Cardiac Arrhythmias: Management of Atrial Fibrillation in the Critically Ill Patient

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Atrial fibrillation (AF) is a common arrhythmia in the ICU, second only to ventricular tachycardia. A study of prevalence of arrhythmias showed that AF may occur in up to 31% of patients in medical, cardiac, and surgical ICUs [1]. AF is associated with a significantly longer ICU stay. In-hospital mortality associated with acute myocardial infarction (MI) is higher in patients who have AF (25% versus 16%) [2]. AF is associated with a twofold increase in mortality in the community, and it is influenced by the severity of underlying heart disease [3,4].

It is estimated that 2.2 million people in the United States have AF. The prevalence of this disease increases with age. The burden of AF is expected to rise as population ages, and it will continue to be associated with significant health care costs [5].

Etiology and associated conditions

AF is associated with various cardiac or extracardiac conditions, some of which are chronic, while others are short lived. In the setting of acute illness, AF may present de novo, or it may recur in patients who have a history of AF. Surgery, especially cardiac or thoracic, pulmonary embolism or other pulmonary conditions, myocarditis, electrocution, alcohol consumption, thyroid disorders, and other metabolic conditions may contribute to the development of AF.

AF also often is associated with history of hypertension and coronary artery disease (CAD). Eleven percent of patients presenting with acute MI

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develop AF during their hospitalization [6]. Left ventricular (LV) hypertrophy and associated diastolic dysfunction likely play a role in the genesis of AF because of an increase in stretch in the left atrium or the pulmonary veins [7]. Valvular heart disease, especially mitral stenosis and mitral regurgitation resulting in left atrial (LA) dilatation, commonly are associated with atrial arrhythmias. AF also may be related to hypertrophic cardiomyopathy (HCM) or dilated cardiomyopathy, and various forms of congenital heart disease in adults, especially atrial septal defect. Less common causes of AF include restrictive cardiomyopathies (such as amyloidosis, hemochromatosis, and endomyocardial fibrosis), pericarditis, and cardiac tumors. The known causes of AF are listed in Box 1.

Among noncardiac chronic conditions, obesity is an important, recently identified risk factor for developing AF [8,9]. There is a direct relationship between LA size and body mass index (BMI). An association between obstructive sleep apnea (OSA) and AF also has been reported [10].

The term lone AF is used to describe AF in individuals younger than 60 years of age who have no clinical or echocardiographic evidence of cardiac disease. In approximately 45% of patients who have paroxysmal AF and 25% of patients who have chronic AF, no cardiac disease can be identified [11]. Fluctuations in autonomic tone appear to play a role in the initiation of AF, especially in structurally normal hearts. Both vagal and sympathetic tone may surge in the minutes that precede initiation of AF [12,13].

Definitions

Various terms have been used in the literature to describe patterns of AF occurrence. The North American Society of Pacing and Electrophysiology and the European Society of Cardiology recently endorsed a new nomenclature [14]. Episodes are classified as first-detected, recurrent, paroxysmal, persistent, or permanent. When a patient has had two or more episodes of AF, AF is considered recurrent. If it terminates spontaneously, AF is designated as paroxysmal; when it is sustained beyond 7 days, it is called persistent. If cardioversion has failed or had not been attempted, and the patient has been in AF for longer than 1 year, AF is referred to as permanent.

Pathophysiology

The mechanisms responsible for AF are multifactorial [15]. Multiple wavelet reentry [16], anisotropic reentry with high-frequency focal sources and centrifugal fibrillatory conduction [17], and perturbations in the autonomic innervation of the atrium [18] have been proposed as potential mechanisms of AF. Pulmonary veins have arrhythmogenic activity and are implicated in the initiation [19] and perpetuation of paroxysmal AF [20]. In patients who have persistent and permanent AF, fibrosis is thought to
Box 1. Etiologies and factors predisposing patients to atrial fibrillation

Electrophysiological abnormalities
- Enhanced automaticity (focal AF)
- Conduction abnormality (reentry)

Increase in atrial pressure
- Mitral or tricuspid valve disease
- Myocardial disease (primary or secondary, leading to systolic or diastolic dysfunction)
- Valvular abnormalities (causing ventricular hypertrophy)
- Systemic or pulmonary hypertension (pulmonary embolism)
- Intracardiac tumors or thrombi

