Atrial fibrillation: a contemporary update

Authors: Keenan Saleh and Shouvik Haldar

Atrial fibrillation (AF) is the most common cardiac arrhythmia and imposes a significant healthcare burden. The landscape of AF has changed considerably over the past few years, with the advent of novel diagnostic approaches, advances in therapies and changing recommendations on best practice from the latest major trials. In this article, we review our evolving understanding of the natural history of AF and explore the contemporary landscape of its diagnosis and management.

Introduction

Atrial fibrillation (AF) is an arrhythmia characterised by irregular and disordered atrial electrical activity that suppresses normal sinus rhythm. Public Health England estimates that ∼1,300,000 people are living with AF in the UK and projections indicate that this could reach as high as 1,850,000 by 2060. AF has significant health implications on both an individual and population level, being a major risk factor for thromboembolic stroke, heart failure and mortality.

Natural history

Early AF is driven primarily by focal triggers, typically originating from muscular sleeves around the pulmonary veins. Hence, electrical isolation of the pulmonary veins forms the cornerstone of all AF ablation procedures. Atrial stretch, myocardial ischaemia, autonomic dysfunction, genetic factors, obesity and oxidative stress can all change the structural and electrical properties of the atria. These changes predispose to further AF initiation and can enable AF to sustain itself for longer, eventually progressing to a persistent phenotype. Advanced structural remodelling, with development of significant atrial dilatation and fibrosis, suggests disease severity and predicts rhythm control treatment resistance. Recent evidence indicates that intervening early in the AF natural history could prevent disease progression.

Diagnosis

AF is an ECG diagnosis, with hallmark features of absent P waves and an irregular R–R interval on a 12-lead ECG. However, the European Society of Cardiology (ESC) 2020 guidelines indicate that a ≥30 second rhythm strip demonstrating AF is also acceptable to definitively diagnose AF.

AF is traditionally classified by its temporal pattern and the mode of termination of AF episodes (Box 1).

Box 1. AF classification

- First diagnosed AF: new-onset AF irrespective of symptoms or duration
- Paroxysmal AF: AF episodes terminate spontaneously within 7 days
- Persistent AF: AF episodes sustain beyond 7 days and require cardioversion to restore sinus rhythm
- Longstanding persistent AF: AF is sustained beyond 12 months and rhythm control is being considered or undertaken
- Permanent AF: AF is sustained, and it is accepted by both the patient and clinician that no further attempts will be made to attain rhythm control because of the futility of maintaining sinus rhythm

Therefore, the burden of AF needs to be considered in its temporal and structural phenotypes.

Key points

- AF is the most common cardiac arrhythmia, particularly among the ageing population, and is a major risk factor for thromboembolic stroke, heart failure and mortality.
- AF primarily begins as a paroxysmal condition, driven by focal triggers, but progresses over time to a persistent phenotype through electrical and structural atrial remodelling.
- A 12-lead ECG or >30-second rhythm strip is diagnostic for AF according to the latest European Society of Cardiology guidelines. Subclinical device-detected AF does not carry the same prognostic risk and must be interpreted in the context of AF burden and stroke risk.
- Holistic care with lifestyle and cardiovascular risk factor modification is a key treatment priority to prevent AF recurrence and improve the efficacy of AF rhythm management.
- Maintenance of sinus rhythm should be prioritised in early disease states to prevent AF disease progression and to improve long-term clinical outcomes.

KEYWORDS: atrial fibrillation, AF, ablation, arrhythmia, ECG, devices

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Novel ECG wearables and devices

Recent technological advancements have generated a wealth of commercially available wearables and handheld devices that can produce single-lead ECG recordings. These devices are becoming ubiquitous and are being increasingly adopted within clinical practice, enabling patients to provide more accurate symptom–rhythm correlation. As such, they potentially offer increased diagnostic yield for AF detection and could enhance rhythm management. In contrast to the ESC, the National Institute of Health and Care Excellence (NICE) 2021 guidelines still insist on either a 12-lead ECG or ambulatory ECG monitoring to diagnose AF. However, this has not detracted from the rapid uptake of these direct-to-consumer single-lead ECG recorders by digitally engaged patients and clinicians, who recognise their value in rhythm diagnostics and screening.

