Post-operative atrial fibrillation: should we anticoagulate?

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Abstract: The prevalence of atrial fibrillation (AF) is estimated to be 12 million by the year 2030. A subset of those patients fall into the category of post-operative atrial fibrillation (POAF) and either develop POAF after cardiac procedures [coronary artery bypass graft (CABG) and valvular procedures] or non-cardiac procedures. With the rise in surgical procedures, POAF represents a significant economic burden. POAF usually converts to sinus rhythm on its own, prompting questions about whether there is a need to treat it and if there is a need for anticoagulation. This review discusses risk factors, pathophysiology, complications of POAF, and mechanisms of risk stratifying patients to determine when to anticoagulate.

Keywords: Atrial fibrillation (AF); post-operative; anticoagulation; arrhythmia

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Introduction: post-operative atrial fibrillation (POAF) in cardiac and noncardiac scenarios

Atrial fibrillation (AF) is a relatively common disorder affecting between 2.7 and 6.1 million individuals in the US alone, based on 2010 data, and having a projected prevalence of up to 12 million by the year 2030, based on logarithmic growth trends (1). AF from a reversible cause is known as secondary AF (2,3). These secondary causes include cardiac and noncardiac surgery in the past 30 days, acute myocardial infarction occurring in the past 30 days, acute infection, acute alcohol intoxication, thyrotoxicosis, acute pericarditis or tamponade, and acute pulmonary phenomena (including pulmonary embolism, pneumothorax, and bronchoscope intervention) (3,4). Focusing on the subpopulation of POAF, there are two major categories: cardiac and non-cardiac. The incidence of AF among adults aged 45+ is only 3% for non-cardiac surgery but ranges from 20% to 40% among those undergoing thoracic or cardiac surgery (5,6). In fact, patients undergoing both coronary artery bypass surgery (CABG) as well as valvular surgery have the greatest risk of developing POAF, at 60–80% (5,7).

POAF typically converts to sinus rhythm without intervention (8,9), creating questions about whether to treat the arrhythmia or begin anticoagulation. The most critical complication of untreated AF is stroke, including stroke severity and mortality from stroke (1), which is especially common in the post-cardiothoracic surgery AF population (5). Because recent data suggests that new-onset POAF has a similar long-term thromboembolic risk profile when compared to non-valvular AF (9,10), it is imperative to consider POAF when assessing stroke risk.

Risk factors, pathophysiology, and complications of POAF

Pathophysiology

The pathophysiology of POAF is multifactorial (5). First, patients undergoing surgery are generally hypercoagulable with a high risk of bleeding (5). Post-surgically, sympathetic activation leads to heart rate elevation and catecholamine release, which predisposes the myocardium to arrhythmias. Electrolyte imbalances, transient hypoxemia, and electrophysiological disturbances may additionally be contributory. Next, hypervolemia from intraoperative fluid administration can lead to right atrial stretching, causing an arrhythmia. In post-cardiac surgery populations, specifically, coronary artery disease in atrial-supply vessels independently predicts new onset POAF (5,11). Finally, elevated C-reactive protein, interleukins, and leukocyte count may also play a role in especially post-cardiac surgery patients; though, this mechanism is not as well defined (5).

Risk factors & predictive models

The major risk factors for POAF among both non-cardiac surgery and cardiac surgery patients are male sex, advancing age, congestive heart failure (CHF) history, and hypertension (5,6,10,12). Lung disease and elevated brain natriuretic peptide are also predictors in non-cardiac surgery patients (12). Among cardiac surgery patients, specifically, history of arrhythmias, history of vascular disease, and type or surgery are also implicated (5,6,13,14). In general, older patients and those with more preoperative comorbidities will be more likely to develop POAF, and this has been used to create predictive scoring systems.

Based on a study of 856 patients, of whom 147 (17.2%) developed POAF, Passman *et al.* derived a POAF risk score based on the most key predictors (15). One point was given to each of male sex and heart rate ≥72, age 55–74 was given 3 points, and age ≥75 was given 4 points. Zero percent of patients with a score of 0 developed POAF, while 35.3% with a score of 6 developed POAF (P<0.001 for the trend).

Recently, Mariscalco *et al.* created the POAF Score to predict the risk of POAF post-cardiac surgery (14). Points are given for predictors of AF, where there is one point for each of age 60–69, COPD history, estimated glomerular filtration rate <15 mL/min/1.73 m^2 or dialysis, emergency surgery, preoperative need for intraaortic balloon pump, left ventricular ejection fraction <30%, and valvular surgery. Additional points are given for each decade above 70, where 70–79 years old receives 2 points and age ≥80 receives 3 points. Those with a score ≥3 had higher rates of complications, ranging from mortality to stroke to need for renal replacement therapy.

Complications

Arrhythmias contribute to a longer hospital course and higher mortality rates (8,9), and patients are more likely to develop complications (5). These include CHF, myocardial infarction, cardiac arrest, and even bacterial pneumonia (5). The most well-documented and critical consequence of POAF (and AF overall) is stroke.

