

# **Surgical management of atrial fibrillation in patients undergoing cardiac surgery: a systematic review of clinical practice guidelines and recommendations**

Niraj S Kumar<sup>1,2</sup>, Mohammed Y Khanji<sup>1,3,4</sup>, Kush P Patel<sup>1,5</sup>, Fabrizio Ricci<sup>6</sup>, Rui Providencia<sup>7</sup>, Anwar Chahal<sup>8</sup>, Afzal Sohaib<sup>9</sup>, Wael I Awad<sup>1,10,11</sup>

<sup>1</sup> Barts Heart Centre, St. Bartholomew's Hospital, London, UK

<sup>2</sup> National Medical Research Association, London, UK

<sup>3</sup> Newham University Hospital, Barts Health NHS Trust, London, UK

<sup>4</sup> NIHR Barts Biomedical Research Centre, William Harvey Research Institute, Queen Mary University of London, London, UK

<sup>5</sup> Institute of Cardiovascular Sciences, University College London, UK

<sup>6</sup> Department of Neuroscience, Imaging and Clinical Sciences, G.d'Annunzio University of Chieti-Pescara, Chieti, Italy

<sup>7</sup> Department of Cardiac Electrophysiology, Barts Heart Centre, St. Bartholomew's Hospital, Barts Health NHS Trust, London, UK

<sup>8</sup> Division of Cardiology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA

<sup>9</sup> NHLI, Imperial College London, London, United Kingdom.

<sup>10</sup> Centre for Cardiovascular Medicine and Devices, William Harvey Research Institute, Queen Mary University of London, London, UK

<sup>11</sup> University of South Wales, Cardiff, UK

## **Corresponding Author:**

Wael I Awad

**Professor of Cardiovascular Surgery**

Barts Heart Centre, St. Bartholomew's Hospital,

West Smithfield

London, EC1A 7BE,

United Kingdom.

+44 2037658744

wael.awad@nhs.net

Word Count: 4943

Keywords: atrial fibrillation, surgical ablation, cardiac surgery, guidelines

## **Abstract**

### Aims:

Surgical ablation of atrial fibrillation (AF) has been demonstrated to be a safe procedure conducted concomitantly alongside cardiac surgery. However, there are conflicting guideline recommendations surrounding indications for surgical ablation. We conducted a systematic review of current recommendations on concomitant surgical AF ablation.

### Methods and results:

We identified publications from MEDLINE and EMBASE between January 2011 and December 2022 and additionally searched Guideline libraries and websites of relevant organisations in accordance with PRISMA guidelines. Of 895 studies screened, 4 were rigorously developed (AGREE-II >50%) and included. All guidelines agreed on the definitions of paroxysmal, persistent, and longstanding AF based on duration and refractoriness to current treatment modalities. In the Australia-New Zealand (CSANZ) and European (EACTS) guidelines, opportunistic screening for patients >65 years is recommended. The EACTS recommends systematic screening for those aged >75 or at high stroke risk (Class IIa, Level B). However, this was not recommended by AHA or STS guidelines. All guidelines identified surgical AF ablation during concomitant cardiac surgery as safe and recommended for consideration by a Heart Team with notable variation in recommendation strength and the specific indication (3 guidelines fail to specify any indication for surgery). Only the STS recommended left atrial appendage occlusion (LAAO) alongside surgical ablation (Class IIA, Level C).

### Conclusion:

Disagreements exist in recommendations for specific indications for concomitant AF ablation and LAAO, with the decision subject to Heart Team assessment. Further evidence is needed to develop recommendations for specific indications for concomitant AF procedures and guidelines need to be made congruent.

Word Count: 250/250

## **Introduction**

Atrial fibrillation (AF) is the most common cardiac arrhythmia in patients undergoing cardiac surgery and is associated with an increased risk of ischaemic stroke, hospitalisation, and death. AF affects approximately 10% of patients undergoing cardiac surgery. [1][2]

AF is classified by the duration of the episodes: paroxysmal AF is defined by recurrent AF episodes terminating within 7 days; persistent AF by episodes 7 days or longer, and longstanding persistent AF lasts for 1 year or more. [3]

Concomitant AF ablation can vary from pulmonary vein isolation (PVI) to a bi-atrial ablation or a full Cox-Maze procedure. The latter is the gold standard treatment for typical AF and consists of biatrial incisions isolating the pulmonary veins to disrupt reentrant circuits which perpetuate fibrillatory conduction, with >90% success rate by restoration of sinus rhythm at 1 year. [4] In recent years, various modifications have been made to simplify this procedure to reduce bypass and cross clamp times, such as the use of alternative lesions and energy sources for ablation. This

has resulted in the wider use of surgical ablation which can be simply performed in patients undergoing concomitant cardiac surgery.

