

# Perspectives on the modern management of non-valvular atrial fibrillation

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## INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia affecting approximately 1-2% of the population in the developed or western world. There is a dearth of data on the prevalence of AF in Africa, small studies have indicated a figure of 0.7%, but this is likely to be an underestimate.<sup>(1)</sup> Moreover, it is likely that this figure will rise with an ageing population, and therefore AF will become an important public health issue.

The RELY-AF registry provides contemporary data on AF risk factors and anticoagulation in Africa. The key findings being that, compared to Europe and North America, patients were younger and had a much higher prevalence of rheumatic heart disease. Nevertheless, hypertension appeared to be a stroke risk factor associated with AF. Furthermore, anticoagulation rates were lower in comparison compared (40-50%) despite a higher prevalence of rheumatic heart disease. Interestingly INR control (i.e. 2-3) was better compared to South America and South East Asia (41%), but countries in the developed world had modestly better rates averaging 60%. Whilst this data is interesting, it is important to note that just over 1 000 patients were studied, therefore larger population studies are needed to clarify these findings.<sup>(2)</sup>

The definition of non-valvular AF is important as patients with valvular AF have a higher risk (with specific reference to rheumatic mitral stenosis and prosthetic mechanical valves)<sup>(3)</sup> of thrombus formation, and that NOACs have not been tested

## ABSTRACT

**Atrial fibrillation is the most common clinical arrhythmia.**

**The mainstay in the prevention of atrial fibrillation related stroke is oral anticoagulation. The 2 most important aspects in the management of patients with atrial fibrillation, is therefore risk stratification for stroke and risk assessment for bleeding. Assessment of risk factors is in fact a dynamic process. In appropriate patients, novel anticoagulants are safe and better tolerated, and may be considered as an alternative to warfarin. In patients who are truly intolerant of, or where an absolute contra-indication to anticoagulation exists, occlusion of the left atrial appendage may be considered. Patients are to be carefully counselled with regards this therapy as currently, questions surrounding its safety and long-term efficiency remain unanswered. This is an area of on-going research and further evidence is awaited.**

**Catheter ablation of atrial fibrillation is a highly effective therapy to achieve freedom of recurrent arrhythmia and relief from symptomatic atrial fibrillation. Recent systematic reviews demonstrate a low incidence of periprocedural complications with regards catheter ablation of atrial fibrillation, with acute complication rates having decreased significantly in recent years. This may be attributed to increasing experience and improved catheter technology. SAHeart 2015;12:66-73**

in valvular AF and are therefore not suitable for use in this context. The definition of non-valvular AF has been contentious; however in an effort to standardise definitions, De Caterina, et al. have suggested the term 'mechanical and rheumatic mitral valvular AF (MARM-AF) to represent valvular AF. Patients with AF and bio-prosthetic valves in the aortic position (and those with mitral valve repair) or mitral regurgitation or hypertrophic cardiomyopathy, do not appear to have an increased additional risk of thromboembolism.<sup>(3)</sup> This definition will be adopted for this review.

## DIAGNOSING ATRIAL FIBRILLATION

An ECG is required to confidently diagnose AF. This can be a straightforward process, if the patient is in AF at the time; however, as AF can be paroxysmal, documenting the arrhythmia on ECG can be challenging. Ambulatory ECG monitoring in the form of Holter recording can be useful, but sometimes prolonged monitoring may be required. Novel technologies, such as implantable loop recorders or event recorders, may be

necessary for rhythm recording. A particular challenge is the asymptomatic patient with AF. Opportunistic screening, e.g. pulse checks or ECGs done as part of health checks or annual reviews in patients with conditions like hypertension may be necessary. Although AF can be asymptomatic, the stroke risk it confers is no different to patients who have symptoms.

Implantable devices (including loop recorders) have increased the detection of AF. Studies suggest that the stroke risk is related to the burden of AF<sup>(4)</sup> and that, in patients with paroxysmal AF, the period when patients go into AF may pose the highest stroke risk. Controversies exist as to the minimum burden of AF that is required to institute anticoagulation, as even a few minutes can be sufficient in certain patients.<sup>(5)</sup> Indeed in patients who have suffered ischaemic stroke (>40 years old), AF was detected in 12% of patients who were implanted with a loop recorder by one year, compared to 2% without.<sup>(6)</sup> This does raise issues as to how hard we look for AF in patients who are potentially vulnerable, or whether patients with additional risk factors such as smoking, hypertension, diabetes and obesity should be treated upfront?

