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Review

Surgical treatment of atrial fibrillation: State of the art, 2012

Takashi Nitta, MD, PhD*, Yosuke Ishii, MD, PhD, Shun-ichiro Sakamoto, MD, PhD

Cardiovascular Surgery, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8602, Japan

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ABSTRACT

The development and introduction of radiofrequency ablation devices allowed maze procedure to be performed safely and easily, further enabling off-pump pulmonary vein isolation through mini-thoracotomy or thoracoscopy. The outcomes of the maze procedure include the prevention of stroke and other complications related to atrial fibrillation (AF), improvement in cardiac performance, and relief of symptoms. The indications for the maze procedure have been discussed on the basis of available evidence. Pulmonary vein isolation has been shown to be effective in most patients with paroxysmal AF, and can be performed with both endocardial catheter ablation and minimally invasive epicardial ablation. These 2 modalities should be compared in terms of the success rate, occurrence of cerebral microembolic signals, capability adding other lesions indicated for persistent or long-standing persistent AF, and closure of the left atrial appendage. Noncontinuous or nontransmural lines of conduction block as a result of incomplete ablation can result in the recurrence of AF and induction of atrial tachycardia. Intraoperative verification of a conduction block across the ablation lines is recommended to prevent these complications. Volume reduction of the enlarged left atrium or a box lesion to isolate the entire posterior left atrium may be effective in patients with a dilated left atrium, but the potentially impaired atrial transport function should be considered. Mapping of active ganglionated plexi and their ablation may improve the outcome of the procedure; however, the long-term effect on AF and autonomic nerve activities should be examined. Because the mechanism underlying AF varies in each patient, a tailor-made therapy, using a stepwise approach, with a hybrid procedure combining epicardial and endocardial ablation offers promising prospects in the nonpharmacological treatment of AF.

Contents

1. Introduction

It has been a quarter of a century since the maze procedure was first performed in a patient with atrial fibrillation (AF). Initially, all lines of conduction block were created by a "cut-and-sew" technique in conjunction with cryoablation at the atrioventricular annuli. The use of the maze procedure has been limited by its complexity, the potential risk of bleeding, and the prolonged ischemic time. However, the introduction of radiofrequency (RF) ablation devices enabled performing the procedure in a minimally invasive manner, and it is now widely performed as a standard surgical procedure.

* Corresponding author. Tel.: +81 3 5814 6219; fax: +81 3 5685 0985.
E-mail address: nitta@nms.ac.jp (T. Nitta).

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The outcomes of the maze procedure have been extensively investigated with regard to cardiac function, prevention of thromboembolism, long-term mortality, quality of life, and others. Many studies have demonstrated that the maze procedure relieves symptoms, decreases the morbidities associated with AF, and improves patient survival. The indications and recommendations for the procedure have been published as a guideline or a consensus statement.

The establishment of a minimally invasive procedure for AF will benefit patients with lone AF and without any structural heart disease. An off-pump and beating heart pulmonary vein (PV) isolation procedure with a bipolar RF ablation device, through a small thoracotomy or thoracoscopy, has been developed and shown to be effective in some patients, mainly those with paroxysmal AF. Currently, PV isolation can be effectively attained with a high success rate by catheter ablation, particularly in patients with paroxysmal AF. A prospective study will be directed toward the modification of the PV isolation procedure for terminating AF, even the persistent or long-standing persistent AF.

The surgical and catheter approaches both have advantages and limitations in AF ablation. PV isolation and excision of the left atrial appendage can be easily performed through small thoracotomy or thoracoscopy. Catheter ablation is more suited for isthmus or focal ablation guided by electrophysiological findings. A hybrid therapy combining these approaches may be a promising prospect.

The use of ablation devices simplifies the procedure, and decreases the procedure time and the risk of bleeding. However, these ablation devices can create nontransmural or noncontinuous lines of conduction block, and result in failure to convert AF or induce reentrant atrial tachycardia (AT) postoperatively. Further improvement of these ablation devices and technical artifices, including intraoperative verification of a conduction block, are mandatory to decrease the incidence of incomplete conduction blocks.

The maze procedure may not be able to cure AF in a certain group of patients, including those with a severely dilated left atrium, long-lasting AF, and low-amplitude atrial activity on the electrocardiogram. Volume reduction of the left atrium in addition to the maze procedure may lessen the blood stasis in the left atrium and increase the chance of terminating AF even in this subgroup of patients. The more the atrial myocardium is isolated, such as in the box lesion set, the higher the chance for AF to be terminated, but the lesser the recovery of the atrial transport function.

Increased autonomic nervous activity is known to play an important role in the initiation and maintenance of AF. Recently, identification of active ganglionated plexi (GP) and their ablation, with or without the maze procedure, has been shown to contribute to the elimination of AF. The long-term effect of GP ablation on the maintenance of sinus rhythm, as well as the adverse effect on the physiologic variability of heart rate, will need further investigation.

This review will describe the recent progress and future perspective in surgery for AF.

