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## Perioperative Atrial Tachyarrhythmias

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THE new onset of brady- or tachyarrhythmias of supraventricular origin can occur before the administration of anesthesia, intraoperatively but most frequently during the first postoperative week.<sup>1-6</sup> Although severe bradyarrhythmias requiring treatment have been reported in 0.4% of 17,021 patients ( $\geq 18$  yr) undergoing general anesthesia, they respond well to short-term pharmacologic therapy or noninvasive transesophageal atrial pacing, and rarely require invasive temporary cardiac pacing, even in the presence of preoperative asymptomatic bifascicular block or left bundle branch block.<sup>2</sup> In contrast, it is estimated that perioperative rapid atrial arrhythmias affect close to one million elderly Americans annually and are often associated with significant morbidity, greater hospital stay, and related costs.<sup>1-8</sup> A greater number of patients undergoing noncardiac surgery may suffer these arrhythmias (but with a lower overall incidence) since many more patients undergo noncardiac surgery compared with cardiac surgery.<sup>6,7</sup> 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 life threatening hemodynamic instability in the elderly. This commentary will focus on recent progress in the epidemiology, etiology, mechanisms, management, and prevention of common perioperative atrial tachyarrhythmias including atrial fibrillation-flutter (AF) and ectopic supraventricular tachyarrhythmias (SVT) other than AF.<sup>5,7,9</sup> Less common perioperative arrhythmias include uniform atrial tachycardia which may be seen in children or multiform atrial tachycardia seen in acutely ill patients or in those with advanced pulmonary disease. Nonectopic tachycardias due to atrial, SA, or AV node reentry or reentry involving an accessory AV pathway are relatively rare in the perioperative setting.<sup>2</sup>

### Epidemiology

Little information exists in the literature on how many patients are admitted to the operating room with new

onset AF or SVT requiring treatment before the administration of anesthesia. Arrhythmias in this setting are typically observed in asymptomatic patients who are usually but not always elderly, may be having significant pain (*i.e.*, hip fracture) or severe anxiety, situations that are consistent with high adrenergic tone. Once the rapid ventricular rate is controlled in these cases, the practicing anesthesiologist is then faced with the dilemma of whether to proceed with or delay surgery to find a possible cause for the arrhythmia such as acute myocardial infarction, pulmonary embolism, pericarditis, or thyrotoxicosis. In the absence of suggestive signs or symptoms, the frequency of new atrial arrhythmias associated with any of the above mentioned etiologies is less than 1%.<sup>9</sup> Thus, in nonsurgical patients presenting with new onset AF recent consensus guidelines recommend performing a transthoracic echocardiogram to rule out significant structural heart disease.<sup>9</sup> Because outcomes data in patients with new onset preoperative AF or SVT are sparse, it is reasonable to extrapolate the above guidelines to preoperative patients and proceed with surgery providing the ventricular rate is controlled, there are no signs of acute illness, or evidence of structural heart disease on echocardiography (fig. 1). With loss of sinus rhythm the potential for thromboembolism develops within 48 h. Therefore, it is important for the physician to try to determine the approximate duration of the arrhythmia ( $<$  or  $>$  48 h), since this will help estimate the potential risk for thromboembolism and the possible need for early anticoagulation after surgery.

A recent prospective study of 4,181 patients ( $\leq 50$  yr) in sinus rhythm before major noncardiac (including intrathoracic) surgery, showed that supraventricular arrhythmia reported as persistent or requiring treatment occurred in 2% of patients during, and in 6.1% after, surgery.<sup>6</sup> During the intraoperative period the prevalence ratio of SVT to AF was 2:1 whereas the reverse was true after surgery.<sup>6</sup> Using medicare data it is estimated that the total annual number of patients projected to be at risk for perioperative atrial tachyarrhythmias may be 1.2 million.<sup>†</sup> The clinical symptoms, time of onset, and