### AETIOLOGICAL RISK FACTORS IN ATRIAL FIBRILLATION<sup>(7)</sup>

AF is a complex arrhythmia, and although there may be little in the way of difference in ECG appearance between patients, the aetiology and prognosis may differ markedly. This, in part, is reflected by the way in which AF is managed clinically - from accepting it as permanent and not pursuing sinus rhythm, to extensive atrial ablation and complex surgical procedures.

The discovery of the importance of the pulmonary vein/left atrial junction mediating AF, and the finding that AF can be potentially cured by eliminating the focus, has been central to the increase in the use of catheter ablation.<sup>(8,9)</sup> Broadly AF can be thought of as trigger dependent due to electrical instability (e.g. tissue inhomogeneity at the left atrial/pulmonary vein junction) and AF perpetuation because of abnormal atrial substrate (e.g. fibrotic scar secondary to chronically elevated left ventricular end diastolic pressure). The majority of patients probably have both mechanisms present, with the added insult from AF itself causing further electrical and structural (negative) remodelling - AF begets AF. A basic concept of these mechanisms is helpful when attempting to understand the management of AF.

Trigger dependent AF is usually paroxysmal, but if the atrial tissue remodels then the episodes can become longer and more persistent. An increase in left ventricular end diastolic pressure results in an increase in atrial pressure, hypertrophy and stretch as well as the development of scar tissue. It is therefore not surprising that hypertension and heart failure are commonly associated with AF. However, patients with normal pressures can also develop AF and it is now recognised that certain patients can have a primary atrial cardiomyopathy,

resulting in gross atrial scarring and AF. Furthermore, AF can run in families where a number of genes have been implicated affecting ion channels; this adds "electrical" substrate as another factor in the causation of AF. Non-valvular AF therefore covers a complex spectrum of heterogeneous, overlapping phenotypes. The importance of these varied mechanisms is that the treatment of AF not only involves rhythm management but the treatment of conditions that predispose to AF, even before AF develops.

### PATHOPHYSIOLOGY OF ATRIAL FIBRILLATION

The fibrillating atrium transforms a chamber that fills and empties in a co-ordinated fashion to an essentially still compartment. In addition, the rapid activity transmitted to the AV node results in an irregular and rapid ventricular response. Whilst ventricular filling is mainly passive, loss of atrial contraction can result in a 20% reduction in cardiac output. Furthermore, rapid and irregular ventricular contraction impairs ventricular filling and further reduces cardiac efficiency.<sup>(10)</sup>

Loss of atrial contractility reduces atrial flow. As discussed before, many of these patients have abnormal substrate and therefore abnormalities in atrial structure. Moreover, conditions such as diabetes and hypertension are not uncommon in AF and are pro-inflammatory states. These factors constitute Virchow's triad for thrombogenesis and thus explain why AF is associated with thrombus formation in the atria and thromboembolism. The left atrial appendage is the origin of most clots.

### STRATEGIES TO PREVENT NON-VALVULAR ATRIAL FIBRILLATION

#### Primary prevention

Early and optimal management of conditions that predispose to AF such as heart failure, hypertension and diabetes intuitively could prevent the onset of AF by limiting the exposure of the atrium to high left ventricular end diastolic pressure. The LIFE trial suggested a potential role in the use of angiotensin 2 receptor blockers in primary prevention.<sup>(11)</sup> These drugs, that are not anti-arrhythmic agents, are generally referred to as upstream treatment. There is some supportive data for the use of atorvastatin in the prevention of AF post cardiac surgery, but patients need to be on it beforehand.<sup>(12)</sup>

#### Secondary prevention

Once AF has developed there is little data to support upstream drug therapy in preventing further episodes of AF. Early treatment of AF, for example when paroxysmal, could potentially attenuate negative remodelling as AF begets AF. There is however a lack of data to support this currently, and in the majority of patients the effect of pre-existing conditions (e.g. hypertension, sleep apnoea) may have a much greater negative impact, even after AF ablation.<sup>(13,14)</sup>

Recent data from the LEGACY trial has suggested that patients who are overweight and receive a planned management

strategy to lose weight appear to benefit with not only improved rhythm control, but quality of life. At least 10% weight loss, which is then sustained is required, but this data is encouraging because it is a particularly relevant secondary prevention strategy when the prevalence of obesity worldwide is increasing.<sup>(15)</sup>

**MANAGEMENT OF NON-VALVULAR ATRIAL FIBRILLATION**

Two key issues that need to be addressed in patients with AF are how to prevent thromboembolic complications and whether to offer rate or rhythm control.