2. Effects of the maze procedure and guidelines

A number of studies have examined the effects of the maze procedure, including parameters such as the relief of symptoms, incidence of hospital readmission, morbidities associated with AF, quality of life, incidence of thromboembolism, and mortality. Whereas the relief of symptoms such as palpitations is a simple aim of the maze procedure for patients with paroxysmal AF, the prevention of stroke and long-term survival are the most important goals of any treatment for both paroxysmal and chronic AF.

The prevention of stroke has been recognized as an important reason for performing the maze procedure since the era of the cut-and-sew technique [1]. Lall et al. [2] demonstrated that the early results, such as 30-d mortality, early atrial tachyarrhythmias, late stroke, and survival, after the maze procedure with a bipolar RF ablation device were similar to those with the cut-and-sew technique. Beukema et al. [3] examined the intermediate to long-term results after the maze procedure with an irrigated unipolar RF ablation device in 258 patients with structural heart disease and permanent AF. Oral anticoagulation drugs were taken by 99% of these patients. Stroke was reported in 4 patients. The mortality rate was 28.3% during a mean follow-up of 43.7 ± 25.9 months. The postoperative rhythm was not predictive of all-cause mortality, cardiac mortality, and stroke. Kim et al. [4] investigated whether the type of the mitral surgery affects the outcome in 435 patients who underwent the maze procedure concomitant to either a mitral repair or mitral replacement. No significant differences were found between the types of mitral surgery in terms of survival, stroke incidence, or sinus rhythm restoration rate. More recently, Fujita et al. [5] evaluated the long-term outcomes of a combined mitral repair and maze procedure for patients with nonrheumatic mitral regurgitation and chronic AF. The 15-year survival was 71%, and 11 thromboembolic episodes were detected during a mean follow-up period of 7.4 ± 4.3 years, of which 7 occurred in patients with recurrent AF (Fig. 1).

A guideline for AF surgery was published by the Japanese Circulation Society in 2000, and revised in 2011 [6]. The guideline focused on the prevention of stroke and the complications associated with AF and was constructed on the basis of the

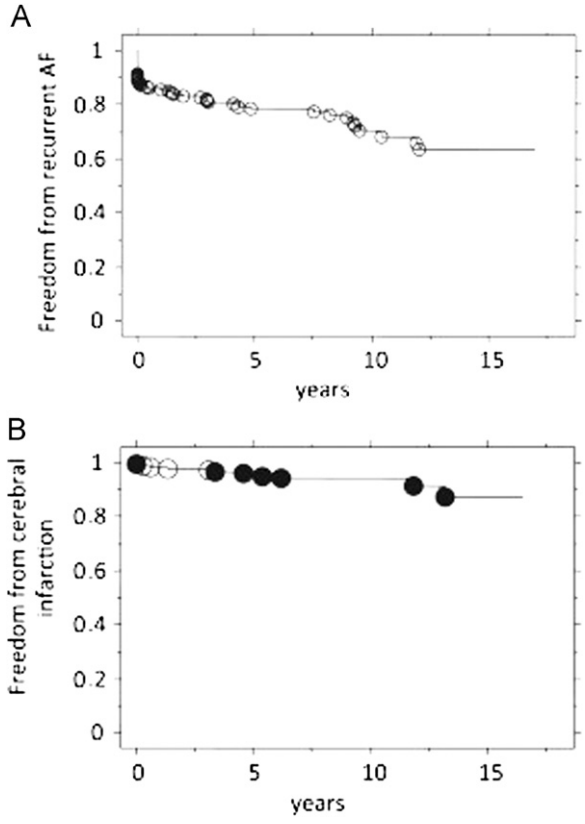

Fig. 1. (A) Rate of freedom from recurrence of atrial fibrillation (AF). (B) Rate of freedom from cerebral infarction. Open circle: cerebral infarction in patient with sinus rhythm. Closed circle: cerebral infarction in patient with recurrent AF. (Cited from Ref. [5] with permission: J Thorac Cardiovasc Surg. 2010;140:1332-7.).

evidence obtained from previous maze procedures. Surgery for AF in patients undergoing surgery for mitral valve disease is recommended as a class 1 indication because multiple studies have demonstrated a significantly lesser incidence of stroke in patients undergoing a concomitant maze procedure compared with those without. In AF patients undergoing other cardiovascular surgeries, AF surgery is recommended as a class IIa indication.

In 2012, a revised consensus statement for AF surgery was published by the Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society as a part of the "Expert consensus statement for catheter and surgical ablation for AF" [7]. The statement was focused mainly on the relief of symptoms associated with AF and the safety of the procedure, as shown in Table 1.

The consensus conference of the International Society of Minimally Invasive Cardiothoracic Surgery (ISMICS) aimed to determine whether surgical AF ablation during cardiac surgery improves the clinical and resource outcomes compared with cardiac surgery alone in adults undergoing cardiac surgery for valve or coronary artery bypass grafting [8,9]. The available evidence, including systematic reviews, randomized trials, and nonrandomized trials, was reviewed by the consensus panel and considered in descending order of validity and importance. Then, evidence-based statements were created and consensus processes were done to determine the ensuing recommendations. Six questions were formulated and statements were drawn for each question, except for question 6, as shown in Table 2. Although the evidence level was B and the class of recommendation was IIa, the consensus panel reached an agreement that a concomitant surgical ablation is recommended to reduce the risk of stroke and thromboembolic events and improve the long-term survival of patients (Fig. 2).

