Atrial Fibrillation After Cardiac Surgery: Clinical Update on Mechanisms and Prophylactic Strategies

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ATRIAL FIBRILLATION (AF) is a common complication after cardiac surgery and is associated with increased cost, morbidity, and mortality.[1–3] Minimally invasive surgical techniques such as transcatheter aortic valve replacement (TAVR) have not substantially reduced the risk of developing AF.[4–6] The development of AF after cardiac surgery remains common and significantly increases mortality, morbidity, and total hospital costs, including readmission.[7–9] In an effort to reduce these adverse consequences of this complication, considerable research recently has focused on identifying prophylactic strategies for AF after cardiac surgery.[10] A thorough understanding of the mechanisms underlying the genesis of AF in this setting may aid in designing preventative paradigms and standardizing treatment. The purpose of this expert review is to highlight the incidence, pathogenesis, and preventative strategies for AF after cardiac surgery.

INCIDENCE OF ATRIAL FIBRILLATION AFTER CARDIAC SURGERY

The incidence of AF after cardiac surgery ranges from 15%-50% depending on the cardiac surgical procedure, patient population, and perioperative exposure to prophylactic interventions.[1,2,10,11] A recent large single-center clinic trial (N = 999: University-affiliated medical center) found a 30.5% incidence of AF after coronary and/or valve surgery.[1] Based on a comprehensive analysis, including a multivariate risk model tested with bootstrapping, the risk of AF after cardiac surgery was excessive in patients older than 65 years with left atrial enlargement and mitral valve disease.[1] In a recent registry analysis (N = 12,260 thoracic aortic surgical procedures from 2004 to 2008 in Japan), the overall incidence of AF was 17.1%.[8] Independent risk factors for AF in this trial included advanced age, smoking history, hypertension, congestive heart failure, urgent surgery, and emergency coronary artery bypass grafting.[8] Although AF may occur at any time after cardiac surgery, it most commonly occurs within 4 days of surgery, with a peak incidence on postoperative day 2.[12–15]

THE PATHOGENESIS OF ATRIAL FIBRILLATION AFTER CARDIAC SURGERY

Although the mechanisms underlying AF are not understood completely, an extensive set of bench and clinical studies have yielded clues (Table 1). Atrial dilation is important in the development of AF and often is secondary to chronic structural heart disease, including hypertension, myocardial ischemia, and valvular pathologies.[1,16] The consequences of chronic atrial stretch include myocyte hypertrophy, fibrosis, and altered protein distribution.[17–19] These induced anatomical atrial abnormalities may alter normal cardiac impulse conduction through atrial tissue, which may be evidenced by alterations in P-wave morphology and conduction on the electrocardiogram.[20–22] As in the case of chronic atrial stretch, acute atrial dilation also causes extensive electrophysiologic atrial changes, including increased susceptibility to AF.[23,24] Although acute and chronic atrial dilation may not be the precipitating causes for acute postoperative atrial fibrillation, they may generate the electrical substrate that facilitates development and maintenance of AF after cardiac surgery.

Three electrophysiologic models have been postulated to describe the pathophysiology of AF. The first model is known as the "multiple-wavelets" hypothesis that was popularized by Moe et al.[25,26] In this paradigm, numerous waves of impulses that depend on a short refractory period to maintain conduction are randomly conducting and colliding. Consequently, reducing the number of waves or increasing the refractory period of atrial tissue should increase the likelihood of arresting the

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Table 1. Mechanisms and Prophylactic Strategies for Atrial Fibrillation After Cardiac Surgery

