

# Postoperative atrial fibrillation: Formulating the problem may be more challenging than the solution

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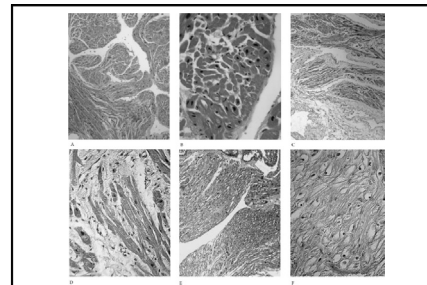
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*The formulation of the problem is often more essential than its solution, which may be merely a matter of mathematical or experimental skill.*

—Albert Einstein

Postoperative atrial fibrillation (POAF) is a common complication after cardiac surgery. The risk for POAF peaks at around 48 hours after surgery, but its incidence remains significant up to 7 days postsurgery.<sup>1</sup> Historical rates suggest an incidence of POAF as high as 50% in cases involving valve surgery but only up to 30% to 35% in more recent reports.<sup>2,3</sup> The relatively lower incidence reported in recent studies and databases likely is related partly to broader use of perioperative beta blockers, prophylactic antiarrhythmic therapies, and better myocardial preservation in many centers.<sup>4,5</sup> The significance of POAF as reported by multiple studies is its association with perioperative complications, early and late mortality, and increased cost.<sup>2</sup> The ongoing challenge we have with the interpretation of these findings is related to the fact that many of the variables associated with inferior outcomes after cardiac surgery are very similar to those associated with POAF. Therefore, in many instances we should perhaps consider POAF as a marker for more complicated or high-risk patients and postoperative course rather than the sole cause for inferior outcomes.

In addition, more clarity is required in terms of the clinical significance of POAF. This should be based on the timing and the state of the patient at the time of the occurrence, true clinical impact in terms of hemodynamics and symptoms, duration, and the need for treatment, including anticoagulation. Regardless, societal efforts should be made to promote research to improve our understanding of the pathophysiology as well as gathering information on the most effective preventive and treatment protocols to reduce the incidence of POAF, even in the most complex patients. A better understanding of the real net impact of POAF on procedural cost



Ad N, Snir E, Vidne BA, Golomb E. Histologic atrial myofibrillar myolysis is associated with atrial fibrillation after cardiac operation. *Ann Thorac Surg.* 2001;72:688-93.

### Central Message

Preexisting atrial substrate changes may contribute to higher susceptibility to develop postoperative atrial fibrillation following surgical manipulation and the associated inflammatory response.

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is required, because current data available are not granular enough, and in most instances circumstantial evidence is being presented by the use of general billing tools that may include variables other than the cardiac surgery event only.<sup>2</sup>

When considering the potential etiologies associated with POAF, the multifactorial aspects of this complication should be recognized and understood. Irrespective of the etiology, POAF is an atrial arrhythmia and perhaps should be looked at as a final common pathway of multiple different pathologic events and clinical scenarios. The electrophysiologic aspects and basic mechanisms of POAF are less studied in humans but probably are a combination of single or multiple foci, single or multiple rotors, and reentry mechanisms that are directly related to operative stress, changes in myocardial properties, and surgical incisions.<sup>6</sup>

Clinical studies have defined a few common clinical variables associated with greater incidence of POAF, with the most consistent being age, chronic obstructive pulmonary disease, heart failure, obesity, renal failure, peripheral vascular disease, and possibly male sex.<sup>7,8</sup> The role of perioperative inflammation was investigated in multiple studies, with conflicting evidence found regarding the efficacy of anti-inflammatory treatment and the impact on reduction in the incidence.<sup>9,10</sup> The lack of consistency in the effect of anti-inflammatory

treatment in general and more specifically steroids begs for a better understanding of the inflammatory process and its interaction with other clinical variables such as low cardiac output, poor oxygenation, use of inotropes, postoperative infection, and the specific patient's atrial substrate properties.<sup>11,12</sup>