3. Surgery for failed catheter ablation for lone AF

Although most patients with paroxysmal AF are effectively treated by catheter ablation, one or more additional sessions of ablation are required in some of these patients and in a considerable number of those with persistent or long-standing persistent AF. Ad et al. [10] performed the maze procedure in 40 patients with recurrent AF who underwent at least one left-sided ablation. Ninety-five percent of the patients presented with long-standing persistent AF. Careful inspection of the left atrial endocardial surface revealed multiple spots of scar tissue, but with no definite linear or continuous scar formation. At the time of the operation and before surgical ablation, 96 PVs were assessed for an exit block. Ninety-five percent of the veins tested were found to conduct across the ablation line, even though all tested veins had a documented confirmed conduction block at the time of percutaneous catheter ablation. After the maze procedure, the sinus rhythm was maintained in 76%, 89%, and 93% of the patients during the follow-up periods of 6, 12, and 24 months, respectively, without taking class I/III antiarrhythmic drugs (Fig. 3).

4. Minimally invasive surgery for lone AF

The minimally invasive surgical procedure was developed for patients with lone AF without any structural heart disease. The procedure includes PV isolation with or without connecting

Table 1
Consensus indications for catheter and surgical ablation of AF. (Cited from Ref. [7] with permission.)

Indications for catheter ablation of AF	Class	Level
Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication		
Paroxysmal: Catheter ablation is recommended*	I	A
Persistent: Catheter ablation is reasonable	IIa	B
Longstanding Persistent: Catheter ablation may be considered	IIb	B
Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent		
Paroxysmal: Catheter ablation is reasonable	IIa	B
Persistent: Catheter ablation may be considered	IIb	C
Longstanding Persistent: Catheter ablation may be considered	IIb	C
Indications for concomitant surgical ablation of AF		
Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication		
Paroxysmal: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Longstanding persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent		
Paroxysmal: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Longstanding Persistent: Surgical ablation may be considered for patients undergoing surgery for other indications	IIb	C
Indications for stand alone surgical ablation of AF		
Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication		
Paroxysmal: Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach	IIb	C
Paroxysmal: Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation	IIb	C
Persistent: Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach	IIb	C
Persistent: Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation	IIb	C
Longstanding Persistent: Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach	IIb	C
Longstanding Persistent: Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation	IIb	C
Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent		
Paroxysmal: Stand alone surgical ablation is not recommended	III	C
Persistent: Stand alone surgical ablation is not recommended	III	C
Longstanding Persistent: Stand alone surgical ablation is not recommended	III	C

* Catheter ablation of symptomatic paroxysmal AF is considered a Class 1 indication only when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced center.

Table 2
A consensus statement of the ISMICS 2009. (Modified from Ref. [9] with permission.)

Question 1:	Does Surgical Ablation Result in Higher Rates of Sinus Rhythm Prior at Discharge and is the Effect Sustained Long-Term (6 Months, 1 Year, 3 Years, and 5 Years)? Statement: In patients with AF undergoing cardiac surgery, surgical ablation improves the achievement of sinus rhythm at discharge and 1 year (level A). This effect is sustained up to 5 years (level B).
Question 2:	In Patients Undergoing Cardiac Surgery, Does Surgical AF Ablation Reduce the Need for Pharmacologic Treatment of AF, DC Cardioversion, or Pacemaker Insertion? Statements: i. In patients with AF undergoing cardiac surgery, surgical ablation did not reduce the use of antiarrhythmic drugs at 12 months after surgery (level A; 36.0% vs. 45.4%), although trials were not designed to answer this question. ii. In patients with AF undergoing cardiac surgery, surgical ablation did not increase the requirement for permanent pacemaker implantation (4.4% vs. 4.8%; level A), although level B evidence raises the possibility of increased need for pacemaker.
Question 3:	In Patients Undergoing Cardiac Surgery, Does Surgical AF Ablation Reduce the Risk of Stroke, MI, Heart Failure, and Other Complications? Statements: i. In patients with AF undergoing cardiac surgery, surgical ablation does not increase the risk of perioperative mortality (level A), stroke (level A), MI (level B), cardiac tamponade (level A), reoperative bleeding (level A), esophageal injury (level B), low cardiac output (level A), intraaortic balloon (level B), congestive heart failure (level B), EF (level B), pleural effusion (level A), pneumonia (level A), renal dysfunction (level B), mediastinitis (level A). The incidence of esophageal injury remains low (level B). ii. In patients with AF undergoing cardiac surgery, surgical ablation does not reduce mortality at 1 year (level A). There is a possible reduction in mortality beyond 1 year (level B).There was no difference in stroke (level A), MI (level A), and heart failure (level B). EF is increased (+4.1% over control; level A).
Question 4:	Does Ablation Improve QOL, Functionality, or Other Patient-Reported Outcomes? Statement: In patients undergoing cardiac surgery, surgical AF ablation: i. Has been shown to improve exercise tolerance at 1 year (level A); however, the methodology used and the number of trials studying this outcome are insufficient. ii. Has not been shown to impact QOL at 3 months and 1 year (level A); however, the methodology used and number of trials studying this outcome are insufficient.
Question 5:	In Patients Undergoing Cardiac Surgery, Does Surgical AF Ablation Reduce Total Costs, ICU and Hospital Length of Stay, Need for Repeat Cardiac Surgery, Readmissions, and Cost-Effective? Statement: In patients undergoing cardiac surgery, concomitant surgical ablation increases CPB and cross-clamp times (level A), with no difference in ICU and hospital length of stay (level A). Overall costs were not reported.
Question 6:	In Patients With AF Undergoing Cardiac Surgery Plus Ablation, How Do Different Ablative Techniques Compare With Each Other for Conversion to Sinus Rhythm Cut-and-Sew, Cox Maze I, II, and III, Pulmonary Vein Isolation, Radiofrequency Ablation, Ultrasound Ablation, Laser Ablation, and Cryoablation? No statement.

