Prevention and Management of Perioperative Arrhythmias in the Thoracic Surgical Population

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Severe perioperative bradyarrhythmias requiring treatment have been reported in 0.1% to 0.4% of 17,021 patients, of whom 6.4% were American Society of Anesthesiologists physical status III or IV [1]. In general, perioperative bradyarrhythmias respond well to short-term pharmacologic therapy, noninvasive transesophageal atrial pacing in anesthetized individuals or to noninvasive transcutaneous pacing in awake or anesthetized patients [2]. With the easy access to noninvasive pacing modalities, the preoperative insertion of temporary cardiac pacing wires rarely is required unless a patient is symptomatic and/or meets criteria for permanent pacemaker placement, even in the presence of preoperative asymptomatic bifascicular block or left bundle branch block [3]. Sustained (> 30 seconds) ventricular arrhythmias that cause symptoms and require immediate treatment are rare in the perioperative setting [1,2]. Little data are available on whether repeated or frequent ventricular ectopy after noncardiac surgery is associated with poor long-term cardiovascular outcome. To date only one study evaluated the relationship of the development of ventricular tachycardia (VT) in patients without ischemia during hospitalization following noncardiac surgery and showed that VT was not associated with adverse long-term outcome [4]. The author and colleagues determined the incidence and short-term outcome of nonsustained ventricular arrhythmias in 412 patients who had lobectomy (n = 243) or pneumonectomy (n = 169) and were continuously monitored with Holter recorders for 72 to 96 hours postoperatively [5]. Sixty-one of
the 412 patients (15%) developed one or more episodes of nonsustained VT (three or more consecutive wide complexes) [5]. There were no episodes of sustained VT, and no patient required treatment for hemodynamic compromise associated with any VT episode. Patients who had nonsustained VT had a greater incidence of a preoperative left bundle branch block but did not differ unit from those who did not have VT in other clinical characteristics, operative data, or core temperature on arrival to the postanesthesia care. On multivariate logistic regression analysis, only the occurrence of postoperative atrial fibrillation/flutter (AF) was associated independently with nonsustained VT (relative risk, 2.6; 95% confidence interval, 1.4–4.8) [5]. The incidence of sustained VT or fibrillation following cardiac surgery has been reported to be 0.5% to 1.6% in large observational studies of patients who were monitored postoperatively [6–8]. Patients who developed postcardiac surgery VT/ventricular flutter had a greater 30-day mortality [8,9]. Attempts to suppress nonsustained ventricular arrhythmias after cardiac surgery prophylactically with lidocaine failed to show that such a strategy improves outcome [10]. Surprisingly, when used for the prophylaxis of AF after cardiac surgery amiodarone, a class III antiarrhythmic drug approved for the treatment of malignant ventricular arrhythmias, did not prevent sustained VT from occurring in a study comparing patients receiving and not receiving amiodarone [7]. The mortality rate from VT/ventricular flutter in patients who had chronic class II or III congestive heart failure and an ejection fraction of less than 35% who were assigned randomly to amiodarone was similar to that in patients assigned to placebo [11]. In patients who are hypomagnesemic, magnesium prophylaxis reduces the incidence of ventricular arrhythmias and perhaps AF after heart surgery [12].

Guidelines are not available for the work-up of patients developing perioperative ventricular arrhythmias. In the general population or following an acute myocardial infarction, electrophysiologic testing in patients who have no symptoms or only mild symptoms related to frequent ventricular ectopy or nonsustained VT now is considered inappropriate because of the lack of evidence that therapeutic strategies for such events have improved outcome [13]. Exceptions to these guidelines may be applied to highly symptomatic patients who have a low ejection fraction and a positive signal-averaged ECG. Because current data in surgical patients do not show a clear link between nonsustained ventricular arrhythmias and poor outcome, it is reasonable to adapt these published practice guidelines to perioperative patients [13].