Ambulatory ECG monitoring

Diagnosis of paroxysmal AF is best achieved with ambulatory ECG monitoring, usually up to 7 days depending on symptom frequency, or with implantable loop recorders for monitoring durations. As well as determining the temporal nature of AF (ie paroxysmal versus persistent), ambulatory ECG monitoring establishes the AF burden and symptom–rhythm correlation, and provides information on ventricular rate control and the occurrence of bradyarrhythmias. These data inform subsequent management decisions regarding optimal treatment approach (rate/rhythm control) and drug titration in response to therapy.

Device-detected AF

High-frequency signals detected on the atrial lead of a pacemaker or cardiac defibrillator can represent underlying AF; however, they are not straightforward to interpret. First, they are susceptible to artefact and noise, which can lead to false positive detection if the recordings are not manually analysed. Second, the prognostic significance with regard to thromboembolism of asymptomatic device-detected AF has yet to be established in robust clinical trials, but might be lower than the stroke risk associated with clinical AF. The presence of AF symptoms, burden of AF and overall stroke risk profile are likely to influence the clinical significance of these episodes. The ESC advocate consideration of anticoagulation for patients with sustained episodes >24 h and a high individual stroke risk. However, within clinical practice, there remains significant variation in thresholds for initiating anticoagulation and large international multi-centre trials that will attempt to address this are ongoing.

AF screening

Up to one-third of patients with AF are asymptomatic at diagnosis and identifying such patients early could enable prompt initiation of therapeutic anticoagulation to prevent embolic stroke. However, despite a higher detection rate for AF, large randomised controlled trials of AF screening have not demonstrated significant benefit on hard clinical endpoints of stroke and death. Therefore, at present, population-level screening for AF is not recommended, although guidelines do suggest opportunistic or targeted screening for high-risk individuals.

The role of echocardiography

Echocardiography is a key baseline investigation in AF to assess for coexisting left ventricular dysfunction, valvular heart disease and/or left atrial dilatation, the latter being an important marker of AF disease severity that can guide clinicians on the likelihood of success and suitability for rhythm control.

Management

AF management has transformed in recent years and now highlights the importance of lifestyle, risk factor modification and early rhythm control, particularly the role of catheter ablation. The 2020 ESC guidelines advocate a holistic approach to AF management (Box 2).

Assessment of thromboembolic risk

Timely assessment of thromboembolic risk is crucial to AF management, given the fivefold increased risk of stroke compared with the general population. Patients with AF are typically risk stratified using the CHA\(_2\)DS\(_2\)-VASc score (Table 1). Anticoagulation should be considered for AF patients with ≥1 non-sex stroke risk factors.

**Box 2. The AF Better Care (ABC) integrated pathway**

**A: Avoid stroke: optimise stroke prevention**

- Assessment of thromboembolic and bleeding risk
- Anticoagulation for high-risk patients

**B: Better symptom management: treat symptoms**

- Patient-centred and symptom-directed decisions on rate versus rhythm control

**C: Cardiovascular and other comorbidities: manage risk factors**

- Hypertension (aim for blood pressure ≤130/80 mmHg)
- Heart failure (guideline-directed therapies)
- Diabetes (optimise glycaemic control)
- Ischaemic heart disease
- Obstructive sleep apnoea (continuous positive airway pressure compliance)
- Lifestyle changes: weight loss, diet optimisation, regular exercise, alcohol reduction, smoking cessation

**Table 1. CHA\(_2\)DS\(_2\)-VASc score**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Points awarded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure: clinical heart failure</td>
<td>1</td>
</tr>
<tr>
<td>objective evidence of moderate–severe LV dysfunction or hypertrophic cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age 75 years or older</td>
<td>2</td>
</tr>
<tr>
<td>Age 65–74 years</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke, TIA or systemic thromboembolism history</td>
<td>1</td>
</tr>
<tr>
<td>Vascular disease: angiographically significant coronary artery disease, previous myocardial infarction, peripheral arterial disease or aortic plaque</td>
<td>1</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>1</td>
</tr>
</tbody>
</table>

LV = left ventricular; TIA = transient ischaemic attack.
factor (ie CHA₂DS₂-VASc score >0 in men, >1 in women) to reduce risk of cardioembolic stroke. Direct oral anticoagulants should be used in preference to warfarin, given their similar risk reduction for stroke, improved bleeding risk profile and ease of use, with no routine requirement for blood monitoring. However, warfarin remains the gold standard in patients with moderate–severe mitral stenosis and mechanical prosthetic valves.

