

# Does Minimal Invasive Cardiac Surgery Reduce the Incidence of Post-operative Atrial Fibrillation?

## Abstract

Atrial fibrillation (AF) is the most common post-operative complication and tends to be the most common arrhythmia after cardiac surgery. The etiology and risk factors for post-operative AF are poorly understood, but older age, large left atrium, diffuse coronary artery disease, a history of AF paroxysms and in general, pre-existing cardiac conditions that cause restricting and susceptibility towards inflammation have been consistently linked with post-operative atrial fibrillation (POAF). It has been traditionally thought that post-operative AF is transient, well-tolerated, benign to the patient and self-limiting complication of cardiac surgery that was temporary and easily treated. However, recent evidence suggests that POAF may be more “malignant” than previously thought, associated with follow-up mortality and morbidity. Several minimally invasive approaches, including the right parasternal approach, upper and lower mini-sternotomy (MS), V-shaped, Z-shaped, inverse-T, J-, reverse-C and reverse-L partial MS, transverse sternotomy and right mini-thoracotomy, have been developed for cardiac surgery operations since 1993 and have been associated with better outcomes and lower perioperative morbidity compared to full sternotomy (FS). The common goal of several minimally invasive approaches is to reduce invasiveness and surgical trauma. According to a statement from the American Heart Association (AHA), the term “minimally invasive” refers to a small chest wall incision that does not include a FS. This review is aimed to evaluate the use of minimally invasive techniques like mini-sternotomy, mini-thoracotomy and hybrid techniques versus conventional techniques which are used in cardiac surgery and to compare the frequency of post-operative AF and its effect on post-operative complications, morbidity and mortality, after cardiac surgery operations with FS versus cardiac surgery operations with the use of minimally invasive techniques.

**Keywords:** Atrial fibrillation, hybrid cardiac surgery, mini sternotomy, minimal invasive cardiac surgery, valve surgery.

## Introduction

Atrial fibrillation is the most common post-operative complication and most common arrhythmia after cardiac surgery.<sup>[1-3]</sup> Its peak incidence is between second or third post-operative day.<sup>[2,4-6]</sup> Post-operative AF incidence varies and is depending on surgery type.<sup>[2,4,5]</sup> Especially, AF occurs in nearly 30% of patients undergoing coronary artery grafting (CABG) and in 40% and 50% of patients after valve surgery alone or combined valve and CABG surgery, respectively.<sup>[2,4,5]</sup> AF is often temporary and disappears after the recovery of mechanical and metabolic functions.<sup>[7]</sup>

The etiology and risk factors for post-operative AF are poorly understood, but older age, large left atrium, diffuse

coronary artery disease, a history of AF paroxysms and in general pre-existing cardiac conditions that cause restricting and susceptibility towards inflammation have been consistently linked with post-operative atrial fibrillation (POAF).<sup>[6,8]</sup> The pathogenesis of post-operative AF seems to be multifactorial.<sup>[1]</sup> It has been traditionally thought that post-operative AF is transient, well-tolerated, benign to the patient and self-limiting complication of cardiac surgery that was temporary and easily treated.<sup>[9-11]</sup> However, recent evidence suggests that post-operative atrial fibrillation (POAF) may be more “malignant” than previously thought, associated with follow-up mortality and morbidity.<sup>[12,13]</sup>

It is an expensive complication, it results a prolonged hospital stay (an additional 2-5 days in the hospital), 12-24 hours of

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prolonged ICU time and approximately \$10,000-\$20,000 in additional hospital costs.<sup>[3,6]</sup>

Post-operative AF is associated with numerous detrimental sequelae,<sup>[7,14-16]</sup> and may cause hemodynamic instability and may predispose to stroke and increase mortality.<sup>[2]</sup> It is an independent predictor of early and long-term complications including a 2- to 4-fold increased risk of stroke, infection, renal or respiratory failure, cerebral complications, thromboembolic events, need for permanent pacemaker placement and cardiac arrest and is associated with reoperation for bleeding, longer hospitalization, increased cost of hospitalization and increased post-operative mortality (a 2-fold increase in all-cause 30-day and 6-month mortality).<sup>[6,7,17,18]</sup>

