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Atrial fibrillation: relieving symptoms and managing risk

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Introduction

One in four of us who live beyond the age of 40 will experience atrial fibrillation (AF) at some point during our lives. Its prevalence doubles with each advancing decade, from 0.2% at the age of 45–55 years to almost 8% at the age of 75 or over.[1] The condition ranges from what appears to be an isolated electrical abnormality in an otherwise normal heart, to an electrical complication of widespread damage to the myocardium in a patient with multiple comorbidities. The approach to therapy needs to be tailored to the individual characteristics of the patient. In considering the benefits to be gained from therapy, two key areas need to be considered: relief of symptoms and managing prognostic risk.

Classification

The EuroHeart Study showed that the presentation of AF occurs in approximate thirds: 36% as paroxysmal, with spontaneous reversion within 1 week of onset; 28% as persistent, requiring cardioversion to revert to sinus rhythm or with duration of episodes over 1 week; and 36% permanent, where the condition persists and no attempt is deemed appropriate to return the patient to sinus rhythm.[2] Symptomatic problems are more typical in patients with repeated episodes of paroxysmal AF (PAF),[3] but can also significantly impair quality of life in patients with persistent AF.[4]

Risk assessment and management of thromboembolic risk

In older patients with minor symptoms and good tolerance of drugs to maintain rate control, the main concern is to ensure adequate prognostic therapy. Prevention of thromboembolism and stroke is paramount and risk-scoring systems, such as $CHADS_2$ and CHA_2DS_2VASC, have gained wide acceptance in general practice (GP) over the past few years.[5] Their assessment is now built in to the financial incentive system for GP surgeries. This is gradually improving the delivery of effective anticoagulation to the population. Arguably, bleeding risk scores, such as HASBLED, have been less useful. Given that most of the factors increasing bleeding risk are the same as those increasing stroke risk, these often seem to provide conflicting advice. Our approach is to ask the patient for evidence of significant bleeds in their history or any known haematological condition predisposing them to severe bleeds and, where anticoagulation is indicated ($CHADS_2$ ≥1 or CHA_2DS_2 VASC ≥2), to adapt therapy in light of this information.

Such information can also influence the decision about whether to treat with warfarin or one of the novel oral anticoagulant agents (NOAC), of which three are currently approved by the National Institute for Health and Care Excellence (NICE): dabigatran, rivaroxaban and apixaban. Until the 'antidotes' that are under development for these agents have been released, it will remain harder to be sure that reversal has been adequately achieved when a patient presents with a severe bleed requiring therapy. Management guidelines for such situations are available and need to be understood by emergency department and on-call haematological and/or blood-bank services in all hospitals.[6] For patients with elevated bleeding risk, warfarin might still be the agent of choice. It might also be preferable in patients undergoing invasive therapies, such as ablation, because of the availability of immediate and measurable reversibility with agents such as Beriplex® and Octaplex®. However, the safety in appropriately selected patients of a strategy of stopping NOAC administration for the half-life immediately before ablation appears to carry little risk in reported series.[7] Although, for many patients, the lack of need for frequent blood tests chasing variable international normalised ratios (INRs) will be attractive, including those in whom maintenance in the therapeutic range with warfarin has been difficult.

It is necessary to bear in mind the different pharmacokinetics of these drugs, avoiding administration of full dose in patients with impaired renal and/or liver function depending on the primary route of excretion (renal in dabigatran, whereas liver in rivaroxaban and apixaban). Manufacturer's guides also need to be carefully followed for prescription of the correct doses depending on age, weight, renal function and co-prescribed interacting drugs. For low-weight patients or those with mild renal impairment, we prefer the lower dose of dabigatran (110 mg twice daily). The guidelines mandate the 150 mg twice-daily dose in those patients under 80 years of age, but the lower bleeding risk compared with warfarin with equivalent efficacy, seen in the RE-LY trial,[8] makes the lower dose a pragmatic choice where there is a smaller volume of distribution and slower excretion. Similar specifically attractive features for particular patient groups apply to

Key points

In considering the benefits to be gained from atrial fibrillation (AF) therapy, two key areas need to be considered: relief of symptoms and managing prognostic risk.

Both require individually tailored therapy rather than a one-size-fits-all approach.

Where beta-blocker therapy gives inadequate symptomatic relief, decide whether to start an anti-arrhythmic drug in patients with paroxysmal atrial fibrillation (PAF) or direct current cardioversion (DCCV), with or without supporting anti-arrhythmic therapy, in patients with persistent AF.

The availability of novel oral anticoagulant agents and increasing knowledge of the value of AF ablation are two aspects demanding the attention of a wide spectrum of healthcare professionals. The response to this initial rhythm-control therapy will determine whether to consider early referral for ablation.

rivaroxaban and apixaban, but space does not permit further discussion here.

Management of symptoms

In patients who are symptomatic, NICE and European guidance reasonably advise beta-blockade in the first instance (with rate-slowing calcium antagonists an alternative for those with a history of bronchospasm; adjustment of the NOAC dose might be required because of potentiation by verapamil and diltiazem). The lack of adverse prognostic data associated with beta-blockade means that, if symptoms become tolerable owing to blunting of the peak ventricular rate in AF, this is the safest strategy. All true anti-arrhythmic drugs carry potential adverse prognostic impacts in some patient groups and invasive therapies carry small but always-present risks of complications.