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† It has been projected that in the next 10-20 yr 13.3 million Americans over the age of 65 yr will undergo noncardiac surgery annually.<sup>10</sup> Of these, approximately 266,000 (2%) patients will develop atrial tachyarrhythmias requiring therapy during surgery and 810,000 (6.1%) after surgery.<sup>6</sup> In addition, of the 600,000 Americans who undergo cardiac operations annually, approximately 25% (10-25% after "off-pump" beating heart surgery, 10-40% after conventional coronary artery bypass grafting with cardiopulmonary bypass, up to 65% after valvular surgery) will develop these arrhythmias.<sup>3,5,8,11</sup>

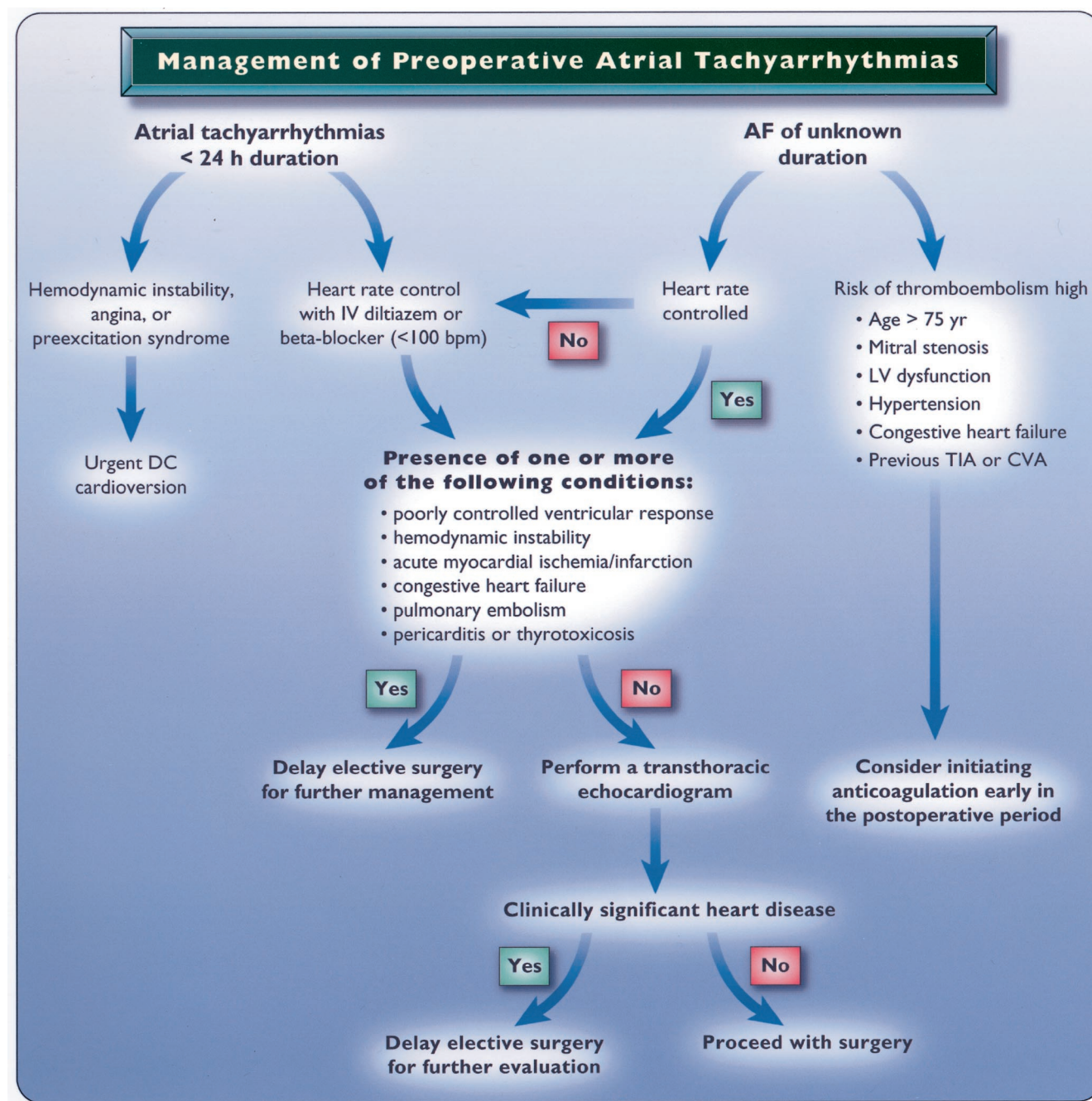


Fig. 1. AF = atrial fibrillation-flutter; DC = direct current; bpm = beats/min; LV = left ventricular; TIA = transient ischemic attack; CVA = cerebrovascular accident.

natural course of atrial arrhythmias are identical regardless of whether a patient has had cardiac, thoracic, or other surgery.<sup>3-7</sup> Atrial arrhythmia onset peaks 2 to 3 days after surgery with close to 85% of these episodes reverting to sinus rhythm with rate or rhythm control strategies during hospitalization.<sup>5,12,13</sup> The timing of onset of atrial arrhythmias is intriguingly similar to that of postoperative myocardial ischemia and is likely related to autonomic nervous system changes associated with an inflammatory response.<sup>7,10,14,15</sup> Approximately 15%

of patients have persistent AF on discharge from the hospital, and of these 98% are free of AF 2 months after surgery.<sup>5</sup> Despite this good prognosis, patients with postoperative AF have a greater risk of stroke, especially when AF is persistent.<sup>3,5,8,11</sup> It has been reported that AF after cardiac surgery extends hospital stay by an average of 1 to 2 days with a median cost of \$1,600 per patient<sup>8</sup> and that 5% of patients who had "fast track" cardiac surgery require readmission to the hospital for AF management.



