Keynote Lecture Series

Surgical options for atrial fibrillation treatment during concomitant cardiac procedures

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Current guidelines recommend concomitant surgical ablation (SA) of atrial fibrillation (AF) in the context of mitral valve disease. A variety of energy sources have been tested for SA to perform effective transmural lesions reliably. To date, only radiofrequency and cryothermy energies are considered viable options. The gold standard for SA is the Cox-Maze ablation set, especially for non-paroxysmal AF (nPAF), with the aim of interrupting macro-reentrant drivers perpetuating AF, without hampering the sinus node activation of both atria, and to maintain the atrioventricular synchrony. Although the efficacy of SA in terms of early and late sinus rhythm restoration has been clearly demonstrated over the years, concomitant AF ablation is still underperformed in patients with AF undergoing cardiac surgery. From a surgical standpoint, concerns have been raised about whether a single (left) or double atriotomy would be justified in AF patients undergoing a "non-atriotomy" surgical procedure, such as aortic valve or revascularization surgery. Thus, an array of simplified lesion sets have been described in the last decade, which have unavoidably hampered procedural efficacy, somewhat jeopardizing the standardization process of ablation surgery. As a matter of fact, the term "Maze" has improperly become a generic term for SA. Surgical interventions that do not align with the principles of forming conduction-blocking lesions according to the Maze pattern, cannot be classified as Maze procedures. In this complex scenario, a tailored approach according to the different AF patterns has been proposed: for patients with concomitant nPAF, a biatrial Cox-Maze ablation is recommended. Conversely, it might be reasonable to limit lesions to the left atrium or the pulmonary veins in patients with paroxysmal AF (PAF) in some clinical scenarios. The aim of this review is to provide an overview of the current ablation strategies for patients with AF undergoing concomitant cardiac surgery.

Keywords: Atrial fibrillation (AF); concomitant atrial fibrillation ablation (concomitant AF ablation); cardiac surgery; Cox-Maze

Submitted Dec 09, 2023. Accepted for publication Feb 12, 2024. Published online Mar 14, 2024.
doi: 10.21037/acs-2023-afm-0208
View this article at: https://dx.doi.org/10.21037/acs-2023-afm-0208

Introduction

Among patients undergoing cardiac surgery, the incidence of preoperative atrial fibrillation (AF) is about 30% (1). In those who present with mitral valve diseases, this can increase to 50% (2). A lower incidence amongst patients listed for coronary artery bypass graft (CABG) is found, at approximately 5% (3). Prior studies have illustrated that concomitant surgical AF ablation alongside valvular surgery and/or CABG promotes sinus rhythm (SR) restoration and improves long-term outcomes, with demonstrated safety and effectiveness (4-7), while patients with untreated AF experienced a lower quality of life due to the persistence of arrhythmia-related symptoms and reduced exercise tolerance (8). Notwithstanding the clear

benefits and guideline recommendations, concomitant AF ablation is still under-performed in patients with AF undergoing cardiac surgery (9,10). At present, the most effective approach for concomitant AF treatment in terms of SR restoration is represented by the biatrial (BA) Cox-Maze operation. This technique has evolved since its first introduction by simplifying the lesion-set and replacing the "cut-and-sew" technique with ablation lines. As a result of this evolution, the Cox-Maze IV (CM-IV) technique has improved the outcomes of surgical ablation (SA) by reducing surgical times and operative complications (4). Nevertheless, the BA endo-epicardial approach for SA is still perceived as too invasive and time-consuming. For this reason, surgeons are inclined to perform a CM-IV only when the treatment of cardiac disease requires an atriotomy, and are often reluctant to perform a CM-IV in patients that do not require atriotomy for the principal procedure, such as in CABGs or aortic valve replacement (AVR) (10). In this scenario, besides the CM-IV, which still represents the gold standard of therapy, simplified ablation schemes that limit the ablation lines to just the left atrium (LA) or to the pulmonary veins (PVs) with pulmonary vein isolation (PVI) have been developed. However, this wide variety of lesion sets with different indications may generate more confusion in the field of AF ablation and feed skepticism toward the efficacy of surgical AF treatment. This review will illustrate the current ablation strategies for patients with AF undergoing concomitant cardiac surgery and will attempt to shed light on the controversies regarding concomitant AF ablation in "non-atriotomy" surgeries.

