Electrical and Pharmacologic Cardioversion for Atrial Fibrillation

Susan S. Kim, MD, Bradley P. Knight, MD*

KEYWORDS

• Atrial fibrillation • Cardioversion • Electrical

Cardioversion is a useful tool in managing patients who have atrial fibrillation (AF) when rhythm control is appropriate. It is used most frequently for those who are symptomatic or newly diagnosed. Transthoracic electrical cardioversion is the overwhelmingly preferred method because of its relative simplicity and efficacy, even in patients who have multiple comorbid conditions and significant structural heart disease. In selected circumstances, pharmacologic cardioversion is preferred. This article discusses indications for cardioversion and management of pericardioversion anticoagulation and describes electrical and pharmacologic cardioversion in detail. Finally, management strategies are offered for initial failure to convert or immediate recurrence of AF (IRAF).

PATTERNS OF ATRIAL FIBRILLATION

Before discussing the indications for cardioversion, it is useful to define the clinical patterns of the occurrence of AF. Generally, patients who have AF demonstrate one of three clinical patterns: paroxysmal, persistent, or permanent AF (**Fig. 1**).[1] Paroxysmal AF consists of self-terminating episodes, each usually lasting fewer than 7 days and often less than 24 hours. Persistent AF consists of non–self-terminating episodes, each lasting more than 7 days, whereas permanent AF is defined as a long episode with failed or no attempt at cardioversion.

Given these definitions, cardioversion can be clinically useful in some patients who have paroxysmal AF and in many who have persistent AF. By definition, cardioversion is not used for patients who have permanent AF.

INDICATIONS FOR CARDIOVERSION

Broadly, cardioversion should be considered for two populations of patients: those who are symptomatic with AF and those who present with AF for the first time.

Patients who have symptomatic AF can have severe enough symptoms, such as severely decompensated heart failure, hypotension, uncontrolled ischemia, or angina, to mandate urgent cardioversion. Other patients who have AF may have less severe symptoms, such as palpitations, fatigue, lightheadedness, and exertional dyspnea. Regardless of the degree of severity, any symptoms caused by atrial fibrillation warrant consideration of cardioversion as a management option.

Restoration of sinus rhythm is a reasonable goal in patients who have a first-time diagnosis of AF, regardless of symptoms, unless some indication shows that the AF has been present for many years before identification. The purpose of cardioversion, even in patients who are asymptomatic or newly diagnosed, is to slow the progression of the clinical pattern of AF. Many lines of evidence support the principle that "atrial fibrillation begets

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Section of Cardiology, Department of Medicine, University of Chicago Medical Center, 5758 South Maryland Avenue MC9024, Chicago, IL 60637, USA
* Corresponding author.
E-mail address: bknight@medicine.bsd.uchicago.edu (B.P. Knight).

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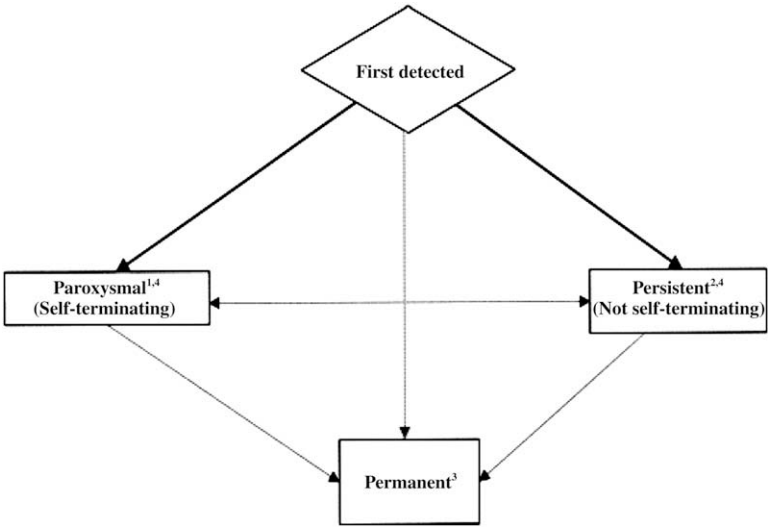

Fig. 1. Patterns of AF. (1) Episodes that last generally 7 days or fewer (most less than 24 hours); (2) episodes that last usually longer than 7 days; (3) cardioversion failed or not attempted; and (4) paroxysmal and persistent AF may be recurrent. (*From* Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation. Circulation 2006;114:e257–354, © 2006; with permission from the American Heart Association.)

atrial fibrillation''.[2] Natural history studies show that AF can be a progressive disease: patients who have paroxysmal AF progress to persistent and permanent AF. Even those who have lone paroxysmal AF may progress,[3] and the tendency to progress seems to correlate with the duration of the paroxysmal AF episodes.[4]

In addition, many clinical trials show that pharmacologic and electrical cardioversion are more likely to succeed in patients experiencing shorter episodes.[5] A study comparing short- versus longer-duration episodes of AF in goat hearts showed that with longer-duration episodes, the rate, inducibility, and stability of AF increased significantly. In addition, a marked shortening of the atrial effective refractory period was seen.[2] These lines of evidence strongly support the principle that AF begets itself; this principle underlies the rationale for cardioverting patients who have newly diagnosed AF.

