

Atrial fibrillation post-coronary or cardiac surgery: A transient inflammation-related event or the expression of a pre-existing arrhythmogenic atrial substrate?

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Related article

by Smukowska-Gorynia et al.

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Atrial fibrillation (AF) is a common cardiac arrhythmia, occurring as a result of a complex interaction between cardiac substrate, triggers, precipitating factors, and altered autonomic nervous system activity [1]. AF may occur in the setting of patients undergoing both cardiac and non-cardiac surgery and may depend on several factors (Figure 1) [2–5]. Postoperative AF (POAF) usually occurs during the first postoperative week, more frequently after cardiac surgery than after non-cardiac surgery, and it is associated with worse outcomes as compared to patients who do not develop AF [2–5]. A recent systematic review and meta-analysis pooling data from six studies enrolling more than 2 000 000 patients showed that patients developing POAF after non-cardiac surgery had a four-fold higher risk of stroke and mortality as compared to controls during a median follow-up of 12 months [2]. In the setting of patients undergoing cardiac or coronary surgery, POAF usually occurs within the first 2 weeks, with a peak of incidence on the second and third postoperative day. POAF is considered the expression of an inflammatory process occurring at the cardiac level, which may be transient [5–7]. However, it is associated with lengthening of hospitalization, need for acute treatment, and need for anticoagulation [6].

In the current issue of *Kardiologia Polska* (*Polish Heart Journal*), Smukowska-Gorynia et al. [7] reported an interesting study on neopterin as a biomarker associated with the

occurrence of AF following coronary artery bypass grafting (CABG). Neopterin is a marker of cellular inflammation linked to processes involving macrophages and dendritic cells, and its increase expresses increased oxidative stress [7]. The authors evaluated 101 consecutive patients with advanced coronary artery disease and without a history of AF undergoing CABG. They found that preoperative neopterin levels were associated with the occurrence of POAF, which was observed in 30% of patients. Other significant predictors of POAF were (1) higher body mass index, (2) history of pulmonary disease, (3) increased diastolic thickness of the interventricular septum, and (4) duration of operation. Most patients experienced POAF within the first 2–3 days after intervention and AF recurrence was observed in one-third of patients during the hospital stay. POAF required treatment with intravenous amiodarone in almost all cases, while only 1 patient was treated with electrical cardioversion. These findings suggest that preoperative neopterin levels may be a marker of AF occurrence, whose mechanism may be linked to the activation of inflammatory pathways. According to these interesting findings, this marker could be clinically helpful in discriminating between episodes of POAF elicited by transient inflammatory factors and episodes of POAF that are mainly an expression of a pre-existing arrhythmogenic atrial substrate, characterizing an “AF susceptibility” whereby patients are more prone to

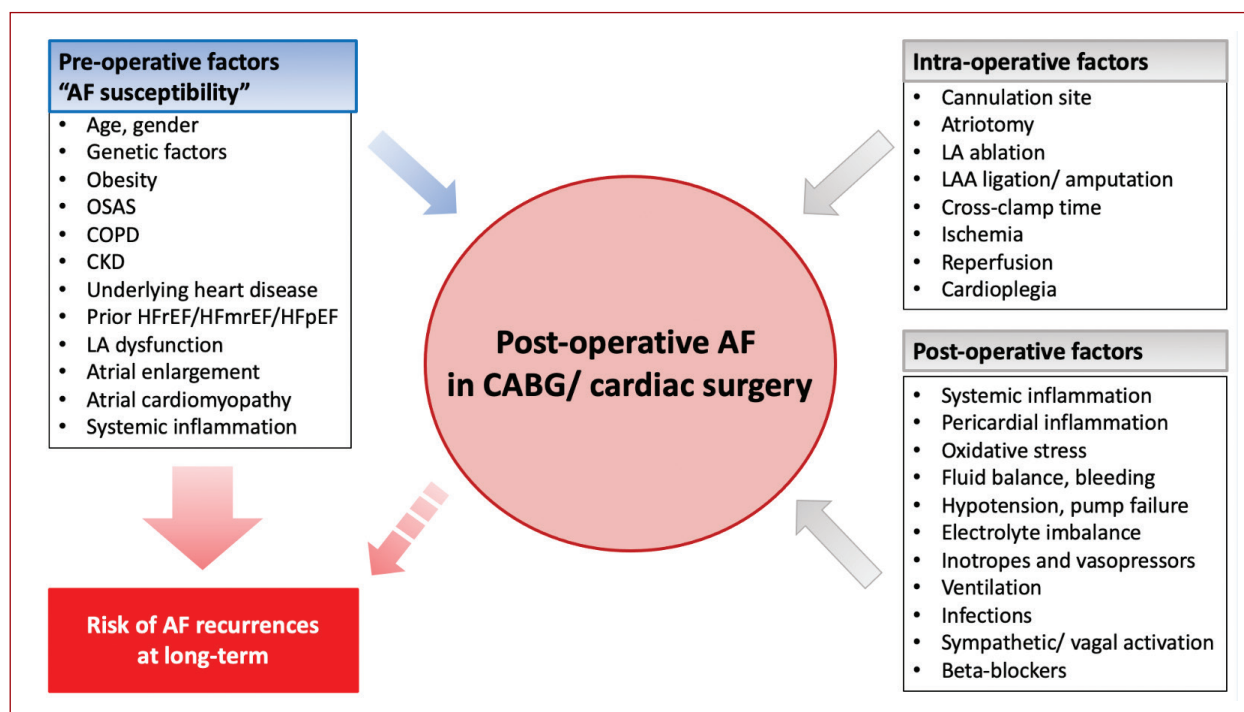


Figure 1. Pre, intra, and postoperative factors associated with postoperative atrial fibrillation after cardiac surgery and risk of long-term recurrences