Intervention	Mechanism
Serum electrolytes	
1. Potassium	1. Suppresses ectopic foci automaticity within cardiac conductive tissue
2. Magnesium	2. Raises automaticity threshold and increases atrial refractoriness; magnesium repletion facilitates potassium repletion in the setting of hypokalemia to activate the inhibitory mechanism of renal outer medulla potassium channels to reduce potassium secretion
Beta-blockers	Prevents adverse ventricular remodeling with decrease in atrial and ventricular end-diastolic pressures; decreases sympathetic drive, therefore reducing ectopic foci automaticity
Amiodarone	Prolongs action potential duration and increases refractory period in cardiac conductive tissue, which prolongs repolarization; class III antiarrhythmic agent, inhibits adrenergic stimulation, affects sodium, potassium, and calcium channels; strong vasodilator but may be used in patients with hemodynamic instability when administered intravenously as low-dose bolus (150-300 mg) followed by prolonged infusion
Sotalol	Class III antiarrhythmic agent, inhibits adrenergic stimulation, affects sodium, potassium, and calcium channels; prolongs action potential duration and increases refractory period in cardiac conductive tissue, which prolongs repolarization; relatively contraindicated in patients with hemodynamic instability
Steroids	Mitigation of perioperative inflammatory response
Colchicine	Inhibits microtubule formation of neutrophils, therefore inhibiting inflammation caused by migration, activation, and degranulation of neutrophils
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Inhibits cyclooxygenase, therefore preventing formation of prostaglandins, prostacyclins, and thromboxanes
Fish oil	Unknown exactly but may decrease cardiac arrhythmias by long-chain n-3 polyunsaturated fatty acids (eg, eicosapentaenoic acid and docosahexaenoic acid), therefore modifying myocyte electrophysiology
Statins	Inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A. Reduces serum low-density lipoprotein, stabilizes vascular plaques, and possesses anti-inflammatory properties
N-Acetylcysteine	Inhibits oxidative stress via breakdown of disulfide bonds
Vitamins C, E	Antioxidative and anti-inflammatory properties, therefore reduces oxidative stress and promotes radical scavenging
Angiotensin blockade	Inhibits angiotensin II, which typically is produced postoperatively as a result of atrial stretch
Cardiac pacing	Overdrive atrial pacing suppresses ectopic foci and reduces abnormal refractoriness of atrial tissue
Posterior pericardiotomy	Small incision in posterior pericardium will effectively drain pericardial blood or fluid into left pleural space, reducing the incidence of pericardial effusions, which may trigger atrial fibrillation

NOTE. Discussion and relevant references are located in the relevant section of the article.

fibrillatory activity.[27] Atrial mapping studies support this multiple-wavelet hypothesis by showing numerous wavelets that wander in a disorganized fashion.[28,29]

A second proposal to explain the genesis of AF is known as the single- or multiple-driver model. In this paradigm, single or multiple rapidly firing foci form a closed re-entry loop with a short cycle length that produces fibrillatory conduction.[30,31] A single focus may fire continuously or multiple foci may reactivate each other, thus sustaining AF.[32] Conditions that shorten the atrial wavelength impulse or decrease the atrial refractory period may increase the risk of initiation and maintenance of AF.[33]

More recently, a third model has emphasized the role of focal activity, in which AF is induced by focal bursts originating in the pulmonary veins.[34] These rapidly firing foci most commonly are found in 1 or more pulmonary veins, the inferior and superior vena cava, and the left atrial free wall. These sites are frequently the targets of interventional procedures, such as cardiac ablation, aiming to isolate the foci and eliminate conduction to surrounding atrial tissue.[35] Based on the existence of multiple plausible models, it is now well-accepted that there may be multiple mechanisms for AF and no single model may be applied universally to all patients. AF frequently leads to electrical remodeling of atrial tissue, including alterations in ion channels that shorten both the refractory period and the action potential.[36,37] These alterations appear within days of developing AF, preventing a prompt return to normal sinus rhythm.[33] Furthermore, prolonged fibrillation leads to atrial dilation, which supports sustained AF.[38] In adult cardiac surgical patients, it remains unclear which of the underlying mechanisms of AF predominates. The frequency of AF suggests, however, that the electrophysiologic alterations due to cardiac surgery increase patient susceptibility to AF.

RISK FACTORS FOR ATRIAL FIBRILLATION AFTER CARDIAC SURGERY

Although multiple risk factors have been associated with AF after cardiac surgery, advanced patient age consistently is recognized as a powerful independent risk factor across multiple studies; for every 10-year increase in patient age, the odds of developing AF increase by 75%.[1,2,8–15] Other clinical risk factors for AF after cardiac surgery include male gender, obesity, prior paroxysmal AF, left atrial enlargement, left ventricular hypertrophy, decreased left ventricular systolic function, chronic pulmonary obstructive disease, chronic renal failure, diabetes mellitus, rheumatic heart disease, and perioperative withdrawal from chronic medications such as