Atrial ischemia
- Coronary artery disease

Inflammatory or infiltrative atrial disease
- Pericarditis
- Amyloidosis
- Myocarditis
- Age-induced atrial fibrotic changes

Drugs
- Alcohol
- Caffeine

Endocrine disorders
- Hyperthyroidism
- Pheochromocytoma

Changes in autonomic tone
- Increased parasympathetic activity
- Increased sympathetic activity

Primary or metastatic disease in or adjacent to the atrial wall

Postoperative
- Cardiac, pulmonary, or esophageal

Congenital heart disease

Neurogenic
- Subarachnoid hemorrhage
- Nonhemorrhagic, major stroke

Idiopathic (lone AF)

Familial AF

promote AF by facilitating reentry. Loss of intercellular coupling caused by alterations in the number and distribution of gap junctions and connections may be important in creating a substrate capable of maintaining AF [21].

Adrenergic stimulation and inflammation, common among postoperative and critically ill patients, are involved in the genesis of AF by means of complex and incompletely understood mechanisms. AF is associated with an up-regulation of angiotensin subtype 1 receptor [AT (1)] in the left atrium [22]. Renin-angiotensin-aldosterone system (RAAS) promotes development of atrial fibrosis, which is thought to be a substrate for anisotropic reentry. Levels of C-reactive protein (CRP) are higher in patients who have AF, and they increase with higher AF burden [23,24]. AF increases production of superoxide by the left atrium and LA appendage [25]. Pronounced increases in white blood cell (WBC) count have been described as an independent risk factor in patients after cardiac surgery [26]. Statins, which have anti-inflammatory properties, have been shown to suppress electrical remodeling in an animal model of AF [27], and they may reduce the incidence of postoperative AF. This effect may be caused by their inhibition of metalloproteinases, oxidants, and mediators of inflammation [28]. High levels of these stress mediators may be responsible for increased burden of AF in critically ill patients.

**Hemodynamic consequences of atrial fibrillation**

AF can lead to a decrease in cardiac output, which can manifest as a fall in blood pressure and pulmonary congestion. AF worsens New York Heart Association (NYHA) heart failure class even in patients with relatively well-controlled ventricular response [29]. Hemodynamic deterioration is particularly problematic in patients who have already impaired systolic or diastolic function, and other underlying heart disease, such as significant mitral stenosis and hypertrophic obstructive cardiomyopathy.

Several mechanisms have been proposed to explain the adverse hemodynamic effects of AF. They include a rapid heart rate, loss of atrial systole, irregularity of ventricular rhythm, and activation of neurohormonal mediators such as norepinephrine and angiotensin II [30–33].

Rapid heart rate limits the amount of time available for ventricular filling. Loss of atrial systole may be associated with a 20% reduction in LV stroke volume in patients who have preserved LV function, and up to 35% reduction in patients with recent MI [30] Patients who have diastolic dysfunction or poorly compliant left ventricle rely heavily on atrial systole for filling. In patients who have hypertrophic cardiomyopathy, mitral stenosis, aortic stenosis, and severe cerebrovascular disease, these effects may be more profound.

Irregular rhythm may affect cardiac output adversely by inefficient ventricular mechanics caused by abrupt changes in ventricular cycle length, variations in preload, and in myocardial contractility. Resumption of
ventricular regularity with AV nodal ablation and ventricular pacing improves cardiac output beyond what would be expected in patients who have AF and adequate rate control [31].

The fall in cardiac output in critically ill patients who develop AF with rapid ventricular response may activate neurohormonal vasoconstrictors further, which can lead to an increase in systemic vascular resistance (afterload) and coronary vascular resistance (decrease in coronary perfusion). AF episodes are associated with increases in atrial natriuretic peptides and B-type natriuretic peptides, which decrease rapidly after restoration of sinus rhythm [32,34]. The results of these assays should be interpreted carefully in the presence of AF. High levels of ANP and BNP may lead to diuresis and hypotension [33].

