

Reducing the risk of post-surgery ischemic stroke caused by new atrial fibrillation

In a study of more than 250,000 adults who underwent noncardiac surgery, we found that new-onset postoperative atrial fibrillation (POAF) occurs at a predictable rate and is associated with an increased risk of ischemic stroke. Postoperative oral anticoagulation eliminated the POAF-attributable risk of stroke during the first year after surgery.

This is a summary of:

Azimaraghi, O. et al. Role of anticoagulation therapy in modifying stroke risk associated with new-onset atrial fibrillation after non-cardiac surgery. *Nat. Med.* <https://doi.org/10.1038/s41591-024-03206-0> (2024).

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Published online: 3 October 2024

The question

Approximately 50 million patients in the USA undergo non-cardiac surgical procedures annually, and it is estimated that up to one-quarter of these individuals may experience at least one episode of perioperative atrial fibrillation¹. Atrial fibrillation is an irregular heart rhythm that can lead to the formation of blood clots in the heart, and increases the risk of stroke, heart failure, myocardial infarction and pulmonary embolism².

Mechanistically, the interplay of increased inflammatory response, hypercoagulability, and the withdrawal of regular antiplatelet or anticoagulation treatment in the perioperative setting contribute to an increased risk of stroke after non-cardiac surgery. New-onset post-operative atrial fibrillation (POAF) may be temporary and self-terminate, although even short-lived episodes can be followed by recurrent atrial fibrillation and a heightened risk of stroke. Unfortunately, evidence-based guidelines for the prevention of POAF and its complications are lacking^{3,4}. We created a computational tool to determine a patient's risk of developing POAF and examined whether, in patients with POAF, postoperative anticoagulation treatment can reduce the risk of stroke.

The discovery

In this multicenter study, we utilized large and diverse populations from two academic healthcare networks in the USA in Massachusetts and New York. We enrolled 251,837 adult patients who underwent non-cardiac surgery with no prior history of atrial fibrillation, to examine whether POAF after non-cardiac surgery is a risk factor for ischemic stroke within one year after surgery. Furthermore, we examined whether oral anticoagulation helps to reduce the added risk of stroke in individuals with POAF. Modified Poisson regression models with robust error variances were used to account for residual differences in the baseline clinical characteristics of the comparison groups. We validated a widely applicable prediction instrument for POAF based on age, sex, body mass index, ASA physical status, emergency status, surgical service, type of anesthesia,

and history of respiratory failure before surgery (Fig. 1). Its predictive value was slightly improved by including left atrial diameter.

The incidence of ischemic stroke one year after surgery was 3.6% in 4,538 patients who developed POAF and 2.3% in 247,299 patients without POAF (adjusted risk ratio (RR_{adj}) of 1.60, 95% confidence interval (CI) 1.37–1.87; absolute risk difference (ARD) 0.4%, 95% CI 0.2–0.6%). This association was modified by oral anticoagulants, defined as three or more prescriptions of oral anticoagulation therapy within 1 year after surgery. Anticoagulant treatment was only given to 27% of patients with POAF. The POAF-attributable risk of stroke in individuals who were not prescribed oral anticoagulants was 0.33% compared with no POAF-attributable risk in patients who received oral anticoagulation therapy. Major bleeding events occurred in 3.7% of all cases, and oral anticoagulation increased this risk (RR_{adj} of 1.62, 95% CI 1.47–1.78, $P < 0.001$).

The implications

POAF after non-cardiac surgery is a relevant risk factor for stroke during the first postoperative year. Adequate postoperative anticoagulation is associated with a significant, 54% reduction in risk of postoperative ischemic stroke within 1 year, and no risk of stroke that is attributable to POAF. Based on our data, stroke can be prevented for 1 in every 146 high-risk patients treated with oral anticoagulants. These data add important information to the reported beneficial effects of anticoagulation on postoperative ischemic stroke in patients with high risk of postoperative stroke⁵.