Abbreviations: CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HF_mrEF, heart failure with mildly reduced ejection fraction; HF_pEF, heart failure with preserved ejection fraction; HF_rEF, heart failure with reduced ejection fraction; LA, left atrial; LAA, left atrial appendage; OSAS, obstructive sleep apnea syndrome

develop AF in case of stressors typical of a post-operative phase, but also with a tendency to have recurrences of AF in the long term [2, 8] and AF progression. From a wider perspective, we could hypothesize that neopterin could be of clinical value in differentiating between the two conditions previously described and, therefore, help in better predicting the risk of AF recurrence in the long term after CABG, related to the underlying atrial substrate, independently of inflammation, thus contributing to improved knowledge in this complex field. Indeed, POAF has been traditionally considered as an event substantially linked to transient factors, therefore, with a limited risk of recurrences. However, recent long-term observational studies [2, 5] showed that both the risk of recurrences and the risk of stroke in the long term are much higher in patients with POAF (either after CABG or other types of surgery) as compared to controls. Unfortunately, no controlled study on the management of patients presenting with *de novo* AF in the postoperative phase is available, and also the guidelines [6] do not deliver evidence-based recommendations on how to manage patients with POAF in the long term. In the European Society of Cardiology guidelines [6], the recommendations for long-term oral anticoagulants (OAC) in POAF patients at risk of stroke (according to the CHA₂DS₂-VASc score) are of relatively low-grade: class IIb for patients in the setting of post-cardiac surgery and class IIa for non-cardiac surgery. In the setting of patients with AF treated with rhythm control, recent evidence-based

recommendations suggest that early restoration of sinus rhythm is associated with a lower risk of adverse cardiovascular outcomes in the long term [9]. However, these recommendations are not strictly related to POAF and direct evidence is needed in this context. Indeed, no specific trial addressed the issue of cardioversion of recent-onset AF after surgery. We think that in POAF with no resumption of sinus rhythm within a few hours, a personalized approach to cardioversion should be advocated, including a "watch-and-wait" approach, pharmacological cardioversion, or electrical cardioversion depending on the patient's profile (e.g.: hemodynamic status, presence of structural heart disease, symptoms, and fluid and electrolyte balance) and organizational issues [10].

We think that the findings of the study by Smukowska-Gorynia et al. [7] can help to characterize the occurrence of POAF as mainly related to transient inflammatory factors rather than linked to an underlying arrhythmogenic substrate prone to AF. This distinction can be of value for future prospective studies aiming to assess the risk of stroke and adverse outcomes in the long term and the effectiveness of OAC in POAF patients at risk. Unfortunately, the study by Smukowska-Gorynia et al. [7] did not provide information on long-term follow-up. Therefore, long-term clinical implications of high levels of neopterin and the real incidence of AF in the long-term in this cohort of patients remain at present unknown and deserve future prospective studies.

The issue of detecting POAF is particularly complex since AF may occur as an asymptomatic event, and the ability to identify this arrhythmia may strictly depend on the intensity of cardiac monitoring. This may vary and range from the duration of monitoring with telemetry, execution of 12-lead ECG at standardized time intervals after surgery, up to the planning of intermittent Holter recordings, or even continuous monitoring through implanted devices, further enhanced by remote monitoring functions [11]. In the latter context, indeed, it is known that episodes of atrial tachyarrhythmia lasting a few minutes are commonly detected by cardiac implantable electronic devices and may progress to clinical AF in up to 30% of patients at 2-year follow-up [12, 13]. Since AF is strictly linked to a variety of factors (Figure 1), such as patients' age and a variable combination of cardiac substrate, triggers, precipitating factors, and altered autonomic modulation, it appears that, in this context, individualized decision-making is needed also with regard to indication for long-term OAC and extent of monitoring for patients in whom anticoagulation is not established or is prescribed for a limited period after surgery [14]. In the future, improved and more specific diagnostic tools to better characterize the underlying cardiac substrate in terms of atrial cardiomyopathy will help to predict the risk of AF in the long term, independently of transient risk factors, and this is a field of increasing interest and research [15]. So far, clinical guidelines [6] have not specifically addressed in depth the complex scenario of POAF, either in coronary/cardiac surgery or non-cardiac surgery. Notably, it is still unclear how to optimally stratify the risk of recurrences and the risk of stroke in these patients [2, 6].

Finally, the findings by Smukowska-Gorynia et al. [7] can open the way to prospective studies evaluating the impact of interventions aimed to reduce inflammation in patients at higher risk of POAF, who could be identified by higher baseline neopterin levels. A baseline status prone to more intense activation of the inflammatory pathway may portend a higher risk of POAF and identify a subset of patients who may benefit from specific prophylactic interventions aiming at reducing peri-operative inflammation. In more general terms, improvement in risk stratification and effectiveness of treatments for AF patients, including patients with POAF, will depend on the close collaboration between basic scientists and physicians involved in clinical trials, trying to bridge the gap between bench and bedside.

Article information

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