As evidenced in large-scale, randomized clinical trials, repeated cardioversion and other attempts to maintain sinus rhythm are unlikely to have a meaningful clinical impact on older patients who are asymptomatic. Also, by definition, cardioversion is not applied to patients who have permanent AF. Both populations of patients, however, should undergo therapeutic anticoagulation or antiplatelet therapy as dictated by their risk for a thromboembolic event versus the risks from this therapy.[6,7]

Another group of patients who may benefit from cardioversion are those who have postoperative AF. Postoperative AF occurs most commonly in the first few days after surgery, when anticoagulation may be undesirable. Many episodes of postoperative AF resolve spontaneously. Patients who do not experience spontaneous resolution may be cardioverted before an AF duration of 48 hours to avoid anticoagulation.

RATE OF SUCCESSFUL CARDIOVERSION

With electrical cardioversion and use of biphasic waveforms, cardioversion success rates are consistently at or greater than 90%.[8,9] These high rates of successful cardioversion apply even in populations of patients who have advanced age, multiple comorbid conditions, and significant structural heart disease. In one study of 1355 patients who had persistent AF (>7 days) undergoing electrical cardioversion,[8] 92% were successfully converted to sinus rhythm. With biphasic energy cardioversion, multivariate analysis showed that no patient characteristic, gender, age, comorbid condition, or cardiac structural abnormality (eg, reduced left ventricular ejection fraction, enlarged left atrium, other structural heart disease) was associated with failure to convert to sinus rhythm. Therefore, although these baseline characteristics should be considered with regard to successful maintenance of sinus rhythm, they should not necessarily deter attempts at cardioversion.

PERICARDIOVERSION ANTICOAGULATION

AF results in mechanical stasis in the atria and is associated with a proinflammatory and therefore potentially prothrombotic state.[10] Therefore, patients who have AF are at risk for developing intracardiac thrombi and subsequent embolization. The risk for a thromboembolic event is particularly high around cardioversion for two reasons. First, if an unstable thrombus is present precardioversion,

the recovery of atrial contraction postcardioversion and the force of atrial contraction may cause fragmentation and embolization of the preexisting thrombus.[11,12] Second, in many patients, the recovery of atrial mechanical function can lag behind restoration of normal electrical function.[13] This period of atrial mechanical ''stunning'' after cardioversion can last up to 4 weeks postcardioversion. Thus, stasis in the atria and the risk for clot formation may endure for several weeks postcardioversion, even with persistent sinus rhythm. Therefore, the goals of pericardioversion anticoagulation for AF are twofold: (1) to minimize the likelihood of an unstable thrombus being present at cardioversion and (2) to prevent the formation of new thrombus in the postcardioversion phase. Without anticoagulation, the risk for a thromboembolic event postcardioversion can be as high as 5%.[14]

To minimize the likelihood of an unstable thrombus being present at cardioversion, one of two different strategies may be used: (1) empiric anticoagulation for 3 weeks or (2) short-term anticoagulation and transesophageal echocardiography (TEE)-guided cardioversion. Presuming that an unstable thrombus takes approximately 2 weeks to organize and adhere to the atrial wall, under the empiric anticoagulation strategy patients should be treated for a minimum of 3 weeks with warfarin (target international normalized ratio [INR], 2.5; range, 2.0–3.0) or enoxaparin before cardioversion.[1,12,15]

The 3 weeks' duration allows for organization and even potential resolution of preexisting thrombus in addition to minimizing the risk for new thrombus formation. When using warfarin, a therapeutic effect must be verified with weekly INR levels before cardioversion. One retrospective study examined 1435 patients who had AF greater than 48 hours' duration who were receiving warfarin and undergoing direct current cardioversion. In these patients, embolic events were significantly more likely when the INR was 1.5 to 2.4, compared with an INR greater than or equal to 2.5 (0.93% versus 0%; $P = .012$).[16]

Alternatively, patients may be therapeutically anticoagulated with heparin followed by TEE. If no thrombus is seen on TEE, cardioversion is performed. The advantage of TEE-guided cardioversion is a shorter time to cardioversion and, potentially, a shorter total duration of anticoagulation.

The validity of TEE-guided cardioversion was shown in a randomized clinical trial involving 1222 patients.[17] Patients who had AF requiring cardioversion were randomized to 24 hours of unfractionated heparin and TEE-guided cardioversion versus empiric anticoagulation for 3 weeks before cardioversion. In both strategies, patients were anticoagulated for 4 weeks postcardioversion. After 8 weeks, no significant difference was seen in the rate of embolic events (0.8% versus 0.5%; $P = .50$) between the TEE-guided versus warfarin-only groups. However, a significantly decreased rate of hemorrhagic events (2.9% versus 5.5%; $P = .03$) and a shorter time to cardioversion (3.0 versus 30.6 days; $P<.001$) were seen in the TEE-guided versus warfarin-only groups.

A smaller, randomized, controlled trial compared low molecular weight heparin with unfractionated heparin plus oral anticoagulation.[15] Of the 496 patients in the trial, 431 underwent TEE-guided cardioversion, whereas the remaining 65 were anticoagulated empirically and cardioverted after 3 weeks. In all strategies, patients underwent 4 weeks of anticoagulation postcardioversion. The use of low molecular weight heparin was found to be noninferior in the empiric-anticoagulation and TEE-guided treatment arms, compared with the use of unfractionated heparin plus oral anticoagulation, for the primary end point of preventing ischemic and embolic events, bleeding complications, and death.

