patients who had mitral valve surgery and no surgery for AF. Adjusting for preoperative characteristics, patients undergoing mitral valve repair and concomitant AF ablation did not have a significantly increased mortality risk compared with patients undergoing only mitral valve surgery (OR, 1.00 [95% CI, 0.83, 1.20]).

STANDALONE SURGICAL THERAPY FOR ATRIAL FIBRILLATION

The minimally invasive standalone maze technique is a key nonpharmacologic therapeutic option in the modern era. According to Cox, the ideal surgery for AF "would be performed via a minimally invasive incision (or endoscopically or robotically), off bypass, in less than 1 hour, with hospital discharge planned for the next morning" (37). Surgeons have strived to meet this objective, attempting to reap the efficacy benefits of the Cox Maze III technique while preventing the related morbidity and complexity. The minimally invasive standalone maze procedure includes left atrial appendage (LAA) exclusion, PVI, and ablation of the ganglionic plexuses (GPs) and the ligament of Marshall, all combined into one surgery (38). For nonparoxysmal patients, linear lesions can also be added (39). This procedure can decrease the risk of emboli, enable extensive mapping of the GPs and ligament of Marshall, and help prevent catheter ablation–related adverse events. However, compared with medical therapy, minimal access surgery does have some risks: lengthier hospitalizations and recovery periods, the required use of general anesthesia, greater patient discomfort, and the bleeding risk associated with LAA excision.

CryoMaze is one variety of such minimal-access AF ablation. Although called minimal access, it does utilize cardiopulmonary bypass with retrograde perfusion and employ a groin incision for cardiopulmonary bypass as well as a minimal-access mini-thoracotomy incision, as described by Gammie and colleagues (40). Between July 2002 and November 2005, 119 patients underwent CryoMaze. Thirty-three patients had preoperative intermittent AF, and 28 (85%) were in NSR at late follow-up (>3 years). However, for the 58 patients with continuous AF, the results were less impressive, with 27 patients (47%) being in NSR ($P < 0.0001$). The overall rate of freedom from AF was 60% at late follow-up. There was one perioperative stroke, which was entirely resolved within 1 month, and there were no late strokes. Another study was conducted using CryoMaze, this time with the multiple–purse-string technique, wherein atriotomies are avoided via the placement of sutures on the left and right epicardial surfaces (41). A total of 12 patients underwent this procedure, either combined with CABG (n = 9), combined with aortic valve replacement (n = 2), or as a standalone surgery (n = 1). Five additional patients required a small left atrial atriotomy to ensure that the mitral valve isthmus lesion was complete. There were no cerebrovascular accidents/

transient ischemic attacks or perioperative mortalities. There was 1 late death, and 91% of the patients were free of AF or flutter at a mean follow-up of 13 ± 6 months.

Also influencing the progress of surgical therapy for patients with AF is video-assisted technology. Wolf et al pioneered this innovation, conducting a video-assisted bilateral PVI and LAA exclusion via minithoracotomy in 27 patients with AF (18 with paroxysmal AF, 4 with persistent AF, and 5 with permanent AF) whose condition was intolerant to or refractory to pharmacologic interventions (42). At a follow-up of >3 months, 21 patients (91.3%) had freedom from AF. There were no deaths or conversions to sternotomy or full thoracotomy. Yilmaz et al performed a study of video-assisted totally thorascopic PVI with GP ablation and LAA amputation, for which data on the first 30 patients are available (43). With a mean follow-up of 11.6 months, 77% of the patients were free of AF. The mean operation time was 137.4 ± 24.7 minutes, and the mean length of hospital stay was 5.1 ± 1.8 days. No cerebrovascular accidents, pacemaker placements, or deaths occurred. Additionally, Edgerton and colleagues conducted a study in which video-assisted technology was utilized for PVI and partial autonomic denervation for 74 patients with AF (44). At a follow-up of 6 months, overall, 92.9% of the patients were in NSR as determined by an electrocardiogram, and 74.2% of the patients with longer-term observation had no indications of AF. By AF type, 56.5% of the patients with persistent/longstanding persistent (LSP) AF and 83.7% of the patients with paroxysmal AF were free of detectable AF (AF episodes >15 seconds). Partial autonomic denervation combined with PVI is proposed to be an effective and safe surgical option for patients with AF.