Studies of patients with AF who are undergoing concomitant cardiac surgery have demonstrated the safety and effectiveness of ablation in restoring normal sinus rhythm. [5,6] Moreover, the evidence for superior postoperative morbidity and mortality outcomes following concomitant surgery is subject to controversy, and as such there is hesitation from surgeons (with concerns regarding increased operative and cross-clamp times, and the need to open left and right atria leading to a perceived increased risk of intraoperative complications) and guidelines regarding whether the concomitant procedures should be routinely performed. [5,6]

This study adds to a series in which we have analysed inconsistencies in international guideline recommendations for the management of cardiovascular disease. [7] The objective of this systematic review is to assess current guidelines and recommendations from professional societies for the diagnosis and management of AF in patients undergoing cardiac surgery. Additionally, this study highlights areas of agreement, disagreement, and potential gaps in literature to aid surgical decision-making and identify areas of future research.

## **Methods**

### **Data sources and searches**

We planned, conducted, and reported this systematic review under the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations, with the checklist being provided within the supplementary material. [8] Our methodology for systematic review of guidelines has been described in detail previously. [7]

We searched MEDLINE and EMBASE for guidelines in the English language containing recommendations for the diagnosis and surgical management of AF in adult patients undergoing concomitant cardiac surgery, published between 1 January 2011 and 31 December 2022. We also searched websites of cardiac societies and guideline development organisations (listed in Supplementary material), the National Library for Health Guidelines Finder, the Canadian Medical Association Clinical Practice Guidelines Infobase, the National Guideline Clearinghouse, and the Guidelines International Network International Guideline Library. Websites, as well as reference lists of all identified articles, including manual searching of reviews, were also appraised for additional relevant studies. We included search terms relevant to surgical management of atrial fibrillation and guideline recommendations. The specific search terms used and websites searched are included in the supplementary material.

### **Study selection**

We included only references that met the Institute of Medicine's definition of a guideline. [9] We excluded expert consensus documents, paediatric guidelines, or guidelines that were not produced on behalf of a professional organisation. If more than one guideline from the same organisation existed, we only assessed the most recent one.

### **Data extraction and quality assessment**

Titles and abstracts were assessed by two independent reviewers (NK and WA). Articles were excluded only if both reviewers agreed they were ineligible. Discrepancies were resolved by consensus and involving a 3<sup>rd</sup> reviewer to adjudicate as appropriate (MK). Both reviewers performed the final selection for full data extraction. We used the 23-item Appraisal of Guidelines for Research and Evaluation (AGREE) II system to determine the rigour of

development for each of the guidelines. [8] The AGREE II domain considers reporting of methods to search for evidence; criteria for selection of evidence; strengths and limitations of the body of evidence; methods for formulating the recommendations; health benefits, side effects, and risks; explicit link between recommendations and evidence; procedures for external expert peer review; and the updating process. Each item is rated on a 7-point Likert scale. Two reviewers (NK and WA) independently rated the items, conforming to the instructions of the AGREE II tool, with any disagreements being resolved via discussion.

Both reviewers assessed background information on the guideline development process from the developer's website. The average rigour scores were obtained by expressing the sum of the individual scores as a percentage of the maximum possible score. Guidelines were ranked according to this scoring system. Editorial independence from the funding body, external funding, and disclosure of relationships with the industry by individual guideline group members were also assessed.

### **Data synthesis and analysis**

Two reviewers (NK and WA) extracted all of the relevant recommendations from the guidelines that had an AGREE II score  $\geq 50\%$  conforming to our previous protocol. [8] Information on definition of AF, screening at time of cardiac surgery, safety, indications, and impact on outcomes of concomitant AF surgery & left atrial appendage occlusion. The recommendations were extracted into a table and compared (Table 1).

### **Results**

The search yielded a total of 895 titles. After removing duplicates and review of titles and abstracts, we retained 4 guidelines and recommendations on the management of concomitant AF

and cardiac surgery after full-text review (Figure 1). The guidelines from the Society of Thoracic Surgeons (STS), Cardiac Society of Australia and New Zealand (CSANZ), American Heart Association (AHA) and the European Society of Cardiothoracic Surgery (EACTS), had a rigour score >50% and formed the object of our review. [10-13] Table 1 summarises these guidelines and highlights rigour scores and Author's conflicts of interest (if applicable). Figure 2 summarises the relevant areas of agreement, disagreement, and gaps in guideline recommendations.

### **Definition of AF**

All 4 guidelines agreed on the definitions of paroxysmal, persistent, and longstanding AF based on the length of the AF and refraction to current treatment modalities. Three of the guidelines (AHA, EACTS, and CSANZ) also defined "permanent AF" whereby the patient and the clinician accepted the presence of AF with no attempt of rhythm control surgery to restore sinus rhythm.

These 3 guidelines also agreed upon AF being defined clinically by 30 seconds or longer incidents of shortened R-R intervals and absent P waves, as detected by an electrocardiogram (ECG) or continuous 24-hour monitoring (Holter monitoring). The STS guideline made no comment regarding the assessment of AF and did not include permanent AF as a defined variant.