Again, given the delay of up to 4 weeks for recovery of atrial mechanical function postcardioversion, patients should undergo at least 4 weeks of therapeutic anticoagulation postcardioversion.[1,12] Especially in the early postcardioversion period, meticulous attention should be given to anticoagulation status, because most thromboembolic events occur within the first few days postcardioversion (**Fig. 2**).[18] In particular, overlapping therapy with heparin (unfractionated or low molecular weight) should be administered if the INR is less than 2.0.

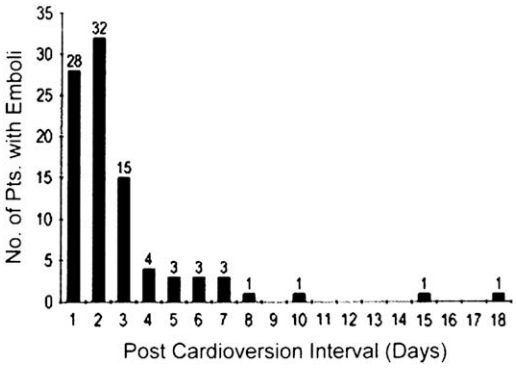

Fig. 2. Interval between cardioversion and thromboembolic events in 92 patients. (*From* Berger M, Schweitzer P. Timing of thromboembolic events after electrical cardioversion of atrial fibrillation or flutter: a retrospective analysis. Am J Cardiol 1998;82:1545–7, © Elsevier 1998; with permission.)

One analysis that pooled data from 32 studies and included 4621 patients examined the timing of embolic events,[18] finding that 92 (2%) patients experienced embolic events. Only 11 of the patients were anticoagulated before cardioversion. Of the 92 episodes, 75 (82%) occurred within the first 72 hours postcardioversion (see **Fig. 2**). Notably, 98% of the embolic events occurred within the first 10 days postcardioversion.

For AF episodes lasting less than 48 hours, the likelihood of thrombus formation and subsequent embolization after cardioversion is low. Therefore, anticoagulation is not recommended routinely for patients who have episodes lasting less than 48 hours.[1] Neither pre- nor postcardioversion anticoagulation is recommended for these short-duration episodes.

One prospective observational study followed 375 patients admitted to the hospital for AF who were found to have an episode lasting less than 48 hours.[19] Patients treated with anticoagulation using warfarin (INR >1.6) or heparin at presentation were excluded. Spontaneous conversion occurred in 250 patients, whereas 107 underwent pharmacologic or electrical conversion. Three patients (0.8%; 95% CI, 0.2%–2.4%) had a clinical thromboembolic event. Thus, overall, the thromboembolic risk for patients who have short-duration AF seems low.

Determining the true onset of an AF episode can be difficult in the absence of electrocardiographic documentation (eg, telemetry or 12-lead ECG). Symptoms generally are unreliable as a marker of the presence of absence of AF. One study in patients who had pacemakers showed that more than 90% of atrial tachyarrhythmia events documented by the pacemaker were not perceived by the patients, even in those who were believed to have symptomatic arrhythmias.[20] Therefore, in the absence of electrocardiographic evidence of the true onset of an episode of AF, it is most prudent to assume that the episode has been ongoing for more than 48 hours.

CARDIOVERSION

Most patients who require cardioversion undergo transthoracic electrical cardioversion rather than an attempt at pharmacologic conversion because of its shorter overall procedure duration and high rate of success (as high as >90%).[21] Although at least deep sedation is required for transthoracic electrical cardioversion, if short-acting agents are used, patients may be discharged within hours after recovery from anesthesia. Antiarrhythmic medications play two primary roles in cardioversion for AF. Used alone, they are effective in timely termination of symptomatic AF of short duration. Used together with electrical cardioversion, they help facilitate persistent sinus rhythm in two distinct populations of patients: those who have IRAF (successful conversion to sinus rhythm, even just one beat, followed by recurrence of AF within minutes) and those for whom cardioversion truly fails with no achievement of sinus rhythm.

Electrical Cardioversion

Biphasic waveforms superior to monophasic waveforms

The success of cardioversion and defibrillation depends on the delivery of adequate current flow through the heart.[22] However, excessive current delivery can lead to myocardial damage, leading to ST-segments changes, enzyme release, depression of myocardial function, and reduced mean arterial pressures.[23,24]

The two major determinants of current delivery through an external defibrillator are energy selection and the shock waveform used. When Bernard Lown[25] reported the first series of AF cardioversions using an external defibrillator in 1963, he was using what is termed *monophasic damped sinusoidal* (*MDS*) *waveform*, or the *Lown waveform*, for energy delivery (**Fig. 3**).[26] This waveform, displayed as current amplitude over time, is characterized by an initial high peak followed by an exponential decay of the current to zero. The MDS waveform remained the dominant waveform in external defibrillators until biphasic waveforms emerged. Under pressure to reduce the size of implantable defibrillator generators, device manufactures developed biphasic waveforms, which showed a significant decrease in defibrillation energy requirements for ventricular fibrillation.[27,28] Given their superiority in implantable defibrillators, biphasic waveforms then were tried in external defibrillators. Currently, two types of biphasic waveforms are used in most commercially available external defibrillators: biphasic truncated exponential (BTE) waveforms and rectilinear biphasic waveforms (RBW) (see **Fig. 3**). Both biphasic waveforms are characterized by lower peak current amplitudes (compared with monophasic waveform energies of similar clinical efficacy) and a second phase with a negative or inverted polarity. The lower peak current amplitudes may be associated with less myocardial injury than higher peak current shocks.[29]