Effective ways for prophylaxis of post-operative AF is vital as it reduces hospitalization and overall morbidity<sup>[2]</sup> and as post-operative AF is a potentially morbid complication following cardiac surgery.<sup>[6]</sup>

Decades of research have explored interventions to prevent or limit the incidence of POAF, but most are only partially effective. Due to the widespread incidence and numerous comorbidities associated with POAF, additional research focusing on the precise mechanisms of its pathogenesis is needed to yield a greater understanding of this complication, and to thereby produce more effective prophylactic and treatment options.<sup>[6]</sup>

Several minimally invasive approaches (including the right parasternal approach, upper and lower mini-sternotomy (MS), V-shaped, Z-shaped, inverse-T, J-, reverse-C and reverse-L partial MS, transverse sternotomy and right mini-thoracotomy,) have been developed for cardiac surgery operations (AVR, MVR, CABG) since 1993<sup>[19]</sup> and have been associated with better outcomes and lower perioperative morbidity compared to full sternotomy.<sup>[20-27]</sup> The common goal of several minimally invasive approaches is to reduce invasiveness and surgical trauma.<sup>[19]</sup>

According to a statement from the American Heart Association, the term “minimally invasive” refers to a small chest wall incision that does not include a FS.<sup>[28]</sup>

This review article is aimed to evaluate the use of minimally invasive techniques like ministernotomy, minithoracotomy and hybrid techniques versus conventional techniques which are used in cardiac surgery and to compare the frequency of post-operative AF and its effect on post-operative complications, morbidity and mortality.

### **Full Sternotomy Versus Right Anterior Mini-Thoracotomy or Mini-Sternotomy for Isolated AVR**

Conventional aortic valve replacement (CAVR) via a full sternotomy is the standard therapy for aortic valve diseases.<sup>[29]</sup> The term “minimally invasive” refers to a small incision in the chest wall. Over the past 2 decades,

minimally invasive cardiac surgical techniques have been increasingly adopted with the goal to reduce the invasiveness of the surgical procedure and to offer the same quality, safety and results as the standard conventional procedure. The main goal of such approaches is to reduce the invasiveness and the intraoperative trauma and bleeding and to accelerate post-operative recovery without compromising the quality, safety and results of the conventional approach.<sup>[3,30]</sup> In addition, small surgical scars and fast recovery times increase patient satisfaction. Since the mid-1990s, several minimally invasive approaches for aortic valve operations have been introduced and used with increasing frequency: upper partial sternotomy,<sup>[31,32]</sup> anterolateral right mini-thoracotomy,<sup>[33]</sup> right parasternal approach<sup>[34]</sup> and transverse sternotomy.<sup>[35]</sup>

Gilmanov *et al.*, through a 9-year propensity matched study, compared full sternotomy versus right anterior mini-thoracotomy for isolated AVR in octogenarians.<sup>[36]</sup> Minimally invasive AVR (MIAVR) has been shown to offer numerous advantages. Several earlier reports favourably compared right anterior mini-thoracotomy (RAMT) with full and partial sternotomy.<sup>[37-40]</sup> In the experience of Gilmanov *et al.*'s center, the RAMT was the most promising surgical approach for AVR.<sup>[27]</sup> Within a 9-year study period (August 2004-September 2013), 516 patients underwent AVR through RAMT. They selected 116 of them, aged  $\geq 80$  years. 116 elderly patients underwent AVR through median sternotomy between February 2001 and September 2013. Before propensity matching, patients in the RAMT group were slightly older, had lower prevalence of arterial hypertension, AF, left ventricular dysfunction and pulmonary hypertension, and were also less likely to have a critical preoperative status.<sup>[36]</sup> New-onset AF was defined by the documentation of AF of any duration at any point in the post-operative period on a rhythm strip or 12-lead electrocardiogram.<sup>[36]</sup> They registered the same rate of new-onset atrial fibrillation (0,28) for both groups. New-onset AF (OR 3.16, 95% CI 1.53-6.58,  $P = 0.002$ ) was one of the five factors that was associated with prolonged hospital stay (7 days or more).

