White Paper on Atrial Fibrillation

Dr U. Maden-Weinberger
Dr C. Crockford
What is Atrial Fibrillation?

Atrial fibrillation (AF) is the most commonly occurring cardiac arrhythmia1, 2 and a major cause of stroke, cardiovascular morbidity and mortality3, 4. More than 33.5 million people worldwide suffer from AF with 5 million new cases each year5. Early detection is emerging as a priority issue in medicine, because AF is very common and associated with poor health outcomes, which imposes a substantial cost burden on healthcare systems6.

The European Society of Cardiologists (ESC) has termed Atrial Fibrillation a “major cardiovascular challenge in modern society”, with medical, social and economic aspects all set to worsen over the coming decades7. Fortunately, these negative prospects can be averted through early diagnosis and appropriate management with anticoagulants.

Pathophysiology

Each heartbeat originates as an electrical impulse in the right upper chamber (atrium) of the heart. This impulse initially causes both atria to contract and then spreads through the lower chambers (ventricles), causing these to contract and thereby generating a synchronised heartbeat. In AF, the electrical impulses controlling the heartbeat become uncoordinated, so that the heart beats irregularly. The consequence of this is a serious deterioration of the mechanical function of the heart, with blood output from the heart reducing by as much as 30%. The loss of atrial contraction leads to blood pooling in the left atrium and increased risk of clot formation. These thrombi can break off and travel through the body, thereby causing ischaemic strokes, transient ischaemic attacks (TIAs) and congestive heart failure8, 9.

Symptoms and Classification

AF is a chronically progressive disease that is classified into four types or temporal patterns:

- **First detected episode of AF**
- **Paroxysmal AF**: Episodes that self-terminate within seven days
- **Permanent AF**: Episodes last longer than seven days but can self-terminate after seven days or respond to pharmaceutical or electrical cardioversion (restoration of sinus rhythm)
- **Persistent AF**: Established AF where cardioversion is accepted to be unsuccessful10, 11.

Singular paroxysmal episodes of AF are very rare; the normal progression of AF is from short, rare episodes increasing in duration to more frequent events and over time, more than 75% of patients will develop persistent or permanent AF. Symptoms of AF can be non-specific, such as general malaise, fatigue and dizziness. Some patients may present with breathlessness, chest pains, palpitations, or, on rare occasions, fainting. However, only about two-thirds of people with AF experience symptoms; a large number of studies have indicated that approximately 30-40% of all cases are asymptomatic (“silent AF”). As many patients start off with silent paroxysmal episodes, this life-threatening disease is often not detected early enough12, 13.

Large epidemiological studies have shown that approximately one-third of patients with paroxysmal as well as persistent AF are not diagnosed due to lack of symptoms1. Admission to hospital with acute ischaemic complications, e.g. stroke, is often the first manifestation of the arrhythmia, when the disorder is first diagnosed14. However, the stroke risk is the same in all types of AF and irrespective of the presence of symptoms.

Risks, Causes and Comorbidities

AF is associated with a five-fold increase in stroke risk, a three-fold increase in the risk of chronic heart failure and doubling of mortality15, 16. Due to the physiological mechanisms that cause the blood clots in patients with AF, these emboli tend to be very big and result in more severe strokes, greater mortality, greater disability, longer hospital stays and lower discharge rate to patients’ own home17, 18. If these large emboli fragment, the resulting ischaemic events can also affect several critical areas at the same time.

Patients with AF also appear to have more recurrent and fatal strokes independent of age and other risk factors for stroke19. Additionally, a growing body of evidence suggests that AF significantly increases the risk of cognitive deterioration even in the absence of stroke. People with AF experience cognitive impairment or dementia at earlier ages and their cognitive decline is significantly accelerated compared to those without AF20, 21. However, studies also found that even patients with asymptomatic AF have lower global life satisfaction compared to healthy individuals22.

A number of factors can contribute to AF development. In the report of the 3rd Atrial Fibrillation Competence NETwork/European Heart Rhythm Association consensus conference23, these are divided into ‘established’ and ‘emerging’ factors, distinguishing those that have been validated through extensive research and those that are indicated in ongoing research, but are not well established yet.

The best validated factors that lead to the development of AF are age, hypertension, heart failure and diabetes mellitus. Age is one of the key risk factors for AF24.

The overall lifetime risk of developing AF is about one in four for men and women aged 40 years and older.

The majority of patients with AF, however, are over 65 years old, and each decade of advancing age increases the likelihood of developing AF more than two-fold. One of the reasons for this is that AF is more likely to occur in patients who also have other heart conditions, which are, again, more likely to develop with advancing age. While in developing countries the main cause of AF is rheumatic heart disease (as a result of infection), the spectrum in Western populations has shifted to hypertension, atherosclerosis, congestive heart failure and mitral valve disease25.

As people begin to live longer with the background of these conditions, the risk for AF as a comorbidity also increases. Metabolic factors, such as diabetes mellitus and hyperthyroidism have been recognised as independent risk factors for AF26, 27. Conversely, AF occurring at a younger age is associated with genetic factors, which is one of the emerging factors mentioned above28. Additionally, lifestyle factors such as smoking, excessive alcohol intake, obesity, sleep apnoea and psychological stress have recently been identified as previously underappreciated risk factors29.