### **Screening for AF**

In the CSANZ and EACTS guidelines, opportunistic screening for patients >65 years is recommended at primary care level when a patient presents for any reason. The EACTS further recommends systematic ECG screening for those aged >75 or at high risk of stroke (Class IIa, Level B). However, this indication was not recommended by the AHA or STS guidelines,

showing inconsistency in the need for screening practice. There was no specific recommendation regarding AF screening in patients undergoing cardiac surgery.

### **Recommendation for concomitant surgical intervention**

All 4 guidelines identified surgical AF ablation during concomitant cardiac surgery for any other indication to be safe and recommended for consideration by a multidisciplinary Heart Team. The same recommendation, however, is made at varying evidence levels: the STS gives Class I strength recommendation and the CSANZ uses a Strong recommendation, in contrast to a IIa recommendation given by the AHA and the EACTS. [9-12]

### **Indications for concomitant ablation in cardiac surgery**

There is notable variation in the strength of recommendation and the specific indication by which surgical ablation is listed in guidelines. The EACTS, AHA, and STS guidelines fail to specify any indication for AF surgery based on the classification of AF experienced by the patient nor the experienced benefit for the patient.

This decision is left to the best judgement of the Heart team with respect to benefits and risk, as justified by a paucity of trial evidence exploring outcomes specific to individual types of AF, and the concerns of an increased risk of pacemaker insertion and a range of ablation strategies, including cryoablation and radiofrequency. Thus, at present it is unclear which is the agreed recommendation for surgical ablation for each type of AF and for symptomatic vs asymptomatic AF.

The CSANZ guidelines are the only guidelines which specify that concomitant surgical ablation is to be considered in patients with symptomatic paroxysmal, persistent, or long-standing



persistent AF (GRADE quality of evidence: Moderate; GRADE strength of recommendation: Strong).

### **Indications for Left Atrial Appendage (LAA) surgery**

All 4 guidelines also discuss accompanying LAA surgery alongside other cardiac surgery for the reduction of stroke risk and thromboembolism. Again, there is a general consensus that this is a decision to be closely considered by a multidisciplinary Heart Team in the context of the patient's overall surgical tolerance and their specific needs for thromboprophylaxis and risk management, but with acknowledgement that not performing LAA occlusion (LAAO) may lead to thrombotic risk arising from AF being undertreated in patients who are not able to tolerate anticoagulation therapy. Notably, these recommendations are not made to a consistent standard: the EACTS makes a IIb, C recommendation, AHA IIb, B-NR, CSANZ GRADE quality of evidence: Moderate; GRADE strength of recommendation: Strong, and STS IIa, C.

The STS do not specifically comment on LAAO, but they make the recommendation for LAA exclusion or excision to be conducted alongside surgical AF ablation (Class IIA, Level C limited data), and is the only body to provide guidance on this. Three guidelines (EACTS, STS, and CSANZ) recommended the usage of LAA exclusion, either in isolation or in conjunction with surgical ablation and concomitant cardiac surgery.

Significantly, there are no clear alternatives specified to LAA occlusion or excision, and no mention is made of other procedures such as the cut and sew method or the AtriClip.

Additionally, there were no clearly specified indications or contraindications to LAA surgery listed in any of the guidelines included in this systematic review, with the decision being left to the best judgement of risk and benefit to the patient by the Heart team.

## **Postoperative surveillance**

After ablation, regular community monitoring using ECG or Holter have been conventionally thought of as reasonable methods by which to confirm a diagnosis of AF and therefore to assess recurrence. However, this recommendation is not consistently made across guidelines. The STS is the only guideline to refer to postoperative monitoring for AF arrhythmia, but even so do not make a recommendation for monitoring, simply mentioning that “at least periodic 24-hour Holter monitoring should be routine”.

## **Discussion**

In this systematic review, we identified 4 guidelines which provided recommendations on the surgical ablation of AF. We reported consensus generally on the definitions and assessment of AF, and the recommendation to surgically ablate or conduct LAA procedures concurrently with other cardiac surgery. This is in line with current evidence as AF has consistently been demonstrated as an independent predictor of mortality and morbidity in cardiac surgery, and thus the concomitant ablation of AF to restore sinus rhythm can serve as an important component of clinical management to improve outcomes by reducing risk of stroke, bleeding, heart failure, or readmission from AF. [6,14] Concomitant surgical ablation was additionally found to provide significant improvement in quality of life, which is even greater when the ablation leads to successful restoration of SR. [15]

However, there is clear disparity and lack of consensus over the indications and contraindications for which types of AF surgical ablation ought to be considered for, and the risk cut-offs for deciding on offering surgical ablation.

None of the recommendations mention AF screening in a more general population (<65 years or with other risk factors), usage of anticoagulation in management of stroke risk following ablation, or the specific indications for when LAAO may be appropriate for patients.