Current indications for concomitant AF ablation

The 2020 European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) guidelines recommended concomitant AF ablation as a class IIa indication, suggesting that for non-paroxysmal atrial fibrillation (nPAF), a BA lesion pattern is more effective than left-sided only (11). Moreover, the 2023 Society of Thoracic Surgeons (STS) guidelines recommended surgical AF ablation at the time of concomitant mitral operations, isolated AVR, isolated CABG, and AVR plus CABG operations to restore SR (class I indication) (10). In the 2023 American College of Cardiology (ACC)/American Heart Association (AHA)/Heart Rhythm Society (HRS) guidelines, concomitant surgical AF ablation has a class IIa recommendation (12). Finally, the 2017 HRS/European Heart Rhythm Association (EHRA)/European Cardiac Arrhythmia Society (ECAS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Society of Cardiac Stimulation and Electrophysiology [Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología (SOLAECE)] expert consensus statement indicated a class I category for concomitant open (such as mitral valve) or closed (such as CABG and AVR) SA of paroxysmal AF (PAF) and nPAF for symptomatic AF refractory or intolerant to at least one class I or III antiarrhythmic medication (13).

Ablation schemes in atriotomy surgery

The rationale of concomitant surgical AF treatment is to restore a stable SR in order to maximize the benefits of surgical correction. Present evidence showed better SR restoration rates, cumulative overall survival, and survival freedom from stroke or morbidity at 5 years compared to no ablation in patients undergoing concomitant SA in atriotomy surgery (5,14). Therefore, SA should be adopted in as many patients presenting with preoperative AF history as much as possible.

In patients with AF linked to mitral valve disease, the amount of atrial substrate is maximal due to pressure and volume overload, often leading to LA dilation and remodeling. In such a context, significant myocyte and interstitial alterations contribute to the increasing electrical inhomogeneity, determining the micro- and macro-reentrant circuits at the level of the atria, thus perpetuating AF and flutter (15). Therefore, limiting SA to PVs alone without interrupting large re-entry circuits tends to provide unsatisfactory results, especially in persistent and long-standing persistent AF (16). The concept behind the Maze procedure is to interrupt the micro- and macro-reentrant AF drivers usually located around the atrial circular structures [i.e., PVs ostia, mitral valve annulus, LA appendage (LAA) ostium, coronary sinus ostium, tricuspid valve annulus, superior and inferior vena cava and right atrial appendage (RAA) ostium]. Atrial lesions are arranged such that a sinus-generated impulse can activate both atria and maintain atrioventricular (AV) synchrony (17). A left-sided Maze including LA posterior wall ablation, mitral isthmus, LAA ablation line, coronary sinus ablation, and LAA exclusion should be thus guaranteed in mitral patients with concomitant AF. However, the ideal strategy advocates completion of the SA by means of right ablation lines, namely the superior and inferior vena cava, tricuspid isthmus, right atrial (RA) free wall, and RAA ablation,

completing a full CM-IV ablation set.

In this scenario, physical energy sources [bipolar radiofrequency (BRF) and or cryothermy (cryo)] are used to perform the key corner lesions at the base of the CM-IV: the Box-lesion set isolating the four PVs and the posterior aspect of the LA, the LAA line connecting the Box-lesion with the LAA ostium, the mitral isthmus ablation line, and completed by the ablation at the level of the coronary sinus. Of paramount importance is managing the LAA, aiming both at stroke and cerebrovascular accident prevention, and providing electrical isolation to increase the chance of SR conversion (11,12). To date, the most reliable options to reach both goals are provided by either epicardial exclusion by means of AtriClip (AtriCure Inc., Manson, OH, USA), or by surgical excision, either stapling or by endocardial suture, with the latter showing to be largely unreliable in stroke prevention, and ineffective in terms of electrical isolation (18). In order to successfully complete a CM-IV SA, the right-sided lines should never be forgotten (19).

Adding a CM-IV SA is generally accepted when concomitant mitral and tricuspid surgery is needed (BA access). Evidence clearly demonstrates perioperative morbidity and mortality are not increased when a BA ablation is performed in patients with AF undergoing mitral surgery (20). However, in the case of PAF in patients with a high surgical risk profile, a left-Maze alone might be the preferred alternative to a complete CM-IV, compared to no ablation. Moreover, the widespread adoption of minimally invasive techniques in mitral and tricuspid valve surgery should not discourage the application of concomitant SA. As a matter of fact, the devices used for SA have been highly adaptable to minimally invasive techniques, allowing surgeons to perform a complete ablation procedure through a right mini-thoracotomy (21), utilizing video assistance with the support of cardiopulmonary bypass (CPB) via femoral cannulation. This approach has not only sustained excellent results comparable to a sternotomy, but also reduced surgical complications and hospital length of stay (21).