Assessment of bleeding risk

The decision to start anticoagulation must be balanced against individual patient bleeding risk. The HAS-BLED and ORBIT scores are both validated tools to assess bleeding risk (Table 2). A high bleeding risk should not necessarily preclude anticoagulation but should prompt clinicians to address modifiable bleeding risk factors; it also guides frequency of clinical review once anticoagulation has been started.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>HAS-BLED: high risk (≥3)</th>
<th>ORBIT: low risk (0–2), medium risk (3), high risk (≥4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncontrolled hypertension: SBP &gt;160 mmHg</td>
<td>1 point for each</td>
<td>Older age: 75+ years</td>
</tr>
<tr>
<td>Abnormal renal and/or hepatic function: dialysis dependent, transplant, serum creatinine &gt;200 μmol/L, cirrhosis, bilirubin more than twice upper limit of normal, AST/ALP more than three times upper limit of normal</td>
<td>1 point for each</td>
<td>Reduced haemoglobin/haematocrit/history of anaemia: Hb &lt;130 g/L in men, &lt;120 g/L in women; haematocrit &lt;40% in men, &lt;36% in women</td>
</tr>
<tr>
<td>Stroke history: ischaemic or haemorrhagic</td>
<td>1</td>
<td>Bleeding history or predisposition: previous major haemorrhage or anaemia or severe thrombocytopenia</td>
</tr>
<tr>
<td>Labile INR: time in therapeutic range &lt;60% in patient taking warfarin</td>
<td>1</td>
<td>Older patients: aged &gt;65 years or with extreme frailty</td>
</tr>
<tr>
<td>Drugs or excessive alcohol drinking: concomitant use of antplatelet or NSAID; and/or excessive alcohol intake per week</td>
<td>1</td>
<td>Drugs or excessive alcohol drinking: concomitant use of antplatelet or NSAID; and/or excessive alcohol intake per week</td>
</tr>
<tr>
<td>ORBIT score: low risk (0–2), medium risk (3), high risk (≥4)</td>
<td>1 point for each</td>
<td>Treatment with antplatelets</td>
</tr>
</tbody>
</table>

Left atrial appendage occlusion

AF-related strokes are consequent to the ineffective contraction of the left atrium, and the left atrial appendage is often a nidus for thrombus formation. Left atrial appendage occlusion is a strategy that could provide effective thromboembolism prophylaxis without the need for oral anticoagulation, potentially in patients with major anticoagulation contraindications. Evidence of overall net benefit for this approach has not been borne out in clinical trials to date and, therefore, careful patient selection is required to determine those most likely to benefit.

Pharmacological rate control

Rate control reduces the rapid ventricular rate associated with AF and is typically the initial treatment approach as well as background therapy in nearly all patients with AF. This is achieved using drugs that prolong atrioventricular node (AVN) refractoriness, namely beta blockers, diltiazem, verapamil, digoxin and, less frequently, amiodarone. During rest, a lenient target heart rate of <110 beats per minute (bpm) is adequate; however, a strict target of <80 bpm is recommended if patients remain symptomatic, have suspected tachycardiomyopathy or have a biventricular pacemaker. Rate control can exacerbate bradycardia, particularly with concomitant sinus node dysfunction or AV block (ie tachybrady syndrome); therefore, pacemaker implantation might additionally be required in some cases to enable safe escalation of rate control therapy.

Non-pharmacological rate control: ‘pace and ablate’

Pacing and AVN ablation is a useful strategy for managing drug-refractory permanent AF with high ventricular rates. Disruption of AV nodal conduction dissociates the atria from the ventricles, enabling the ventricular rate to be controlled from a prior implanted pacemaker. This technique is safe and highly effective at managing AF-related symptoms. The main drawback is irreversible pacemaker dependence; hence, the approach is reserved for select patient groups and avoided in younger patients. Biventricular pacemakers (cardiac resynchronisation therapy; CRT) are commonly implanted to mitigate against the long-term deleterious impact of right ventricular pacing post-AVN ablation. More recently, conduction system pacing by lead implantation into the His bundle or left bundle branch area can achieve more physiological biventricular activation and is a promising alternative approach for long-term pacing.

Rhythm control

Rhythm control is the restoration and maintenance of sinus rhythm and is advocated for patients who are symptomatic with AF despite adequate rate control, to improve quality of life. This includes patients who experience significant symptomatic improvement with restoration of sinus rhythm post cardioversion and patients with AF-related exercise intolerance.