It is estimated that perioperative rapid atrial arrhythmias affect more than 1 million elderly Americans annually and often are associated with significant morbidity, longer hospital stay, and related costs [14]. A greater number of patients undergoing noncardiac surgery may suffer these arrhythmias (but with a lower overall incidence), because many more patients undergo noncardiac surgery than cardiac surgery [14]. The incidence of AF is less than 4% after exploratory thoracotomty or wedge or segmental resection of the lung. In contrast, in age-matched patients who undergo an anatomic resection
such as lobectomy, bilobectomy, or pneumonectomy, the incidence of AF is very similar, ranging between 12.5% and 33% [14–24]. Despite the belief that minimally invasive surgery is associated with fewer adverse effects, the authors found no difference in the occurrence of AF after lobectomy done by open thoracotomy versus that done by the video-assisted approach in 244 age- and gender-matched patients [17]. One retrospective analysis found that in patients undergoing single or bilateral pulmonary transplantation the incidence of AF was 39% within 14 days of surgery [23]. The incidence of AF/supraventricular tachycardia (SVT) after esophagogastrectomy is reported to be 17% and ranges between 13% and 25%. Some authors have made an association between increased mortality and AF following esophagogastrectomy, but others have not [24–26].

When comparing the rates of arrhythmia occurrence reported in the literature, one must consider the definitions of AF used, monitoring techniques, and age matching of groups. At the onset of these arrhythmias patients often present with one or more of the following: dyspnea, palpitations, dizziness, syncope, respiratory distress, and/or hypotension. Although usually well tolerated in younger patients, perioperative atrial arrhythmias can be associated with hemodynamic instability in elderly patients. For nonsurgical patients presenting with new-onset AF, newly revised consensus guidelines recommend performing a transthoracic echocardiogram to rule out significant structural heart disease as part of a minimum evaluation [27]. A prospective study of 4181 patients (age ≥ 50 years) in sinus rhythm who had major noncardiac (including intrathoracic) surgery and routine postoperative monitoring showed that supraventricular arrhythmia including AF that was persistent or required treatment occurred in 2% of patients during surgery and in 4% after surgery [16]. The clinical symptoms, time of onset, and natural course of atrial arrhythmias are identical, whether a patient has had cardiac, thoracic, or other surgery [14]. Atrial arrhythmia onset peaks 2 to 3 days after surgery with nearly 85% of these episodes reverting to sinus rhythm with rate- or rhythm-control strategies during hospitalization [28,29]. The timing of the onset of atrial arrhythmias is intriguingly similar to that of postoperative myocardial ischemia and probably is related to autonomic nervous system imbalance. Few patients have persistent AF on discharge from the hospital; of these, 98% are free of AF 2 months after surgery [14]. Despite this good prognosis, patients who have postoperative AF have a greater risk of stroke, especially when AF is persistent [7,14,28].

**Risk factors and mechanisms**

To date, the only consistent preoperative risk factor for an increased incidence of atrial arrhythmias following surgery has been an age of 60 years or older [14–20,24]. In addition to older age, male gender, history of AF, prolonged preoperative P wave duration from the 12-lead ECG, and low
postoperative cardiac index also have been implicated as independent, albeit softer, predictors of AF after cardiothoracic surgery [20,30]. Using logistic regression analysis and weighted scores for AF occurrence, the author and colleagues found that male gender (1 point), preoperative heart rate higher than 72 beats per minute (1 point), an age between 55 and 74 years (3 points), and age greater than 75 years (4 points) were predictive of AF risk in both the derivation and validation models [20]. For patients who had scores of 4, 5, and 6 points, the risk of developing AF was approximately 14%, 21%, and 32%, respectively [20]. The author and colleagues recently showed that a twofold elevation in white blood cell count on the first postoperative day corresponded to a 3.3-fold increase in the odds of developing AF after thoracic surgery [31]. Adrenergic predominance after surgery probably is responsible for the lymphocytosis and leukocytosis that is mediated by β2-adrenergic receptors of the spleen and venular system. A more recent paper showed that elevated perioperative N-terminal pro-B-type natriuretic peptide levels predict atrial fibrillation after thoracic surgery for lung cancer [32].