Atrial substrate associated with greater susceptibility to develop POAF may have a more significant role than we previously thought. Research by others and us<sup>13-15</sup> identified potential atrial myocardial properties that suggest greater susceptibility of developing POAF. Therefore, a better understanding of the role of preoperative atrial changes and potential markers for atrial substrate with greater vulnerability to develop POAF should be attempted. These studies recognized atrial myolysis, nuclear derangement, and atrial tissue aging as significant, and a better understanding of their role may improve efforts to control POAF and patient outcome.<sup>13</sup> Mitochondrial dysfunction and poor response to simulated ischemic reperfusion injury also should be studied, because it may be possible to identify vulnerable atrial substrate very early after surgery so that better prophylactic strategies in reducing POAF could be applied.<sup>13-15</sup>

In this issue of the *Journal*, Ishii and colleagues<sup>16</sup> demonstrated the potential impact of a perioperative steroids regimen on attenuating the impact of the inflammatory response associated with right atrial atriotomy. A total of 18 mongrel dogs were divided to 3 groups of 6 dogs each. The first group was exposed to anesthesia only (control). The 2 other groups underwent right atriotomy, one without any treatment (atriotomy group) and the second with methylprednisolone treatment starting 1 week before the intervention and continued for 3 days after the intervention. A previous report by the authors also studied a fourth group that underwent pericardiectomy only.<sup>17</sup> The animal model is unique because it demonstrates the impact of surgery on the atrial myocardial properties and how such changes may be associated with acute response to surgery.

Interestingly, in their previous publications,<sup>17,18</sup> the pericardiectomy-only group demonstrated significant changes in atrial tissue inhomogeneity index of atrial conduction, heart rate, and heart rate variability, changes that were found to be significant compared with the control and steroid-treated groups. This study also showed significantly greater inflammatory activity as measured by myeloperoxidase activity and neutrophil infiltration with a strong correlation between inhomogeneity in atrial conduction and the degree of inflammation. The degree of inhomogeneity of atrial conduction and inflammation correlated very well with the ability of inducing and maintaining atrial fibrillation (AF) longer than 2 minutes in the untreated atriotomy and the pericardiectomy group. Prophylactic treatment with steroids was found to be very effective in attenuating the inflammatory process and electrophysiologic changes.

This impact was well correlated with lower rates of induction of AF by burst pacing and shorter duration of AF if induced for the atriotomy group treated with steroids and to the control group.<sup>16,17</sup> In the current report, left atrial studies also were shared, which demonstrated very minimal impact on the left atrium.

This study is unique and important because it may indicate that inflammation has a primary role and impact on the measured changes and the electrophysiologic characteristics of the atrial tissue that may have led to greater tendency to develop and sustain AF after stimulation. The findings presented regarding the left atrium weaken to some extent the claim of inflammation as the only driver that is leading to these changes. Therefore, it also could suggest that the atriotomy and surgical manipulations of a specific atrial chamber are important and the inflammatory process seen is mainly the one that is associated with myocardial healing. It is well known that after myocardial injury there are 3 overlapping phases of healing: the inflammatory phase, in which inflammatory leucocytes are recruited and activated to clear the area of dead cells; the proliferative phase, in which suppression of proinflammatory signaling together with infiltration of cells secreting matrix proteins in the affected area; and the maturation phase.<sup>19</sup> Therefore, one of the questions that should be asked is did the authors capture mainly an isolated inflammatory response or a mixture of the former and a response that is part of a physiological process that is associated with myocardial repair?

In their study in 2005, it clearly was demonstrated that inflammation is significant even in the pericardiectomy-only group with no atriotomy; however, it is important to remember that the right atrium was manipulated for mapping and that the pericardium adjacent to the right atrium was manipulated surgically. Both may result in increased inflammation. The studies clearly demonstrated that both the systemic and local inflammatory processes are important modifiers of atrial tissue properties and the ability to induce and sustain AF.<sup>16,17</sup> It would be imperative to better understand the potential implications of such findings with pathologic hearts, significant comorbid events, and the different atrial substrates.

There are a few important questions that can be raised and serve for future studies to further improve our understanding of POAF and help identify the best clinical approaches to reduce its incidence:

1. What is the impact of modification and attenuation of physiologic inflammatory response to myocardial injury on myocardial healing? The findings of the study clearly demonstrated that there is a significant inflammatory activity associated with a thoracotomy and the different atrial manipulation, such as atriotomy, pericardiectomy, and intracardiac mapping. The clinical impact of

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