Where beta-blocker therapy gives inadequate symptomatic relief, the next step is to decide whether to start an anti-arrhythmic in patients with PAF and whether to move to direct current cardioversion (DCCV), with or without supporting anti-arrhythmic therapy, in patients with persistent AF. At this stage, it is helpful to decide whether the strategic plan is to consider the patient for AF ablation should this second step fail. Several features are helpful in guiding these choices. Dilatation of the atria, low left ventricular ejection fraction, myocardial hypertrophy, high body mass index or a history of symptomatic heart failure are all adverse features for the maintenance of sinus rhythm.[9] Therefore, an echocardiogram will be valuable.

New risk factors predicting the likelihood of recurrence of AF after ablation are now being reported[10,11] and could help to refine this process further in forthcoming years. In patients with multiple adverse features, there is likely to be little point in subjecting them to intensive medical intervention with adverse effects and a high risk of failure, but equally, patients with significantly symptomatic PAF or persistent AF will benefit from prompt referral for ablation rather than trials of a succession of drugs and repeated cardioversions while the AF substrate progresses and becomes more difficult to eradicate by ablative therapy.[12] A short history (<1 year of continuous AF), lack of marked left atrium dilatation (corrected for patient size), and previously good fitness mark a patient out as someone likely to gain significant benefit from early ablation.

The role of DC cardioversion

In patients with persistent AF who are symptomatic, a single attempt at DCCV will usually be worthwhile. Although reversion to AF occurs in approximately 75% of patients within 1 year,[13] the choice of the next step in management will be helped by instructing the patient to take particular notice of how much symptomatic improvement they feel in the initial weeks after cardioversion to sinus rhythm compared with how they felt in the week or two preceding the procedure. This of course helps to identify how much of their symptomatology is attributable to the arrhythmia and how much to other problems. There are steeply diminishing returns from repeated cardioversions and, in those suitable patients, ablation might be a better way forward than committing the patient to drugs with high risks of significant adverse effects. One in five patients has to be withdrawn from amiodarone because of toxicity, and sotalol has a 2% overall rate of *torsade de pointes*. In those patients where the initial cardioversion conferred little symptomatic benefit, a detailed discussion with the patient over the merits of accepting AF with rate control as the long-term strategy is indicated.

AF ablation therapies

Can we consider ablation to be curative? Conversely, are we doing patients a disservice advising them to accept long-term rate control? We still have few good randomised data on the long-term efficacy of AF ablation in maintaining sinus rhythm. The CABANA trial[14] might provide some data when it reports, but as is often the case in a fast-moving field, the procedural data run the risk of being obsolete and historical by the time trial follow-up duration becomes meaningful. Series indicate a late recurrence rate (after 1 year of freedom from AF) following ablation of approximately 7% per annum;[15] therefore, we should probably avoid claiming current techniques amount to a 'cure'. However, efficacy from procedures continues to increase, with radically new approaches still being introduced.[16,17] In general, approximately 75% of patients will be free from symptomatic recurrences of AF after ablation with a redo procedure required in approximately 15% of patients with PAF and 40% of patients with persistent AF to achieve this. In many centres, including our own, approximately 80% of both patients with PAF or persistent AF are either AF-free or getting sufficiently infrequent AF to feel that their therapy has been a success.[18]

Some centres are claiming that data already collected show such good prognostic outcomes for patients who have undergone ablation that there is probably a true prognostic gain from ablation in patients who achieve long-term sinus rhythm.[19] They argue that this might not merely represent self-selection of a favourable group. Although fast ventricular rates in AF are clearly associated with the development of cardiac tachymyopathy, more subtle long-term negative effects on ventricular function might have a part in the observed prognostic impact of the condition. If this is true, by leaving relatively asymptomatic 50- and 60-year-olds in persistent AF, we might be unnecessarily consigning them to a higher likelihood of going on to develop gradually progressive heart failure and to accept the 1.5- to 2-fold excess mortality year on year that is shown to be the effect of permanent AF.[20] Although this remains a serious concern, such a prognostic recommendation for AF ablation remains to be proven. In terms of provision of services and health economics, it would be a huge undertaking to try to offer AF ablation to all those affected on prognostic grounds.

Prevention

So-called 'upstream therapy' for the prevention of AF has been disappointing. Trials of the role of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, statins, aldosterone agonists and polyunsaturated fatty acids have reported mixed and inconclusive results.[5] Designing preventative strategies is difficult when we understand so little of the fundamental

mechanisms that underlie the development of AF. There is a widespread belief that high caffeine consumption provokes attacks, but trials have failed to confirm this. However, high alcohol consumption (over 35 units per week) does increase the incidence and, paradoxically, it seems that those trying hardest to maintain cardiovascular fitness by prolonged duration training, such as for marathon running, also increase their likelihood of developing AF.

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