As such, there are clear directions for which future evidence will be needed to guide surgical practice and to help inform decisions made by Heart teams regarding individual patient management, which exemplify the need for clear trial data which will provide clarity and confirmation on the benefits and limitations of surgical intervention for AF alongside other cardiac surgery.

### **Ablative techniques in cardiac surgery**

AF ablation can briefly be summarised as closed or open. Closed surgery does not require incisions to be made to open the atria, and so is achieved with the majority of concomitant cardiac procedures, such as CABG or aortic valve surgery. In such cases, the subtype of AF is significant in determining the optimal surgical procedure, since the management will vary on the circuits causing AF. For patients with a paroxysmal AF, the inducing triggers causing the arrhythmia are believed to originate most commonly from the pulmonary veins, and hence PVI is the most reasonable management, with a freedom from AF at 1 year follow-up at approximately 80%. [14] For non-paroxysmal AF, it is more common for the trigger to be self-perpetuating macro-re-entrant circuits in the atrium, and to address this a more invasive ablation technique such as the Cox-Maze is most effective, with a biatrial lesion set proving to offer greater ability to restore sinus rhythm. [16]

Open surgery is typically for mitral valve procedures, where the left atrium has already been dissected for access to the mitral valve, allowing for more incisions to be made in the ablation

procedure. It is typically on such patients where the Cox-Maze procedure is used, and these patients will often receive LAA surgery if indicated as well due to the ease of access. This is thought to be the best practice for all subtypes of AF, given effectiveness in restoring non-sinus rhythm is over 90%. [3,16]

### **Role of screening for AF in context of surgery**

There is inconsistency in the recommendations for opportunistic AF screening, with the CSANZ and EACTS guidelines offering supporting recommendations, albeit for differing age groups. The rationale for this recommendation is based on a combination of risk profile (since 70% of patients with AF are aged 65-85) and the actionable management at this stage. Patients over 65 are indicated to receive direct oral anticoagulant (DOAC) therapy for stroke prevention, justified by studies analysing cost-effectiveness and the risk of stroke increasing with age, thus allowing early detection and management. [14] Hence in the context of cardiac surgery it is important to include opportunistic screening to identify patients amidst a population at elevated risk of stroke or mortality from AF to provide necessary surgical management. Repeated hand-held ECG recordings over 2 weeks in an unselected population aged 75-76 years increased the detection of asymptomatic AF by up to 7.4% in subjects with >2 stroke risk factors. [14, 17]

### **Safety of concomitant surgical ablation**

Surgeons are documented as being hesitant to perform concomitant ablation outside of mitral valve surgery, due to a perceived increase in risk and an unwillingness to subject patients to additional incisions or cross-clamp time in the presence of multiple comorbidities. [2] However, in spite of this, many studies have demonstrated that ablation results in no additional perioperative risk and no difference in length of stay, permanent stroke, renal failure, 30-day

readmissions, and 30-days mortality. [14, 18] Nevertheless, it is still unclear which patients would benefit most from it and whom may be at higher risk of further mortality and morbidity given their relative surgical risk. The defining surgical pre-operative risks for morbidity and mortality outcomes following surgical ablation are well-documented in the literature: left atrial size, patient age, AF duration, heart failure with reduced ejection fraction, and renal dysfunction. [14, 16] These are specified within the EACTS guidelines to be considered for patients and are generally thought to be similar to the risks identified for catheter ablation. However, there is paucity of literature and recommendation in the guidelines regarding significant risk factors or concerns for a surgical team influencing the decision to undertake an ablation. No guideline in our review specified any such risk factors for concomitant surgical ablation of atrial fibrillation or LAA procedure.

### **Indications for surgical ablation**

Consensus guidelines from the Heart Rhythm Society (HRS), in collaboration with the European Heart Rhythm Association (EHRA), and the European Cardiac Arrhythmia Society (ECAS), have clarified the relative roles of catheter and surgical ablation of AF. [14] They state that surgical ablation is indicated for: 1) all symptomatic AF patients undergoing other cardiac surgery, 2) selected asymptomatic AF patients undergoing cardiac surgery in which the ablation can be performed with minimal additional risk, and 3) symptomatic AF patients who prefer a surgical approach, have failed one or more attempts at catheter ablation, or are not candidates for catheter ablation. Notably however, these indications were not reflected in any of the guidelines that were included within our systematic review and there was no recommendation provided regarding the specific surgical technique of AF ablation to be used, setting an example for further refinement and congruency to be achieved. These guideline recommendations are also more

consistent in the concomitant usage of ablation, with a recommendation Class I for open surgery (e.g. concomitant mitral valve procedure), and Class IIa for closed surgery (e.g. concomitant CABG), across all subtypes of AF. Figure 3 summarises the consensus writing group recommendations.