Comparison between bi-atrial and left-atrial lesions sets

Currently, there is conflicting evidence regarding the superiority of BA ablation over the left-Maze. A meta-analysis by Guo *et al.* reported BA ablation was not superior to LA ablation strategies in reducing AF recurrences in unselected surgical patients, and there were no differences in regard to early mortality and permanent pacemaker (PPM) (22). Similar results were shown by Li *et al.*, who depicted no significant differences in the rates of restored SR, risk of death, and cerebrovascular events, but higher rates of PPM implantation when BA was compared to LA ablation (23). On the other hand, Cappabianca *et al.* reported BA ablation to be superior to LA ablation alone in efficacy, but was associated with a higher risk of bleeding and PPM implantation, thus suggesting LA approaches in some subset of patients (24).

Such controversial results feed into the debate on the correlation between RA lesions and PPM. However, if correctly performed, the CM-IV should not cause PPM implantation by AV block as the procedure was improved from previous iterations by avoiding an atrial septal lesion (19), and moving the superior vena cava ablation line more posteriorly would avoid nodal injuries (17). Of note, the rate of PPM implantation for AV block in patients undergoing concomitant surgery could be largely influenced by the fact that valvular surgery entails a certain risk of PPM implantation. Most importantly, sick sinus syndrome is reported as the primary indication for PPM in many studies (25), and is known to be associated with AF (26): the PPM rate may be linked to preoperative sinoatrial node dysfunction. Despite most sources of mapped AF originating in the LA, nearly 25% patients may have AF sources in the RA (27). This is particularly true for nPAF; therefore, BA ablation is particularly recommended, because when the right lesions are omitted, one-half of the atrial continuum remains untreated, leaving a large amount of "untreated" atrium accessible for re-entry circuits. As a consequence, current guidelines on concomitant AF ablation recommended BA ablation for nPAF, while it may be reasonable to use a unilateral left atrial approach in the case of PAF and normal LA (16). Lastly, Cox and colleagues suggested that adding at least the cavo-tricuspidal isthmus ablation line to the LA Maze may improve efficacy without compromising procedural complexity and, possibly, the PPM rate (28).

The role of CM-IV in non-atriotomy surgeries

While the relationship between mitral valve disease and AF is well known, AF can be associated with coronary artery disease (CAD) due to multiple mechanisms. Firstly, AF and CAD can frequently simply coexist in the same patient. The occurrence of AF following a myocardial infarction or chronic CAD is partly due to structural changes stemming from ischemia and inflammation, resulting in

atrial remodeling and increased atrial fibrosis. Both factors contribute to an arrhythmogenic substrate within the atria (29). Various animal studies have demonstrated that chronic coronary artery occlusion creates an environment favorable for the spontaneous occurrence of atrial ectopy AF (30,31). Furthermore, myocardial ischemia and/or infarction can lead to ventricular dysfunction, inducing AF.

Aortic stenosis or regurgitation can progressively affect the atrial hemodynamics and prompt structural atrial remodeling. In pressure or volume overload cases, the elevated stress on the atrial wall results in atrial enlargement, thus initiating pathways that lead to fibrosis and modifications in myocyte function and coupling (32). Consequently, electrical conduction within the atria becomes disrupted, potentially leading to regions with slow and fragmented conduction that could serve as a substrate for tachyarrhythmias. Despite this, many studies supporting the results of CM-IV have been performed on patients undergoing atriotomy surgery, while the data regarding the BA endo-epicardial approach in non-atriotomy surgery are scant, and the evidence in this field is less solid (10).

There is a general reluctance to fulfill the complete Maze lesion set by adding atriotomies that would not have been otherwise needed, as in aortic valve or revascularization surgery. In these patients, the adoption of non-sternotomy surgical approaches (including robotic-assisted, left mini-thoracotomy, upper hemi-sternotomy, or right anterior thoracotomy) represents an anatomical limit for extensive AF management. Therefore, AF treatment is limited in such patients to epicardial PVI encircling using BRF clamp or the Box-lesion with LAA external exclusion, as these ablation lines can be performed with no atriotomy, with or without CPB. These approaches have high adoption rates and low complexity. However, their efficacy is limited, especially in the treatment of nPAF (persistent and long-standing persistent AF), because they leave the mitral and tricuspid isthmus and the connection between the Box and LAA untreated, which represent critical locations of macro-reentrant circuits in nPAF.

