Is there a role for cardioversion in the management of atrial fibrillation?

Electrical cardioversion was originally used for the treatment of ventricular arrhythmias but has increasingly been used for atrial fibrillation in an attempt to restore sinus rhythm and correct the electrophysiological abnormalities associated with arrhythmias. Data have now accumulated demonstrating that cardioversion confers no survival benefit compared with a rate-control strategy and that even in patients who are successfully converted into sinus rhythm, oral anticoagulation needs to be maintained owing to the high rate of relapse. This is true for high-risk patients, such as those who also suffer from heart failure. Cardioversion should be reserved for patients with acute onset of atrial fibrillation and those who remain symptomatic despite medical therapy.

KEYWORDS: atrial fibrillation ■ cardioversion ■ oral anticoagulation

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Electrical cardioversion was first described by Zoll and colleagues in the context of ventricular fibrillation [1]. The procedure has changed very little over the years since the original procedure was described as the application of paddles in an antero-apical position with conductive paste between the skin and paddle, applied with firm pressure [2]. A 2.5 ms pulse of direct current energy was given timed to the R-wave with energies between 0 and 400 J. The same group published a study in 50 patients, most of whom had associated mitral valve disease and who had 65 episodes of atrial fibrillation (AF) [3]. An 89% success rate was claimed after up to five shocks. Only one complication was documented within this study, relating to thromboembolism in a nonanticoagulated patient.

From these and subsequent studies, it became clear that cardioversion was unsuccessful in at least 30% of patients [4]. Predictors of failure included the age of the patient, the duration of the arrhythmia, comorbidity and the etiology of the arrhythmia. The role of electrical cardioversion has waxed and waned since its first clinical utilization with opinion generally polarized around those who support its use wholeheartedly and those who resist any use of cardioversion. This article discusses where cardioversion fits in with treatment options for AF in the 21st century. Thertefore, in order to understand the impact of cardioversion, we need to understand the pathophysiology of AF.

Pathophysiology of AF

It has become clear that AF requires triggers for its initiation and the correct environment (sometimes referred to as 'a substrate') for its maintenance. Haissaguerre and colleagues were the first to highlight the importance of rapidly firing ectopic foci in and around pulmonary veins [5]. It is now apparent that these foci (and ectopic activity arising largely from other venous–atrial interfaces) are critical in AF induction. This is the basis for the pulmonary vein isolation procedure. Current theories suggest that areas of both fixed and functional blocks in the atria interact with these foci, setting up multiple wavelets of anisotropic re-entry. In addition, parts of the myocardium may not be able to conduct one-to-one with these rapidly firing foci, leading to so-called fibrillatory conduction. These foci may also perpetuate the arrhythmia. With time, owing to the rapid and repeated activation of atrial myocytes both structural and electrophysiological remodeling occurs. Ion-channel changes alter myocyte electrophysiology – conduction velocity decreases and the action potential shortens, as does the atrial refractory period. There is also a loss of the normal variation in the refractory period with changes in heart rate. These, and other, electrophysiological changes are progressive and lead to the perpetuation of AF [6]. If sinus rhythm can be induced, by whatever means, these short-term electrophysiological changes are potentially reversible, at least in experimental preparations (i.e., animals). Therefore, at this stage, cardioversion has the potential to halt or reverse this electrical 'remodeling'. However, as AF persists, irreversible structural changes occur, including fibrosis and cell death (both necrotic and apoptotic) contributing to the AF substrate, thus

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increasing the risk of recurrence. This explains why cardioversion is less successful the longer the fibrillation has been present.

Physics of cardioversion/defibrillation

Much of what is known about the physics of defibrillation is derived from studies of ventricular fibrillation. As previously discussed, AF is an arrhythmia characterized by multiple, random re-entrant wavelets circulating in both atria. Cardioversion aims to induce a coordinated change in the action potential in a significant proportion of the atrial myocardium (a critical mass), such that the wavelets terminate and normal electrical activity can resume. If too little energy is used, sufficient wavelets may persist to reinitiate the arrhythmia. The shock produces a current gradient across the myocardium that affects the myocytes according to their state of activation; depolarization or hyperpolarization may occur depending on their location with respect to each individual electrode. If the shock occurs during the action potential little effect may be seen, although if it is of large enough magnitude and occurs early enough, the action potential may be prolonged. Later in the action potential, further depolarization may be induced. However, the precise mechanisms of defibrillation at a microscopic level remains poorly understood.

From an electrophysiology perspective, the major determinant of shock success is the current density. This depends upon the energy used, the current path and the transthoracic impedance (TTI) between the shock electrodes. Too little energy will not terminate the arrhythmia. When utilizing external shocks, perhaps as little as 4% of the energy given affects the myocardium. There are a number of determinants of TTI, including paddle characteristics (size, constitution and positioning), the couplant used to conduct the charge from the electrode to the skin, the number of shocks, the timing between shocks, and the electrical conductivity of the tissues between the electrodes and the heart [7]. In simple terms, a low charge delivered poorly in an obese individual is less likely to be successful than a large charge delivered effectively in a slim person.

