Atrial Fibrillation after Cardiac Surgery—To Infinity and Beyond!

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Thromb Haemost 2021;121:1391–1393.

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> "It isn't that they can't see the solution. It is that they can't see the problem."
> G.K. Chesterton, "The Scandal of Father Brown" (1935)

New-onset atrial fibrillation (AF) is common after cardiac surgery, with an incidence of 30 to 50%.[1–3] Patients developing de novo AF after cardiac surgery (AFACS) have a higher risk of developing persistent/long-term AF in the community.[4] An episode of AFACS, even if terminated prior to discharge from hospital, is associated with an increased long-term risk of embolic stroke[5] and higher 10-year all-cause mortality.[6] Considering this, it is then perhaps not surprising that AF has been named as one of the top 10 research priorities for cardiovascular surgery.[7]

Pathophysiology of Atrial Fibrillation after Cardiac Surgery

Accurate risk quantification for AFACS has been one of the holy grails of research in cardiothoracic perioperative medicine. The quest for risk factors and models has been relatively unrewarding so far, despite a lot having been published. A recent PubMed search using the key words "atrial fibrillation" and "cardiac surgery" rendered 7,716 publications between 1957 and 2021, with 2,449 papers mentioning or entirely focusing on risk prediction for AFACS.

Even though little detail is known about the precise molecular mechanisms underlying the onset and perpetuation of AFACS, recent evidence points to proarrhythmic mechanisms acting on a background of structural remodeling. Disease- and surgery-related triggers accelerate or even tip the risk balance toward AF in patients who are already at risk, due to age, gender, and comorbidities; hence, the importance of proper AF characterization as part of clinical evaluation.[8] Risk factors are also dynamic in nature, changing with age and incident comorbidities[9] (►**Fig. 1**).

A remodeled atrial tissue, with structural changes, increased wall strain, and increased chamber dimensions, is much more sensitive to the effects of proinflammatory cytokines, reactive oxygen species, and increased adrenergic drive.[10] Surgical trauma and ischemia and reperfusion from the use of cardioplegia and cardiopulmonary bypass lead to oxidative stress and production of proinflammatory molecules, resulting in endothelial activation. Systemic inflammation and oxidative stress have been shown to be associated with increased incidence of AFACS.[10,11] Details of the conceptual model underpinning this are beyond the scope of this editorial note. Nevertheless, it is worth pointing out that structural remodeling of the atrial tissue, together with connexin and ion-channel remodeling, is among the possible mechanisms proposed.[12]

Risk Models for Atrial Fibrillation after Cardiac Surgery

There have been several AFACS-predictive models published, the most notable of which are Postoperative AF,[13] Atrial Fibrillation Risk Index,[14] and even a stroke prediction score[15] as a prediction tool for risk of new-onset AFACS in the setting of cardiopulmonary bypass grafting.[16] However, the predictive ability of these scores has not been supported by external validation, with the best area under the receiver operator characteristic curve of 0.68 (95% confidence interval: 0.67–0.69),[17] typical of clinical-factor-based risk scores.

Aristotle famously said that "the whole is something besides the parts" (Aristotle, Metaphysics, translated by W. D. Ross). It is likely that none of these scores performed well because we have been asking the wrong question. Instead of a static, almost reductionist approach, we should perhaps consider the alternative view of a dynamic risk trajectory for AFACS. It is a well-known fact that the pathogenesis of AFACS is heterogeneous, with acute changes in physiology

received
May 6, 2021
accepted
May 10, 2021
published online
May 11, 2021

Georg Thieme Verlag KG,
Rüdigerstraße 14,
70469 Stuttgart, Germany

DOI https://doi.org/10.1055/a-1506-8744.
ISSN 0340-6245.