For this reason, the most effective approach to AF treatment remains the CM-IV, although in some selected cases, a left-Maze can be a reasonable compromise. The use of such an extensive approach must be carefully balanced, taking into account three factors:

- AF weight: duration, burden, signs of atrial remodeling (LA >55 mm).
- AF clinical drivers: symptoms (palpitation, dizziness, and dyspnea) and impact on daily activities (modified EHRA symptoms score).
- Surgical friendliness (low surgical risk, high center expertise in arrhythmia surgery).

In straightforward nPAF patients experiencing arrhythmia-related symptoms and at low surgical risk, the CM-IV is recommended during non-atriotomy cardiac surgery, particularly in young patients who may benefit from stable SR restoration in the long term. In such patients, a complete left-Maze should be at least performed. When dealing with an increased surgical risk or complex pathology associated with a nPAF substrate, the decision to adopt extensive ablation strategies needs to be substantiated by the belief that restoring SR could enhance both survival and quality of life. In such cases, a left-Maze lesion set might be more reasonable in order to simplify a surgery, particularly when the right atrium is not dilated, and the AF duration is relatively short. However, surgeons should at least aim for thromboembolic risk reduction by managing the LAA unless contraindicated. Lastly, for patients not undergoing an atriotomy, a combination of PVI/Box lesion and external exclusion of the LAA can be contemplated for those with a PAF substrate. This approach was proved to be effective in younger patients without predictive factors for treatment failure (i.e., severe atrial dilation) (33).

Energy sources

The modern innovation in arrhythmia surgery was represented by the transition from a "cut-and-sew" technique to the use of physical energy sources to create all the ablation lines. This technical innovation sped up the procedure, and reduced bleeding complications (34). A variety of energy sources have been tested, from BRF to cryo, microwave, high-frequency ultrasound, and laser. To date, only the BRF and cryo have been demonstrated to be effective in producing consistent and durable transmural lesions, thus increasing the success rate of SA. Modern AF ablation devices are characterized by the generation of uniformly continuous transmural lesions, resulting in complete conduction blocks that interrupt activation wave propagation. Besides, their safety is controlled by limiting the excessive energy delivery and collateral damage to surrounding structures (35). Transmurality depends on extrinsic factors such as the type of energy, application duration, and contact with the tissue that is critical especially when using cryo. Intrinsic factors include factors such as local variation in atrial wall thickness, the composition of epicardium and myocardium, and endocardial blood

cooling (36).

Despite the BRF and cryo being the most frequently recommended energy sources for AF ablation, only a limited number of studies in literature directly compared these energies, with inconsistent outcomes (37-39).

Radiofrequency (RF)

RF creates thermal injury by means of high-frequency, alternating current produced by myocytes, leading to irreversible protein denaturation and cellular desiccation (40). RF energy can be unipolar or bipolar, irrigated or dry. Unipolar RF studies have shown that it was unable to consistently create transmural epicardial lesions (41). Moreover, several complications were attributed to its use, the most worrisome being esophageal injury, which is usually fatal (42). Therefore, it has been abandoned over time. On the contrary, BRF clamp devices supply energy on both sides of the tissue (biparietal contact) between the jaws of the clamp, permitting better heat penetration with negligible thermal spread outside the bite of the jaws. By clamping the atrial myocardium, BRF also neutralizes the cooling effect of the circulating blood (heat sink effect) when used on the beating heart.

Currently, the available BRF devices recommended for RF energy ablation in concomitant surgical are Cardioablate Gemini (Medtronic, Minneapolis, USA), Cardioablate BP2 (Medtronic), Cardioablate LP (Medtronic), Isolator Synergy Clamp (AtriCure, Manson, USA) for RF energy ablation. The Cardioablate Gemini, BP2, and LP ablate tissues through resistive heating due to irrigated BRF energy. The Gemini is characterized by a flexible neck design that provides the ability to access various anatomies, utilizing a neck curve through the full range from 0- to 180-degree configuration, while the BP2 and LP have flexible malleable electrodes that can be rotated through 300°, and can conform to address even the most challenging cardiac anatomy. The closure of the jaws of these devices has hinged mechanisms. The Isolator Synergy bipolar clamp device is available in both fixed (OLL2) and articulated (EMT1) jaws configurations, with both devices having a parallel jaw closure mechanism. These devices use a dynamic monitoring algorithm that measure the tissues response to RF delivery 50 times per second. The system responds to specific tissue properties, and adjusts the energy output and time accordingly. The result is a custom-made column-shaped lesion specific to a tissue's length, width, and composition.