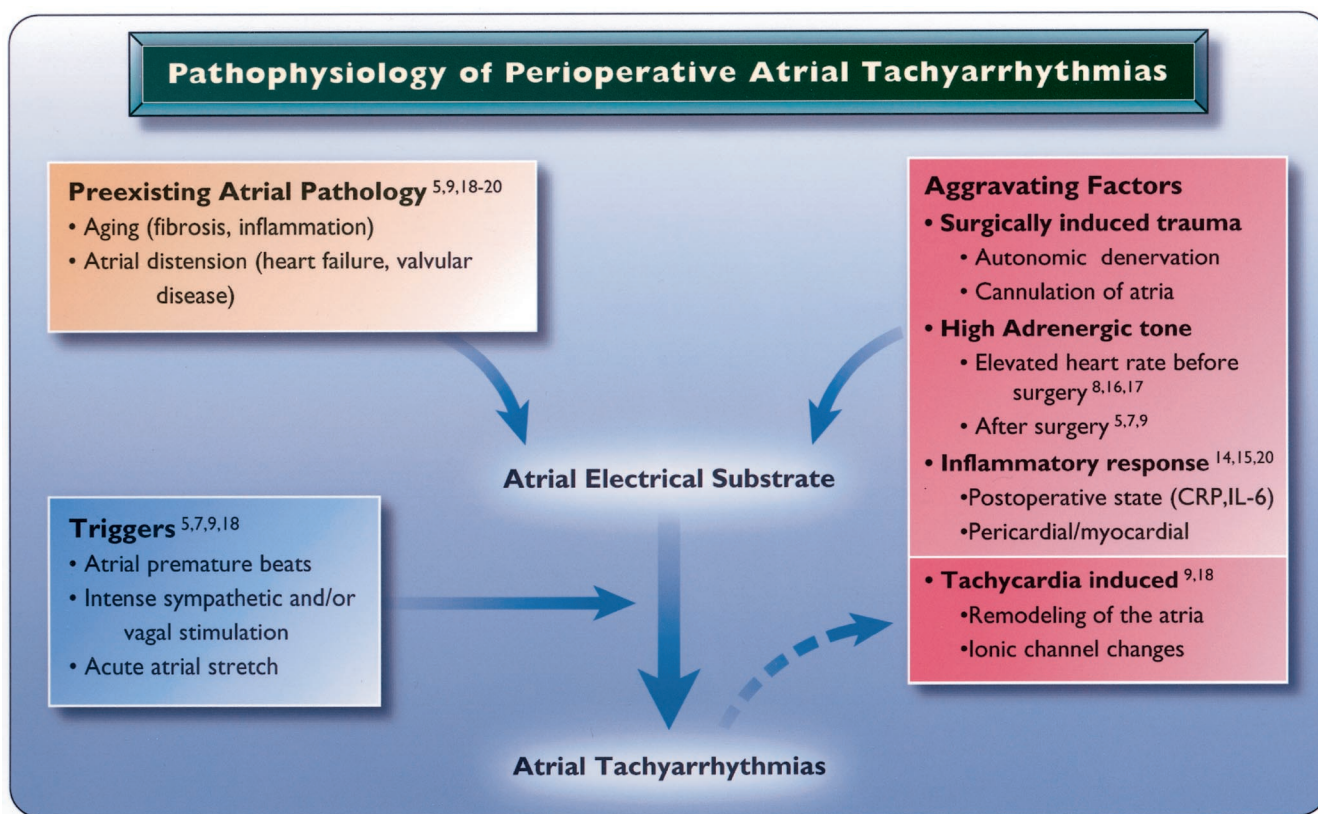


Fig. 2. CRP = C reactive protein; IL-6 = interleukin 6.

#### Risk Factors and Possible Mechanisms

To date, the only consistent preoperative risk factor for an increased incidence of atrial arrhythmias after surgery has been age greater than 60 yr.<sup>3-8</sup> In addition to older age, we and others have observed that a greater preoperative heart rate was an independent predictor of AF after cardiothoracic surgery, suggesting that preoperative sympathetic dominance further stratifies those susceptible to AF.<sup>8,16,17</sup> Other independent risk factors include history of hypertension and congestive heart failure.<sup>5</sup> It is well known that aging causes degenerative and inflammatory changes in atrial myocardium that lead to alterations in electrical properties of the SA and AV nodes and atria, including prolonged SA and AV nodal conduction times and shorter atrial effective refractoriness, all of which contribute to fragmentation of the propagating impulse.<sup>9,18,19</sup> The concept of a preexisting anatomic or electrophysiologic substrate for arrhythmias due to aging, which may be present in varying severity among individuals who are susceptible to AF, possibly explains why some but not other patients who undergo the exact same operation develop postoperative atrial arrhythmias.<sup>7,18,20</sup> In comparison to the 6.1% incidence of postoperative atrial arrhythmias among elderly patients who undergo major abdominal or peripheral 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 repair or replacement) operations most likely corresponds to the amount of blunt or sharp surgical trauma to the atria and to sympathovagal fibers innervating the sinus node.<sup>5,7,8,13</sup> Autonomic neural injury may then sensitize the atrial myocardium to catecholamines (denervation supersensitivity) to promote arrhythmias. AF and SVT are often initiated by an atrial premature contraction and later degenerate into one or more circuits that continuously reenter themselves or one another (random reentry).<sup>5,9,18</sup> Once initiated, atrial tachyarrhythmias 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.<sup>18</sup> The current view of the pathophysiology underlying the genesis of perioperative atrial tachyarrhythmias is depicted in figure 2.

#### Prevention of Perioperative Atrial Tachyarrhythmias

Because of the greater incidence of atrial arrhythmias in the postoperative period most efforts on prevention have focused on this and not the intraoperative period. A recent review summarized the results of numerous studies examining the efficacy of a variety of drugs to prevent this complication.<sup>5</sup> It is unclear whether prophylactic treatment against postoperative atrial arrhythmias im-