**Prevention of thromboembolic complications**

In any patient with AF, the risk is greater (at least 5 times) than that in a similar subject in sinus rhythm.<sup>(7)</sup> The most common complication is stroke; however, embolism can occur anywhere in the systemic circulation for example the small bowel. Outcomes, including mortality in patients who have stroke as a result of AF, are often worse than in those who do not have AF; the consequences are far more costly than in patients with sinus rhythm.<sup>(16)</sup> The cornerstone of management is the prevention of thrombus formation, through the use of anti-thrombotic therapy which includes antiplatelet agents or anticoagulation. It has now been increasingly recognised that anti-platelet treatment confers no benefit in stroke prevention and can result in harm. The prescription of these drugs is therefore not recommended by current guidelines.<sup>(17,18)</sup>

Oral anticoagulation unfortunately predisposes to an increase in bleeding risk, and therefore in an individual the risk/benefit of bleeding versus thrombotic complications has to be carefully considered. The key question is not who to anticoagulate, but to identify the patient who is at very low risk and in whom anticoagulation will not be beneficial. Various scoring systems have been developed over the years with initial classification into low, medium and high risk followed by the CHADS2 score. This score has now been updated by CHA<sub>2</sub>DS<sub>2</sub>VaSc which includes vascular disease and increases weighting in patients over 75 and females (provided they have another risk factor).<sup>(19)</sup> Both the CHA<sub>2</sub>DS<sub>2</sub>VaSc and HASBLED scores are used in assessing the risk of stroke, and bleeding, respectively (Table 1). In essence, in the setting of AF, an individual requires a score of 1 (if male) and 2 (if female) to warrant anticoagulation. Categories such as hypertension are in fact shared between the scoring systems. Regardless of the HASBLED score, (and in particular in the setting of multiple modifiable risk criteria here), oral anticoagulation is still recommended by current guidelines if the individual qualifies by the CHA<sub>2</sub>DS<sub>2</sub>VaSc score.

Following the consideration of the risks of thrombo-embolism and bleeding, systemic anticoagulation is considered, and Vitamin K antagonists such as warfarin are prescribed. It is very clear from clinical data that systemic anticoagulation significantly reduces the risk of stroke in patients with AF, and the threshold of initiating treatment has been lowered over the last

few years. Stroke in patients with AF is associated with greater mortality and disability, and hence investment in anticoagulation is cost effective.

Vitamin K antagonists operate with a narrow therapeutic index, and the dose response curve varies markedly from patient to patient. Therefore monitoring is required in the case of warfarin with INR. Because of the unpredictable pharmacodynamics of Vitamin K antagonists, together with the fact that their actions could be modified by diet (alcohol, leafy vegetables), medication (e.g. amiodarone) and by lack of compliance, a not uncommon problem is suboptimal INR control (either too high or too low). To an extent the morbidity with sub-therapeutic anticoagulation is worse than with over-anticoagulation.<sup>(20)</sup>

The concept of time in therapeutic range (TTR) has recently been a topical issue with the development of novel oral anticoagulants or non-vitamin K dependent oral anticoagulants (NOACs). Data from Rely-AF show South African patients to only have been within TTR approximately 58% of the time. It is also pertinent to note that South Africa was the only country from the African continent in fact represented in the study. This index (TTR) calculated the time that patients have maintained

**TABLE 1: Assessing risk for stroke and bleeding using the CHA<sub>2</sub>DS<sub>2</sub>VaSc and HASBLED scores**

<b>CHA<sub>2</sub>DS<sub>2</sub>-VASc</b>	
<b>CHA<sub>2</sub>DS<sub>2</sub>-VASc criteria</b>	<b>Score</b>
CHF/LV dysfunction	1
Hypertension	1
Age ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease	1
Age 65-74 years	1
Sex category (i.e. female gender)	1
<b>Max score</b>	<b>9</b>
<b>HAS-BLED</b>	
<b>HAS-BLED risk criteria</b>	<b>Score</b>
Hypertension	1
Abnormal renal or liver function (1 point each)	1 or 2
Stroke	1
Bleeding	1
Labile INRs	1
Elderly (e.g. age ≥65 years)	1
Drugs	1
Alcohol	1
<b>Max score</b>	<b>9</b>

Adapted from Lip G, et al. *Chest* 2010;137:263-72; Lip G, et al. *Stroke* 2010;41:2731-8; Camm J et al. *Eur Heart J* 2010;31:2369-429; Hart RG, et al. *Ann Intern Med* 2007;146:857-67 and Pisters R, et al. *Chest* 2010;138:1093-100; ESC guidelines: Camm J, et al. *Eur Heart J* 2010;31:2369-429.