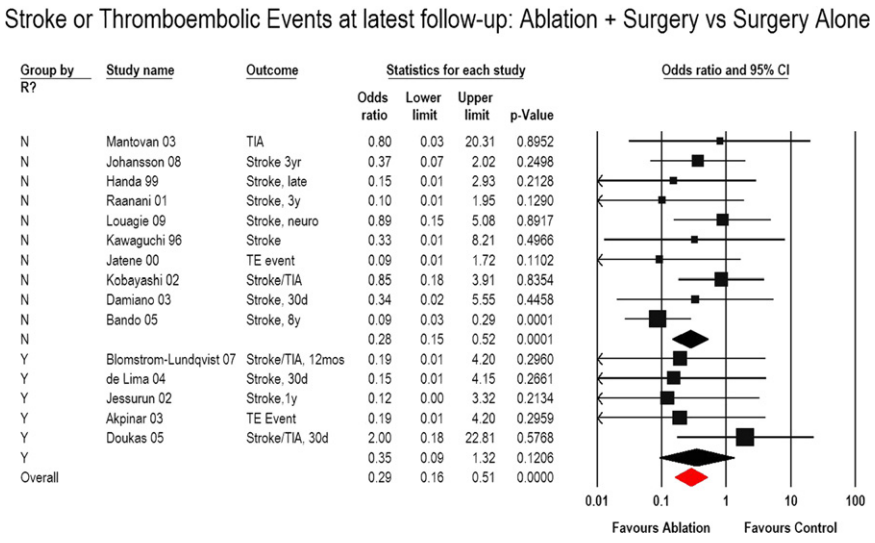

Fig. 2. Meta-analysis of stroke or thromboembolism at latest follow-up. (Cited from Ref. [8] with permission: Innovations. 2010;5:84–96.)

lesions, excision or closure of the left atrial appendage, or ablation of the active GP, performed through small thoracotomy or a thoracoscopic approach. This procedure avoids the use of cardiopulmonary bypass, cardiac arrest, and a full sternotomy. Initially, the indication of the minimally invasive procedure was paroxysmal AF; however, more recently, it has been extended to persistent and long-standing persistent AF [11]. Nevertheless, PV isolation alone has been shown to be insufficient in treating long-standing persistent AF, and the need for connection lines between the PV isolation lines and the mitral annulus has been raised [12]. Various epicardial techniques were tested to create a linear block line on the atrial free wall on the beating heart [13–16].

Compared with the full-maze procedure with cardiopulmonary bypass, cardiac arrest, and full sternotomy, the minimally invasive procedure reduces the potential risk of bleeding, myocardial damage and other complications, and mortality. PV isolation can be performed both with catheter ablation and surgical ablation. Sauren et al. [17] investigated the occurrence of cerebral microembolic signals as a surrogate marker for the risk of neurological impairment of 2 different PV isolation methods: percutaneous

Survey Period	Overall Return to SR
6 months Off AA's	34/38(89%) 29/38(76%)
12 months Off AA's	24/26(92%) 23/26(89%)
24 months Off AA's	13/14(93%) 13/14(93%)
36 months Off AA's	8/8(100%) 8/8(100%)

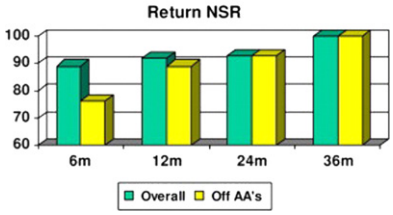

Fig. 3. Outcome after the maze procedure for patients with failed radiofrequency catheter ablation. Return to sinus rhythm rate. (AA, antiarrhythmic drugs; NSR, normal sinus rhythm; SR, sinus rhythm.) (Cited from Ref. [10] with permission: Ann Thorac Surg. 2011;91:1371-7.)