It is well known that aging causes degenerative and inflammatory changes in atrial myocardium that lead to alterations in the electrical properties of the sinoatrial and atrioventricular nodes and atria, including prolonged sinoatrial and atrioventricular nodal conduction times and shorter atrial effective refractoriness, all of which contribute to fragmentation of the propagating impulse [33,34]. The concept of a pre-existing anatomic or electrophysiologic substrate for arrhythmias caused by aging, which may be present in varying severity among individuals who are susceptible to AF, may explain why some patients, but not others who undergo exactly the same operation, develop postoperative atrial arrhythmias [14].

In comparison with the overall 4% incidence of postoperative atrial arrhythmias among elderly patients who undergo major noncardiac surgery, the greater incidence of postoperative arrhythmias observed in elderly patients who had thoracic (20%) or cardiac (30% average for coronary artery bypass grafting and up to 65% for valvular surgery) operations probably corresponds to the amount of blunt or sharp surgical trauma to the atria and to sympathovagal fibers innervating the sinus node. Autonomic neural injury then may sensitize the atrial myocardium to catecholamines (denervation supersensitivity) to promote arrhythmias. AF and SVT often are initiated by a premature atrial contraction and later degenerate into one or more circuits that continuously re-enter themselves or one another (random re-entry) [2,33,34]. Once initiated, atrial arrhythmias cause alterations in atrial electrical and structural properties (remodeling), including both rapid functional changes and slower alterations in ion channel gene expression, which promote the maintenance of the arrhythmia and facilitate its reinitiation should it terminate [34]. In comparison with matched controls, patients who developed AF after major noncardiac thoracic surgery demonstrated significant changes in heart rate variability that are consistent with vagal
resurgence competing in a background of increasing sympathetic activity as the primary autonomic mechanism responsible for triggering postoperative AF [35]. These novel results represented the largest study using heart rate variability to understand autonomic influences preceding postoperative AF and suggest that interventions that modulate both the sympathetic and parasympathetic nervous systems may be beneficial in suppressing postoperative AF [35].

The author and colleagues could not demonstrate an association between right or left heart dysfunction on serial transthoracic echocardiograms done before and after major thoracic surgery [18,36]. The role of inflammation and a genetic predisposition to postoperative atrial arrhythmias has been proposed recently by assessment of the interleukin-6 promoter gene variant [37]. Elevations in C-reactive protein levels were described in patients who had atrial arrhythmias unrelated to surgery but not in comparably large studies involving patients undergoing cardiac or thoracic surgery [38–40]. In contrast with the general population [38], there is controversy as to whether C-reactive protein elevations in the postsurgical patient indicate general systemic inflammation or more specific myocardial inflammation of atrial muscle injury that may be associated with AF promotion. Use of high-dose prednisone in an animal model also attenuated the electrophysiological remodeling seen with rapid pacing and AF promotion [41]. These laboratory data were confirmed by a recent clinical trial in patients having cardiac surgery and suggest that anti-inflammatory agents may have a role in AF prevention strategies [42]. Other pathophysiologic mechanisms proposed for the occurrence of postoperative AF are alterations in atrial oxidative stress and elevations in the gap-junctional protein connexin40 expression [43,44]. Whether ectopic atrial activity from the pulmonary veins contributes to the genesis of AF after major pulmonary resection remains unknown.

