The pharmacological considerations of atrial fibrillation ablation

In this second article on the management of patients with atrial fibrillation Gurpreet Virdi and Sotiris Antoniou describe the interventional procedure of catheter ablation and explain its role as a form of treatment for this condition.

Introduction

The aim of this article is to discuss the management of patients with atrial fibrillation undergoing an interventional procedure of catheter ablation as a form of treatment. New interventional procedures are increasingly being developed to improve treatment options for patients with atrial fibrillation (AF). These can be performed as sole therapy in patients whose symptoms have not responded to other interventions or in those who are intolerant to medication. Alternatively, they can be used in conjunction with medication to help manage a patient.[1] An example of this practice seen routinely is in the management of patients with ischaemic heart disease who can be treated surgically and/or with drug therapy. As the number of patients undergoing interventional procedures increases, it has become more important for pharmacists to understand these procedures and how pharmacotherapy impacts on the management of patients in these situations.

The NICE guidelines for AF (June 2006)[1] and percutaneous radiofrequency ablation for AF (April 2006)[2] intend to meet the Department of Health's public service agreement (PSA) targets of reducing mortality rates from heart disease and stroke by at least 40% by 2010.[1,3] Along with the medical treatment of patients with AF there has been an increased investment in cardiac services and catheterisation laboratories in line with the above initiatives. As a result an increasing number of patients are being referred for interventional procedures such as catheter ablation where the aim is to treat malfunctioning parts of the heart. This can provide a cure for patients who suffer from palpitations who may then no longer require medication.[4]

Catheter ablation would not only help to improve care for this large patient group but can make a significant contribution to the delivery of the target for reducing unnecessary and costly emergency admissions to hospital for acute episodes of these chronic diseases. This article discusses the pharmacological considerations that should be made for catheter ablation.

The following learning outcomes are anticipated — you should be able to:

- ☐ list the types of patients referred for percutaneous radiofrequency ablation (catheter ablation) for AF
- ☐ describe how to manage the pharmacological therapy before and after catheter ablation.

The case

Robert Walker is an 80-year-old male (80kg) who was admitted to hospital for an elective procedure of catheter ablation for his persistent AF. Four years ago he experienced his first sudden onset of palpitations, which were diagnosed as AF. An electrocardiogram (ECG) was performed that showed he had a generally fast, irregular heart rate (up to 200 beats per minute). He underwent a direct-current cardioversion (DCCV) which despite keeping him in sinus (normal) rhythm for six months, reverted back to AF. While his heart was in sinus rhythm his AF was controlled with atenolol and he felt well. His symptoms soon deteriorated where he felt increasingly short of breath, was often fatigued and still experienced palpitations. He was referred by his GP to the arrhythmia clinic at the hospital after trying various antiarrhythmic medications, where his condition and the benefits and risks of catheter ablation were discussed in detail. Mr. Walker agreed to have an ablation procedure.

A computerised tomography scan (a series of X-rays taken at slightly different angles to produce very detailed pictures of the inside of the heart) was then arranged before his admission. Mr Walker had pre-existing hypertension but did not have any other cardiac problems and his recent echocardiogram (ultrasound of the heart) was normal. His current medications were:

- ☐ Flecainide 100mg BD
- ☐ Atenolol 50mg once per day
- ☐ Warfarin (INR range of between 2 and 3) in the evening.

Mr Walker attended the hospital pre-admission ablation clinic two weeks before his admission where he was instructed to stop taking his warfarin five days before his procedure. He was also taught how to self-administer the enoxaparin replacement. It was explained to him that all other medications were to continue until the morning of the procedure.

On the morning of Mr Walker's admission, a transoesophageal echocardiogram

(TOE) was performed to ensure there was no blood clot inside the heart. The TOE was negative so he progressed to have his procedure with no complications.

Mr Walker resumed taking his warfarin in the evening of the procedure and continued to administer his daily enoxaparin until his INR was therapeutic again. His flecainide was stopped after the ablation and his atenolol was continued. He was discharged the day after his procedure taking the following medicines:

- ☐ Enoxaparin 120mg S/C OM until two consecutive INRs are in range (2–3)
- ☐ Warfarin (dependent on INR) in the evening.
- ☐ Atenolol 50mg once per day.