Biphasic waveforms have proven to convert AF at much lower energies and higher rates than the MDS waveform. In one study comparing the RBW and MDS waveforms,[21] 165 patients who had AF were randomized to monophasic shocks

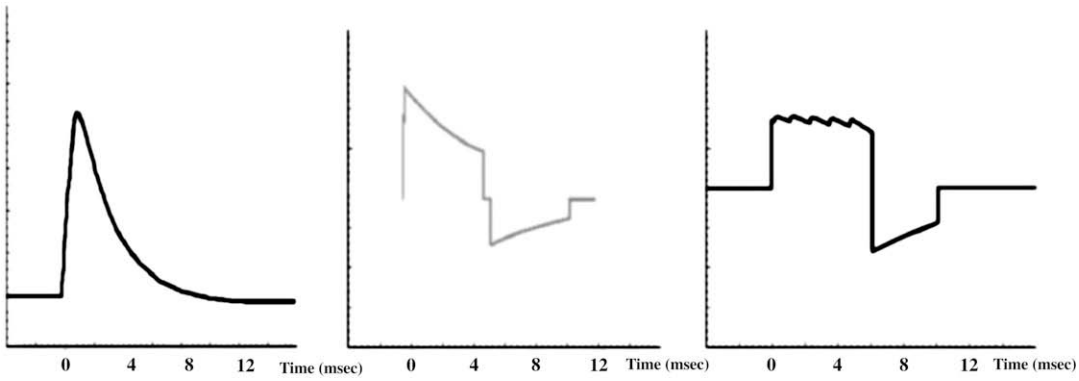

Fig. 3. Shock waveforms: (*left*) MDS waveform; (*middle*) BTE waveform; (*right*) RBW. The vertical axis represents current amplitude. (*From* Mittal S, Stein KM, Markowitz SM, et al. An update on electrical cardioversion of atrial fibrillation. Card Electrophysiol Rev 2003;7:285–9, © 2003 Springer; with permission from Springer Science and Business Media.)

using a dose escalation of 100, 200, 300, and 360 J or biphasic shocks using 70, 120, 150, and 170 J. With the first shock, the RBW was significantly more successful than the MDS shock, with a 60/88 (68%) versus 16/77 (21%) ($P<.0001$) conversion rate. A significantly higher success rate was still seen in the biphasic shock group after the highest energy shock (83/88 [94%] versus 61/77 [79%]; $P = .005$). At all comparable energy levels and across all impedances, peak currents in the biphasic shocks measured at approximately 50% of the peak current amplitude seen with monophasic shocks.

Two randomized studies compared the BTE waveform with the MDS waveform for AF cardioversion. In the first study, 57 patients were randomized to either cardioversion with 150 J and then 360 J with a MDS defibrillator or 150 J followed by another 150 J with a BTE defibrillator. With the first shock (each at 150 J), the cardioversion success rate was 16/27 (59%) in the MDS group versus 26/30 (86%) in the BTE group.[30] Cumulative success rates after the second shock and after crossover were not significantly different between the groups (88% versus 93% and 92% versus 96%, respectively).

In the second study, 203 patients were randomized to an MDS versus a BTE waveform with delivery of 100, 150, or 200 J, then maximum-output (360 and 200 J, respectively) shocks.[31] At each of the first three energy levels, the cumulative cardioversion success rate was significantly higher in the BTE group versus the MDS group: for example, at 200 J, the success rate was 86/96 (90%) versus 57/107 (53%), respectively ($P<.0001$). At the highest energies, no statistically significant difference in outcome was seen between the groups: 87/96 (91%) versus 91/107 (85%), respectively ($P = .29$). Also, at equal energy levels, the BTE waveform was associated with significantly less dermal injury than the MDS waveform.

Finally, biphasic external defibrillators are more efficacious in patients who have AF resistant to monophasic cardioversion.[32] Fifty-six patients who had AF for whom at least one 360-J monophasic shock had failed were randomized to progressive 150-J, 200-J, and 360-J BTE shocks or one 360-J monophasic shock. Sinus rhythm was restored in 17 of 28 (61%) patients who had biphasic versus 5 of 28 (18%) who had monophasic shocks ($P = .001$). With crossover allowed after failed shocks, 78% of patients who had a failed monophasic shock were cardioverted successfully with a biphasic shock, whereas only 27% of those patients who had failed biphasic shocks converted with the high-energy monophasic shock.

Currently, most evidence favors the use of biphasic external defibrillators for AF cardioversion because of their categorically lower energy requirements and greater efficacy compared with monophasic defibrillators.

Practical considerations

Anesthesia Patients undergoing elective cardioversion should receive at least deep sedation, because high-energy shock can cause significant discomfort. Short-acting agents, such as midazolam, fentanyl, and propofol, are desirable given their rapid onset and short half-life. In some cases, general anesthesia may be indicated. Anesthesia and cardioversion should be performed in the postabsorptive state. Even when urgent cardioversion is required, as in cases of hypotension, severe decompensated heart failure, angina, or ischemia,

attempts should be made to sedate patients when circumstances allow.