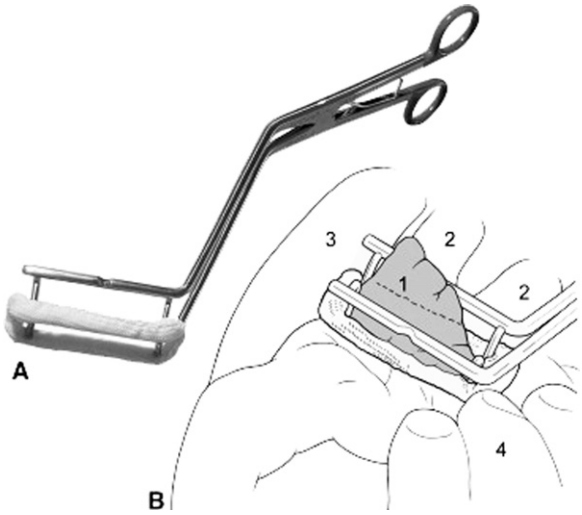

Fig. 4. Left atrial appendage (LAA) clip, deployment tool, and deployment. (A) Reusable Miltex deployment tool, as used in all cases. The LAA clip is loaded onto the jaws of this tool. (B) LAA mobilized within the clip (1), right pulmonary veins (2), and pulmonary artery (3), and operator's hand (4) gently mobilizing the heart to demonstrate the LAA and allow placement of the clip with the left hand. (Cited from Ref. [21]: J Thorac Cardiovasc Surg. 2010;139:1269-74.)

endocardial RF ablation and thoracoscopic epicardial ablation with RF energy.

The incidences of AF and AT have been shown to be relatively high after minimally invasive AF surgery [18–20]. Edgerton et al. [18] demonstrated that freedom from AF or AT should be assessed by long-term monitoring. Kron et al. [19] showed that 40% of patients could undergo bilateral PV isolation and ablation of GP and the ligament of Marshall through a minimally invasive thoracoscopic procedure. An electrophysiological study investigated patients with atrial arrhythmias and found that the underlying mechanism behind the arrhythmias was the reconnection of the previous PV isolation and isthmus-dependent reentry. Zeng et al. [20] examined patients with recurrent atrial tachyarrhythmias after minimally invasive PV isolation with an electro-anatomical mapping system, and found gaps at the roof and bottom of the PV isolation. They also found gaps in the PV isolation ring and ectopic focus between the left atrial appendage and left superior PV.

Closure of the left atrial appendage is an important procedure both in the full-maze and minimally invasive AF procedures, with regard to the prevention of stroke. Staples have been used to close the left atrial appendage in the minimally invasive AF procedure. Recently, a new clip device was introduced and tested in animals and patients [21,22] (Fig. 4). The initial results were favorable, and further trials are required to test the long-term safety and to evaluate the role of the left atrial appendage occlusion in stroke prevention.

5. Postoperative AT

Although the maze procedure is the gold standard in surgical therapy for AF, the restoration ratio of sinus rhythm from AF is about 90%. Five percent to 10% of patients experience recurrences of AF or AT after the maze procedure [23]. While recurrent AF occurs in some patients with a large left atrium (cardiothoracic ratio $>70\%$ and left atrial diameter >80 mm) preoperatively, the mechanism of postoperative AT differs from that of recurrent AF. It has become clear that the most common mechanism of postoperative AT is incomplete ablation of the mitral valve annulus and coronary sinus. Wazni et al. [24] reported that incomplete surgical ablation of the PVs, or the mitral or tricuspid annulus causes postoperative AT after the traditional cut-and-sew maze procedure. Postoperative AT is cured by catheter ablation of the incomplete conduction block. McElderry et al. [25] described a 15% incidence of AT after a modified maze procedure. They found macro-reentries around the surgical incisions caused by residual conduction at the incomplete ablation site in AT patients.

The rationale behind the surgical treatment of AF is to create a conduction block. The cut-and-sew technique provides a complete conduction block, and a line of conduction block prevents propagation of abnormal activation and interrupts reentrant circuits. Alternative ablation devices have been developed to replace the cut-and-sew lesions of the original maze procedure in order to simplify the surgical procedure, decrease the risk of bleeding, and shorten the cardiac arrest and operative times during the surgery. However, ablation devices such as traditional cryoablation, RF ablation, microwave, or ultrasound do not necessarily guarantee a transmural and continuous necrosis. However, Lall et al. [2] described that AF surgery with a RF ablation device cured AF in $>90\%$ of patients, which is a similar result to that with the traditional cut-and-sew maze procedure. Stulak et al. [26] and Doty et al. [27] reported that the traditional cut-and-sew maze procedure was superior to RF AF surgery for the treatment of AF. Ishii et al. [28] emphasized the importance of complete ablation of the coronary sinus and PVs during AF surgery. They recommend an intraoperative evaluation of the conduction block by pacing from the coronary sinus or PVs in order to prevent postoperative AT (Fig. 5). Krul et al. [29] demonstrated that the periprocedural confirmation of ablation lesions contributed in achieving a high success rate of thoracoscopic video-assisted PV antrum isolation with GP ablation. Henry et al. [30] showed that recurrent AT can be safely and effectively treated by catheter ablation postoperatively, suggesting that the combination of catheter and surgical ablation can improve outcome even in complex patients.