**TABLE 2: The NOACs**

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Mechanism of action	Direct thrombin inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
Dose*	150mg bd	20mg od	5mg bd	60mg od
Superiority over warfarin for thrombo-embolism	150mg bd	Non-inferior only	Yes	Not tested
Reduced major bleeding when compared to warfarin	More with 150mg bd	No	Yes	Yes

\*All require dose adjustments in renal impairment. These drugs' effects can be potentiated by CYP-3A4 and P-glycoprotein inhibitors and vice versa; it is important to check the formulary.

a therapeutic INR level over a period of time, and the better the TTR the greater the efficacy of oral anticoagulation.<sup>(21)</sup> Considerable research efforts have been made to develop anticoagulants that do not require therapeutic monitoring and provide effective anticoagulation. Dabigatran, a direct thrombin inhibitor, was the first agent to be tested in a clinical trial and compared against warfarin. The key findings were that it was non-inferior, and the higher dose was potentially better than warfarin.<sup>(22)</sup>

Three other agents have been compared to warfarin in clinical trials since then. These are all factor Xa inhibitors and include apixaban,<sup>(23)</sup> rivaroxaban<sup>(24)</sup> and edoxaban.<sup>(25)</sup> These agents offer similar advantages to dabigatran. There appears to be a clear non-inferiority effect, and a potential superiority effect, especially when the TTR is taken into account. Table 2 summaries the key features of currently used NOACs.

Since there have been no head to head trials between different NOACs, it is very difficult to be definitive about which one to use, especially as their results are quite comparable. There are however certainly patients for whom warfarin use may still be preferable and these include:

- Patients for whom NOAC use will lead to an unacceptable increase in cost.
- Patients, already on warfarin, who do not mind periodic INR checks and who have had relatively easy INR control.
- Patients with severe chronic kidney disease who have an estimated CrCl (creatinine clearance) less than 30mls/min.
- Patients where NOACs are contra-indicated e.g. those on anti-epileptic or protease-inhibitor based anti-retroviral therapy agents.

**TABLE 3: Advantages and disadvantages of NOACs when compared to warfarin**

Advantages	Disadvantages
Convenience (no routine INR checks)	Lack of blood level monitoring and compliance
Reduction in intracranial haemorrhage risk	Lack of approved antidote
Less susceptibility to drugs and dietary interactions	Restrictions in severe chronic kidney disease
Shorter plasma half-life	Higher cost

A number of meta-analyses support the concept that NOACs are, in fact, preferable to warfarin in many cases. These are based on the findings that NOACs are associated with a significant reduction in intra-cranial haemorrhage, stroke/systemic embolism as well as a marked reduction in haemorrhagic stroke and a trend towards reduced major bleeding.<sup>(26)</sup> Nevertheless, Vitamin K antagonists clearly have advantages over NOACs as well (Table 3).

Clinicians certainly need to familiarise themselves with the host of drug interactions and dosing schedules, for example in chronic kidney disease, applicable to these agents. It is highly recommended that rivaroxaban needs to be taken with food, for instance.

An extensive description, including recommendations for transitioning of these agents, or that involving pending surgery, unfortunately falls beyond the scope of this article.

As regards the future of anticoagulation in AF, new work on factor XI inhibitors looks very promising.