Pad or paddle positioning and size A handful of studies have examined the effect of anterior-posterior (AP) versus anterior-lateral (AL) electrode (pad or paddle) positioning on cardioversion success. One study randomized 301 patients who had AF to AP or AL pad positioning. The AP position was associated with a significantly higher rate of successful cardioversion and lower cumulative energy requirement (**Fig. 4**).[33] Two subsequent studies show no effect of pad placement on cardioversion success in AF.[34,35] The second study also showed that an increased pad size (13 cm versus the standard 8.5 cm) did not improve the likelihood of cardioversion.[35]

Shock delivery To avoid shock delivery during the vulnerable phase of the cardiac cycle ("shock on T") and subsequent ventricular fibrillation, shocks should be delivered in a synchronized fashion. In the synchronized mode, intrinsic R waves are sensed and shock delivery is timed to minimize the risk associated with delivery during the vulnerable period. This technique is different from the defibrillation mode, which delivers shocks in an asynchronous or random fashion without regard to the cardiac cycle. This mode is appropriate for ventricular fibrillation or very rapid ventricular tachycardia, for which synchronized delivery is not possible and immediate shock is desired.

Energy selection Energy level is related directly to current amplitude, and adequate current delivery determines successful cardioversion. Therefore, one choice may be to start with the highest energy for every cardioversion (360 J with monophasic defibrillators and 200 J or even 360 J in some biphasic defibrillators). The advantage is a high probability of successful cardioversion and, thus, a shorter duration of sedation. The greatest disadvantage of higher energy shocks, especially with monophasic defibrillators, is thermal injury to the skin.[31,36] Any potential myocardial damage, from even high-energy cardioversion, rarely is of clinical consequence.

Because current is related inversely to impedance, increased transthoracic impedance can diminish current delivery to myocardium. One study found increased transthoracic impedance to be significantly and independently associated with lower rates of successful cardioversion.[21] Incomplete pad or paddle contact also may increase transthoracic impedance. Adequate contact medium (usually gel or paste) and firm pad or paddle contact should be assured. Other factors that increase transthoracic impedance include obesity, emphysema, and asthma. In patients who have these conditions, selecting a high level of energy is appropriate. Delivering shocks during the expiratory phase of the respiratory cycle also may decrease transthoracic impedance.

Patients who have AF of longer duration have lower rates of successful cardioversion.[21,33] They also may have more success with higher energy shocks.

Lower-energy shocks are appropriate when patients are smaller in size or have AF of shorter

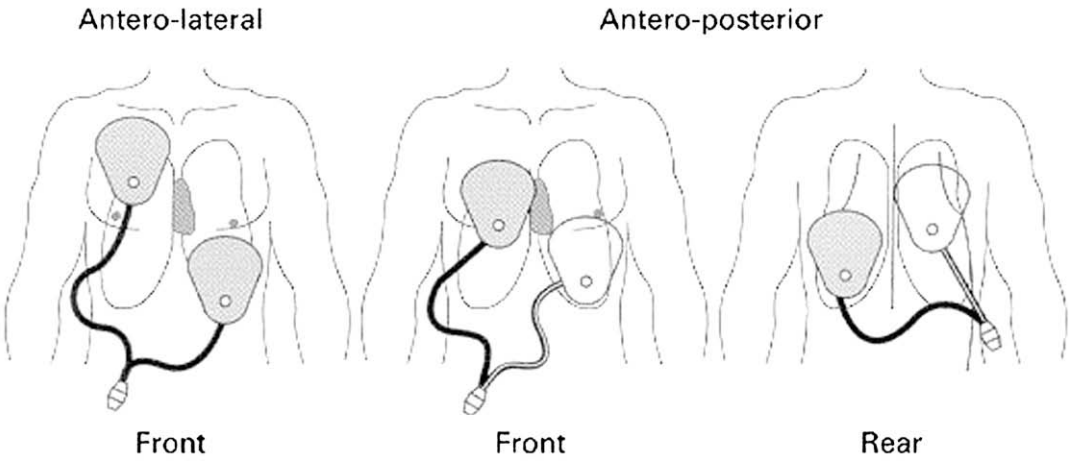

Fig. 4. Electrode positions. Anterolateral, ventricular apex-right infraclavicular area paddle position; (modified) anteroposterior, right sternal body at the third intercostal space-angle of the left scapula paddle position; front, front view; rear, rear view. (*From* Botto GL, Politi A, Bonini W, et al. External cardioversion of atrial fibrillation: role of paddle position on technical efficacy and energy requirements. Heart 1999;82:726–30; with permission from the BMJ Publishing Group.)

duration. Furthermore, patients who have atrial flutter may successfully convert with low energies (as low as 100 J monophasic or 50 J biphasic) for successful cardioversion. Even with lower energy shocks, patients can experience significant discomfort and still should undergo at least deep sedation.

Patients who have implanted devices Under the proper circumstances, patients who have implanted devices (permanent pacemakers or implantable cardioverter-defibrillators [ICDs]) can undergo external cardioversion with minimal risk to their devices and themselves. Potential risks at shocking include alteration of programmed data or, if electricity is conducted down an implanted lead, endocardial injury with transient or permanent exit block. These risks are maximized when pads or paddles are placed with one over the pulse generator and one at the apex of the heart. AP positioning seems to lower these risks.[1] Pre- and postcardioversion, devices should be interrogated with complete lead testing and device reprogramming as needed.

In patients who have ICDs, cardioversion may be achieved with a commanded internal shock delivered through the device. Device-mediated cardioversion has the advantage of avoiding potential damage to the implanted system. A disadvantage is that each shock contributes to significant decrease in battery life of up to approximately 1 month for each maximum-energy shock. Internal shocks can cause significant discomfort, and therefore patients still should receive at least deep sedation. For patients who have atrial flutter, device-delivered antitachycardia pacing should be attempted because it is painless and sedation is unnecessary.