Clinical presentation

Patients who have AF have variable clinical presentations. Many patients are asymptomatic or complain of palpitations, shortness of breath, or fatigue. Some patients experience chest pain, especially when ventricular rate is not controlled well, regardless of whether they have underlying CAD. Sustained AF with rapid ventricular response may lead to tachycardia-mediated cardiomyopathy, especially in patients unaware of their condition [35]. Syncope is rare in patients without other cardiovascular conditions, but may be more common in patients who have sinus node dysfunction, an accessory pathway, hypertrophic cardiomyopathy, or aortic stenosis. Thromboembolism may be the sole presenting symptom resulting in cerebrovascular accident or ischemic extremity.

In the ICU setting, onset of AF may be associated with hemodynamic compromise and hypoxemia. Patients who have subclinical heart failure are likely to experience an exacerbation. Anticoagulation issues related to AF may complicate management of critically ill patients with trauma, malignancy, intracranial or gastrointestinal hemorrhage, platelet disorders, or history of heparin-induced thrombocytopenia.

Management

Treatment of AF is directed at three major objectives: control of ventricular rate, restoring normal sinus rhythm, and prevention of thromboembolic complications. Acute management largely depends on the clinical status of the patient. Patients who have ongoing cardiac chest pain, pulmonary edema, or who are hemodynamically unstable, should be considered for an emergent cardioversion. Management of patients who can tolerate AF initially focuses on adequate control of the ventricular rate appropriate for the hemodynamic status and underlying cardiac substrate of the ICU patient.
Acute rate control of atrial fibrillation

Agents such as beta receptor blockers, some calcium channel antagonists, and digoxin can be used acutely to control ventricular rate. Dihydropyridine calcium channel blockers such as nifedipine or amlodipine besylate have no effect on the atrioventricular node, and they are not recommended to control ventricular response. Beta-blockers are likely to be effective in postoperative patients who may have high adrenergic tone. Metoprolol is given in doses of 2.5 to 5 mg intravenously over 2 to 5 minutes. The onset of action occurs within a few minutes, and the drug can be repeated up to three times every 5 to 10 minutes as long as patient does not develop hypotension or other adverse effects. Once adequate rate control has been achieved, patients may be transitioned to oral doses of metoprolol. Esmolol, an intravenous, short-acting beta-blocker, may be very helpful in patients who are at risk for hemodynamic instability, as the drug is eliminated quickly when discontinued. Beta-blockers may result in bronchospasm in patients who have chronic obstructive pulmonary disease (COPD), asthma, or reactive airway disease. In patients who do not tolerate beta-blockers, or in whom beta-blockers are insufficient to control ventricular rate, diltiazem may be administered at 0.25 mg/kg intravenously over 2 minutes followed by 5 to 10 mg/h continuous infusion, or verapamil 0.075 to 0.15 mg/kg intravenously over 2 minutes (Table 1).

Digoxin may be useful in patients with heart failure and those who have marginal blood pressures, as it increases myocardial contractility and does not result in hypotension. Digoxin can be loaded intravenously at 0.25 mg intravenously every 2 hours, up to 1.5 mg, or given orally. Caution should be exercised in patients who have kidney disease. In patients who have renal insufficiency, digitoxin, another cardiac glycoside, may be used. Unlike digoxin (which is eliminated from the body through the kidneys), digitoxin is eliminated by the liver [36].

Amiodarone causes slowing of rapid ventricular rate, most of which occurs in the first hour after administration of the drug, although other antiarrhythmic properties of this drug may not manifest until several days later [37]. This may be because of predominant beta-adrenergic and calcium channel blockade observed early after intravenous amiodarone injection.

Beta-blockers and nondihydropyridine calcium channel blockers should be avoided in patients presenting with pulmonary edema or severe LV dysfunction. Intravenous beta-blockers, nondihydropyridine calcium channel blockers, and digitalis should be used with caution in patients who have a history of pre-excitation and Wolf-Parkinson-White syndrome, because these agents can facilitate antegrade conduction over the accessory pathway and may result in acceleration of tachycardia and degeneration to ventricular fibrillation [38,39]. Patients who have ventricular pre-excitation and AF may be treated with intravenous procainamide or amiodarone. ECG during AF in a patient who has an accessory pathway may show an irregular wide complex tachycardia caused by ventricular pre-excitation of
the accessory pathway (Fig. 1). In select patients who have Wolf-Parkinson-White syndrome, oral beta-blockers and calcium channel blockers may be used for rate control as chronic therapy with careful monitoring [5].