The ability to generate consistent transmural lesions is a key feature in being the appropriate tool for SA of AF. The main difference between clamp devices is represented by the type of the jaws closure mechanism. Hinged closure devices were demonstrated to have a progressively reduced contact force and pressure on the clamped tissue from the hinge to the tip of the jaws. This effect is less prominent in devices with parallel jaws closure systems. However, pressure and contact forces are of paramount importance in achieving transmurality (43).

Cryo

Cryo produces a direct physical injury using thermal conduction, and molecular-based cell death occurs by freezing. Moreover, intracellular and extracellular ice crystals form during the ablation process, disrupting the cell membrane (44). A liquid refrigerant (nitrous oxide or argon) is pressurized to the inner lumen of the ablation probe; here, it is transformed from liquid to gas and it cools the tissue by energy absorption (45).

For cryoablation, the cryoICE (AtriCure), the cryoFORM (AtriCure), the Cardioablate Cryoflex (Medtronic) and Cardioablate Cryoflex Clamp (Medtronic) are at the surgeon's disposal. The cryoICE or the cryoFORM have a retractable handle to expose the active probe length. In addition, their flexible tube set allows for a tight bending radius. They are both nitrous oxide powered. On the other hand, the Cardioablate CryoFlex Probes are distinctly malleable, allowing them to be easily shaped and reshaped by hand to address varying anatomical situations. They are argon-powered. Of note, the CryoFlex Clamp combines the utility of the CryoFlex probe with the familiarity and useful delivery of a clamp. Two commercially accessible cryo-thermal energy sources can be employed in cardiac surgery: those manufactured by AtriCure, Inc. (Cincinnati, OH, USA) utilize nitrous oxide, while argon is being utilized by Medtronic ATS (Minneapolis, MN, USA). Nitrous oxide (–88.5 ℃) and argon (–185.8 ℃) possess boiling points significantly below 0 ℃. However, does the efficacy of a colder cryoprobe change the rhythm outcomes? An observational study, with all its biases, reported better rhythm outcomes for the nitrous oxide probe compared to the argon one (46). In contrast, a recent randomized controlled trial showed no significant difference between the two probes at 1- (47) and 5-year (48) follow-up.

Cryo ablation devices were the first devices used to replace the "cut-and-sew" technique and were particularly effective

and reliable in transmural lesion creation. Specifically, cryo energy proved valuable in establishing a lesion along the mitral region, effectively reaching the fibrous annulus, or in conducting ablation procedures near coronary arteries. By leaning directly on the endocardial side, cryo is particularly convenient in the perimitral and peritricuspid areas where the AV tissue is too thick for the standard bite of BRF clamps to be effective (49). Nevertheless, specific techniques allow for the dissection of the AV groove tissue away from the AV junction (50), and the deployment BRF directly on the atrial myocardium. However, cryoenergy may be easier as it requires no additional dissection that might be cumbersome in a minimally invasive setting. Finally, cryo is considered safer because directly cooling the coronary arteries does not induce coagulative necrosis. Nevertheless, injury of the major coronary branch in the AV groove has been reported to occur with any ablation energy, including cryo (51). When performing any ablation at the level of the mitral and tricuspid annulus, it is advisable to tailor the ablation direction to the specific coronary anatomy (52). Despite such advantages, cryo is a much more time-consuming procedure in creating linear ablation compared to BRF. Ideally, a combination of both energy sources could combine advantages while reducing the drawbacks of cryo and BRF when used alone. This approach aims at reducing the potential for coronary thrombosis and stenosis, in contrast to the risks associated with RF energy (37).