6. Hybrid approach

A hybrid approach that combines surgical epicardial PV isolation with an excision or closure of the left atrial appendage and catheter-based endocardial ablation of the atrioventricular isthmuses or focal ablation may enhance the advantages and lessen

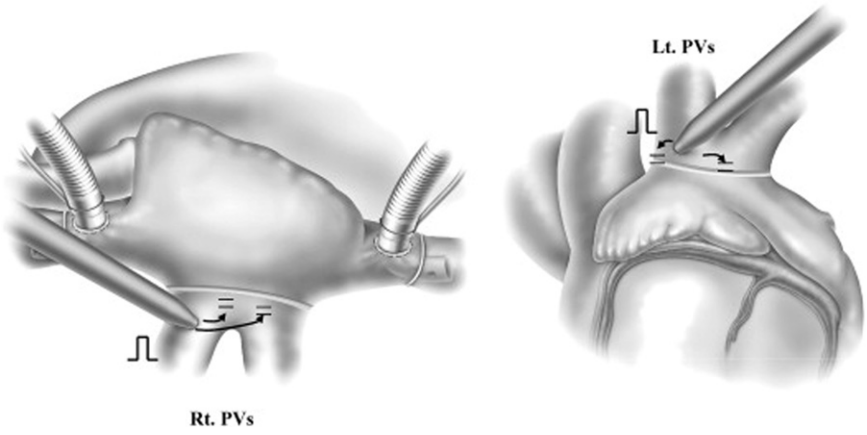

Fig. 5. Confirmation of pulmonary vein (PV) isolation. Each of the 4 PVs is paced using a bipolar electrode after PV ablation. The conduction block between the PVs and the left atrium is determined by the failure of atrial capture despite the maximum output of the stimuli of the PV pacing. If any residual conduction is observed between any of the PVs and the left atrium, repeat ablation is performed until a complete conduction block is confirmed. Pacing sites (rectangles). Rt. PVs, right pulmonary veins; Lt. PVs, left pulmonary veins. (Cited from Ref. [28]: J Thorac Cardiovasc Surg. 2008;136:998–1004.)

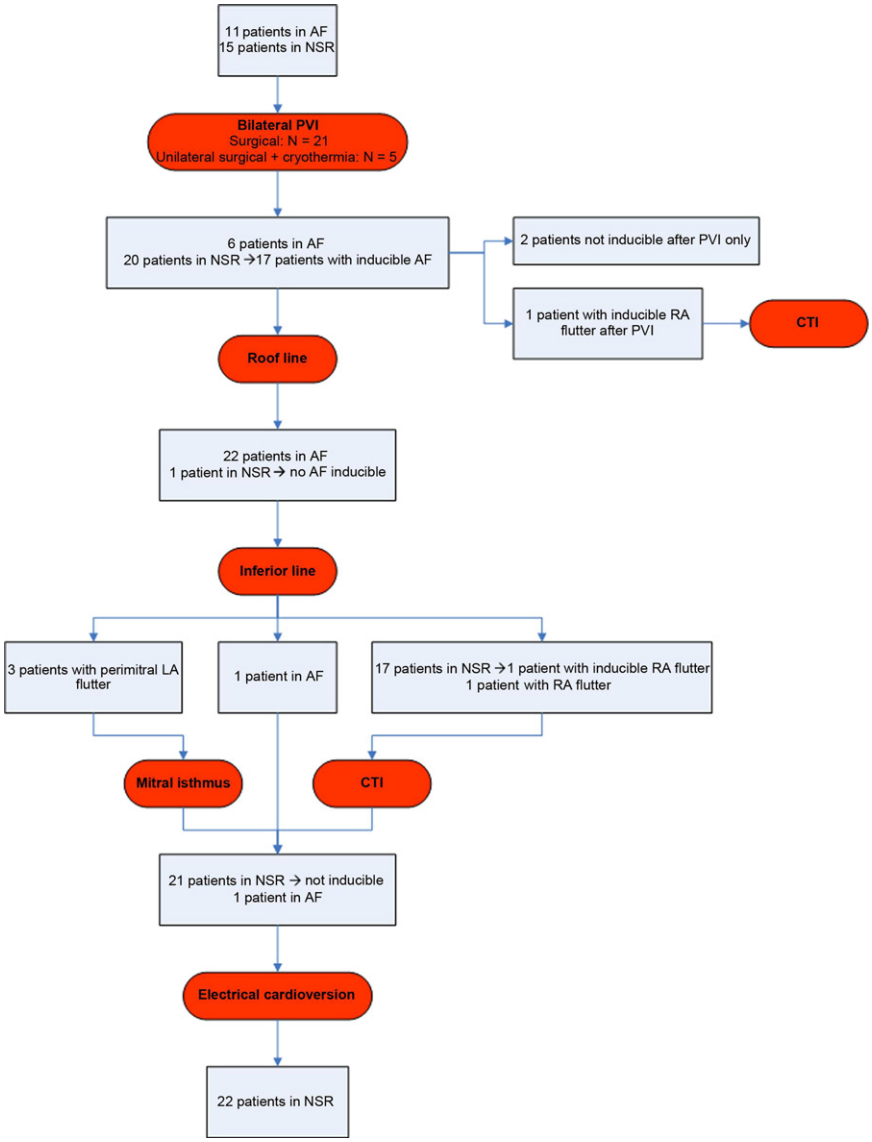

Fig. 6. Flow diagram of the stepwise lesion sets. CTI, cavotricuspid isthmus; LA, left atrium; NSR, normal sinus rhythm; PVI, pulmonary vein isolation; RA, right atrium. (Cited from Ref. [33] with permission: J Am Coll Cardiol. 2012;60:54–61.)