Pharmacologic cardioversion

Various agents are available for cardioversion of AF. The overall acute success rate is lower with pharmacologic cardioversion than with electrical cardioversion and ranges from 40% to 70% [40,41]. Class I antiarrhythmic agents work primarily by blocking sodium channel (Na⁺) and class III agents primarily by blocking potassium slow rectifier channel (I_{kr}). Not all pharmacological agents can be employed in the intensive care setting because of their pharmacodynamics and the many comorbidities that may be contraindications for their use. Class IA (quinidine, disopyramide, procainamide) and IC agents (flecainide and propafenone) are contraindicated in patients who have structural heart disease. The Cardiac Arrhythmia Suppression Trial provided evidence against use of flecainide and encainide in patients with CAD [42]. Other agents may be available in oral preparations only, which limits their usefulness in the intensive care environment. Amiodarone and procainamide are two antiarrhythmic agents most frequently used in the ICU.

The conversion rate from AF to sinus rhythm during amiodarone load is about 30% [43]. Amiodarone often is used to maintain sinus rhythm after cardioversion in patients who have AF. Amiodarone also is used for managing ventricular arrhythmias. Its advantages include low acute adverse effect profile and a neutral effect on mortality in patients following MI and in the presence of structural heart disease. Its long-term extracardiac toxicity potential, however, is significant. Amiodarone can be administered intravenously as a bolus of 150 mg over 10 minutes, followed by a continuous drip at 1 mg/min for 6 hours, then at 0.5 mg/min for 18 hours or until the patient can take amiodarone orally. Hypotension may occur with intravenous amiodarone, especially in patients who have overt heart failure and severe LV dysfunction [37]. The maintenance dose of amiodarone for AF is usually 200 mg orally per day.

Upon initiation of therapy with amiodarone, thyroid and liver panels, and chest radiograph should be obtained. Patients who are maintained on amiodarone should undergo monitoring every 6 months and have periodic pulmonary function tests with diffusing capacity of lungs for carbon monoxide [44]. Four types of lung injury from amiodarone have been reported: chronic interstitial pneumonitis, bronchiolitis obliterans, acute respiratory distress syndrome, and a solitary lung mass. Amiodarone pulmonary toxicity correlates most closely with cumulative dose received, and it is rare in patients receiving 200 mg daily [45,46]. Acute lung injury with smaller doses of amiodarone, however, have been reported, especially following thoracotomy [47–51].

According to a recent meta-analysis, amiodarone facilitates conversion of recent-onset AF to sinus rhythm, with a 44% superiority in efficacy compared
<table>
<thead>
<tr>
<th>Drug</th>
<th>Loading dose</th>
<th>Onset</th>
<th>Maintenance dose</th>
<th>Major adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute setting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esmolol</td>
<td>500 µg/kg intravenously over 1 min</td>
<td>5 min</td>
<td>60 to 200 µg/kg/min intravenously</td>
<td>↓ BP, HB, ↓ HR, asthma, HF</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>2.5 to 5 mg intravenous bolus over 2 minutes, up to three doses</td>
<td>5 min</td>
<td>N/A</td>
<td>↓ BP, HB, ↓ HR, asthma, HF</td>
</tr>
<tr>
<td>Propranolol</td>
<td>0.15 mg/kg intravenously</td>
<td>5 min</td>
<td>N/A</td>
<td>↓ BP, HB, ↓ HR, asthma, HF</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>0.25 mg/kg intravenously over 2 min</td>
<td>2 to 7 min</td>
<td>5 to 15 mg/h IV</td>
<td>↓ BP, HB, HF</td>
</tr>
<tr>
<td>Verapamil</td>
<td>0.075 to 0.15 mg/kg intravenously over 2 min</td>
<td>3 to 5 min</td>
<td>N/A</td>
<td>↓ BP, HB, HF</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>150 mg over 10 min</td>
<td>Days</td>
<td>0.5 to 1 mg/min IV</td>
<td>↓ BP, HB, pulmonary toxicity, skin discoloration, hypothyroidism, hyperthyroidism, corneal deposits, optic neuropathy, warfarin interaction, sinus bradycardia</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.25 mg intravenously each 2 h, up to 1.5 mg</td>
<td>60 min or more</td>
<td>0.125 to 0.375 mg intravenously daily or orally</td>
<td>Digitalis toxicity, HB, ↓ HR</td>
</tr>
</tbody>
</table>