Video-assisted technology has played a key role in another recent study of a novel minimally invasive surgical method: the totally thorascopic video-assisted PVI, GP ablation, and LAA exclusion, with perioperative electrophysiologic confirmation (45). Krul et al utilized bipolar radiofrequency to treat 31 patients (16 with paroxysmal AF, 13 with persistent AF, and 2 with LSP AF). Eighty-six percent of the patients were free of AF recurrence, atrial flutter, and atrial tachycardia and were not using antiarrhythmic agents at 1-year follow-up. No deaths or thromboembolic events occurred. Therefore, this procedure could be a reliable, cost-effective new therapeutic choice for surgeons treating AF.

Pulmonary vein isolation alone, although effective for paroxysmal AF, is not sufficient treatment for patients with continuous AF, as seen by these preliminary results. Because of the substrate alterations that electrical remodeling brings about, this procedure as standalone therapy is insufficient for patients with persistent and LSP AF (46). The altered left atrial substrate beyond the PVs can initiate and sustain AF. Additional linear lesions are necessary in this group. The "Dallas lesion set" was developed to treat this group of patients. It is a set of linear lesions that replicates the left-sided Cox Maze III procedure and can be applied epicardially, on the full beating heart, with a totally thorascopic technique. The surgeon creates lesions at the roof line, the anterior line, and between the roof line and the LAA in this extended linear lesion set (47, 48). The Dallas lesion set was studied in 30 patients with persistent or LSP AF. The preliminary results are encouraging: 15 of 20 patients (75%) with LSP AF and 9 of 10 patients (90%) with persistent AF had freedom from AF at a follow-up of 6 months (39). PVI and GP ablation are more efficacious in paroxysmal AF (24, 49), but the Dallas lesion set can serve as a valuable surgical therapy option in persistent and LSP AF.

HYBRID PROCEDURES AND FUTURE DIRECTIONS

Hybrid procedures are further advancing the state of the art. A hybrid procedure combines epicardial and endocardial ablation, either staged or as a single procedure, through a partnership between the surgeon and electrophysiologist. Because data from recent studies are still incomplete, it has not yet been established whether the single or staged approach is most likely to produce favorable outcomes.

The nContact trial, performed by Horton, Hume, Natale, and colleagues, is one of the latest studies on the hybrid method. It included 57 patients with LSP AF and a large (≥5 cm) left atrium (50). Patients in group 1 (n = 22) underwent combined closed-chest epicardial monopolar radiofrequency ablation via a transabdominal transdiaphragmatic single port and catheter-based transseptal endocardial ablation. Patients in group 2 (n = 35) received manual catheter ablation alone. In group 1, there were 3 deaths (13.6%): one due to stroke, one due to left atrium-esophageal fistula, and one sudden death. No deaths were reported in group 2. The study demonstrated that this combined technique increases complication rates and does not improve outcomes in patients with a large atrium and LSP AF.

More efficacious and lower-risk bilateral thorascopic hybrid approaches for AF are being investigated. Mahapatra and colleagues performed a study of sequential surgical epicardial ablation with subsequent endocardial evaluation and catheter mapping with targeted ablation during the same hospitalization compared with catheter ablation alone (51). Forty-five patients with persistent or LSP AF received either the sequential ablation (n = 15) or the catheter-alone ablation (n = 30). Of the patients who were treated by catheter ablation alone, 53.3% had freedom from AF and were not using antiarrhythmic agents compared with 86.7% of the patients who received sequential therapy ($P = 0.04$) at a mean follow-up of 20.7 ± 4.5 months. Although small, the study's positive results are promising. Further study is needed.

CONCLUSION

In the past three decades, and particularly in the time since the initial maze procedure was carried out on a patient in 1987, surgical therapy for patients with AF has seen extensive advances. The Cox Maze III technique remains the mainstay of such therapy. However, with innovations in surgical AF ablation by means of alternative energy sources, namely cryothermy and radiofrequency, Maze IV is becoming a feasible, less complex option. Findings from randomized controlled trials (31–35) support the International Society of Minimally Invasive Cardiothoracic Surgery consensus panel recommendation that AF ablation be performed when a patient is already undergoing at

least one other cardiac procedure (30). Video-assisted technology as well as hybrid procedures that combine epicardial and endocardial ablation have brought the future into the present. Prospective, randomized, controlled trials with long-term follow-up are needed as minimal access surgical therapy for AF progresses into the future.

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