



Atrial Fibrillation and its Management

1. Overview of AF

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia (abnormal heart rhythm).¹ It results from abnormal electrical activity, leading to an irregular heart rhythm which prevents the blood from efficiently being pumped toward the rest of the body.

The symptoms of AF

- Common symptoms include palpitations (a rapid, irregular, “flopping” movement or pounding sensation in the chest), shortness of breath, dizziness and/or a feeling of heaviness in the chest. Tiredness and a feeling of being generally unwell also commonly occur.

AF risk factors

- There are several underlying factors which put patients at increased risk of developing AF including age, hypertension, diabetes mellitus, heart failure (HF), myocardial infarction (MI), valvular heart diseases, thyroid disease, pericardial diseases, and obesity.²

Burden of the disease

- Atrial fibrillation is a complex disease that may double the risk of mortality,³ increases the risk of stroke almost five fold⁴ and worsens the prognosis of patients with CV risk factors.^{1,5}
- People with AF have a substantially worse quality of life than healthy individuals.⁶

Socio-economic burden

- Nearly 7 million people in the EU and US have AF and this number is predicted to more than double in the next decades in the US.⁷
- AF represents one third of hospitalisations for arrhythmia.
- 70 percent of the annual cost of AF management in Europe is driven by hospitalisation care and interventional procedures.⁸

Medical burden

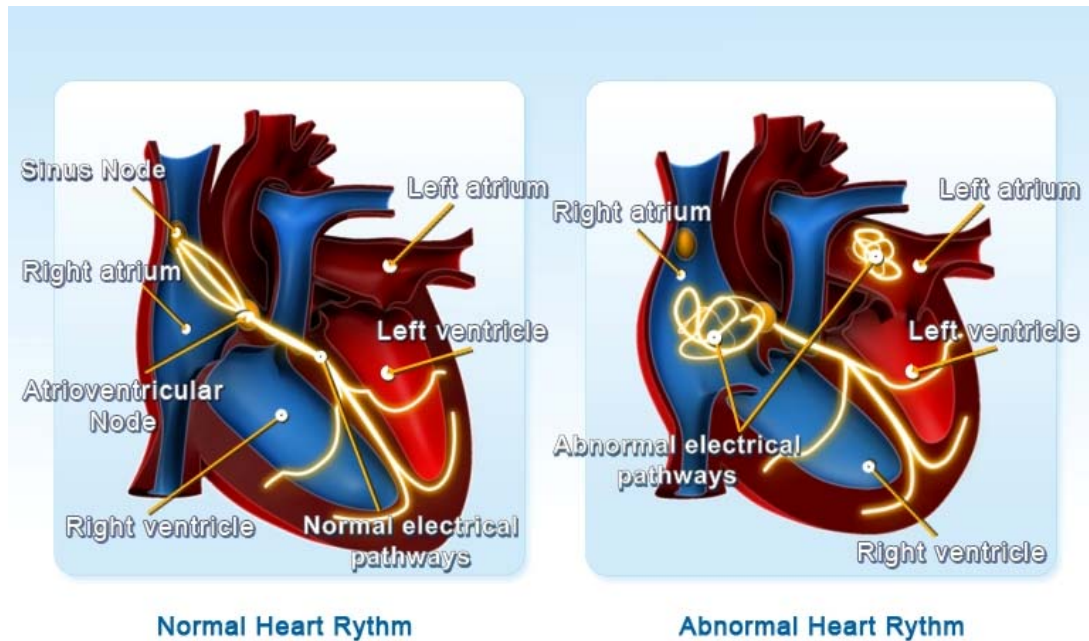
- Although there are multiple options for the treatment of AF, treatment success will vary from patient to patient. Managing AF and its associated complications remain a major challenge with unmet medical needs.



2. Physiology of AF

- In AF, control of heart rhythm by its natural pacemaker, the sinus node, is replaced by abnormal electrical activity from other areas of the upper chambers of the heart, the atria.
- This results in the atria, beating in an uncoordinated and disorganised way, and an irregular and often rapid heart rhythm. This irregular, rapid heart beat leads to deterioration of the heart's mechanical function.

Figure 1: Electrical pathways in normal heart function versus atrial fibrillation



AF can be classified into three groups:

- Paroxysmal - Recurrent episodes that terminate spontaneously within seven days.
- Persistent - Recurrent AF sustained beyond seven days which needs a medical intervention to restore the normal rhythm.
- Permanent - Long standing AF for which cardioversion is either ineffective or has not been attempted.