**Nonacute setting and chronic maintenance therapy**

| Drug       | Loading dose            | Onset     | Maintenance dose                  | Major adverse effects                                      |
|------------|-------------------------|-----------|-----------------------------------|                                                            |
| Metoprolol | Same as maintenance dose| 4 to 6 h  | 25 to 100 mg twice a day orally   | ↓ BP, HB, ↓ HR, asthma, HF                                  |
| Propranolol| Same as maintenance dose| 60 to 90 min | 80 to 240 mg daily in divided doses, orally | ↓ BP, HB, ↓ HR, asthma, HF                                  |
| Diltiazem  | Same as maintenance dose| 2 to 4 h  | 120 to 360 mg daily in divided doses, slow-release available, orally | ↓ BP, HB, HF                                               |

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### Table 1 (continued)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Loading dose</th>
<th>Onset</th>
<th>Maintenance dose</th>
<th>Major adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verapamil</td>
<td>Same as maintenance dose</td>
<td>1 to 2 h</td>
<td>120 to 360 mg daily in divided doses, slow-release</td>
<td>↓ BP, HB, HF, digoxin interaction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>available, orally</td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>800 mg daily for 1 wk, orally</td>
<td>1 to 3 wk</td>
<td>200 mg daily, orally</td>
<td>↓ BP, HB, pulmonary toxicity, skin</td>
</tr>
<tr>
<td></td>
<td>600 mg daily for 1 wk, orally</td>
<td></td>
<td></td>
<td>discoloration, hypothyroidism,</td>
</tr>
<tr>
<td></td>
<td>400 mg daily for</td>
<td></td>
<td></td>
<td>hyperthyroidism, corneal deposits,</td>
</tr>
<tr>
<td></td>
<td>4 to 6 wk, orally (if outpatient, should not receive more than 400 mg a day because of the need for monitoring)</td>
<td></td>
<td></td>
<td>optic neuropathy, warfarin interaction, sinus bradycardia</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.5 mg by mouth daily</td>
<td>2 days</td>
<td>0.125 to 0.375 mg daily, orally</td>
<td>Digitalis toxicity, HB, ↓ HR</td>
</tr>
</tbody>
</table>

↓ BP indicates hypotension; ↓ HR, bradycardia.

**Abbreviations**: HB, heart block; HF, heart failure.


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**Fig. 1.** Atrial fibrillation in a patient with pre-excitation may result in rapid conduction over the accessory pathway, resulting in polymorphic ventricular tachycardia (shown) and eventually ventricular fibrillation and cardiac arrest.
with placebo [52]. Its antiarrhythmic effect on AF is not apparent until 8 to 24 hours after administration. This efficacy is comparable to that of class IC agents at 24 hours after drug administration, although IC drugs showed a more rapid onset of action, with some effect already apparent at 1 to 2 hours after administration. The only significant predictors of cardioversion are the duration of AF and LA size [53].

Amiodarone potentiates the effects of warfarin (it raises international normalized ratio [INR] level); accordingly, the dose of warfarin should be reduced upon initiating amiodarone. Amiodarone also increases digoxin and cyclosporine levels. Adverse effects of amiodarone include bradycardia, hypotension, visual disturbances, nausea, or constipation after oral administration and phlebitis after peripheral intravenous administration. Amiodarone can be used in patients with poor LV function, and it has a very low risk of polymorphic ventricular tachycardia (torsades de pointes) despite QT interval prolongation. In one meta-analysis of four trials involving 738 patients who had MI and LV dysfunction treated for at least a year, low-dose amiodarone caused no cases of torsades de pointes [54]. Amiodarone is more effective than either sotalol or propafenone in maintaining sinus rhythm in patients who have paroxysmal or persistent AF [55]. Amiodarone prevented recurrence of AF in 69% of patients, while only 39% of those on sotalol or propafenone remained in sinus rhythm. Amiodarone has some beta-blocking and calcium-blocking activity, so doses of these agents also should be adjusted appropriately.