What causes atrial fibrillation?

Atrial fibrillation is the result of both a substrate and a trigger. The substrate is most often a pathophysiological process that affects the atria, such as hypertensive heart disease (associated with increased stress on the atrial wall) and is capable of sustaining the AF. Local ectopic beats (extra beats from areas other than the sino-atrial node) have been thought to 'trigger' AF[5] (see Figure 1). These are often located in the muscular sleeves that extend from the left and right atrium into the proximal parts of the pulmonary veins and are often responsible for episodes of AF in patients with otherwise normal hearts. Electrophysiology studies (EPS) can be performed to determine the cause of the arrhythmia if it is unknown. An external pacing catheter is used in EPS to stimulate the onset of the arrhythmia and record electrical activity from specific areas in the heart.[6] Less frequently these ectopic beats may arise from other parts of the left or right atria.

The mechanisms involved in the production of ectopic activity as well as the exact mechanism of initiation of AF remain to be elucidated.[5,7–10]

Once the AF is initiated, the arrhythmia is maintained by a mechanism of re-entry (because of the substrate). This occurs when a continuous loop of atrial depolarization is formed around an anatomical or functional conduction barrier (such as a vein orifice or zone of diseased atrial tissue; see Figure 1). In particular, this occurs when the conduction propagates in one direction around the barrier. During AF many such re-entrant circuits are established in the atria and they sustain themselves more readily in diseased or enlarged atria. The number of these circuits (i.e single or multiple) depends upon the atrial conduction velocity, refractory period (the period following excitation when no response is possible regardless of the intensity of the stimulus) and the atrial mass.[7] Persistence of AF is therefore favoured by a slowed conduction, shortened refractory periods (i.e. the cells recovery quicker and are available for re-activation) and increased atrial mass (i.e. more cells are available for activation; see Figure 1).[5,7–10]

What is percutaneous radiofrequency ablation and is it appropriate for Mr Walker?

This is a treatment option for symptomatic patients with AF that does not respond to anti-arrhythmic drug therapy or where medical therapy is a contra-indication because of co-morbidity or intolerance.[2,11] It involves threading several catheters into the femoral vein in the groin and up towards the heart. A contrast dye is injected, which allows x-ray images to be taken showing the position of the catheters in the heart.[6] Catheter positioning is confirmed by a combination of techniques, such as the CT scan Mr Walker had previously, three-dimensional electroanatomical mapping or intracardiac echocardiography.[11]

The catheters are passed into the right atrium of the heart where the pulmonary veins are targeted for electrical isolation