Internal by way of intracardiac catheters This article has primarily discussed external transthoracic cardioversion. Before the development of biphasic defibrillators, AF cardioversion failure rates were significantly higher. In that setting, internal cardioversion was established as next-line therapy for patients for whom external cardioversion failed. The technique eventually evolved to placement of intracardiac catheters in the right atrium, coronary sinus, and left pulmonary artery, through which low-energy shocks were delivered.[37] This treatment option may be useful in patients for whom all other cardioversion techniques have failed.

Outcomes The three potential outcomes after electrical cardioversion are (1) persistent restoration of sinus rhythm, (2) restoration of sinus rhythm (at least one sinus beat) followed by IRAF, or (3) failed cardioversion with no evidence of sinus rhythm. Results from many studies show that patients who have IRAF can experience rates of long-term freedom from AF[38,39] comparable to patients who have persistent sinus rhythm postcardioversion. The rates of long-term freedom from AF are significantly worse, however, in patients who have true failed cardioversion who ultimately achieve sinus rhythm. Thus, it is critical to distinguish between patients who have IRAF (those who have even just one sinus beat after cardioversion) and those who have true failed cardioversion. Because patients who have IRAF can have favorable long-term outcomes, aggressive measures should be taken to facilitate persistent postcardioversion sinus rhythm.

Immediate recurrence of atrial fibrillation IRAF is defined as AF recurring within the first few minutes after cardioversion. One study suggests that if AF recurs within the first 24 hours postcardioversion, it will occur within the first few minutes after cardioversion.[40] Even when only one beat of sinus rhythm is seen, the subsequent AF is considered IRAF as opposed to true failed cardioversion. The incidence of IRAF ranges from 5% to 25%.[41]

The distinction between IRAF and true failed cardioversion is important because the two populations have different long-term outcomes:[39] patients who have IRAF who ultimately achieve persistent sinus rhythm postcardioversion (usually pharmacologically facilitated) have better rates of long-term freedom from AF than those who have true failed cardioversion who subsequently achieve sinus rhythm.

IRAF seems to be triggered by very early coupled premature atrial beats (PABs). In one study of patients undergoing internal cardioversion for AF, IRAF was noted in 13% (5/38). IRAF in these patients always was seen to reinitiate with non-catheter-induced PABs. PAB-coupling intervals that led to IRAF were significantly shorter than those that did not.[38] Pretreatment with atropine or flecainide facilitated cardioversion without IRAF in three patients, whereas repeat shock alone was successful for two.

In another study in patients undergoing catheter ablation for AF, PABs triggering IRAF also were significantly shorter than PABs not triggering AF.[42] This study documented that 20% of IRAF episodes were initiated by pulmonary vein activity. In every case, the pulmonary vein activity took the form of a rapid pulmonary vein tachycardia.

In a third study, also in patients undergoing catheter ablation for AF, coupling intervals for IRAF-initiating PABs were again significantly

shorter than those not initiating IRAF. IRAF was seen more frequently in patients who had AF lasting less than 1 month than in those who had longer episodes. Long-term, patients who had IRAF experienced similar freedom from AF to those who did not have IRAF.[43]

Another study also showed the increased incidence of IRAF in patients who have shorter-duration episodes of AF.[41] This study involved patients who had implantable atrial defibrillators and those undergoing external transthoracic cardioversion. In patients who underwent cardioversion within 1 hour of the onset of AF, IRAF occurred at a rate of 56%, compared with those whose AF lasted more than 24 hours who had a rate of 12%. This finding suggests a possible lower limit of AF duration below which cardioversion may be less likely to lead to persistent sinus rhythm.

Patients who have IRAF have experienced successful persistent postcardioversion sinus rhythm or suppression of IRAF in many studies using various antiarrhythmic medications. An early demonstration of successful pharmacologic suppression of IRAF was published in 1967 with the use of quinidine.[44] Fifty patients received oral quinidine (1200 mg) 1 day before cardioversion. Successful cardioversion was achieved in 92% patients receiving quinidine versus 64% in control patients ($P<.01$), predominantly because of the prevention of IRAF. Another Vaughan-Williams class IA agent, procainamide, has no effect on the rate of successful cardioversion compared with placebo.[45]

In another study, 50 patients were randomized to propafenone (750 mg/d) or placebo for 2 days before cardioversion. Patients treated with propafenone had a significantly lower likelihood of IRAF and, thus, a higher overall likelihood of persistent sinus rhythm postcardioversion compared with patients receiving placebo (0% versus 17% IRAF, respectively, and 84% versus 65% sinus rhythm, respectively, at 48 hours).[46] A subsequent study showed that adding verapamil to propafenone was superior to propafenone alone in suppressing IRAF.[47]

Sotalol and amiodarone suppress IRAF effectively. Sotalol suppressed IRAF effectively in patients undergoing internal cardioversion.[48] Amiodarone was studied in 27 patients who had either IRAF (group A) or a failed cardioversion (group B).[39] All patients received oral amiodarone loading (600 mg/d for 4 weeks) followed by 200 mg/d for 4 weeks if sinus rhythm was ultimately achieved. Among patients in group A, 5 of 11 (46%) converted during loading compared with only 1 of 16 (6%) patients in group B. After electrical cardioversion, the number of patients in group A in sinus rhythm was 10 of 11 (91%), versus 7 of 16 (44%) in group B. At 1-month follow-up, all 10 of 11 (91%) patients in group A versus only 5 of 16 (33%) patients in group B remained in sinus rhythm. This study, although small, showed a significant outcome difference between patients who had IRAF postcardioversion versus those who underwent failed cardioversion. These findings suggest that restoration of persistent sinus rhythm should be pursued aggressively in patients who have IRAF.