Attempts at stratifying ablation risk by cardiac surgery have been made. Iribarne et al. identified differential outcomes following concomitant surgery between CABG, isolated valve, and combined CABG + valve surgery. [19] Unadjusted HRs for survival at 5 years following concomitant ablation by procedure were 0.55 (95% CI: 0.33-0.91,  $p=0.020$ ) for CABG, 0.42 (95% CI: 0.23-0.63,  $p < 0.001$ ) for isolated valve, and 0.68 (95% CI: 0.44-1.05,  $p=0.079$ ) for CABG + valve. Although the nonsignificant result for combined CABG + valve may be due to lack of statistical power, or a greater operative risk associated with more complex procedures, further assessment and evidence is required to identify best practice.

Currently, the guidelines do not provide any recommendation or clarity regarding specific surgical procedures such as staple closure, double-suture technique, usage of the AtriClip, or any other method to excise or occlude the LAA, and the evidence to determine which method is superior is inadequate.

It is commonly accepted that the Cox-Maze procedure is the gold standard procedure, however this is not always achievable. For example, there is evidence that a bilateral Maze procedure has greater risk of post-operative permanent pacemaker implantation compared to a PVI, particularly in the context of concomitant valve procedures. [20] Since a permanent pacemaker can lead to endocarditis, tricuspid valve regurgitation and right heart failure, there is a need for

individualised patient selection for treatment and further evidence of benefit with respect the different procedures.

It is also worth noting that individual procedures have specific targets and so have variable utility. For example, PVI is often used in the first instance for paroxysmal AF where it has greatest efficacy, and then subsequently more extensive ablation can be done as a redo operation for persistent AF refractory to early catheter ablation attempts. While the evidence for these techniques is limited, particularly in comparing outcomes across procedures, there seems to be little difference in the effectiveness of ablation from the energy source, rather the patient comorbidities and extent of the ablation seems to be more impactful on prognosis. [14] Nevertheless, this has not been clearly demonstrated and there remains a need for appropriate trials and guidelines so that Heart Teams can make effective decisions as to the specific impacts of the choice of surgical methods and the differential risks and benefits this will introduce to the patient.

### **Stroke prevention**

A key benefit of restoring sinus rhythm via AF ablation is to minimise likelihood of stroke, as patients with AF are known to have over fivefold increase in risk. Guidelines were unanimous in recommending surgical AF ablation for its benefit in stroke reduction, as this has been well-documented within literature however the patient-specific indications of this procedure are poorly defined. Registry data from the Taiwanese National Health Insurance Research Database has demonstrated long-term benefit of 22% risk reduction in stroke after discharge (HR: 0.78, 95% CI: 0.67-0.91, p=0.0013). [21]

Additionally, all 4 guidelines in our study mention the utility of LAAO in patients with pre-existing AF alongside other cardiac surgery as a safe procedure effective in reducing stroke risk, again the specific recommendations of when to offer the procedure are minimal. Evidence from a randomised trial by Whitlock et al. has examined the benefit of adjunctive LAAO in reducing thromboembolic events and found a 33% decrease in incidence of stroke or systemic arterial embolism, with no difference in mortality or heart failure, providing a reduction in risk which is additive in combination with existing anticoagulation therapy. [22] This benefit did not extend to patients without AF at baseline with no difference in stroke (HR: 0.95, 95% CI: 0.54-1.68, p=0.87). [23]

It is important to specify that the type of AF can impact stroke outcomes. Patients with paroxysmal AF are shown to have similar outcomes between a biatrial lesion set compared to PVI. In contrast, patients with permanent AF have superior risk reduction from stroke, mediated by an improved freedom from AF, from a more extensive ablation procedure such as Maze. [24]

Given the evidence of the safety of the procedure and the efficacy of effect in reducing thrombotic events, it is pertinent to specify the patients that would benefit most from this procedure within the guidelines. Additionally, further value could be derived from examining whether this benefit can be achieved concomitant to surgical ablation, and whether this will bring further cumulative benefit to the patient. To date, trial data exploring this is not available, although data from observational studies have suggested that LAAO offers limited benefit in patients without AF, and so should the AF ablation be successful, combining both procedures would offer minimal additional benefit. [25-27]



In contrast, in patients with previous stroke LAAO has been shown to provide significant mortality benefit, implying that in patients with risk surgical risk and likelihood of AF recurrence, LAAO may prove an effective treatment option. [25] With this dilemma, further study is needed, and this area ought to be more conclusively explored in guideline recommendations. Currently concomitant AF ablation and LAAO is given a Class IIA, Level C recommendation from the STS based on expert opinion, with no other body making recommendations for a combined procedure.