Procainamide is another intravenous agent that has been used to pharmacologically cardiovert AF. It is a class IA antiarrhythmic drug. It can be given at a rate of 30 mg/min to a maximum dose of 20 mg/kg or in 100 mg boluses every 10 minutes up to a dose of about 2 g. If hypotension or QRS complex prolongation by greater than 50% occurs, infusion of procainamide should be terminated. Procainamide also can prolong QT interval and lead to proarhythmia. Unfortunately, its negative inotropic effects and vasodilation have limited its use in the intensive care setting. Its metabolite NAPA (N-acetylprocainamide) is cleared through the kidneys, and monitoring of NAPA levels is recommended in patients who have renal dysfunction. Procainamide also may cause bone marrow suppression, Coomb's-positive hemolytic anemia, cholestatic jaundice, and lupus-like symptoms. Procainamide is the drug of choice in patients with Wolf-Parkinson-White syndrome who present with AF.

Ibutilide is another class III antiarrhythmic drug. Ibutilide is given intravenously and may be used alone or in conjunction with direct current cardioversion. Ibutilide 1 mg is given as an infusion over 10 minutes, which can be repeated 10 to 20 minutes later if AF persists. Torsades de pointes occurs in up to 4% of patients who are given this medication, but it appears to be limited to patients who have LV dysfunction or baseline prolongation of QT interval, particularly in the presence of hypokalemia or hypomagnesaemia. Therefore ibutilide should not be administered in patients who have a left ventricular ejection fraction less than 35% or corrected (QTc) > 460 milliseconds.
Dofetilide is a newer class III oral antiarrhythmic agent that is a highly selective blocker of the rapid component of the delayed rectifier current causing action potential prolongation. It may take days to weeks before cardioversion occurs while this drug achieves therapeutic levels. This limits its use in the acute setting. Dofetilide has renal clearance. Only the oral form of the drug is available in the United States, and it is approved for both AF and atrial flutter. Inpatient initiation of therapy by certified physicians is mandated by the US Food and Drug Administration. Table 2 provides a side-by-side comparison of various antiarrhythmic agents with proven efficacy for pharmacologic cardioversion.

**Electrical cardioversion of atrial fibrillation**

Direct current (DC) cardioversion is the preferred initial method for termination of AF in critically ill patients because of its high acute efficacy of 67% to 94% [56–58]. Cardioversion results in immediate improvement of LV ejection fraction and stroke volume [59].

The probability of long-term maintenance of sinus rhythm is inversely related to both duration of AF before cardioversion and LA size [60,61]. If cardioversion fails, patients may be premedicated with antiarrhythmic medications before repeat cardioversion. Pretreatment with ibutilide, a class III antiarrhythmic drug, improves the success rate of DC cardioversion and is associated with a reduction in defibrillation energy requirements [62]. Other agents that can be used to enhance the success of DC cardioversion and maintenance of sinus rhythm are amiodarone, flecainide, propafenone, ibutilide, and sotalol [5].

Biphasic waveform defibrillators are more effective in cardioverting AF than are monophasic waveform defibrillators [63,64]. The energy requirement for cardioversion is usually 100 to 200 J for AF and 25 to 50 J for atrial flutter. Higher energy levels are required in patients whose BMI is high, who have had AF for a longer period of time, and whose left atrium is enlarged. Studies have failed to substantiate significant effect of high-energy defibrillation of up to 1370 J on troponin release from cardiac myocytes [65,66]. Pulmonary edema is a rare complication following cardioversion (1.2 %), and may be related to myocardial stunning, but seems not to be related to the amount of energy used [67].