Another study showed favorable outcomes in pharmacologically facilitated cardioversion in patients who had IRAF, this time using intravenous verapamil or ibutilide. These medications have been shown to attenuate the shortening of the atrial refractory period seen in patients post-AF; that is, they prolong the atrial refractory period.[49] Subsequently, both medications were studied in patients who had IRAF.[50] Verapamil (0.15 mg/kg at 2 mg/min) was assigned randomly to 11 patients versus ibutilide (1 mg) over 10 minutes in 9 patients. IRAF occurred in 73% of patients treated with verapamil and in only 22% of patients treated with ibutilide ($P<.05$). After crossover, ibutilide continued to have a higher rate of IRAF suppression than verapamil. These findings correlated with ibutilide's much greater effect on the atrial refractory period compared with verapamil's in the earlier study.[49]

Verapamil was used alone in one uncontrolled study of 19 patients who had IRAF after each of three cardioversions.[51] Each patient received 10 mg intravenously followed by a fourth cardioversion attempt. IRAF was suppressed in 9 of 19 (47%) patients, and sinus rhythm duration before IRAF was increased in patients who experienced IRAF.

For patients undergoing transthoracic cardioversion, same-day options for pharmacologic suppression of IRAF include intravenous verapamil and ibutilide, with higher success rates seen with ibutilide. Because ibutilide is contraindicated in patients who have depressed left ventricular systolic function, intravenous verapamil (in the absence of decompensated heart failure) or outpatient loading with amiodarone should be used.

Failed cardioversion Even in the era of biphasic defibrillation, up to 10% or more of patients may have true failed cardioversion; that is, no evidence of any sinus activity after cardioversion. Certainly the use of monophasic rather than biphasic waveforms is associated with higher failure rates.[21,30,31] Longer duration of episodes and increased transthoracic impedance also are associated with

higher cardioversion failure rates.[21,33] In contrast, younger age and smaller left atrial size are found to be independently associated with successful cardioversion.[5,52]

When conventional external cardioversion fails, several tactics may be effective. First, shocks should be repeated at highest energy. Because success of cardioversion is probabilistic, a failed attempt at maximum output does not imply that it never will work. Although most biphasic defibrillators deliver a maximum of 200 J, some biphasic defibrillators can deliver up to 360 J. The pads or paddles should be repositioned. If the electrodes are in the AL position, they should be moved to the AP position (right sternal body at the third intercostal space and angle of the left scapula [see **Fig. 4**]).[33] The goal is to direct the energy vector optimally through the atria. Manual pressure should be applied on the anterior pad at shock delivery. With the pads in the AP position, while ensuring electrical insulation, mechanical pressure should be applied to the anterior pad to decrease the distance (thus, the impedance) between the two pads. The shock should be delivered during the expiration. In theory, this may decrease transthoracic impedance. Pharmacologic facilitation of cardioversion should be considered (discussed later). The ''double-paddle'' technique should be attempted. In one study, patients who had AF and had failed 360-J monophasic cardioversion were loaded with amiodarone orally. If repeat 360-J monophasic cardioversion failed again, the patients underwent the double-paddle technique: two monophasic defibrillators were used with two sets of paddles for each patient; each defibrillator was set for a synchronous shock at the maximum output of 360 J; they then were discharged simultaneously, resulting in successful conversion of 13 of 15 patients.[53] Finally, internal cardioversion should be considered.

In addition to facilitating persistent sinus rhythm for patients who have IRAF, antiarrhythmic medications are effective in facilitating successful cardioversion for patients who have true failed cardioversion (ie, no evidence of any sinus activity).

Amiodarone and ibutilide show the strongest success in pharmacologic facilitation of cardioversion after true failed cardioversion. Although some data show decreased IRAF when using propafenone, verapamil, and quinidine, it is less clear whether they increase the likelihood of cardioversion in patients who have had true cardioversion failure.

Amiodarone, used pre- and postcardioversion, increases the rate of successful cardioversion in patients undergoing initial cardioversion[54] and in those for whom past cardioversion failed.[39,55] In patients for whom past cardioversion failed, success rates were 7 of 16 (44%) with 4 weeks of amiodarone (600 mg/d by mouth) and 32 of 49 (65%) with amiodarone (6.0-g load by mouth) given before cardioversion.

Ibutilide clearly is shown to facilitate successful cardioversion in patients for whom direct current cardioversion failed.[56] In one study, 100 patients who had long-duration AF (mean 117 $\pm$ 201 days) and a high prevalence of structural heart disease (89%) were randomized to undergo transthoracic electrical cardioversion with or without pretreatment with ibutilide (1 mg). Remarkably, conversion to sinus rhythm occurred in 50 of 50 (100%) of patients pretreated with ibutilide compared with 36 of 50 (72%) of those who did not have pretreatment. Additionally, all 14 patients in the untreated group were cardioverted successfully after ibutilide pretreatment. Sustained polymorphic ventricular tachycardia occurred in 2 of 64 patients treated with ibutilide; both patients had ejection fractions less than or equal to 20%.