- These types of AF are not mutually exclusive – a patient may have several episodes of paroxysmal AF and occasional persistent AF, or vice versa.
- A paroxysmal or persistent AF may become permanent over time.

3. Epidemiology of AF

- AF is one of the growing cardiovascular conditions of the 21st century, along with congestive heart failure, type-2 diabetes, and metabolic syndrome.¹⁵
- In 2001, AF affected about 2.3 million people in North America and 4.5 million people in the European Union.^{1,9} .The lifetime risk of developing AF is one in four for individuals aged 40 years and older.⁴
- AF incidence increases with age¹⁰ to eight percent in people 80 years and older¹¹. Given the ageing population, AF is emerging as a growing public health concern.
- Over the past 20 years, hospital admissions for AF have increased by 60 percent.

4. Symptoms of AF

- Common symptoms include palpitations, chest pain, breathlessness, fatigue or light-headedness.¹
- AF may be asymptomatic and is often only diagnosed because of routine medical checks or investigations for other conditions, such as an embolic complication or exacerbation of heart failure.
- Unfortunately AF may often go undetected and untreated because it can be asymptomatic in 15-35 percent of cases.¹²
- Individuals may experience periods of both symptomatic and asymptomatic AF. Over time, symptomatic palpitations may disappear and patients who are in permanent AF may become asymptomatic; this is particularly common among the elderly.

5. Burden of AF

- An AF individual's quality of life is substantially worse than healthy individuals and can be affected in a multitude of ways such as:
 - Reduction in physical functioning including mobility and self-care by 24%, making it difficult to perform daily activities





- Reduction in social functioning including intimacy, support, and family contact by 23%
- Reduction in psychological well-being including anxiety and depression by 16%
- Reduction in general health by 30%

6. Consequences of AF

- AF is a complex, progressive cardiovascular disease with serious consequences, including HF and stroke, which can have serious and debilitating consequences.^{13,14,15}
- People with AF are five times more likely to suffer a stroke.¹⁶
- AF is an independent risk factor for sudden cardiac death with a risk ratio of 1.31.¹⁷
- AF increases the risk of heart failure by 3.4.¹⁸

7. Management of AF

Maintenance of normal sinus rhythm is often seen as the ultimate goal of therapy for patients with AF but the management of AF is a major challenge because all current therapeutic options have their limitations.¹⁹

Pharmaceuticals

- Drug therapy is the first line treatment choice in AF management.
- Antiarrhythmic drugs (AADs) are widely used and many patients have a satisfactory, complete or nearly complete) response.
- For other patients current agents have limited efficacy, poor tolerability and a potential for serious ventricular proarrhythmia and / or organ toxicity.²⁰
- Side effects have been observed in previous AAD clinical trials and as such, safety is a key consideration in the choice of antiarrhythmic medications.²¹
- None of the current anti-arrhythmic drugs have proven any reduction of morbidity or mortality.



Cardioversion

- Cardioversion resets and restores sinus rhythm in patients with persistent AF. It can be achieved with drugs or electric shocks.
- Cardioversion is a highly effective therapy, especially when AF is of recent onset (days or weeks rather than months or years)
- Cardioversion carries a risk of thromboembolism but appropriate full anticoagulation prophylaxis, initiated for at least 3 weeks prior to the treatment prevents this complication.

Ablation

- In this procedure, one or more thin flexible tubes (catheters) are guided into the blood vessels and directed to the heart muscle with the aid of x-ray.
- Bursts of radiofrequency (heating) or cryo (freezing) energy are then delivered to destroy very small areas of tissue that give rise to abnormal electrical signals.
- Pulmonary vein isolation is a highly effective therapy for patients with symptomatic paroxysmal (and to some extent, persistent) atrial fibrillation.
- Complications are not frequent, but may be severe.
- Atrioventricular nodal ablation in conjunction with permanent pacemaker implantation is another therapy which may provide highly effective control of the heart rate and improves symptoms in selected patients with AF.

Although there are multiple options for the management of AF, drug therapy remains the first-line therapy.

8. The future of AF management

- In light of the limitations of currently available therapies, there remains an unmet medical need for innovative new therapeutic options that will help doctors and their patients manage the complexity and impact of AF in day to day life.²²
- Due to the incidence and complexity of this disease, the current treatment options available and the high risk of cardiovascular complications, there is a need for greater awareness and education about AF amongst patients, their families and the general public.



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