DC cardioversion may be complicated by ventricular fibrillation, bradycardia or tachycardia, ST segment elevation, ventricular dysfunction, transient hypotension, pulmonary edema, and embolism. Cardioversions should be performed in the synchronized mode, in which the shock is delivered during ventricular depolarization. Shock applied during repolarization, shock on T, may result in ventricular fibrillation. Electrolyte status should be normalized when possible before cardioversion to limit proarrythmic complications. DC cardioversion should be avoided in the presence of digoxin intoxication. Ventricular fibrillation may occur following synchronous application of shock.
in patients who have digitalis toxicity, especially in the setting of hypokalemia. If cardioversion must be performed, prophylactic lidocaine should be given and low levels of energy applied. Sinus bradycardia or tachycardia occurs in up to 25% of cardioversions [68]. Patients on antiarrhythmic agents are more susceptible to bradycardia or asystole after the shock, and pacing capability should be available immediately after cardioversion [69]. In patients who

Table 2
Recommended doses of drugs proven effective for pharmacological cardioversion of atrial fibrillation

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route of administration</th>
<th>Dosage</th>
<th>Major adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>Oral</td>
<td>Inpatient: 1.2 to 1.8 g per day in divided dose until 10 g total, then 200 to 400 mg per day maintenance or 30 mg/kg as single dose; Outpatient: 600 to 800 mg per day divided dose until 10 g total, then 200 to 400 mg per day maintenance</td>
<td>Hypotension, bradycardia, QT interval prolongation, torsades de pointes (rare), gastrointestinal upset, constipation, phlebitis (intravenous)</td>
</tr>
<tr>
<td></td>
<td>Intravenous or oral</td>
<td>5 to 7 mg/kg over 30 to 60 min, then 1.2 to 1.8 g per day continuous intravenous dose or in divided oral doses until 10 g total, then 200 to 400 mg per day maintenance</td>
<td></td>
</tr>
<tr>
<td>Dofetilide</td>
<td>Oral</td>
<td>Creatinine Clearance (mL/min) Dose (µg twice daily)</td>
<td>Contraindicated if QT prolongation, torsades de pointes; adjust dose for renal function, body size, and age</td>
</tr>
<tr>
<td></td>
<td></td>
<td>More than 60 500 40 to 60 250 20 to 40 125 Less than 20 Contraindicated</td>
<td></td>
</tr>
</tbody>
</table>
| Fleca
|     | nide Oral               | 200 to 300 mg 1.5 to 3.0 mg/kg over 10 to 20 min                        | Hypotension, atrial flutter with high ventricular rate                                  |
| Ibutilide  | Intravenous              | 1 mg over 10 min; repeat 1 mg when necessary                            | QT prolongation, torsades de pointes                                                   |
| Propafenone| Oral                     | 600 mg 1.5 to 2.0 mg/kg over 10 to 20 min                              | Hypotension, atrial flutter with high ventricular rate                                  |
| Quinidine  | Oral                     | 0.75 to 1.5 g in divided doses over 6 to 12 h, usually with a rate-slowng drug | QT prolongation, torsades de pointes, gastrointestinal upset, hypotension               |

have permanent pacemakers, the lowest energy necessary should be used, and the electrodes should be placed in the anteroposterior position at least 12 cm from the pacemaker generator. Most reports on damage to pacemaker circuitry refer to older devices; however, a prudent approach would be to interrogate the device to assure proper function of the pacemaker following a cardioversion.

*Anticoagulation of patients with atrial fibrillation in the ICU*

Management of patients with AF at risk in the ICU presents a set of challenges. Although these patients are at risk of thromboembolism, many may have relative or absolute contraindications for anticoagulation. Comorbidities that may place patients at risk for complications include postoperative state, stroke, hemorrhage, platelet disorders, renal or liver failure, acute respiratory distress syndrome (ARDS), or trauma. The clinician must make a careful assessment of the risks and benefits of anticoagulation in the individual patient. The decision about whether and when to anticoagulate a patient with AF is made best in consultation of all the physicians involved in the patient’s care.

If AF is of greater than 48 hours duration, or its duration is unknown, and the patient has not been anticoagulated for at least 3 weeks, cardioversion can be performed after ruling out left atrial appendage thrombus by transesophageal echocardiography (TEE) with a low risk of stroke [70]. An example of a large thrombus in the LA appendage is shown in Fig. 2. Of course, if AF is associated with hemodynamic instability in the form of angina pectoris, MI, shock, or pulmonary edema, immediate cardioversion should be done without a TEE, but intravenous unfractionated heparin or subcutaneous injection of a low molecular-weight heparin should be initiated at the time of emergency cardioversion.