In patients with persistent AF undergoing cardioversion, current guidelines recommend a minimum period (at least 3 weeks) of therapeutic anticoagulation. This can be difficult to achieve quickly with drugs like warfarin. However as NOACs achieve therapeutic levels quickly and require no monitoring, as long as the patient is compliant, it can be assumed that therapeutic levels have been achieved over the minimum time period. Furthermore, patients do not need cardioversion postponed because of sub-therapeutic INRs. Cardioversion is now routinely performed on these agents and appears as safe as on warfarin with randomised control data (on rivaroxaban).<sup>(27,28)</sup>

Certain patients may not be able to tolerate oral anticoagulation or may be at high risk of bleeding. Unfortunately many of these have a high risk of thromboembolism. Recent developments have focussed on either internal or extrinsic occlusion of the left atrial appendage. PROTECT AF was a randomised trial comparing warfarin versus left atrial appendage occlusion in non-valvular AF. Approximately 4 year follow up data suggest that the ischaemic stroke rate is similar in both groups, but that there are fewer haemorrhagic complications in the device

group.<sup>(29)</sup> Several other endocardial devices are available, and percutaneous as well as surgical clipping of the left atrium is possible. Although the treatments are new, they offer promise, especially in high risk bleeding patients. It is highly unlikely that device therapy will replace anticoagulation since there is an acute complication rate, and long term real world data is still awaited. Patients need careful counselling before this treatment is considered. Also of note is that the most recently updated AHA/ACC/HRS guidelines make no recommendation for percutaneous approaches with specific reference to either LARIAT or the Watchman LAA occlusion device and that for surgical incision of the LAA in patients undergoing cardiac surgery, a single class 2B, level of evidence C, is given, reflecting the fact that the quality and quantity of data are simply limited.<sup>(17)</sup>

Complications related to anticoagulants are generally treated according to the individual institution's bleeding management protocol. General measures, including withholding the anticoagulant (the NOACs have relatively short half-lives), ensuring adequate haemostasis and colloid resuscitation (including platelet/RBC or plasma administration) while simultaneously maintaining a sufficient diuresis, are often initially employed, depending on the severity of the bleeding and the specific anticoagulant used. Fresh frozen plasma rapidly restores coagulation in the case of VKAs whereas vitamin K usually has a slow onset of action. Often misleadingly referred to as an "antidote" for VKAs, vitamin K restores physiological clotting factor synthesis via a slow, complex process with clinically significant variability between patients. The INR corrects more quickly than the coagulopathy.

In the case of the NOACs obtaining critical information with regards to dosing regimens, last intake and renal function is mandatory and may be ultimately lifesaving as time is often the most important antidote. There is some anecdotal evidence that, in addition to the general measures mentioned above, administration of oral charcoal (NOAC intake within 2 hours), tranexamic acid, desmopressin, prothrombin complex and recombinant factor VIIa may be of some use in major life-threatening bleeding though the evidence base for any of the afore-mentioned is rather scanty.<sup>(30)</sup>

Uniquely, in the case of dabigatran, haemodialysis may be of use. More importantly, however, the humanised monoclonal antibody idarucizumab will almost certainly become available shortly as FDA approval is now pending. After IV administration (2-4g), it has a very rapid onset of action and demonstrates an instantaneous, specific and sustained reversal of anticoagulation that returns the patient to haemostasis. This effect seems independent of age, gender or degree of renal impairment and re-administration of dabigatran 24 hours afterward restores anticoagulation fully. Currently available data has suggested excellent efficacy and shown safety in healthy volunteers.<sup>(31,32)</sup>

### Rate or Rhythm Control

Rate control is the initial step in the management of patients with persistent AF. Use of drugs that block the AV node, such as beta blockers or rate limiting calcium channel antagonists (diltiazem, verapamil), are usually first line and combination therapy can be considered. The role of digoxin is currently controversial as there have been conflicting reports of increased mortality.<sup>(33)</sup> It only exerts a modest rate control effect. Amiodarone or dronedarone do reduce heart rate, but are generally unsuitable because of long term drug toxicity. Further, dronedarone was associated with increased mortality in patients with permanent AF.<sup>(34)</sup>

For patients who are asymptomatic this strategy is sufficient. In those patients who are not considered to be candidates for rhythm control where rate control is difficult (and there are drug intolerances), implantation of a pacemaker followed by AV node ablation is an effective strategy. Patients with symptomatic paroxysmal AF may be prescribed beta blockers or calcium channel antagonists to reduce the heart rate when they experience intermittent symptoms.<sup>(7)</sup>

As demonstrated in the RACE II trial, in patients with permanent AF, a lenient rate control, strategy (resting heart rate  $\leq 110$ bpm) is as effective and easier to achieve than that of a strict (resting heart rate  $\leq 80$ bpm) strategy.<sup>(35)</sup>

The decision regarding rate or rhythm control is principally driven by symptoms. The AFFIRM and RACE trials demonstrated that rate control was non-inferior to rhythm control and maintenance of sinus rhythm was poor.<sup>(36)</sup> Rhythm control strategies were therefore thought to be less useful; however, clinicians in favour of rhythm control argued that rhythm control strategies did not show more benefit because sinus rhythm was either not maintained or that there was morbidity and side effects from anti-arrhythmic drug therapy. Therefore, patients who may benefit from this strategy may be denied the beneficial effects.