proves clinical outcomes or shortens hospital stay and whether to employ rate control or rhythm control drugs for this purpose. Since sympathetic activation is suspected in precipitating postoperative atrial arrhythmias in susceptible patients,  $\beta$ -adrenergic blocker prophylaxis has been studied extensively.  $\beta$ -blockers are useful in this setting but despite their administration, the rate of postoperative AF remains high.<sup>5,8</sup> Partial sympathectomy with epidural analgesia did not reduce AF after cardiac surgery and only marginally attenuated the AF incidence after thoracic surgery.<sup>21,22</sup> It is possible that increased intracellular calcium levels associated with perioperative stress may be caused by alterations in G-protein or adenyl cyclase activity *via* receptors that have important physiologic and pharmacologic mediators (*i.e.*, acetylcholine, adrenocorticotrophic hormone, prostaglandins) and not limited to the  $\beta$ -adrenergic receptor system.<sup>18</sup> Some studies have found diltiazem to be moderately effective in reducing postoperative AF and SVT.<sup>13,23</sup> Prophylactic amiodarone to reduce the incidence of postoperative AF has been safe and particularly effective when given orally for 1 week before cardiac surgery.<sup>5,17</sup> Amiodarone is a Vaughan Williams class 3 drug, but also has  $\alpha$ - and  $\beta$ -adrenergic blocking properties, as well as class 1 and 4 actions. However, the cost, feasibility, and safety (*i.e.*, potential for proarrhythmia) of using amiodarone or other class 3 drugs for global prophylaxis of perioperative supraventricular arrhythmias deserves further study. Unless hypomagnesemia was present the prophylactic administration of magnesium during cardiac surgery did not reduce the incidence of postoperative supraventricular arrhythmias.<sup>24</sup> The role of overdrive biatrial pacing for prophylaxis against postoperative AF after coronary artery bypass grafting has been well demonstrated.<sup>25</sup> Its widespread use, however, will be limited by the availability of necessary specialized personnel and complications related to lead failure.

#### *Treatment of Perioperative Atrial Tachyarrhythmias*

Before initiating specific drug therapy for acute AF or SVT one should assess and correct possible aggravating factors such as respiratory failure or electrolyte imbalance. SVT, but not AF, responds well to treatment with adenosine. Both arrhythmias, however, respond to rate control drugs such as  $\beta$ -blockers (esmolol, metoprolol) or calcium channel antagonists (diltiazem, verapamil).<sup>5,9,26</sup> Calcium channel blockers should be used with caution as single agents in patients with Wolff-Parkinson-White syndrome since they can accelerate the ventricular rate with AF.<sup>2</sup> Uniform or multiform atrial tachycardias usually respond to rate control drugs but are not amenable to direct current cardioversion. 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.<sup>5,9</sup> Intuitively the latter may be associated with less risk of proarrhythmia.<sup>12</sup> Once sinus rhythm is restored, rate or rhythm control drugs may be discontinued at 4–8 weeks after surgery.<sup>5</sup> A proposed algorithm for the treatment of recent onset AF or SVT is presented in figure 3. In general, however, digoxin may be used as a first line drug only in patients with congestive heart failure, since it is not an effective treatment for AF or SVT in high adrenergic states such as after surgery.<sup>9</sup>  $\beta$ -blockers are preferred in patients with ischemic heart disease but may be relatively contraindicated in patients with proven bronchospastic potential, in those with congestive heart failure, or those with severe sinus bradycardia or high degree AV-block.<sup>5,9</sup> Of the class 3 antiarrhythmic drugs, ibutilide has been used recently with moderate success to convert acute AF in 57% of patients after cardiac surgery, however, polymorphic ventricular tachycardia was reported in 1.8% of patients and was attributed primarily to electrolyte imbalance.<sup>9</sup> It is therefore recommended to correct potassium and magnesium levels prior to administration of ibutilide, monitor patients for at least 4 h afterward, and have physicians who are trained to deliver defibrillatory shocks readily available. Although commonly used for the acute management of postoperative AF, amiodarone can control the ventricular response but has not been shown to be superior to placebo in the conversion of recent onset AF unrelated to surgery.<sup>9</sup> In patients with recent onset AF without structural heart disease (defined as the presence of one of the following: left ventricular hypertrophy with wall thickness greater than 1.4 cm, mitral valve disease, coronary artery disease, or heart failure), single oral dose of the class 1c drugs flecainide (300 mg) or propafenone (600 mg) have been shown to be safe with conversion rates at 8 h of up to 91% and 76%, respectively.<sup>9</sup> Although the chronic use of class 1c drugs is contraindicated in patients with coronary artery disease, some clinicians would use them in a single dose to treat AF in patients recovering from cardiac surgery, as long as there is no evidence of acute myocardial ischemia and the patients are continuously monitored with telemetry for at least 24 h for detection of potentially harmful ventricular arrhythmias.

