Medical Cardioversion of Atrial Fibrillation

In managing patients with atrial fibrillation (AF), the clinician is confronted with a series of complex tasks and decisions that directly influence the choice of therapy. These include identifying and treating the underlying causes and precipitating factors; achieving ventricular rate control; determining eligibility and choosing optimal timing and methodology for cardioversion (including appropriate anticoagulation); proceeding with medical or electrocardioversion in eligible patients; choosing appropriate candidates for long-term antiarrhythmic drug therapy, and selecting the optimal agent in such individuals; identifying patients who may benefit from catheter-based, surgical, or device therapy; and ensuring optimal anticoagulation in those with chronic or paroxysmal AF. In their article “Amiodarone as a First Choice Drug for Restoring Sinus Rhythm in Patients With Atrial Fibrillation: A Randomized Controlled Study” in this issue of CHEST (see page 1538), Vardas and colleagues focus on the issue of medical cardioversion. This editorial addresses the significance of their findings within the greater context of medical cardioversion of AF. Before considering the role of antiarrhythmic drug therapy in medical cardioversion, it is important to emphasize that AF of recent onset is associated with a high frequency of spontaneous cardioversion. Reportedly, 44 to 78% of patients whose duration of AF is <24 h will spontaneously convert to sinus rhythm. This frequency decreases progressively when the duration of AF is >24 h, and is ≤16% when the duration is >1 month. Although treatment of precipitating factors may account for spontaneous cardioversion in some cases, the absence of electrophysiologic remodeling of the atria with shorter durations and its persistence with longer durations probably plays a more important role. The high rate of spontaneous cardioversion in patients with AF of recent onset has contributed to the misconception that atrioventricular nodal blocking drugs (digitalis, β-blockers, heart rate-modifying calcium channel blockers) are associated with medical cardioversion. In fact, these drugs, which are quite valuable in achieving ventricular rate control, have not been shown in placebo-controlled studies to restore sinus rhythm.

Vaughn-Williams class IA drugs prolong conduction in the atria by use-dependent sodium channel blockade and prolong action potential duration by blocking repolarizing potassium channels. These agents include quinidine, procainamide, and disopyramide. The reported efficacy of quinidine in producing medical cardioversion of AF ranges from 40 to 86%. These rates are derived mainly from uncontrolled studies. In comparative studies, the efficacy of quinidine was similar to that of amiodarone and flecainide, and greater than that of both sotalol and digoxin. However, the proarrhythmic potential of quinidine has blunted enthusiasm for use of this drug in medical cardioversion. Procainamide is the most commonly used antiarrhythmic drug in medical cardioversion of AF, probably because of its ease of use as an IV agent. The reported efficacy of procainamide in medical cardioversion of AF of recent onset ranges from 43 to 58%. Duration of AF is an important determinant of success. In one study, 90% of patients achieved restoration of sinus rhythm when the duration was <24 h, whereas only 9% cardioverted when the duration was >1 week. Comparative studies have shown that procainamide is similar to quinidine and superior to digoxin in restoring sinus rhythm. It has been shown to be superior to propafenone in achieving medical cardioversion in patients with Wolff-Parkinson-White syndrome. This major side effect of IV procainamide is hypotension. The proarrhythmic potential with acute use is less than that of quinidine. In one uncontrolled study, disopyramide, administered orally at 200 mg every 4 to 6 h up to 500 mg/d, restored sinus rhythm in 92% of patients the first day, in an additional 6% the second day, and in the remaining 2% the third day. There were no serious adverse effects. The lack of placebo-controlled data and the marked negative inotropic and anticholinergic effects have limited the use of disopyramide in patients with AF.

During the 1990s, Vaughn-Williams class IC drugs (flecainide and propafenone) also block sodium channel and at high rates prolong the atrial refrac-
tory period and reduce atrial conduction velocity. Because of the known proarrhythmic effect of class IC agents in patients with ischemic heart disease and because of their potent negative inotropic properties, most studies of these drugs have been confined to patients with little or no structural heart disease. Flecainide has been utilized in both IV and oral doses (as a single loading dose or with serial dosing within 24 h). The reported efficacy of flecainide in restoring sinus rhythm ranges from 52 to 92%. Flecainide has invariably been superior to placebo in achieving medical cardioversion. IV administration has generally produced cardioversion within 3 hours, whereas oral dosing has generally required 6 to 12 h to achieve optimal results. In comparative studies, flecainide has proven to be superior to procainamide and sotalol and similar to amiodarone in producing eventual cardioversion. In one study, flecainide proved to be more efficacious than propafenone in restoring sinus rhythm. Propafenone has been used in IV (bolus plus infusion) and oral forms to cardiovert AF. Its reported efficacy ranges from 41 to 91%, with IV infusion restoring sinus rhythm earlier than a single oral dose. Propafenone was superior to placebo in most but not all controlled studies. In one study, there was a high rate of cardioversion within 6 h using oral propafenone, but by 24 h the cardioversion rates for propafenone and placebo were similar. In comparative studies, propafenone has been proved to be superior to digoxin but less effective than amiodarone, procainamide, and flecainide at restoring sinus rhythm. As with the class IA agents, duration of AF played an important role in predicting drug efficacy for flecainide and propafenone, with durations associated with lower conversion rates. Administration of these agents has been remarkably free from adverse effects, with only sporadic episodes of hypotension or wide complex tachycardia being reported. The ability of a single oral dose of flecainide or propafenone to produce cardioversion in > 40% of patients with recent-onset AF within 6 h has created hope that some of those with structurally normal hearts and acute AF might be safely and effectively treated in the emergency department and not require hospital admission for their arrhythmia. IV preparations of flecainide and propafenone are not currently commercially available in the United States.