the disadvantages of the other procedure and enable a minimally invasive and effective treatment for AF. Surgical PV isolation is easily and safely performed using a bipolar RF clamp-type device, and several devices are available for the excision or closure of the left atrial appendage. These procedures can be performed either through small thoracotomy or by using a thoracoscope.

It is still not certain whether a single or a staged approach is safer and more effective. Natale et al. [31] performed a combined closed-chest epicardial monopolar radiofrequency ablation through a transabdominal transdiaphragmatic single port and catheter-based transseptal endocardial ablation as a single-stage approach in 22 patients with long-standing persistent AF and a large left atrium. The outcome and complications were compared with those in patients who underwent standard manual catheter ablation. The hybrid approach resulted in 13.6% mortality rate, whereas no death was reported in the standard approach. There was no significant difference in AF-free rate (55% vs. 54%) after a single procedure.

Mahapatra et al. [32] performed a sequential surgical epicardial ablation followed by planned endocardial evaluation and ablation during the same hospitalization in 15 patients who failed at least 1 catheter ablation and treatment with 1 antiarrhythmic drug, and compared the results with 30 patients who underwent a repeat catheter ablation. Five of the surgical ablation patients were inducible to atrial flutter and were ablated. After a mean follow-up of 21 ± 5 months, 86.7% of the surgical ablation patients were free of atrial arrhythmias and off of antiarrhythmic drugs, compared with 53.3% in catheter-alone patients.

More recently, Pison et al. [33] reported the 1-year follow-up data of 26 patients who underwent a hybrid thoracoscopic surgical and transvenous catheter ablation of AF. Epicardial PV isolation with a bipolar RF clamp was tested endocardially, and 23% of the patients showed residual conduction across the lesion. The lesion set was determined in a stepwise fashion (Fig. 6) and performed epicardially and endocardially. The 1-year success rate for AF was 93% in paroxysmal AF patients and 90% in persistent AF patients.

7. Challenges for advanced cases

A dilated left atrium, a longer duration of AF, the presence of low-voltage *f*-waves on the electrocardiogram, and others have been reported as risk factors for unsuccessful outcome or AF recurrence after the maze procedure. Damiano et al. [34] confirmed that an increasing size of the left atrium was a significant risk factor for failure of an ablation-assisted maze procedure, and concluded that there might be a need for a more extensive size reduction or expanded lesion sets in patients with a large left atrium. Volume reduction procedures, such as resection of the inferoposterior left atrium [35] or plication of the redundant left atrium along the PV isolation line [36], demonstrated an improved conversion rate of AF and increased left atrial function postoperatively. Damiano et al. [34,37] have shown that the box lesion set (Fig. 7), in which the bilateral PV isolation lines are connected at the roof of the left atrium and the entire posterior left atrium is isolated, decreased the incidence of early atrial tachyarrhythmias and late recurrence of AF. Because the more the atrial wall is isolated, the more the atrial transport function is impaired, the indication of the box lesion set should be examined in terms of atrial function in patients with different sizes of the left atrium.

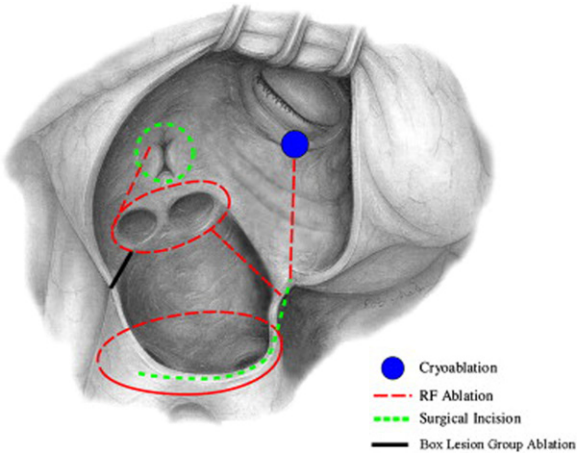

Fig. 7. Box lesion set. Patients either had a single ablation line connecting the inferior right and left pulmonary veins (non-box lesion set) or had an additional ablation line connecting the superior right and left pulmonary veins (box lesion set), which electrically isolated the posterior left atrium. RF, radiofrequency. (Cited from Ref. [37] with permission: J Thorac Cardiovasc Surg. 2008;135:870-7.)