Concomitant AF ablation outcomes

To date, the main achievement in patients undergoing concomitant AF SA is the significant improvement in terms of survival freedom from AF when compared to no ablation (5). Results from the systematic and meta-analysis from McClure and colleagues collecting 23 studies comparing patients with and without concomitant AF ablation pointed out a significantly increased survival freedom from AF recurrence in those receiving concomitant SA at 12 months (53). Moreover, in this study, the bi-atrial approach was deemed superior to lone left-sided lesion sets. More recently, a meta-analysis by Gemelli and colleagues specifically examined the outcomes of concomitant SA in mitral patients and observed that individuals undergoing concomitant ablation experienced improved restoration of SR compared to those who did not (54). Those results were consistent with the 5-year outcomes of the PRAGUE 12 trial, reporting a significantly lower survival freedom from AF recurrence in patients not receiving SA compared to patients with concomitant SA (AF freedom SA: 88.9% *vs.* no SA: 70.4%) (55). These findings support the role of concomitant SA in reducing the impact of AF burden during follow-up. Despite the benefits of SR restoration represent a strong predictor of survival (5), most of the studies failed to demonstrate a positive relationship between SR restoration in patients who underwent concomitant SA and the reduction of thromboembolic events, mortality, and quality of life improvement during follow-up.

Both meta-analyses of McClure and Gemelli reported no difference in terms of mortality between patients undergoing concomitant SA and patients not receiving SA. These findings align with the results of the PRAGUE-12 trial, indicating no significant differences in cardiovascular death during the follow-up period. Different from the above-mentioned metanalyses, the PRAGUE-12 reported a significant difference in developing stroke during follow-up, with a lower incidence in patients receiving SA. This finding may be justified with a more systematic approach to LAA exclusion in SA patients in the trial. A significant improvement in the overall survival for patients receiving SA compared to those no-SA was reported in two propensity-matched analyses derived from a larger series of patients from the STS database (8), and the Polish National Registry of Cardiac Surgery Procedures (KROK) (56). These studies showed lower risk-adjusted mortality and stroke in patients who underwent concomitant SA at 10 years but demonstrated an increased risk of PPM and perioperative renal failure in such patients.

Lastly, a cumulative meta-analysis of randomized clinical trials indicated no significant differences in mortality, pacemaker implantations, and neurological events when comparing SA to no ablation, while a distinct advantage was reported in terms of restoring SR (57). Despite all of this evidence, concomitant SA is still underperformed worldwide. Data from the STS database revealed that between 2011 and 2014, only 48% of patients with AF who underwent non-emergency cardiac operations received concomitant AF ablation, despite a growing trend has been observed over the years (16). Indeed, up to date data from STS database has shown that in 2022 only 30% of eligible patients received neither a SA nor any LAA management (10). In particular, surgeons' experience in SA was found to significantly influence ablation decisions (58). Surgeons with more than 50 SA cases, ablated 57% of AF patients, compared to 22% in surgeons with less than 50 cases. A recent publication from 21 hospitals in the Providence St. Joseph Health system from 2014 to 2020

showed that, on average, only 29.1% of patients with preoperative AF underwent surgical AF ablation, with an increased trend particularly after 2017, when new AF guidelines were published (9). The overall combined rates of AF ablation over the entire study period were 42.6% and 23.4% for mitral valve (± CABG) and non-mitral valve surgeries (CABG, AVR, or CABG + AVR), respectively. This suggests that the addition of a LA atriotomy is a major negative factor in the decision-making process, probably because of the perception that it could be associated with increased operative risk (59-61).

A recent nationwide matched study illustrated how concomitant AF ablation in patients undergoing isolated CABG is safe, and is associated with significantly improved long-term rhythm restoration and survival (14). A BA was mostly performed in nPAF (51%), while PVI was the most frequent scheme for PAF (69%). The authors proved no increase in perioperative mortality or morbidity rates, and a reduction of postoperative AF burden, with better mid-term AF-free survival rates. Ad and colleagues reported that incorporating the Cox-Maze III procedure into AVR or CABG did not lead to increased major morbidity or higher perioperative risk (60). Besides, individuals who underwent the Cox-Maze III procedure exhibited comparable long-term survival, and experienced enhanced health-related quality of life. Kainuma *et al.* compared PVI and the CM-IV in patients with persistent AF undergoing non-mitral surgery after propensity score matching and inverse probability treatment weighting (62). A concomitant Cox-Maze procedure resulted in superior freedom from AF rates at every time point (both with and without antiarrhythmic drugs), and improved survival and freedom from composite adverse events, when compared with PVI alone. It is important to highlight that the freedom from AF was not different between groups when considering patients with limited LA remodeling (LA <45 mm), while a Cox-Maze provided better outcomes in those patients with LA remodeling (LA >45 mm). This emphasizes the importance of evaluating LA remodeling prior to making decisions about the placement of ablation lines.