#### *Prevention of Thromboembolism*

In a study of patients undergoing noncardiac thoracic surgery we found a 1.7% incidence of stroke related to postoperative AF.<sup>13</sup> The risk of stroke or transient neurologic injury of 1.6–3.3% after cardiac operations is consistently greater for patients who develop postoperative AF compared to 0.2–1.4% for those without AF.<sup>3,5,11</sup> In a study of patients after beating heart coronary artery surgery the overall risk of neurologic injury was 1%, however, those who developed persistent AF were at a particularly high risk for stroke at 9%.<sup>11</sup> Risk factors for stroke in patients with AF unrelated to sur-



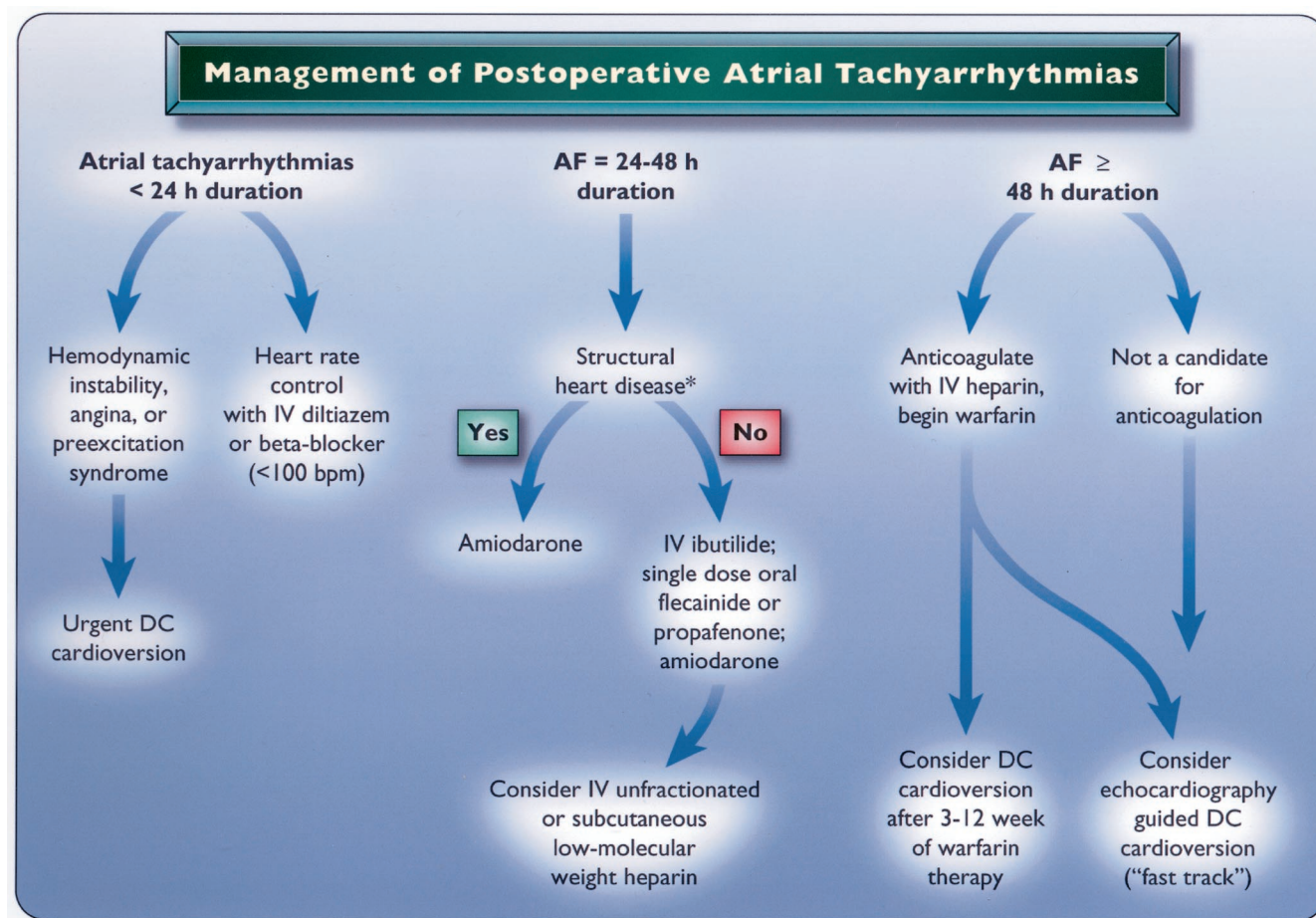


Fig. 3. AF = atrial fibrillation/flutter; DC = direct current; bpm = beats/min; \* = structural heart disease is defined as the presence of one of the following: left ventricular hypertrophy with wall thickness  $\geq 1.4$  cm, mitral valve disease, coronary artery disease, or heart failure.<sup>9</sup>

gery include mitral stenosis, hypertension (including treated hypertension), previous transient ischemic attack or stroke, congestive heart failure or left ventricular dysfunction and an age of more than 75 yr.<sup>9</sup> Since the potential for thromboembolism with new onset AF develops early (24–48 h), prompt attempts to restore sinus rhythm within this period should be made.<sup>5,9</sup> If the arrhythmia persists beyond 24–48 h anticoagulant therapy should be considered after weighing the risk of postoperative bleeding. Although low-molecular-weight heparin has not been approved by the Food and Drug Administration for use in AF or compared in a clinical trial with unfractionated heparin in patients with AF of recent onset, it has been found to be at least as effective in other situations when used for the prevention of arterial thromboembolism and is therefore, a logical alternative to intravenous