Certain anti-arrhythmics utilised in the maintenance of sinus rhythm in AFFIRM, in particular amiodarone, were in fact associated with increasing mortality. AFFIRM had also suggested significantly better symptomatic relief, in particular in heart failure patients where a rhythm control strategy was pursued.<sup>(37)</sup> This has also been re-iterated in very recent studies where AF ablation providing a rhythm control strategy offered heart failure cohorts a significantly improved quality of life, reduced hospitalisation and modestly increased survival.<sup>(38)</sup> In summary, analysis of AFFIRM trial data advocate that rhythm control strategies do offer a survival advantage over one of rate control, if only, however, this could be safely achieved. The search therefore, for more efficacious and safer strategies to enable and maintain the unquestionable benefit of sinus rhythm, continues.<sup>(35)</sup>

Moe, et al. proposed a multiple wavelet hypothesis in AF, and argued that atrial substrate modification may prevent AF perpetuation and encourage sinus rhythm. Surgical AF treatment initially involved cutting and sewing the atria to create lines of block. However, the technique requires open heart surgery and is technically demanding, and was performed in patients undergoing concomitant cardiac surgery, mainly valvular.<sup>(37)</sup>

In 1999 a seminal publication<sup>(8,9)</sup> by the Bordeaux electrophysiology group changed the way rhythm control strategies would evolve. They showed that AF was triggered mainly by the pulmonary veins and that isolation of these veins using radiofrequency ablation catheters could terminate and prevent further episodes of paroxysmal AF.<sup>(39)</sup> As ablation was performed in the veins, the risk of pulmonary vein stenosis was high and further development of this technique, using 3 dimensional atrial geometry creation, involved creating wider lesions more atrially, to isolate the pulmonary veins, reduced this complication.<sup>(40)</sup> This technique was further modified to treat patients with persistent AF.<sup>(41)</sup> The use of percutaneous catheter ablation has been increasing exponentially over the last 10 years, and as the majority of patients with non-valvular AF do not need surgery, catheter ablation is a particularly attractive option. Initially the indications for this procedure were confined to those patients who had failed multiple anti-arrhythmic agents, now it can be offered to patients who may not want to take long term medication or in whom drugs cause side effects.

Current ESC guidelines, as well as ACC/AHA guidelines, recommend the following:<sup>(42,17)</sup>

- AF ablation may be considered a first line therapy in patients with symptomatic paroxysmal AF.
- AF ablation is reasonable for patients who have symptomatic recurrences of AF on anti-arrhythmic therapy.
- AF ablation may be considered for symptomatic long-standing persistent AF to those refractory to class I/III anti-arrhythmics or initially, when a rhythm control strategy is desired.
- It is important to take patient choice into consideration.

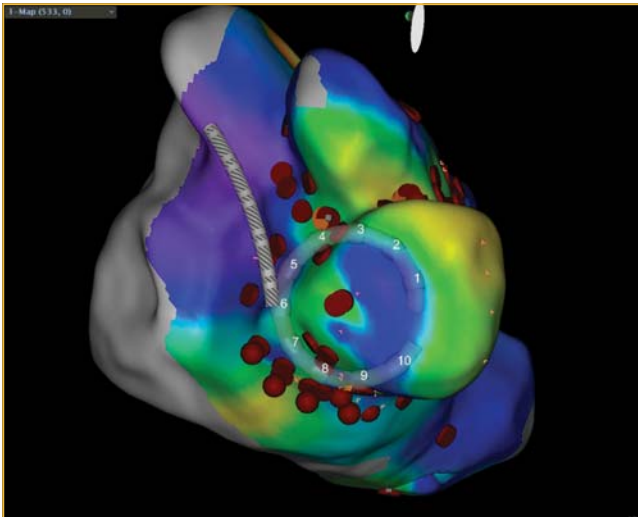
Pulmonary vein isolation is the cornerstone of AF ablation; however, in a number of patients additional substrate modification of the left atrium may be required. Detailed description of these technologies is beyond the scope of this review. Key developments in the field of catheter ablation have been the addition of contact force technology to ablation catheters and the development of balloon based or circular ablation catheters with multiple ablation electrodes that can be applied to the pulmonary vein antrum to isolate pulmonary veins and ablate left atrial substrate<sup>(44,17)</sup> (Figures 1 a,b,c).