Based on data from the POISE trial, "*[a]fter adjustment for perioperative risk factors, POAF remained an independent predictor of stroke within 30 days of surgery (OR 3.51; 95% CI, 1.45–8.52)*" (5). The risk of cardioembolic stroke is especially noteworthy among post-CT surgery AF patients, whereby there is a threefold increased risk of stroke (5). Furthermore, stroke risk is 1.47% at 1 year post-discharge in POAF patients compared to 0.36% in controls without AF (5).

More recent data from a meta-analysis including 2,458,010 patients across 35 studies found a higher risk of stroke in patients undergoing non-cardiac surgery versus those undergoing cardiac surgery [hazard ratio (HR) 2.00; 95% CI, 1.70–2.35 *vs.* HR 1.20; 95% CI, 1.07–1.34; P for difference <0.0001] (9). Butt *et al.* found that the incidence of thromboembolism in POAF versus non-valvular AF patients was similar (HR 0.95; 95% CI, 0.85–1.07) (10). Given the significance of these complications, risk of recurrence of AF must be weighed when treating patients post-operatively.

Recurrence of AF

Addressing the source of the arrhythmia in secondary AF is considered curative, but long-term data on recurrence remains sparse (4). In one study of secondary AF among Framingham Heart Study participants, 56/118 (47%) of recent CT surgery patients and 44/69 (64%) of non-CT patients had AF recurrence (3). A recent meta-analysis on the topic that included 8 multi-national studies of 1,157 participants found that 28.3% of patients with non-invasive monitoring (electrocardiography, telemetry, and wearable event monitors) had AF recurrence in the first 4 weeks post-discharge from cardiac surgery (16). In contrast, 60.9–100% had recurrence over 2 years in the implanted monitoring group (16).

More recently, the MONITOR-AF trial recently completed and found that 14/23 (60.9%) of patients had AF recurrence post-CABG (17). Mariscalco *et al.* noted that among 17,262 cardiac surgery patients, 4,561 (26.4%) developed POAF—primarily within 2 days of surgery. The PRospEctive cohort study of surveillance for perioperative AF RECURRENCE (PREDICT AF RECURRENCE) is an ongoing study that seeks to determine the recurrence of

POAF in patients undergoing major non-cardiac surgery for management of malignancy (18). Because acute AF not only seems to trend towards recurrence (19) but also increases the risk of cardioembolic stroke and systemic embolism (9), there is a need address risk stratification and the importance of anticoagulation in this population.

Risk stratification and anticoagulation

The CHA_2DS_2-VASc score is the guideline-directed risk-stratification tool that is part of the 2014 American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS) Guideline for the Management of Patients with AF (20). Traditionally, oral anticoagulation (OAC) is recommended for CHA_2DS_2-VASc score of ≥2 in males and ≥3 in females, especially in patients with an AF duration of at least 48 hours (5,20). OAC may be optionally started in male patients with a score of 1 and females with a score of 2 (20). This scoring tool is used for all types of AF, including secondary/POAF, despite lack of validation studies in the post-surgical population (5). Because risk of bleeding and subsequent complications is high, OAC should be started carefully, consider the risks.

Current data on the benefit of OAC is mixed. In a general population of patients with secondary AF, Quon *et al.* suggests that anticoagulation does not improve stroke incidence [odds ratio (OR) 1.22; 95% CI, 0.65–2.27) (2), while Butt *et al.* demonstrates that anticoagulation (OAC) significantly reduces the risk of thromboembolic phenomena among non-cardiac POAF-patients when compared to those who were not anticoagulated (HR 0.52; 95% CI, 0.40–0.67) (10). Using their POAF score, Mariscalco *et al.* suggest the consideration of anticoagulation in high-risk patients—those with a score of at least 3—because OAC reduces mortality associated with thromboembolism (14). Other authors similarly suggest anticoagulating those post-surgical patients (cardiac and non-cardiac) who are higher risk (12,21) but acknowledge that most patients will probably not need therapy (12). All authors recommend weighing bleeding risk carefully before starting OAC (5,10,12,14,21).

However, the decision on when to discontinue anticoagulant therapy remains controversial. Yadava *et al.* suggests following the 2005 American College of Chest Physicians guidelines and continuing OAC for at least 30 days after conversion to normal sinus rhythm (22). In contrast, Greenberg *et al.* states that therapy "*should be continued for a minimum of 4–6 weeks after return to sinus rhythm*" (23). Both authors recommend considering a patient's risk factors for stroke and recurrence of AF prior to discontinuing OAC.

Conclusions

Despite low-level evidence in this population, the general consensus per the AHA/ACC/HRS guidelines appears to be that anticoagulation is recommended for patients with prolonged duration POAF (>48 hours) with either multiple stroke risk factors or other AF comorbidities. Expert opinion per the current literature on the subject concurs with this advice. When considering whether to discontinue therapy, a patient's stroke risk must be considered, but patients likely will require a minimum of 4 weeks of anticoagulation.

More questions remain to be answered through future research to strengthen the guidelines. First, should anticoagulation be used only for high risk POAF patients or for all POAF patients? Second, are the scoring systems described in previous studies valid tools for the evaluation of POAF patients who need anticoagulation? Third, what is the risk-benefit ratio for patients who were offered anticoagulation in the long-term, and can we ever stop anticoagulation in those patients? In conclusion, further randomized trials are imperative to guide answers to these questions and to add more depth to the guidelines regarding use of anticoagulation in POAF patients.

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Footnote

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