The emerging importance of early rhythm control

Historically, trials of rate versus rhythm control have shown comparable efficacy and clinical outcomes between both approaches. Several recent trials comparing outcomes in the modern era of AF ablation have challenged this status quo,
suggesting that restoration of sinus rhythm should be a key objective in early AF, not only to improve symptoms, but also to prevent disease progression. Trial data from the past few years indicate a net clinical benefit of early rhythm control (within 1 year of diagnosis) over rate control, with a significant reduction in all-cause mortality, stroke and major adverse cardiovascular events. These encouraging data are not yet reflected in current guidelines, but herald a fundamental change in cardiologists’ approach to AF rhythm management.

Cardioversion

Synchronised DC cardioversion is the primary approach for emergency AF management in haemodynamically compromised patients and is also performed electively for early persistent AF. Pre-treatment with anti-arrhythmic drugs (AADs), usually amiodarone, can further enhance the likelihood of success and reduces the risk of relapse if continued long term. To reduce the risk of thromboembolic stroke, at least 3 weeks of prior anticoagulation is required before undertaking non-emergency cardioversion if AF onset is beyond 48 hours. Otherwise, the procedure should either be delayed or undertaken with transoesophageal echocardiography to exclude left atrial appendage thrombus.

Anti-arrhythmic drugs

AADs can be used to acutely restore sinus rhythm or as chronic therapy to maintain sinus rhythm in patients with recurrent paroxysmal or early persistent AF. Commonly used drugs include flecaïnide, propafenone, sotalol, dronedarone and amiodarone. Each drug has an associated organ toxicity profile and pro-arrhythmic risk, which mandates interval monitoring with ECGs, blood tests and imaging. AADs have modest efficacy overall, with the exception of amiodarone, but this is at the expense of serious adverse effects with long-term use. When compared as first-line therapy with catheter ablation, AADs fared worse with increased atrial arrhythmia recurrence, hospitalisations and AF disease progression. Catheter ablation

Catheter ablation has emerged as a cornerstone strategy for AF rhythm control. The most established and evidence-based technique is pulmonary vein isolation using radiofrequency or cryoballoon ablation. Trials have demonstrated significant clinical benefit in patients with either paroxysmal or persistent AF in terms of freedom from AF, symptomatic benefit and quality of life. Patients with paroxysmal AF derive the greatest benefit from ablation with very high single procedure success rates using the latest generation catheter technologies. Catheter ablation for persistent AF has lower success rates on first-pass ablation, likely because of non-pulmonary vein AF triggers and more established AF substrate. Currently, ESC guidelines recommend catheter ablation for paroxysmal and persistent AF after failure or intolerance of at least one AAD, but ablation can be considered first line in selected symptomatic patients. Catheter ablation is also recommended in patients with AF and heart failure, especially suspected tachycardiomypathy, and is associated with reduced mortality and heart failure hospitalisations, as well as improved left ventricular function. Advances in ablation and mapping technology have dramatically enhanced the safety and efficacy of AF ablation. Life-threatening complications are rare, the most frequent being cardiac tamponade (∼1%). The most common complications are vascular access related (2–4%). Other complications include pulmonary vein stenosis, phrenic nerve palsy, pericarditis and, rarely, peri-procedural stroke or atrio-oesophageal fistula.

Alternative ablation approaches

Hybrid AF ablation combines catheter ablation with minimally invasive surgical ablation. This is achieved via thoracoscopic access to the epicardial space to deliver ablation directly to the epicardial surface. Early single-centre studies showed impressive results in terms of freedom from AF in patients with persistent AF, although there is a relatively higher complication rate compared with catheter ablation alone. Pulsed field ablation (PFA) is a novel non-thermal catheter ablation technique that uses electrical fields to target tissues. Early studies suggest that PFA is very safe with reduced damage to neighbouring structures without detracting from ablation efficacy. Randomised controlled trials are awaited to determine how this technique will fare compared with radiofrequency or cryoballoon ablation.

Conclusion

AF is the most common arrhythmia and is expected to become more prevalent in the coming decades. Early AF recognition and treatment are key to mitigate the potential risk of thromboembolic stroke. Lifestyle and risk factor modification are important to reduce AF burden and improve treatment success. Growing evidence highlights the importance of early intervention, particularly the role of catheter ablation, to prevent disease progression and improve clinical outcomes.

References

Atrial fibrillation


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Address for correspondence: Dr Keenan Saleh, Harefield Hospital, Hill End Road, Harefield, UB9 6JH, UK. Email: ksaleh@doctors.org.uk
Twitter: @DrKeenanSaleh, @Shouvikhaldar