Prevention

In comprehensive reviews the results of numerous studies examining the efficacy of a variety of drugs to prevent postoperative atrial arrhythmias were summarized [12,14]. It is unclear whether prophylactic treatment against postoperative atrial arrhythmias improves clinical outcomes (ie, stroke) or shortens hospital stay. The author and colleagues have found dil-tiazem to be moderately effective and safe in reducing postoperative AF and SVT [28,36]. β-Blockers have not been found useful after thoracic surgery [12] and in one study were associated with a significant incidence of hypotension and bradycardia [45]. Prophylactic amiodarone to reduce the incidence of postoperative AF has been found safe and particularly effective when given orally for 1 week before cardiac surgery [46]. Only one randomized study, however, examined the efficacy of amiodarone in preventing AF after thoracic surgery and showed no difference when compared with verapamil.
at an interim analysis. After this interim analysis, the study was discontinued for fear of the drug’s contributing to postpneumonectomy respiratory failure [47]. Since then the short-term use of amiodarone in the treatment or prevention of AF after thoracic surgery was not found to be associated with a greater risk of respiratory failure [48–50]. The results of these studies, however, showed that amiodarone’s efficacy was not superior to and perhaps was somewhat inferior to conversion rates reported with diltiazem in a similar population [28]. Furthermore, a recent randomized study comparing amiodarone with diltiazem in preventing AF after coronary surgery found no difference in efficacy between the drug groups when compared with historical controls [51]. Guidelines of the American Heart Association/American College of Cardiology task force do not recommend the use of amiodarone as a first-line drug for acute management of AF unless there is evidence of pre-excitation conduction abnormality [27]. Amiodarone is a Vaughan Williams class III drug but also has α- and β-adrenergic blocking properties, as well as class I and IV actions and potential for proarrhythmia. Partial sympathectomy with epidural analgesia did not reduce AF after cardiac surgery or esophagectomy and only marginally attenuated the incidence of AF after thoracic surgery in a small study in which the control and treated arms were poorly matched for age [52–54]. Unless hypomagnesemia is present, the benefit of prophylactic administration of magnesium during general thoracic surgery to reduce the incidence of postoperative supraventricular arrhythmias is not clear. Data are available from only one study in which some control patients who had hypomagnesemia received magnesium after randomization [12,55]. Recent observational studies have made an association between statin use before surgery and a reduction in the rate of AF after cardiac and thoracic surgery [40,56]. A recent randomized, double-blind study of 7 days of preoperative atorvastatin (40 mg) (n = 100) versus placebo (n = 100) showed that atorvastatin reduced the rate of AF after cardiac surgery from 57% to 35% and also shortened hospital stay [57]. Other findings in this study were that concomitant β-blocker therapy was additive to this effect and that patients who had AF had the highest postoperative peak levels of C-reactive protein [57].

**Treatment**

SVT but not AF responds well to treatment with adenosine, but both arrhythmias respond to intravenous rate-control drugs such as β-blockers or calcium-channel antagonists [2]. In patients who have Wolff-Parkinson-White syndrome with AF, amiodarone is recommended as first-line therapy [2]. Recent data suggest that once AF has occurred postoperatively, rhythm control by pharmacologic means or direct current electrical cardioversion offers little advantage to a rate-control strategy [12,14,27,58,59]. Once sinus rhythm is restored, rate- or rhythm-control drugs may be discontinued 4 to 8 weeks after surgery, because more than 98% of patients are free of AF by
this time [14]. In general, digoxin may be used as a first-line drug only in patients who have congestive heart failure, because it is not effective in high-adrenergic states such as after surgery [27]. β-Blockers are preferred in patients who have ischemic heart disease but may be relatively contraindicated in patients who have proven bronchospastic potential, congestive heart failure, or severe sinus bradycardia or high-degree atrioventricular block [14]. Of the class III antiarrhythmic drugs, ibutilide has been used with moderate success to convert acute AF in 57% of patients after cardiac surgery; polymorphic VT was reported in 1.8% of patients, however, and was attributed primarily to electrolyte imbalance [12,27,59]. In the case of chronic AF unrelated to surgery, evidence from well-controlled, randomized trials shows that management with the rhythm-control strategy offers no survival advantages over the rate-control strategy [60]. Other options available in patients who have recent-onset AF without structural heart disease (defined as the presence of one of the following: left ventricular hypertrophy, mitral valve disease, coronary artery disease, or heart failure) include a single oral dose of the class Ic drugs. Flecainide (300 mg) or propafenone (600 mg) have been shown to be safe, with conversion rates at 8 hours of up to 91% and 76%, respectively [27].