Gilmanov *et al.*,<sup>[19]</sup> a year later (2015), in new study, reported the single center experience of minimally invasive AVR (MIAVR) performed through a right anterior minithoracotomy (RAMT) or ministernotomy (MS) and described the surgical technique, complication rates, and patient outcomes.<sup>[19]</sup> New onset AF in Gilmanov *et al.* study was reported for 243 (28,5%) patients.<sup>[19]</sup> Shehada *et al.*<sup>[30]</sup> did a meta-analysis that aimed to compare conventional aortic valve replacement (CAVR) via a full sternotomy and minimal access aortic valve replacement (MAAVR) that is commonly performed via a partial sternotomy and a right minithoracotomy. One of the important findings of this study was that patients that underwent CAVR were likely to experience more post-operative AF (15.9% vs 11.7%,  $P = 0.01$ ).

Numerous studies have addressed the incidence of new onset AF—the most frequent arrhythmia in cardiac surgery—after mini-access and conventional AVR. Notable controversy exists in available literature on the matter: while new onset AF reduction<sup>[23,27]</sup> has been reported in several studies, no difference between minimally invasive and full sternotomy approaches was found by other authors.<sup>[21,38,41-46]</sup> As we see, results from large studies reported a non-significant difference in the incidence of AF and similar rates of PM implantation between both groups.<sup>[43,47,48]</sup> Shehata *et al.*<sup>[37]</sup> reported a non-significant difference in the incidence rate of post-operative AF. On the other hand, Gilmanov *et al.*<sup>[20,27,49]</sup> reported a significantly lower rate of post-operative AF in the lateral minithoracotomy group. A possible explanation is the underlying disease, i.e., aortic stenosis or regurgitation, which could not be evaluated in this meta-analysis, because it was not initially evaluated in all of the included studies. Some also consider that less manipulation of the heart, particularly in cases of MAAVR through lateral minithoracotomy could reduce the incidence of post-operative AF.

### Minimally Invasive Mitral Valve Surgery Through Right Mini-Thoracotomy

Mitral valve surgery using conventional full sternotomy (FS) is the conventional approach for the treatment of the mitral valve disease. Despite this procedure showing excellent post-operative outcomes, in the last two decades, minimally invasive mitral valve surgery (MIMVS) has gained consensus among surgeons as it has provided greater patient satisfaction, maintaining the same quality and safety of the standard mitral valve surgery approach.<sup>[50-52]</sup>

The most common MIMVS approach is the right thoracotomy (RT) followed by the partial sternotomy. Compared with conventional surgery, MIMVS has been shown excellent results in terms of mortality, morbidities and pain, providing shorter hospital stay, less post-operative complications, faster recovery and return to normal activities, better aesthetic appearance, which translate into less use of rehabilitation resources and healthcare costs.<sup>[53-59]</sup>

In 2010, the consensus statement of international society of minimally invasive cardiothoracic surgery (ISMICS) concluded that MIMAVS may be an alternative to conventional mitral valve surgery, given that there was comparable short term and long term mortality, comparable in-hospital morbidity (renal, pulmonary, cardiac complications, pain perception and readmissions), reduced sternal complications, transfusions, post-operative AF, duration of ventilation and ICU and hospital length of stay.<sup>[54]</sup>

Similar results were described by the Society of Thoracic Surgeons of the adult cardiac surgery database as well as

by several meta-analyses confirming the main points of the aforementioned consensus statement.<sup>[53,55-57,60]</sup>

Glauber *et al.*<sup>[61]</sup> reported the early and long-term outcome of 1604 patients that underwent minimally invasive mitral surgery through right minithoracotomy (MIMVS) over a 10-year period.

Post-operative AF is less frequent in mini-mitral valve surgery than in conventional full sternotomy. Also, minimally invasive mitral valve surgery is a safe and reproducible approach associated with low mortality and morbidity, high rate of mitral valve repair and excellent late results.<sup>[61]</sup>

Tang *et al.*<sup>[62]</sup> did a propensity matched study to compare right minithoracotomy versus the conventional median sternotomy for mitral valve surgery in a single high-volume institution. 1,694 patients underwent mitral valve surgery during a 15-year period. Patients who had procedures that were not usually performed through an RT approach were excluded. Using 1:1 propensity score matching, they obtained 215 matched patients in each group for outcomes analysis.<sup>[62]</sup>