Both radiofrequency catheter and cryoablation strategies have been associated with major complications including death, stroke, pulmonary vein stenosis, atrio-oesophageal fistula formation and phrenic nerve injury, amongst others. A recent



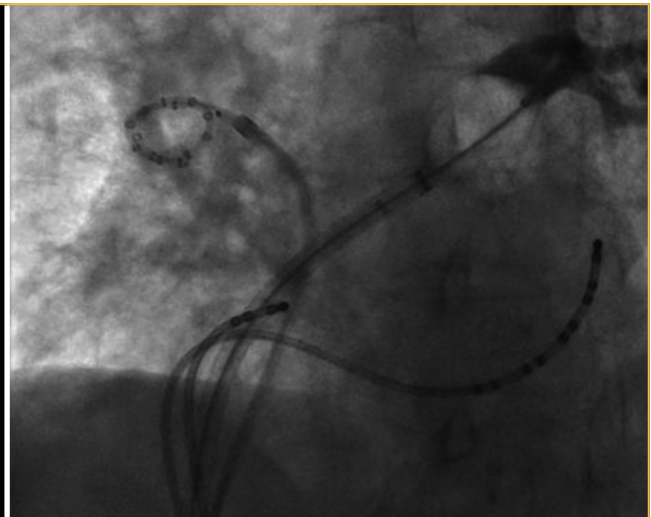
**FIGURE 1: Different strategies to AF ablation**

A. Point by point ablation with irrigated radiofrequency and 3 dimensional mapping system allowing the reconstruction of 3D geometry. Catheter contact is visible as well (Smart Touch, CARTO 3, Biosense Webster).



**FIGURE 1: Different strategies to AF ablation**

B. Wide area circumferential ablation (WACA) and carina at the junction of the left superior/inferior veins and left atrial appendage using a phased multi-electrode irrigated catheter (nMARQ, CARTO 3, Biosense Webster).



C. Cryoablation with a cryoballoon attached to the left superior pulmonary vein ostium (Artic Front, Medtronic).

systematic review however, demonstrates an overall low complication rate and peri-procedural mortality of catheter ablation of AF. As catheter technology improves, experience increases and ablation techniques become more refined, this continuing downward spiral in the incidence of complications is expected to increase.<sup>(45)</sup>

There is ongoing controversy over the optimal method of AF ablation, especially in patients with persistent or long standing persistent AF, and there is certainly evidence to support less atrial ablation.<sup>(46)</sup>

A recent concern with ablation has been silent cerebral emboli. This complication appears to have been more common with non-irrigated multi-electrode catheters, but there have been improvements in design to prevent this.<sup>(47)</sup>

Registry data suggests that AF ablation may reduce the risk of stroke;<sup>(48)</sup> however, data from randomised trials, such as CABANA and EAST, will be important in clarifying whether AF ablation has an impact on long term morbidity and mortality. Currently anticoagulation is generally continued long term in patients with high CHA<sub>2</sub>DS<sub>2</sub>VaSc scores, even if there has been complete abolition of symptoms. This is because of the fact that some patients still get asymptomatic AF and may still have a risk of thromboembolism. Although there is data that indicates that the cessation of anticoagulation therapy may be safe,<sup>(17)</sup> more data is required to affirm this. Indeed, discontinuation of anticoagulation is not an indication for AF ablation. Patients with heart failure appear to benefit from AF ablation, especially those who have tachycardia-induced cardio-

myopathy, and certain subgroups should be considered for an interventional approach early on.<sup>(49,50)</sup>

## SUMMARY

The incidence of non-valvular AF is increasing and will continue to contribute to morbidity and mortality. This is increasingly true, also for countries where communicable diseases were more prevalent as there has been a major change in lifestyle. Anticoagulation is the cornerstone, with rate and rhythm control strategies dependent on symptoms and quality of life.

**Conflict of interest: none declared.**

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