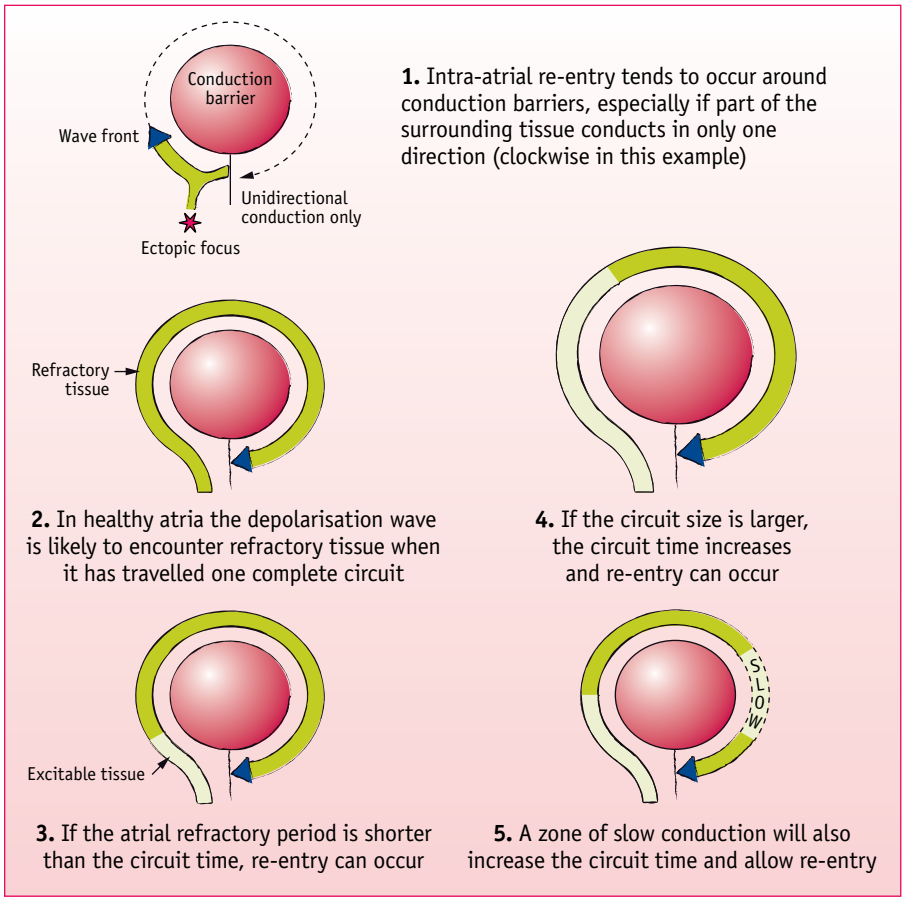

Figure 1. Electrical re-entry, the mechanism responsible for starting and maintaining atrial fibrillation, redrawn from Grubb and Furniss (2001).[10]

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because this is the most common source of AF.[12] The tip of the catheter sends out radiofrequency energy that produces heat (temperatures of 50ºC or higher). The heat damages the targeted area of heart muscle resulting in localized scars that are no longer able to conduct and this disrupts the cause of the arrhythmia. The catheter is then passed into the left atrium via a transseptal puncture (in the absence of an atrial septal defect or patent foramen ovale).[11] The transseptal procedure involves making a hole through the septum separating the left and right atria and therefore allows for electrical isolation of the left pulmonary veins.[2,6] This puncture heals itself after the procedure.

A treatment analysis of the AF follow-up investigation of rhythm management (AFFIRM) trial aimed to compare the effects of rhythm control and rate control on mortality in patients with AF and high risk of stroke or death. It revealed there was no significant difference in all-cause mortality, secondary endpoint (death, disabling stroke, major bleeding, cardiac arrest) or ischaemic stroke. There was, however, an increase in the number of hospitalizations with the use of antiarrhythmic drugs compared with the use of rate-control drugs. Although the trial did not confer any advantage of restoring sinus rhythm, this effect may be overshadowed by the adverse effects of antiarrhythmic drugs.[7,11] Mr Walker was not in sinus rhythm despite being treated with antiarrhythmic drugs so alternative methods were sought to achieve sinus rhythm.

There have been no large multicentre randomised clinical trials that determined whether sinus rhythm achieved with ablation techniques lowers morbidity and mortality compared with rate control alone or treatment with antiarrhythmic therapy.[7] The outcome data of the clinical trials presently published are varied because the trial design has not been standardised for AF ablation trials; the most important selection criterium being the patient population — and this has a large impact on the results. NICE have recognised this and have only recommended the use of percutaneous radiofrequency ablation in patients for whom drug therapy has failed. NICE also mention the possibility of patients undergoing a second or third procedure to achieve long-term maintenance of sinus rhythm.[2] Initial reports have described success rates between 22% and 85% with better results observed in patients with paroxysmal rather than permanent AF.[11]

Mr Walker's AF is sufficiently troublesome to require some form of treatment. The inefficacy of previously tried antiarrhythmic medication and being asymptomatic in sinus rhythm makes him a suitable candidate for ablation.[7]

Was anticoagulant therapy appropriate before and after Mr Walker's procedure?

Maintaining Mr Walker on a safe level of anticoagulant therapy before, during and after ablation was essential because there is a risk of thromboembolic events in AF patients.