Post-cardiac surgery anticoagulation is also indicated for a significant number of patients to reduce stroke risk, with current guidelines specifying that anticoagulation should be continued on a lifelong basis in patients with AF using CHAD<sub>2</sub>VASC score to indicate risk. Upon successful ablation of AF and restoration of sinus rhythm, anticoagulation is indicated by EACTS guidelines to be continued for only 2 months, and then continued using CHAD<sub>2</sub>VASC score for risk management (Class I, Level C). [10] Notably, this does not preclude patients for whom the ablation was unsuccessful, as rhythm status is not a recommended criterion to be included in this decision. In contrast, STS guidelines recommended that DOACs should be continued until a stable sinus rhythm is documented by Holter monitoring 2 to 6 months postoperatively, and that it is common practice to obtain an echocardiogram before discontinuing to ensure adequate emptying of the left atrium, suggesting that atrial status and heart rhythm ought to be considered. [13] It is likely that optimum management of stroke risk is a combination of both factors, and so guidelines ought to consider CHA<sub>2</sub>DS<sub>2</sub>VASc and patient rhythm status more holistically. Additionally, it is notable that guidelines do not consider bleeding risk, both in the risk of haemorrhagic events from anticoagulation therapy, but also in that discontinuing anticoagulation after AF ablation can also offer benefit in reduction of haemorrhagic stroke in addition to

reduced risk of thromboembolic events. Meta-analysis comparing LAAO with DOAC or warfarin therapy for AF has shown no difference in stroke outcomes (OR: 1.11, 95% CI: 0.84–1.45,  $p=0.46$  for DOAC and OR: 2.48, 95% CI: 0.28–21.91,  $p=0.41$  for warfarin). [28] These results suggest surgical management is noninferior to anticoagulation, however with sparse trial evidence it is premature to suggest LAAO can replace medical therapy, and results from studies evaluating LAAO ought to be critically appraised in light of the fact that patients will receive anticoagulation during follow-up as per current best practice guidelines.

## **Mortality**

As a result of the previously examined benefits of surgical AF ablation or LAAO, concomitant procedures are linked to improved mortality outcomes. Surgical AF ablation has been shown to have similar short-term mortality rate but offers increasing benefit translating to a long-term 25% decrease in mortality (HR: 0.75; 95% CI: 0.69-0.81;  $p<0.0001$ ) after 11 years follow-up. [21] This result was consistently noted across all types of concomitant procedures except mechanical valve replacement, where benefit may be seen only in lower risk patients. [29]

The benefit accrued from LAAO is also associated with long-term improvement. A meta-analysis of 540,111 patients showed that there was no difference in all-cause mortality in the perioperative period (risk ratio (RR): 0.84, 95% CI 0.56-1.28,  $p = 0.42$ ), but this was significantly lower in the LAAO arm after 2 or more years follow-up (RR: 0.81, 95% CI: 0.68-0.97,  $p=0.02$ ). [30] While this evidence may suggest that the impact of surgical ablation on mortality is greater than that of LAAO, it is important to evaluate these findings in the context of heterogeneity both in the included samples and the follow-up of these patients.

## **Surveillance post-ablation**

Recent evidence has shown the benefit of short-term ECG usage and external or internal loop recorders to monitor AF following surgical ablation, resulting in accurate estimation of AF burden and recurrence. [31,32] There has also been discussion surrounding the use of 24-hour Holter monitoring, which has been shown to be noninferior to loop recorders. [33] However, there is currently no consistent indication for the use of permanent pacemakers or any other form of post-operative surveillance such as 24-hour Holter testing. As such, further evidence is needed to ascertain best practice in assessing and preventing recurrence of AF and whether outcomes are improved.

## **Cost effectiveness**

None of the guidelines mentioned the cost effectiveness of concomitant surgery or assessed this in relation to decision-making for a Heart Team. Given the cost of cardiac surgery, postoperative monitoring in community, anticoagulation treatment, and subsequent hospital stay there is importance in assessing the value of healthcare delivered to a patient and the saving that may be made from a procedure. Concomitant surgical AF ablation has only minimal additional impact on hospital stay and incisions required and thus does not bring a large additional cost. Any cost which is occurred is offset by a reduction in cost from lower follow-up management of AF and a reduced readmission rate and intensity. A study by Rankin et al. showed from analysis of Medicare database revealed that concomitant AF ablation with CABG revealed an additional \$2476 average in equipment to conduct the surgery, but after 2 years follow up the total median cost was no different (\$42,816 vs \$43,472, respectively,  $p=0.17$ ). [34] More general and

contemporary evidence including a greater variety of cardiac procedures is needed to help inform resource allocation and surgical decision-making.

## **Limitations**

Our findings are subject to certain limitations that may introduce bias and require attention to the generalisation of our findings. The guidelines reviewed in our study arose from Western national organisations, and as such may not be applicable to different populations and institutions. Whilst we did consider the strength of the evidence and the guideline development process, we did not verify the surgical validity of individual recommendations as it was beyond the scope of this review. We did not detail the thoracoscopic or catheter ablation of AF, even if conducted concomitantly alongside other cardiac surgery. Finally, we did not explore the association between recommendations and guideline panel composition or conflicts of interest in this systematic review. Recommendations in guidelines could have been influenced by conflicts of interest in the underlying evidence, or how it was interpreted, which could have impacted the conclusions of clinical trials and systematic reviews and thereby indirectly affected guideline recommendations and potentially resulted in effect modification. Furthermore, financial conflicts of interest can be associated with favourable recommendations of treatments and devices in clinical guidelines.