Thus, amiodarone and ibutilide facilitate cardioversion effectively in patients who have true failed cardioversion. Conveniently, ibutilide can be administered over a short time frame for same-day treatment. Ibutilide, however, should not be used in patients who have low ejection fractions. In patients who have ejection fractions less than or equal to 30%, oral loading with amiodarone is the preferred option.

Complications The risks and complications of cardioversion fall largely into three categories: (1) risks associated with sedation, (2) thromboembolic events (<1% with appropriate anticoagulation),[15,17] and (3) postcardioversion arrhythmias. Overall, the risk for electrical cardioversion is low in patients who are selected properly.[1,57]

Pharmacologic Cardioversion

General considerations

Because of the relative simplicity and high efficacy, most cardioversions are performed electrically. Pharmacologic cardioversion is used primarily in two settings: (1) for short-duration AF in highly symptomatic patients who have little or no structural heart disease, and (2) as adjunct therapy to facilitate electrical cardioversion in patients who have undergone failed cardioversion or have IRAF. In rare instances, such as to avoid anesthesia, pharmacologic cardioversion also may be indicated.

The principles of pericardioversion anticoagulation apply whether cardioversion is performed electrically or pharmacologically. That is, if

patients' AF episodes have persisted for more than 48 hours or for unknown duration, those patients should undergo therapeutic anticoagulation for 3 weeks or TEE with heparin administration before initiation of any antiarrhythmic medication, even those with low efficacy. In particular, amiodarone frequently is used in patients who have AF. Because amiodarone has the potential to convert the AF to sinus rhythm, pericardioversion anticoagulation principles should be applied.

Short-duration atrial fibrillation

In patients who have little comorbid disease and short-duration AF, antiarrhythmic agents show no significant difference in long-term cardioversion outcomes compared with placebo. Class IC agents, however, show a faster time to cardioversion and therefore may be useful in terminating short-duration episodes of AF more rapidly for patients who are highly symptomatic.[58,59]

This finding underlies the ''pill-in-the-pocket'' approach to management of symptomatic, short-duration AF in patients who have little to no structural heart disease. One study examined 268 patients who had little structural heart disease and presented to an emergency department for symptomatic AF.[60] On discharge from the hospital, patients were instructed in out-of-hospital self-administration of flecainide or propafenone after the onset of symptoms. Patients weighing more than 70 kg received flecainide (300 mg) or propafenone (600 mg); those weighing less than 70 kg in weight received flecainide (200 mg) or propafenone (450 mg). This approach was successful in 94% of episodes (534/569), with time to resolution of symptoms at 113 $\pm$ 93 minutes. In 139 of 165 patients, the medication was effective for all arrhythmic episodes. Also, the number of monthly emergency room visits and hospitalizations decreased significantly after the initiation of this management strategy. Overall, 12 of 268 patients (7%) experienced adverse effects, including nausea, asthenia, and vertigo. One episode of atrial flutter with 1:1 AV conduction occurred. Given its overall safety and efficacy, the pill-in-the-pocket strategy can be useful in a select population of patients who have AF.

Longer-duration atrial fibrillation

In patients who have structural heart disease and longer-duration AF, pharmacologic cardioversion shows only modest success (20%–30%).[56,61] Therefore, electrical cardioversion is used more commonly. Antiarrhythmic medications provide useful adjunct therapy for patients experiencing IRAF postcardioversion or those who have true cardioversion failure.

ATRIAL FLUTTER

Generally, the principles discussed previously are valid for atrial flutter, except as specifically noted. In particular, anticoagulation for patients who have atrial flutter should be handled just as it would for patients who have AF.

SUMMARY

In summary, cardioversion is a useful option in managing patients who have AF. It is useful especially for patients who are symptomatic or newly diagnosed or for some patients who have postoperative AF. To minimize the presence of thrombus at cardioversion, patients who have AF of more than 48 hours' duration should undergo therapeutic anticoagulation for 3 weeks prior (full-dose low molecular weight heparin or warfarin; INR target, 2.5; range, 2.0–3.0) or TEE accompanied by heparin before cardioversion. To minimize the formation of thrombus postcardioversion in patients who experience AF for more than 48 hours, therapeutic anticoagulation should be continued for 4 weeks, keeping in mind that the greatest risk for systemic embolization occurs during the first few days postcardioversion. Electrical, pharmacologic, or a combined approach to cardioversion can be taken. In most cases, transthoracic electrical cardioversion is indicated, given its simplicity and high efficacy, especially in the era of biphasic-waveform defibrillators, even in patients who have multiple comorbid conditions and significant structural heart disease.

Pharmacologic cardioversion with class IC agents may be useful for early conversion to sinus rhythm in patients who have minimal structural heart disease and short-duration, symptomatic AF. Antiarrhythmic agents also are useful in the setting of two distinct postcardioversion outcomes: (1) IRAF, which is recurrence within minutes post cardioversion after even just one sinus beat, and (2) true failed cardioversion (no sinus beats seen). Patients who have IRAF and who experience persistent sinus rhythm may have good rates of long-term freedom from AF and should be treated aggressively with pharmacologically facilitated cardioversion. Ibutilide, amiodarone, and verapamil along with propafenone and quinidine are effective. For patients who have true failed cardioversion, ibutilide and amiodarone are effective. Given its short administration period and strong clinical efficacy, ibutilide is an excellent agent for facilitated cardioversion, except in patients who have ejection fractions less than or equal to 30%. Because of the potential for cardioversion, regardless of indication or level of efficacy, antiarrhythmic medications should be given only with

proper application of the principles of pericardioversion anticoagulation.

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