8. Role of GP ablation

Increased autonomic nervous activity has long been known to play a potentially important role in the initiation and maintenance of AF. Vagal nerves innervate the heart more heterogeneously than the sympathetic nervous system, resulting in spatial heterogeneity of refractoriness. Therefore, increased vagal activation may be more important than the effect of the sympathetic discharge in the arrhythmogenesis of AF.

Recently, the identification of the GPs and their ablation has been expected to reduce the vagal activity that may facilitate the triggered activity in the PVs and prevent the recurrence of AF after surgical treatment. High-frequency stimulation at a rate of 800 beats/min is delivered to the fat pad beside the PVs and atrial tissue; then, a specific area with a vagal reflex (reduction in heart rate) during stimulation is defined as an active GP. Mehall et al. [38] ablated the GPs in a minimally invasive operation for AF. Forty-one patients with paroxysmal and chronic AF underwent the operation, and on average, 3 active GPs were identified in each patient. More than half of the GPs were found in the area of the superior aspect of the interatrial groove and the ligament of Marshall. In addition to PV isolation, each GP was isolated or ablated, resulting in the complete elimination of vagal reflexes after the ablation. Mcclelland et al. [39] performed precise mapping of GP activity in 21 patients with paroxysmal or persistent AF. Their data showed that bilateral PV isolation eliminated 79% of the GP active sites and additional GP ablation achieved extensive elimination (94%) of GP activity. During a mean follow-up time of 17 ± 3.5 months, there was only 1 recurrence in a patient with paroxysmal AF, while 4 of 9 patients (44%) with persistent AF had postoperative recurrence. On the other hand, Onorati et al. [40] reported that GP ablation combined with the maze procedure improved the short-term outcome compared with the maze procedure alone in the treatment of persistent AF during mitral valve surgery.

GP ablation has been regarded as a vagal denervation procedure that reduces the vagal tone in the atria and the vulnerability to AF. However, it is unclear how much vagal effect on the atrium is attenuated and how much of the atrium is denervated after the ablation. According to the GP mapping by Mcclelland et al. [39], a vagal reflex was present in the GPs near the atrioventricular groove even after the ablation. A histoanatomical study showed that more than 700 ganglions and 40,000 neurons are distributed in the whole atria and linked with each other. These data suggest that it is difficult to eliminate every GP activity to exclude all

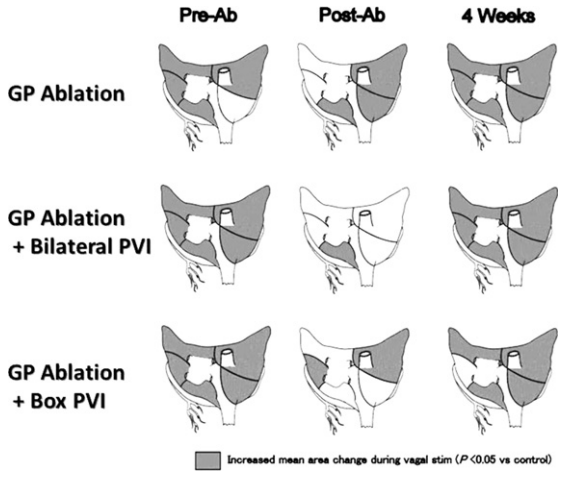

Fig. 8. Mean QRST area changes at 5 atrial regions before ablation (Pre-Ab), immediately after ablation (Post-Ab), and 4 weeks after ablation. Significantly increased area changes against control values ($p < 0.05$) are indicated by shading. stim, stimulation. (Cited from Ref. [42] with permission: J Thorac Cardiovasc Surg. 2010;139:444-52.)

neural networks from the atrium. Lall et al. [41] examined the vagal denervation effects after a maze IV procedure with canine atria, and showed that the maze procedure partially denervated the atrium. However, Voeller et al. [37] demonstrated in patients that the box lesion isolating the entire posterior left atrium in the maze III procedure showed a significantly higher freedom from AF compared with a single connecting lesion between the inferior PVs, suggesting that connecting the lesion between the superior PVs denervated the GPs more extensively in the left atrial roof. More recently, Sakamoto et al. [42] examined the electrophysiologic attenuation and recovery of the atrial vagal effects after GP ablation alone or with standard surgical lesion sets for AF. They demonstrated that GP ablation significantly reduced atrial vagal innervation with restoration of vagal effects at 4 weeks, suggesting early atrial reinnervation (Fig. 8).

9. Future perspective

The results of the surgery for AF are still less than satisfactory. This is largely because of the various and undetermined underlying mechanisms for the initiation and sustenance of AF in each patient. These mechanisms include atrial electro-pathophysiological abnormalities, autonomic nerve activity, and others. Therefore, no single surgical procedure may be sufficient to cure all types of AF in every patient. A new modality is needed to examine each patient preoperatively or intraoperatively, in order to "characterize" the AF and then determine the ideal surgical procedure for each individual. The hybrid procedure combining epicardial and endocardial ablation with a stepwise approach may enable the development of a tailor-made therapy for AF.

Conflict of interest

There is no conflict of interest.

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