Thrombosis and Haemostasis

Atrial Fibrillation After Cardiac Surgery – To Infinity and Beyond!

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Abstract:
No Abstract

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

Pathophysiology of atrial fibrillation after cardiac surgery
Accurate risk quantification for AFACS has been the 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 AF after cardiac surgery.

Even though little detail is known about the precise molecular mechanisms underlying the onset and perpetuation of AFACS, recent evidence points to pro-arrhythmic mechanisms acting on a background of structural remodelling. Disease and surgery related triggers accelerate or even tip the risk balance towards AF in patients who are already at risk, due to age, gender and co-morbidities. Hence, the importance of proper AF characterisation as part of clinical evaluation. Risk factors are also dynamic in nature, changing with age and incident comorbidities.

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

Risk models for atrial fibrillation after cardiac surgery
There have been a number of AFACS predictive models published, the most notable of which are POAF\textsuperscript{13}, Atrial Fibrillation Risk Index\textsuperscript{14}, and even a stroke prediction score\textsuperscript{15} as a prediction tool for risk of new-onset AFACS in the setting of cardiopulmonary bypass grafting (CABG)\textsuperscript{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% CI 0.67 – 0.69)\textsuperscript{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 atrial fibrillation after cardiac surgery. It is a well-known fact that the pathogenesis of AFACS is heterogeneous, with acute changes in physiology compounding the preoperative co-morbidities and genetic predisposition\textsuperscript{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\textsuperscript{20-22} and validated in guidelines\textsuperscript{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, 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 pre-existing 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 paper by Hofer et al.\textsuperscript{24} fills an important gap – it quantifies the degree of cardiomyocyte strain as expressed by the levels of circulating atrial natriuretic
peptide contributing to AFACS. Atrial natriuretic peptide (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. The focus in the Hofer et al. paper is apparently on the atrial natriuretic peptide. However, as the authors astutely highlight in their analysis, it is also the combined levels of ANP and BNP which point to a higher risk of AFACS.

**Future perspectives**

Investigations into risk modelling 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 non-specific, being predictive of outcomes beyond what the scores were proposed for, indicative of a sick patient or a sick heart.

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.

**Conflicts of interest – None to declare**

**References:**


Figure 1: Risk factors associated with new onset AF after cardiac surgery highlights the main risk factors associated with AFACS.

<table>
<thead>
<tr>
<th>Authors, Year</th>
<th>Type of surgery</th>
<th>Number of patients</th>
<th>Area under ROC in external validation model²⁷</th>
</tr>
</thead>
<tbody>
<tr>
<td>El-Chami et al., 2012</td>
<td>CABG, single centre</td>
<td>18,517</td>
<td>0.56, 95% CI: 0.52 to 0.60</td>
</tr>
<tr>
<td>Chua et al., 2013</td>
<td>CABG, valve, CABG + valve; single centre</td>
<td>277</td>
<td>0.59, 95% CI: 0.55 to 0.62</td>
</tr>
<tr>
<td></td>
<td>(using CHADS2 and CHA2DS2-VASc scores)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mariscalco et al., 2014</td>
<td>CABG, valve, CABG + valve surgery; multi-centre</td>
<td>17,262</td>
<td>0.65, 95%. CI: 0.62 to 0.68</td>
</tr>
</tbody>
</table>