Prevention of thromboembolism

The overall risk of a perioperative stroke in all patients undergoing anesthesia has been estimated at 0.08% in a retrospective study of 24,641 patients who had general and vascular surgery [61]. In a study of patients undergoing noncardiac thoracic surgery the authors and colleagues found a 1.7% incidence of stroke related to postoperative AF [28]. The reported incidence of stroke or transient neurologic injury (1.6%–3.3%) after cardiac operations is consistently greater for patients who develop persistent postoperative AF than in those who do not develop AF (0.2%–1.4%) [14]. Because the potential for thromboembolism with new-onset AF develops early (within 24–48 hours), prompt attempts should be made to restore sinus rhythm within this period. If the arrhythmia persists beyond 24 to 48 hours, anticoagulant therapy should be considered after weighing the risk of postoperative bleeding. Whether these individuals require long-term or even short-term anticoagulation is not clear, and the decision must be individualized for each patient based on the intrinsic risk for thromboembolism [14,27]. Several large trials have established that oral anticoagulation with warfarin is associated with a 60% to 70% reduction from the 9.2% overall risk of ischemic stroke in patients who have persistent or chronic nonvalvular AF not receiving warfarin [27]. Factors creating a high risk for stroke in patients who have AF unrelated to surgery include mitral stenosis, previous transient ischemic attack, stroke, or embolism, and a prosthetic heart valve. Moderate risk factors include age of 75 years or greater, hypertension (including treated hypertension), heart failure or a left ventricular ejection
fraction of less than 35%, and diabetes mellitus [27]. Short- or long-term therapy in nonsurgical patients may range from aspirin alone (81–325 mg/d) in patients who have no risk factors, to aspirin and/or anticoagulation depending on the presence of moderate- or high-risk factors [27]. Whether intravenous heparin is needed in patients who develop postthoracotomy AF requires further study, and individual practice may vary by institution. Later, warfarin may be given to maintain an international normalized ratio in the range of 2.0 to 3.0. In patients who have multiple risk factors for thromboembolism who are not candidates for or do not wish to receive systemic anticoagulation, transesophageal echocardiography is an acceptable and frequently used approach to conversion of AF when such services are available [14,27]. Patients who received standard anticoagulation therapy on discharge from the hospital can return for cardioversion between 3 to 12 weeks after initiation of anticoagulant therapy [27].

Summary

In this era of cost containment, the use of proposed prediction rules defining the subgroup of patients who are at highest risk for perioperative atrial arrhythmias will help target the most aggressive pharmacologic therapies to these patients [20,30]. Use of a minimally invasive, non–rib-spreading video-assisted thorascopic surgery approach does not decrease the incidence of postoperative AF when compared with standard thoracotomy, nor does off-pump cardiac surgery [17,62]. Patients deemed at high risk preoperatively should be considered for proven prophylactic therapy regardless of the planned operative approach. This important step will lead to more useful studies to determine whether reduction of atrial arrhythmias among high-risk patients improves outcomes and shortens length of hospital stay. Finally, current data suggest that once postoperative AF has occurred, a rate-control strategy during the first 24 hours is reasonable, because more than 85% of those episodes resolve during this period. Beyond this period, a more aggressive approach using class Ic or III antiarrhythmic drugs may reduce drug-related toxicity and the number of patients requiring anticoagulation [14,27]. Early anticoagulation in high-risk patients is likely to reduce the risk of devastating cerebrovascular events.

References