## **Conclusions**

Contemporary guidelines on the diagnosis and surgical management of AF concomitantly with other cardiac surgery agree on the importance of Heart team involvement and unanimously recommend consideration of surgical ablation to restore sinus rhythm and alleviate symptoms. However, there are significant discrepancies in indications/contraindications for ablation and LAA surgery, opportunistic screening, and risk factors for surgical ablation. These need to be clarified in the guidelines to improve practice and surgical decision-making. Further research is

required in the areas of cost-effectiveness, surveillance following AF ablation, and the specific indications for concomitant surgery.

**Acknowledgements:** None

**Funding:** None received

**Conflicts of interest:** None to be declared

**Data availability:** The data underlying this article are available within the article and online supplementary material. Any further reasonable requests for information may be made to the corresponding author.

## **References**

1. M. Zoni-Berisso, F. Lercari, T. Carazza, S. Domenicucci, Epidemiology of atrial fibrillation: European perspective, *Clin Epidemiol*, 2014,6:213-220
2. Mistirian AA, Yates MT, Awad WI. Concomitant Atrial Fibrillation Procedures During Cardiac Surgery in a UK Center: Reflection of Worldwide Practice? *Front Cardiovasc Med*. 2022 Mar 10;9:780893. doi: 10.3389/fcvm.2022.780893.
3. Markides V, Schilling RJ. Atrial fibrillation: classification, pathophysiology, mechanisms and drug treatment. *Heart*. 2003;89(8):939-43.
4. Stulak JM, Suri RM, Burkhart HM, et al. Surgical ablation for atrial fibrillation for two decades: are the results of new techniques equivalent to the Cox maze III procedure? *J Thorac Cardiovasc Surg*. 2014;147(5):1478–86.
5. Petersen, J., Vettorazzi, E., Hakmi, S et al. Should concomitant surgical ablation for atrial fibrillation be performed in elderly patients?. *J Thorac Cardiovasc Surg* 2021;161(5): 1816-1823.
6. Huffman MD, Karmali KN, Berendsen MA, et al. Concomitant atrial fibrillation surgery for people undergoing cardiac surgery. *Cochrane Database of Systematic Reviews*. 2016(8).
7. Khanji MY, Ricci F, Galusko V, et al. Management of aortic stenosis: a systematic review of clinical practice guidelines and recommendations. *European Heart Journal- Quality of Care and Clinical Outcomes*. 2021 Oct;7(4):340-53.
8. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Plos Medicine*. 2021;18(3):1-5.

9. Brouwers MC , Kho ME , Browman GP , Burgers JS , Cluzeau F , Feder G et al. II: advancing guideline development, reporting and evaluation in health care. *CMAJ* 2010;182:18.
10. Hindricks G, Potpara T, Dagres N, et al. 2020 EACTS Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS) The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (EACTS) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ECS. *European Heart Journal*. 2021 Feb 1;42(5):373-498.
11. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Journal of the American College of Cardiology*. 2019;;74(1):104-32.
12. Brieger D, Amerena J, Attia J, et al. NHFA CSANZ Atrial Fibrillation Guideline Working Group National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand: Australian clinical guidelines for the diagnosis and management of atrial fibrillation *Heart Lung Circ*. 2018;27:1209-66.
13. Badhwar V, Rankin JS, Damiano Jr RJ, et al. The Society of Thoracic Surgeons 2017 clinical practice guidelines for the surgical treatment of atrial fibrillation. *The Annals of Thoracic surgery*. 2017;103(1):329-41.

14. Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial. *Heart Rhythm*. 2017 Oct;14(10):e275-444.
15. Maesen B, van der Heijden CA, Bidar E, Vos R, Athanasiou T, Maessen JG. Patient-reported quality of life after stand-alone and concomitant arrhythmia surgery: a systematic review and meta-analysis. *Interactive cardiovascular and thoracic surgery*. 2022 Mar;34(3):339-48.
16. Cox JL. A brief overview of surgery for atrial fibrillation. *Annals of cardiothoracic surgery*. 2014 Jan;3(1):80.
17. Kim JS, Lee SA, Park JB, Chee HK, Chung JW. Preoperative risk factor analysis of postoperative stroke after Cox-maze procedure with mitral valve repair. *BMC Cardiovascular Disorders*. 2014 Dec;14(1):1-6.
18. Ad N, Henry LL, Holmes SD, Hunt SL. The impact of surgical ablation for atrial fibrillation in high-risk patients. *The Annals of thoracic surgery*. 2012 Jun 1;93(6):1897-904.
19. Iribarne A, DiScipio AW, McCullough JN, Quinn R, Leavitt BJ, Westbrook BM, Robich MP, Sardella GL, Klemperer JD, Kramer RS, Weldner PW. Surgical atrial fibrillation ablation improves long-term survival: a multicenter analysis. *The Annals of thoracic surgery*. 2019 Jan 1;107(1):135-42.
20. Hald MO, Lauritzen DJ, Heiberg J, Juhl W, Moss E, Vodstrup HJ. Biatrial ablation vs. Pulmonary vein isolation in atrial fibrillation patients undergoing cardiac surgery: a retrospective study. *Scandinavian Cardiovascular Journal*. 2021 Apr 5;55(2):116-21.