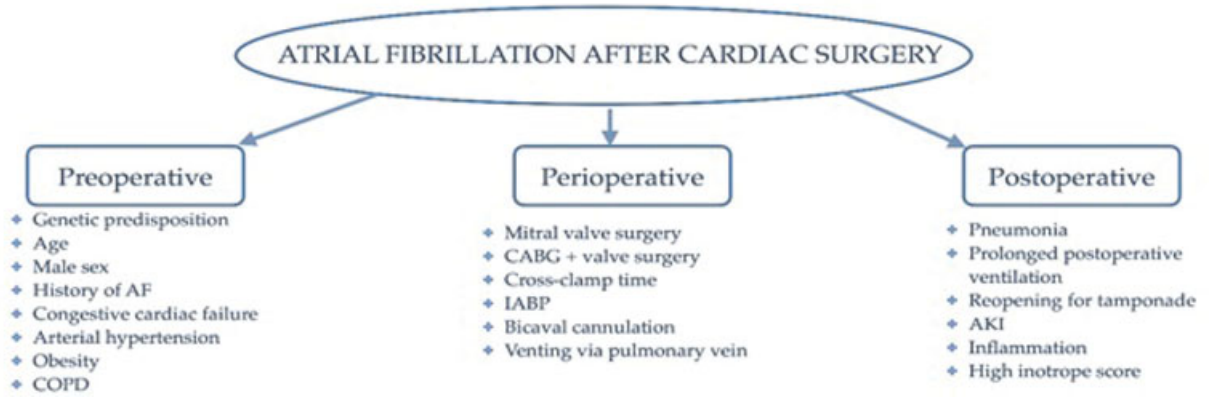

Fig. 1 Risk factors associated with new-onset AF after cardiac surgery (AFACS) highlight the main risk factors associated with AFACS. AF, atrial fibrillation.

Table 1 Atrial fibrillation after cardiac surgery—best validated prediction scores

Authors, year	Type of surgery	Number of patients	Area under ROC in external validation model[17]
El-Chami et al, 2012	CABG, single center	18,517	0.56; 95% CI: 0.52–0.60
Chua et al, 2013 (using CHADS2 and CHA2DS2-VASc scores)	CABG, valve, CABG + valve; single center	277	0.59; 95% CI: 0.55–0.62
Mariscalco et al, 2014	CABG, valve, CABG + valve surgery; multicenter	17,262	0.65; 95% CI: 0.62–0.68

Abbreviations: CABG, coronary artery bypass grafting; CI, confidence interval; ROC, receiver operating characteristic curve.

compounding the preoperative comorbidities and genetic predisposition.[1,18,19] We may then make the argument for a Bayesian approach to risk evaluation for such a complex pathological entity.

Effective acute prophylactic options for AFACS are available[20–22] and validated in guidelines.[23] However, these interventions are not effective in all patients, and some have a high risk of adverse effects. Therefore, it is crucial to be able to identify the individuals at high risk of developing AFACS, as well as to track the risk of developing AFACS throughout their immediate postoperative course as the risk is dynamic and ever-changing in response to the environment and stressors patients are exposed to. The risk of de novo AFACS is dynamic, continuously varying with changes in perioperative physiology.

Tissue samples taken from patients at the end or at the start of surgery provide useful insights into the preexisting substrate and the surgery-induced substrate for the development of AF. However, this approach is obviously not an easy, feasible option for the real-world patients.

In this issue of the journal, the article by Hofer et al[24] fills an important gap—it quantifies the degree of cardiomyocyte strain as expressed by the levels of circulating atrial natriuretic peptide (ANP) contributing to AFACS. ANP is released in response to atrial-wall stretch. An analysis of patients in the sixth examination cycle of the Framingham Offspring Study showed that high levels of ANP are associated with increased risk of AF in the community.[25] The focus in the Hofer et al article is apparently on the ANP. However, as the authors astutely highlight in their analysis, it is also the combined levels of ANP and B-type natriuretic peptide which point to a higher risk of AFACS[24] (►**Table 1**).

Future Perspectives

Investigations into risk modeling approaches for this most common type of secondary AF will still continue. Despite the enthusiasm for biomarker-based scores, the challenge is that many biomarkers are nonspecific, being predictive of outcomes beyond what the scores were proposed for,[26] indicative of a sick patient or a sick heart.[27]

As we enter the third decade of the 21st century, we, as a medical community, are becoming increasingly aware of the possibilities afforded by data science and artificial intelligence. Integrating the ever-expanding information available, sifting through the risk categories and defining the risk trajectory for AFACS is becoming more of a challenge for a single individual and more appropriate for a clinical decision support system based on machine learning, especially given new advances in the latter for the prediction of AF and stroke.[28]

Conflict of Interest
None declared.

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