Our observational study is subject to residual confounding, even after we adjusted for extensive potential confounding variables. We conducted comprehensive sensitivity analysis including falsification analysis, which showed that neither myocardial infarction nor acute heart failure or surgical wound infection within 1 year after surgery, was modified by the use of oral anticoagulant therapy.

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EXPERT OPINION

"This study focuses on an important clinical problem and provides data supporting the need for better postoperative monitoring for atrial fibrillation and the

value of anticoagulation therapy in such patients." **Jeffrey Weitz, Thrombosis and Atherosclerosis Research Institute, Hamilton, Ontario, Canada.**

FIGURE

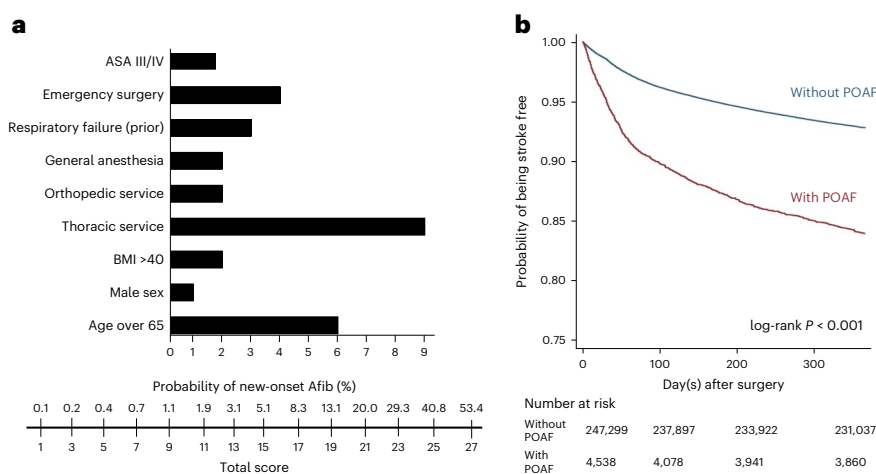


Fig. 1 | Atrial fibrillation after non-cardiac surgery is predictable and preventable. a, New-onset atrial fibrillation after non-cardiac surgery (POAF) can be predicted preoperatively using computational modelling. Each binary predictor variable has an assigned value (x axis). All single values in an individual patient are added up to calculate the total score. The scale at the bottom translates the score value into the probability of developing POAF. ASA III, a patient with severe systemic disease; ASA IV, a patient with severe systemic disease that is a constant threat to life. **b,** Kaplan–Meier survival analysis. The probability of being stroke-free 1 year after surgery is higher in patients without POAF than with patients with POAF. © 2024, Azimaraghi, O. et al.

BEHIND THE PAPER

The Montefiore Einstein Digital Health Team of the Department of Anesthesiology utilizes hospital registry data to identify preventable risk factors for postoperative complications. We have the ability to include any datapoint available in the granular, electronic medical record to our comprehensive pharmaco-physiological outcomes database. In the era of digital healthcare data accumulation, validated data can be used to obtain generalizable knowledge about the effects of innovative treatments on health outcomes, hence complementing results obtained in

randomized controlled trials conducted in smaller sub-cohorts of patients. We are grateful to the 'Boston-NYC Afib after non-cardiac surgery collaborators Consortium', which provided access to data from two Harvard teaching hospitals, validation, and advanced data analytics. I am grateful to Deepak L. Bhatt, with whom I designed and discussed stroke prevention studies for patients undergoing non-cardiac surgery. I am also thankful to Mario Garcia and Luigi Di Biase, cardiology leaders at my institution, for their crucial support of this study. **M.E.**

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FROM THE EDITOR

"Although it's well established that individuals with atrial fibrillation are generally at higher risk for stroke, the clinical course of individuals who develop atrial fibrillation after non-cardiac surgery has not been well characterized. In a large cohort of over 250,000 patients who underwent noncardiac surgery, this study tackles the important question of whether anticoagulation treatment is beneficial for preventing stroke in individuals who developed atrial fibrillation." **Editorial Team, Nature Medicine.**