21. Cheng YT, Huang YT, Tu HT, Chan YH, Wu VC, Hung KC, Chu PH, Chou AH, Chang SH, Chen SW. Long-term outcomes of concomitant surgical ablation for atrial fibrillation. *The Annals of Thoracic Surgery*. 2022 Oct 7.
22. Whitlock RP, Belley-Cote EP, Paparella D, et al. Left atrial appendage occlusion during cardiac surgery to prevent stroke. *New England Journal of Medicine*. 2021 Jun 3;384(22):2081-91.
23. Yao X, Gersh BJ, Holmes DR, Melduni RM, Johnsrud DO, Sangaralingham LR, Shah ND, Noseworthy PA. Association of surgical left atrial appendage occlusion with subsequent stroke and mortality among patients undergoing cardiac surgery. *Jama*. 2018 May 22;319(20):2116-26.
24. Yildirim Y, Petersen J, Aydin A, Alassar Y, Reichenspurner H, Pecha S. Complete Left-Atrial Lesion Set versus Pulmonary Vein Isolation Only in Patients with Paroxysmal AF Undergoing CABG or AVR. *Medicina*. 2022 Nov 7;58(11):1607.
25. Kim HJ, Chang DH, Kim SO, Kim JK, Kim K, Jung SH, Lee JW, Kim JB. Left atrial appendage preservation versus closure during surgical ablation of atrial fibrillation. *Heart*. 2022 Dec 1;108(23):1864-72.
26. Friedman, D.J., Piccini, J.P., Wang, T., Zheng, J., Malaisrie, S.C., Holmes, D.R., Suri, R.M., Mack, M.J., Badhwar, V., Jacobs, J.P. and Gaca, J.G., 2018. Association between left atrial appendage occlusion and readmission for thromboembolism among patients with atrial fibrillation undergoing concomitant cardiac surgery. *Jama*, 319(4), pp.365-374.
27. Romanov A, Pokushalov E, Elesin D, Bogachev-Prokophiev A, Ponomarev D, Losik D, Bayramova S, Strelnikov A, Shabanov V, Pidanov O, Kropotkin E. Effect of left atrial

appendage excision on procedure outcome in patients with persistent atrial fibrillation undergoing surgical ablation. *Heart Rhythm*. 2016 Sep 1;13(9):1803-9.

28. Nso, N., Nassar, M., Zirkiyeva, M., Lakhdar, S., Shaukat, T., Guzman, L., Alshamam, M., Foster, A., Bhangal, R., Badejoko, S. and Ngonge, A.L., 2022. Outcomes of cardiac surgery with left atrial appendage occlusion versus no Occlusion, direct oral Anticoagulants, and vitamin K Antagonists: A systematic review with Meta-analysis. *IJC Heart & Vasculature*, 40, p.100998.
29. Kim JB, Moon JS, Yun SC, Kim WK, Jung SH, Choo SJ, Song H, Chung CH, Lee JW. Long-term outcomes of mechanical valve replacement in patients with atrial fibrillation: impact of the maze procedure. *Circulation*. 2012 May 1;125(17):2071-80.
30. Prasad RM, Saleh Y, Al-Abcha A, Abdelkarim O, Abdelfattah OM, Abdelnabi M, Almaghraby A, Elwany M, DeBruyn E, Abela GS. Left atrial appendage closure during cardiac surgery for atrial fibrillation: A meta-analysis. *Cardiovascular Revascularization Medicine*. 2022 Jul 1;40:26-36.
31. Joshi S, Choi AD, Kamath GS, et al. Prevalence, predictors, and prognosis of atrial fibrillation early after pulmonary vein isolation: findings from 3 months of continuous automatic ECG loop recordings. *Journal of cardiovascular electrophysiology*. 2009 Oct;20(10):1089-94.
32. DeBoard Z, Doty JR. Evaluation of new generation loop recorders placed during surgical ablation for atrial fibrillation. *Journal of Cardiac Surgery*. 2018 Jul;33(7):416-9.
33. Damiano Jr RJ, Lawrance CP, Saint LL, et al. Detection of atrial fibrillation after surgical ablation: conventional versus continuous monitoring. *The Annals of Thoracic surgery*. 2016 Jan 1;101(1):42-8.

34. Rankin JS, Lerner DJ, Braid-Forbes MJ, McCrea MM, Badhwar V. Surgical ablation of atrial fibrillation concomitant to coronary-artery bypass grafting provides cost-effective mortality reduction. *The Journal of Thoracic and Cardiovascular Surgery*. 2020 Sep 1;160(3):675-86.