There was no difference in the median year of operation between the two groups (2002 versus 2001;  $P = 0.142$ ). The RT approach was not a predictor of post-operative mortality. Predictors of mortality included increasing age, diabetes, smoking, preoperative dialysis, lung disease, advanced congestive heart failure class, and peripheral vascular disease. The RT approach was associated with less new-onset atrial fibrillation (8% versus 16%;  $P = 0.018$ ), pneumonia (1% versus 5%;  $P = 0.049$ ), respiratory failure (3% versus 8%;  $P = 0.036$ ), and acute renal failure (2% versus 7%;  $P = 0.006$ ), lower chest tube output (350 versus 840 mL;  $P < 0.001$ ), and fewer red blood transfusions (2 versus 3 units;  $P = 0.001$ ).<sup>[62]</sup> Right mini-thoracotomy compared with median sternotomy for mitral valve surgery was associated with less post-operative atrial fibrillation, respiratory complications, acute renal failure, chest tube output, and use of packed red blood cells. Given study limitations, the RT approach for mitral valve surgery may have advantages over median sternotomy in selected patients.<sup>[62]</sup>

### Hybrid Techniques

A hybrid strategy—firstly performed in the 1990s—is a combination of tools available only in the catheterization laboratory with those available only in the operating room in order to minimize surgical morbidity and face with any cardiovascular lesion. The continuous evolution of stent technology along with the adoption of minimally invasive surgical approaches, make hybrid approaches an attractive alternative to standard surgical or transcatheter techniques for any given set of cardiovascular lesions.<sup>[63]</sup> Coronary artery bypass grafting (CABG) along with percutaneous coronary intervention (PCI), valve replacement in



combination with PCI, endocardial combined with epicardial atrial fibrillation (AF) procedures, aortic debranching procedures combined with endovascular grafting, and carotid artery stenting along with CABG are some examples of hybrid procedures.<sup>[64]</sup> Santana *et al.*<sup>[63]</sup> in 2014 made a study with 22 patients that underwent hybrid valve surgery. Atrial fibrillation was found post-operative in 22,1% of patients (in 49 patients).

### **The Use of Extra-Corporeal and Minimal Extra-Corporeal Circulation as Risk Factors for Post-operative AF**

The use of extracorporeal circulation (ECC) leads to a higher incidence of post-operative atrial fibrillation compared with the use of minimal extracorporeal circulation or with surgery without extracorporeal circulation, probably due to enhanced systemic inflammatory response.<sup>[1]</sup> The use of extracorporeal circulation (ECC) is another possible risk factor for post-operative AF. The contact of blood with the synthetic surfaces of the ECC system leads to the activation of protein and cellular blood components of the systemic inflammatory response syndrome (SIRS).<sup>[65]</sup> Inflammation is one of the predictors of post-operative AF<sup>[7,66]</sup> and affects atrial conduction. Inflammatory markers including IL-6, IL-8, C-reactive protein (CRP), tumour necrosis factor and indices of neutrophil and platelet activation<sup>[66,67]</sup> are significantly increased in the systemic bloodstream after CABG.

It has been proposed that electrical remodeling plays a role in the high incidence of early AF after ischaemic reperfusion myocardial injury caused by cardioplegic arrest. Atrial ischaemia may play a role in the development of post-operative AF. Electrolyte abnormalities also have been implicated as a precipitating factor.<sup>[7]</sup> Jakubová *et al.*<sup>[1]</sup> studied one hundred and ninety-six patients with coronary heart disease (152 men, age  $62.7 \pm 10.1$  years) underwent surgical revascularization. Extracorporeal circulation was used in 64 patients and minimal extracorporeal circulation was used in 75 patients. 57 patients underwent surgery without extracorporeal circulation. During the first 3 post-operative days, subjects were monitored for the duration and incidence of atrial fibrillation, laboratory markers of inflammation (C-reactive protein, leucocytes) and serum potassium.<sup>[1]</sup> The overall incidence of atrial fibrillation was 56% (110 patients). The highest incidence of atrial fibrillation was found in the extracorporeal circulation subgroup, with a significantly lower incidence using minimal extracorporeal circulation, and in patients operated on without extracorporeal circulation (75 vs 47 vs 46%,  $P < 0.001$ ). The longest duration of atrial fibrillation was found in patients operated on with extracorporeal circulation compared with minimal extracorporeal circulation, and without extracorporeal circulation ( $9.7 \pm 11.6$  vs  $4.9 \pm 8.3$  vs  $3.1 \pm 5.2$ ,  $P \leq 0.001$ ). The incidence of post-operative atrial fibrillation significantly correlated