Cardioversion today

Clinical Medicine is a rapidly evolving field where treatments are introduced and subsequently discarded at a relatively high rate. Recent examples of previously standard treatments and theories that have been revised in the light of clinical experience and randomized controlled trials include the demise of vagotomy and pyloroplasty as a standard treatment for peptic ulcers and the absolute contraindication of β-blocker in the treatment of heart failure. Thus, we now treat peptic ulcers almost universally with antibiotics and β-blockers are standard therapy in the treatment of heart failure. I would like to suggest that the next standard treatment to be dispensed with is the routine use of electrical cardioversion in the treatment of AF, despite its inclusion as a therapeutic option in the current National Institute for Clinical Excellence (NICE) AF guidelines [8].

Direct electrical cardioversion has been a mainstay of therapy for the treatment of AF for many years. The theory underpinning its utilization has some face validity, in that by restoring sinus rhythm, any problems associated with AF will be ameliorated. However, this does not take into account the underlying cause of the arrhythmia, with the majority of AF in developed countries caused by ischemic heart disease. It is only relatively recently, however, that evidence for the ineffectiveness of cardioversion has started to emerge. Paradoxically, this evidence has derived from trials designed to prove the effectiveness of the procedure.

The utility of cardioversion was originally explored in the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study [9], which recruited over 4000 patients aged 65 years and over with AF, and one additional risk factor for stroke. These would be described as having at least a moderate risk for stroke according to NICE guidance. Patients were randomly selected for rhythm control, using electrical cardioversion and medication as necessary, or to rate control, using drugs such as β-blockers or digoxin. To the surprise of the investigators, the primary outcome – mortality – was worse (though not statistically) in the rhythm-control group, as were secondary outcomes, such as hospitalization and serious arrhythmias. Certainly cardioversion conferred no benefit to patients. It is important to note that with the AFFIRM trial oral anticoagulation could be stopped at the clinician's discretion following cardioversion.

These results were surprising and the AFFIRM investigators conducted a *post-hoc* 'on-treatment' analysis, which did show some survival advantage if sinus rhythm was maintained [10]. The caveat to this was that the use of antiarrythmic drugs was associated with increased mortality and, in fact, the main predictor of survival was the continued use of warfarin. This left the AFFIRM investigators to

conclude that any advantage from maintaining sinus rhythm through the use of antiarrythmic agents was offset by their toxicity.

Despite the fact that these findings have been repeated in further studies [11,12] and the problems associated with ensuring adequate oral anticoagulation prior to undertaking the intervention, cardioversion has remained a common intervention in patients with AF, particularly if there is associated comorbidity, such as heart failure. This insistence on continued use of cardioversion in the absence of evidence for benefit has been entirely driven by secondary-care cardiologists, with little to no involvement of either primary care or indeed patients in deciding whether or not to attempt cardioversion.

The issue of advantage being conferred in high-risk patients also seems dubious, at best, based on the available evidence. In trying to establish the efficacy of cardioversion for patients with AF and heart failure (defined as left ventricular ejection fraction of 35% or less, or symptoms of congestive heart failure), Roy and colleagues recruited 1376 patients, who were randomized to rhythm control, comprising of cardioversion within 6 weeks of randomization with additional cardioversions as necessary, or rate control with adjusted doses of β-blockers with digoxin [13]. There was no significant difference in primary outcome of death from cardiovascular causes, nor any significant differences in secondary outcomes, including death from any cause (stroke) worsening heart failure. The authors concluded that "in patients with AF and congestive heart failure, a routine strategy of rhythm control does not reduce the rate of death from cardiovascular causes as compared with a rate-control strategy."

There appears to be, therefore, no evidence base to support the use of cardioversion in either high- or low-risk patients with AF. My interpretation of this is that electrical cardioversion has no place in the routine modern management of AF. I would urge nonspecialists and particularly primary cares to question the routine use of this potentially dangerous procedure.

Future perspective

If cardioversion has no place in the routine treatment of AF, nor in the treatment of high-risk patients, for example with heart failure, where does this leave us? To my mind, cardioversion should no longer be offered routinely to patients with AF. The only clinical scenarios where it may be a useful intervention is for patients presenting acutely, within 24 h of onset, or for patients who are very symptomatic despite medical therapy. Even in these instances, oral anticoagulation needs to be considered long-term owing to the high rate of recurrence.

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Executive summary

- Atrial fibrillation occurs due to a combination of triggers within an environment that is conducive to the maintenance of an abnormal rhtythm.
- The use of cardioversion in atrial fibrillation is based on the physics of defibrillation for ventricular fibrillation.
- Many studies have been undertaken assessing the relative merits of cardioversion compared with a rate-control strategy for patients with atrial fibrillation.
- Based on current evidence, cardioversion should be reserved for patients with acute onset of AF and those who remain symptomatic despite medical therapy.
- Even patients who are successfully cartdioverted need to remain on oral anticoagulation in the long-term.

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