unfractionated heparin. It should also be noted that intravenous unfractionated heparin has never been formally evaluated as a therapy for AF of recent onset. Randomized, controlled trials assessing the perioperative use of intravenous heparin in patients with different indications for long-term anticoagulation would provide better data on which to base

management decisions. Intravenous heparin may be initiated to maintain aPTT 2 to 3 times control value but is discontinued if heparin-induced thrombocytopenia develops (platelet count falls by 30% from baseline or below 100,000/mm<sup>3</sup>).<sup>5,9</sup> Lepirudin, a recombinant hirudin and direct thrombin inhibitor, has been approved by the Food and Drug Administration as an alternative to heparin in this situation. Later, warfarin may be given to maintain a prothrombin time international normalized ratio (INR) between 2.0–3.0. Patients may then be considered for early cardioversion with the use of transesophageal echocardiography (fast-track) or returned for cardioversion between 3–12 weeks after initiation of anticoagulant therapy (fig. 3).<sup>9</sup> The prophylactic use of aspirin in postoperative AF has not been studied, and is controversial in patients with AF unrelated to surgery.<sup>9</sup>

## Conclusions

The subgroup of patients who are at highest risk for morbidity related to perioperative atrial tachyarrhythmias requires better definition to target the most aggres-

sive pharmacologic therapies to these patients. Current data suggest that once postoperative AF has occurred, a rate control strategy during the first 8–24 h is reasonable, since 50% of those episodes will resolve during this period. Beyond this period, a more aggressive approach using class 1c or 3 antiarrhythmic drugs will hopefully reduce related drug toxicity and the number of patients requiring anticoagulation.

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