Before ablation

It is important to ensure the correct anticoagulant is prescribed for patients with AF. The choice of drug is dependent upon the patient's risk factors rather than the presenting type of AF. (See previous article for risk assessment for anticoagulation).[13]

In the pre-admission clinic Mr Walker was instructed to stop taking his warfarin five days before the ablation procedure because it might be difficult to manage any potential bleeding complications that could arise if warfarin had been continued. The recommendation is to start taking 0.5–1mg/kg of enoxaparin twice daily from four days before the procedure and continue this until the evening before the procedure.[7] An increased incidence of bleeding complications has been documented with the 1mg/kg enoxaparin twice daily dosing regimen.[7] To achieve adequate anticoagulation, reduce bleeding risks and encourage patient compliance, 1.5mg/kg once daily of enoxaparin (licensed dose for treatment of thromboembolisms) is prescribed according to local agreement, although there is currently no evidence to support this. This dosing regimen, however, allows for once daily nursing support if required.

After ablation

The cardioversion of chronic AF to normal sinus rhythm is recognised to be associated with left atrial mechanical dysfunction. This process, known as atrial stunning, has been implicated in the development of thromboembolic stroke after cardioversion.[14] It is therefore very important to achieve adequate anticoagulation (maintaining INR between 2 and 3) after Mr Walker's ablation procedure. Anticoagulation should be resumed within four to six hours after ablation and enoxaparin should be continued until therapeutic INR is achieved.

After percutaneous radiofrequency ablation what medications does Mr Walker need to continue until his three-month follow-up appointment?

Warfarin should be continued for at least two months after Mr Walker's ablation procedure. It is suggested for patients with a $CHADS_2$ score of 2 or more to continue taking long-term warfarin treatment with a targeted INR of 2–3. It is well recognised that symptomatic or asymptomatic AF may recur during long-term follow-up after an AF procedure and so the stroke risk for these patients remains. However, clinical trials are needed to determine when warfarin should be discontinued after ablation in relation to their stroke risk.[7,15] If warfarin is to be discontinued after the two-month period, aspirin 75–300mg daily should be started unless contraindicated.[7,15]

Because Mr Walker was in sinus rhythm after the ablation he no longer required

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flecainide, which also has proarrhythmic potential. He will continue to take atenolol for three months until his review in clinic. This drug will help to maintain sinus rhythm and will also be beneficial in treating his underlying hypertension.

For ablation patients taking anti-arrhythmic medications before the procedure, some of these medications may be continued after the ablation as a proposed method of reducing relapses within the first three months post-ablation. This is based on findings that 60% of patients may complain of more frequent episodes of AF during this time but will not have any further episodes during long-term follow-up.[7] However, the efficacy of this approach is unknown.

What counselling points does Mr Walker need regarding his anticoagulation?

Mr Walker needs to resume taking warfarin on the evening of the day after his procedure. He is to continue taking his usual dose of warfarin daily until his anticoagulation appointment, which is scheduled in three days at his usual anticoagulation clinic. He will then be advised what dose to take thereafter. He is to continue daily self-injections of 120mg (1.5mg/kg) enoxaparin until two consecutive measurements of his INR are within the recommended range (2–3). (Further counselling points are discussed in the first of our articles on atrial fibrillation management[13]).

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above: *X-ray image of the chest of a person fitted with a pacemaker*

What other treatment options are available?

The ablate and pace technique is another option for patients who do not respond to rate control medication. The atrioventricular node is ablated to produce complete heart block. A pacemaker is then inserted to maintain adequate heart rate. Patients will require long-term anticoagulation because the atrial contractions are not restored.[16]

The surgical MAZE procedure is carried out in patients undergoing cardiac surgery. It requires open heart surgery and involves creating multiple strategically-placed incisions across both the left and right atrium. These incisions are placed in such a way that electrical current from the sinus node can only follow one pathway. This is a very effective procedure where a follow-up at three years has found 90% of patients to be in sinus rhythm at three years.[16] However, because of the complexity, technical difficulty and length of procedure time, the MAZE procedure is currently not the first choice intervention for AF. ✣

Declarations of interest

The author has no interests to declare.

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