with elevation of inflammatory markers (C-reactive protein, leucocytes) compared with patients who were free of atrial fibrillation ( $P \leq 0.001$ ,  $P \leq 0.05$ ). The values of serum potassium were not significantly different. The relationship between post-operative atrial fibrillation and echocardiographic parameters was not confirmed.<sup>[1]</sup> There was no difference in post-operative AF rate between single- and double-atrial cannulation. The occurrence of post-operative AF was significantly associated with prolonged hospitalization in patients operated under ECC compared with those with mini ECC and off-pump. Development of post-operative AF is usually associated with longer hospitalization. This was confirmed in this study where patients operated on using off-pump or mini ECC had a lower incidence of AF and shorter hospitalization than patients operated on with ECC.<sup>[1]</sup> Despite advances in surgical techniques, post-operative AF still remains the most frequent arrhythmic complication after cardiac surgery. ECC plays an important role in the activation of the inflammatory cascade during cardiac surgery. According the international literature, it seems that the use of mini ECC or surgery without ECC were both associated with reduced systemic inflammatory response and lower incidence of post-operative AF compared with the use of ECC. Proper choice of surgical strategy and modulation of inflammation may represent a therapeutic target in the short-term prevention of post-operative AF.<sup>[1]</sup>

### **How Does New-Onset Atrial Fibrillation at Discharge in Patients after CABG Effects on Short- and Long- term Morbidity and Mortality**

Recent evidence suggests that POAF may be more 'malignant' than previously thought, associated with follow-up mortality and morbidity.<sup>[68-71]</sup> Several studies have provided compelling data to demonstrate the link between POAF and short-term mortality.<sup>[72-74]</sup> Phan *et al.*<sup>[3]</sup> did a systematic review and meta-analysis to study new-onset atrial fibrillation following coronary bypass surgery and discuss whether it predicts long-term mortality. To evaluate the long-term survival of POAF versus No-POAF cohorts following coronary bypass surgery, the current meta-analysis with reconstructed individual patient data was performed. Electronic searches were performed using six databases from their inception to August 2014. Relevant studies with long-term survival data presented for POAF versus No-POAF were identified. Data were extracted by two independent reviewers and analysed according to predefined clinical endpoints. The pooled hazard ratio (HR) significantly favoured higher survival in No-POAF over POAF (HR 1.28; 95% CI, 1.19-1.37; I<sup>2</sup> = 96%;  $P < 0.00001$ ). Individual patient data of 69 518 patients were available for inverted Kaplan-Meier survival curve analysis.

Analysis of aggregate data using Kaplan-Meier curve methods for POAF versus No-POAF groups

determined survival rates at the 1-year (95.7 vs 98%), 2-year (92.3 vs 95.4%), 3-year (88.7 vs 93.9%), 5-year (82.6 vs 89.4%) and 10-year (65.5 vs 75.3%) follow-up. Other complications including 30-day mortality, strokes, respiratory failure, pneumonia and hospitalization were significantly higher in the POAF group. New-onset AF following coronary bypass surgery is associated with significantly higher risk of mortality in short- and long-term follow-up. Current evidence suggests the need for stricter surveillance and monitoring of POAF following coronary bypass surgery.<sup>[3]</sup> In the above meta-analysis of 399 patients, significantly higher mortality was associated with POAF compared to No-POAF, both in terms of 30-day and long-term follow-up. Pooled HRs and aggregated survival from reconstructed individual patient data suggested up to 10% higher actuarial survival in the No-POAF versus POAF cohort even at the 15-year follow-up. Significant higher complications including strokes, respiratory failure and longer hospitalization, as well as advanced age, were also found to be associated with POAF.<sup>[3]</sup>

New-onset AF following coronary bypass surgery is associated with significantly higher risk of mortality in short- and long-term follow-up. This difference in survival rate remains even up to the 15-year post-operative follow-up. Whether this association is causal or whether AF is only a marker for underlying cardiovascular disease remains to be elucidated in future studies. However, current evidence suggests the need for stricter surveillance and monitoring of POAF following coronary bypass surgery.

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#### Conflicts of interest

There are no conflicts of interest.

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