Predictors of AF failure and contraindication to SA

In AF SA, a dilated LA (>55 mm) constitutes a risk factor for ablation failure, alongside older age, prolonged AF duration, AF burden, and heart failure (11,63). Indeed, the duration of AF significantly influences the processes that induce LA remodeling and fibrosis. As a result, the effectiveness of ablation is diminished due to an adverse anatomical substrate characterized by intricate electrical disharmony (64). As demonstrated, simplified lesion sets are associated with a reduction in the SR recovery rate. Nevertheless, AF ablation in concomitant cardiac surgery is considered, *per se*, a predictor of AF recurrence during follow-up when compared with stand-alone AF ablation (6,65). Preoperative AF duration was also shown to be a significant predictor of late failure (65). The longer the AF duration, the more irreversible the atrial remodeling, atrial dilatation, atrial mass loss and fibrotic changes that could hamper the effectiveness of the ablation.

Left atrial appendage

It has been demonstrated that in patients with AF, 91% of all thrombi formed within the LAA (45). LAA exclusion represents a consistent feature of the Cox-Maze procedure since its inception (66). The recent LAAOS III trial randomized AF patients with a CHA_2DS_2-VASc score of at least two undergoing cardiac surgery for other indications to LAA closure or not: LAA closure resulted in a significant 33% stroke risk reduction at follow-up (67). In the PRAGUE-17 trial, patients with a history of bleeding requiring intervention or hospitalization, a history of a cardioembolic event while on oral anticoagulation (OAC), and or CHA_2DS_2-VASc ≥3 and HAS-BLED >2 were randomized to either LAA closure or direct oral anticoagulants (DOACs). The trial reported that LAA closure was non-inferior to DOAC in preventing major AF-related cardiovascular, neurological, and bleeding events (68).

Besides the stroke reduction advantage, electrical exclusion of the LAA proved to have an anti-arrhythmogenic benefit with epicardial LAA clip occlusion demonstrated to provide consistent electrical isolation of the LAA (18,69). Clipping or resecting the LAA thus has a potential adjuvant role in AF cure. The recently released 2023 ACC/AHA/American College of Clinical Pharmacy (ACCP)/HRS guidelines recommend surgical LAA exclusion for stroke prevention to be considered in patients with AF undergoing cardiac surgery with a CHA_2DS_2-VASc score ≥2 or equivalent stroke risk in class I (12). This recommendation was confirmed in class I by the recently released 2023 STS guidelines (10).

Conclusions

❖ A biatrial Cox-Maze procedure seems better than a left-

sided only ablation and is particularly indicated for all patients suffering from non-paroxysmal atrial fibrillation (nPAF). A left-sided only ablation may be satisfactory for PAF but should be avoided in patients with concomitant mitral valve diseases.

- ❖ When AF surgery is indicated, a full Cox-Maze IV procedure yields optimal results also in coronary artery bypass graft (CABG), aortic valve replacement (AVR), or both, where atriotomies are usually not required, without increasing postoperative complications.
- ❖ Cryoablation and radiofrequency are the recommended energy sources to be employed during surgical AF ablation.
- ❖ Currently, concomitant AF ablation is underperformed in patients with AF undergoing cardiac surgery, particularly CABG, AVR or both; the great variability of ablation schemes further complicates the analysis of an already intricate disease.
- ❖ While it must be emphasized that a poor or insufficient ablation, inadequate to the specific AF substrate, is usually ineffective if not counterproductive, tailored limited approaches like the left-Maze or pulmonary vein isolation/Box lesion can be considered to adapt the treatment options to non-atriotomy and to minimally invasive surgery.

Acknowledgments

Funding: None.

Footnote

Conflicts of Interest: S.B. receives consulting fee for AtriCure Inc., Allergan, Artivion, Medtronic Inc. The other authors have no conflicts of interest to declare.

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Cite this article as: Baudo M, Rosati F, Lapenna E, Di Bacco L, Benussi S. Surgical options for atrial fibrillation treatment during concomitant cardiac procedures. Ann Cardiothorac Surg 2024;13(2):135-145. doi: 10.21037/acs-2023-afm-0208