Vaughn-Williams class III drugs have been used increasingly in patients with AF. These drugs work primarily by blocking potassium channels, thus prolonging atrial action potential duration and increasing atrial refractoriness. Sotalol, which also possesses β-blocking ability, has not proven to be particularly effective in medical cardioversion. Sinus rhythm has been restored in only 8 to 54% of cases. In one study, its efficacy was no different than placebo. Comparative studies have been shown that sotalol is inferior to flecainide and quinidine in restoring sinus rhythm. Amiodarone is a potassium channel blocker but also possesses many other potential antiarrhythmic properties. It has been studied extensively as a means of medical cardioversion, often after other medical regimens have failed. When used to produce cardioversion of AF, amiodarone has been used primarily in IV form (5 mg/kg or 300 mg over 1 h, then 15 to 20 mg/kg for the remaining 23 h). Most studies have continued amiodarone in oral form after IV loading. When used in this manner in placebo-controlled or comparative studies, amiodarone has been reported to eventually restore sinus rhythm in 47 to 93% of patients with AF. In most, but not all studies, amiodarone was superior to placebo therapy in producing medical cardioversion. Comparative studies show amiodarone to be comparable to flecainide and quinidine and comparable to or more efficacious than propafenone in restoring sinus rhythm. In almost all studies, amiodarone produced its optimal effect in restoring sinus rhythm at 24 h. Adverse effects with IV administration of amiodarone are rare, with transient hypotension being the most common.

Recently, two intravenously administered drugs with short half-lives (ibutilide and dofetilide) have been used to rapidly terminate AF and flutter of variable duration. Both drugs are thought to produce their antiarrhythmic effect via potassium channel blockade. IV ibutilide is administered at a dose of 1 mg, with a second dose of 1 mg provided if needed. Its reported efficacy in restoring sinus rhythm in patient with AF (generally within 3 h) ranges from 32 to 51%. It is more effective in producing medical cardioversion in patients with atrial flutter than in those with AF. In comparative studies, it has proved to be superior to procainamide in restoring sinus rhythm. Dofetilide, administered in doses of 8 to 12 μg/kg, has restored sinus rhythm in 24 to 54% of patients, generally within 3 h. Dofetilide has consistently proven to be superior to placebo in converting AF and flutter to sinus rhythm. Comparative studies are lacking. Although conversion rates for ibutilide and dofetilide are lower than for most other antiarrhythmic drugs, it is important to emphasize that the average duration of AF or atrial flutter in these studies approached 60 days. The major adverse effect of both drugs is proarrhythmia. The average reported incidence of torsades de pointes with ibutilide and dofetilide use was 4.3% and 3.0%, respectively. Sustained monomorphic ventricular tachycardia has also been described.

The study by Vardas and co-workers published in this issue of CHEST shows that approximately 80%
of a typical population of patients presenting with AF can be cardioverted by amiodarone when this drug is chosen first as a therapeutic probe. Moreover, the cardioversion rate was > 90% in those whose duration of AF was < 1 month and in those with a normal or mildly enlarged left atrial dimension. Unlike many of the studies involving class IA drugs that showed high rates of cardioversion, this study was placebo controlled. Unlike many studies of class IC drugs, this study contained a substantial number of patients in both the placebo and amiodarone groups with underlying structural heart disease (45% and 41%, respectively). And, unlike ibutilide and dofetilide, amiodarone, when used in the manner described in this study had no proarrhythmic effect. This study shows that cardioversion continues to occur when short-term oral administration of amiodarone follows IV loading, particularly in those with longer durations of AF. Whether utilization of amiodarone as described by the authors will reduce hospitalization time for patients with recent-onset AF is uncertain. A cost-efficacy analysis of this and other methods of medical cardioversion would be of interest, as would a study focusing entirely on these with underlying structural heart disease. Finally, although studies assessing the efficacy and safety of various methods of medical cardioversion are useful, such methods must ultimately be compared with electrocardioversion of AF, a technique that historically has produced extremely high conversion rates with an excellent record of safety.

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References


Outcome of Lung Surgery

What Patients Don’t Like

The article by Cykert et al, published in this issue of CHEST (see page 1551), is focused on patients’ preferences regarding the possible outcome of lung surgery, and their impact on the final decision of undergoing surgical treatment. The conclusions of this study—if confirmed by larger series—may effect a change in everyday surgical practice.

Firstly—covering a methodologic aspect—it might suggest a revision of standard methods of evaluating postsurgical functional results, not only considering the immediate postoperative period (30 days postoperatively or “transient states”) but, also, long-term functional results—so-called “fixed functional outcomes”—which were felt to be onerous enough to deter patients from the surgical option, and have the potential to expose both the patients and the community to increased health costs.

Secondly—covering a functional aspect—it will help refine the search for predictors of cardiopulmonary reserve in surgical candidates in order to decrease the risk for long-term physical disability. In other words, preoperative workup should predict the long-term possibility for oxygen dependency and limitation in ambulation and routine daily activities. Put it into perspective, the need for a more comprehensive preoperative evaluation including additional...