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Fig. 2. A large thrombus wedged in the left atrial appendage is seen on this transesophageal echogram.
In case–control series, patients undergoing cardioversion of AF or atrial flutter have a 1% to 5% risk of thromboembolism [71,72]. According to data pooled from 32 studies, more than 80% of thromboembolic events occur during the first 3 days, and 98% occur within 10 days of cardioversion [73]. Following successful cardioversion, atrial contractile function is impaired for hours to weeks depending on the duration of AF before cardioversion. Following cardioversion, however, all patients should be anticoagulated unless there is a significant contraindication. Anticoagulation should be continued for at least 4 weeks after a successful cardioversion, and perhaps longer in patients who have a high risk profile for thromboembolic complications. Although LA thrombus and systemic embolism have been documented in patients who have AF of shorter duration, the need for anticoagulation is less clear if AF has been present for less than 48 hours.

**Prevention of atrial fibrillation in ICU patients**

As previously stated, atrial arrhythmias, including AF, complicate 20% to 50% of open heart surgeries. Most postoperative AF occurs in the first 5 days, especially on postoperative day 2. Risks for postoperative AF include advanced age, a history of AF, COPD, valvular heart disease, withdrawal of beta-blockers or ace inhibitors, and pericarditis. Patients who have postoperative AF have a higher inpatient mortality (4.7% versus 2.1%) and longer length of hospital stay than patients without this arrhythmia [74]. Studies on perioperative use of amiodarone, beta blockers, sotalol, and pacing showed varying degrees of benefit. A systematic Cochrane database review analyzing 8565 patients found beta-blockers to be the most efficacious [75]. Perioperative use of amiodarone starting at least 7 days before cardiac surgery has been shown to reduce the incidence of AF by about 50% compared with placebo [76,77]. Sotalol (80 or 120 mg by mouth twice daily) when given in addition to beta-blocker was more effective than beta-blockers alone in some studies [78], but was of no benefit in others. A meta analysis of 10 randomized trials of postcoronary artery bypass graft (CABG) AF suggest that atrial overdrive pacing may reduce occurrence of AF by as much as 54% [79]. Although there are some data suggesting that inhibitors of the RAAS (ACE inhibitors and angiotensin receptor blockers) and statins may reduce the incidence of AF in the general medical population, there are no data on the possible role these agents may play in preventing postoperative AF. One study suggested that withdrawal of ACE inhibitor in the perioperative period may be associated with increased incidence of AF [80].

**Long term outcome of patients who develop atrial fibrillation in the ICU**

AF is associated with increased risk of stroke, heart failure, and all-cause mortality, especially in women [81]. Long-term mortality rate of patients who have AF in the community is about double that of patients who have
normal sinus rhythm. Data on long-term outcomes of patients who develop AF during critical illness is largely lacking, except when associated with specific disease states, such as MI and postoperative state. AF complicating acute MI doubles the in-hospital mortality [2]. In postoperative AF, on the other hand, long-term consequences of AF are more benign, and nearly 90% of patients revert to sinus rhythm after 2 months after surgery. Patients who develop AF in the setting of thyrotoxicosis usually revert spontaneously to sinus rhythm when they become euthyroid. Antiarrhythmic drugs and DC cardioversion are generally unsuccessful until euthyroid state is restored.

Summary

AF is associated with significant morbidity and increased mortality, especially in critically ill patients or in patients who have MI and heart failure. AF is a common arrhythmia in the ICU, and its management can be challenging. Specific therapy should be individualized based on age, clinical and hemodynamic status, underlying cardiac substrate, and comorbidities. Rate control is a reasonable strategy in older patients with asymptomatic or minimally symptomatic AF. In general, rhythm control strategy may be preferred to rate control strategy in ICU patients given their usually tenuous hemodynamic status and overall condition. Anticoagulation is an important aspect of management of AF. Specific measures may be taken to prevent AF in some ICU patients.

References