Until recently, it had been estimated that approximately 12-30% of all AF cases occur without demonstrable underlying disease – so called “lone AF” – in the light of the recent research, especially into biomarkers for AF, it has emerged, however, that these cases are rather due simply to previously undetected reasons.

In any case, though, the implications of an elevated stroke risk and other complications are the same for these patients as for those with comorbidities26, 29, 30.
How common is AF?
Prevalence, Incidence & Projections

AF has been described as an “evolving epidemic” due to its growing prevalence. The recently published findings on the worldwide epidemiology of AF from the 2010 Global Burden of Disease Study provide clear evidence of a burgeoning population of patients with AF on a global level. This study estimates that in 2010, there were 33.5 million people with AF worldwide (approx. 0.5% of the global population).

The likelihood of developing AF appears to be higher in individuals of white European descent in high-income countries, resulting in a higher overall burden of AF in high-income nations. New research into the clinical epidemiology of AF in China has ascertained, however, that prevalence and incidence rates there have risen sharply in the past decade, too, to levels that now mirror closely the rates in North America and Europe.

The current estimate of the prevalence of AF in the developed world is approximately 2% of the adult population. The prevalence of AF increases progressively with age from approximately 1.5% in over 45s to 5% in over 65s, 10% in over 75s and 20% in over 85 year olds.

For Europe, the number of people estimated to have AF stood at 10 million in 2012. As AF is highly age-related and the prevalence of cardiovascular disease is likely to increase at least three-fold by 2050, the number of AF cases is projected to more than double by the year 2050 due to the ageing population.

However, even these approximations may be considered too conservative, because silent (i.e. asymptomatic) AF—which may have a prevalence rate as high as 25-30% in people over the age of 65—often escapes clinical attention.

In the UK, over 1 million people are on the Quality and Outcomes Framework (QOF) register for AF. In France, an estimated 600,000—1 million people are affected by AF, whereas studies in Germany based on data from the statutory health insurance funds report a figure of 1.8 million AF patients.

It has to be kept in mind, though, that the actual figures might be even higher due to silent AF. Annual incidence rates of new cases of AF are reported as 87,000 in the UK, between 110,000 and 230,000 in France and around 360,000 in Germany. Considering the relative population sizes of these three countries, the figure reported from the UK appears to be low. A reason for this might be differing data collection methods whereby AF is not recorded as the primary cause for illness in the UK and therefore not included in the statistics.

What are the cost implications of AF?

Increased risk of ischaemic stroke is the primary hazard of AF. Stroke represents the third single most common cause of death in industrialised countries and is the second biggest cause of cardiovascular death, after ischaemic heart disease, killing an estimated 6.7 million people worldwide and 1.4 million people in Europe every year. The cost of stroke in Europe is estimated at €64 billion annually.

In the UK, more than 150,000 people suffer a first time stroke every year. The same number is reported for France, while Germany reports a number of 200,000-300,000. Over 80% of these are ischaemic strokes and the proportion attributable to AF is mounting with age. It is suggested that, overall, around 15-20% of strokes are directly attributable to AF; but this figure is as high as 25% in people over the age of 80. The primary driver of overall costs related to AF is hospitalisation—mainly due to strokes—which makes up 50% of the overall AF health care expenditure. These strokes, and the considerable associated costs, are largely avoidable through anticoagulation treatment.

How to save £100 million of Primary and Secondary Care costs.

A percentage of strokes due to AF could be preventable in the UK every year. The current NICE atrial fibrillation costing report puts the unit cost of stroke in year 1 at £1,228,000. If just 4% of patients were to receive appropriate treatment and strokes in these patients could be avoided, this would save the NHS around £67 million every year in acute health care costs alone.

The immense burden of AF-related strokes to healthcare budgets and society as a whole is increasingly generating calls for action from cardiologists, European and worldwide health organisations and charities. Reducing the overall burden of stroke, with AF-patients being a significant contributing factor, has been identified by the European Heart Health Charter and EU policy as a key need.

The World Health Organisation has also proposed a target to reduce premature mortality from non-communicable diseases—which includes AF-related stroke—by 25% by the year 2025. Despite all this, AF is not only under-diagnosed, it is also under-treated. When used appropriately, anticoagulation therapy can reduce stroke risk by about 65%. However, despite the availability of guidelines for the use and management of anticoagulation therapy, such therapy is often underused or misused.

Surveys in Italy, Germany and Spain have revealed that the proportion of AF patients with high risk of stroke (established through the validated stroke risk stratification score CHA2DS2-VASc) receiving guideline-adherent anticoagulation was only approximately 25-57%. This is despite the fact that a new group of oral anticoagulation (OAC) drugs (so-called “NOACs”), such as apixaban, rivaroxaban and dabigatran, are available that have several advantages over older OACs, such as warfarin. Not only have they been proven to be at least as effective if not more so, but this efficacy is also accompanied by an improved safety profile due to a reduced risk of intracranial bleeding. Furthermore, NOACs have no food and few drug interactions and do not require continuous routine coagulation monitoring and dose adjustments.

The unit cost of NOACs is more expensive than warfarin (approx. £800 per year, compared to £40 per year), however, lower risk of complications, better adherence prospects and lower monitoring costs mean that they are deemed cost-effective and are recommended in the UK as well as across Europe for effective stroke prevention.
Screening

Although the prevention of AF-related strokes is not only cost-effective compared to the direct cost of treating stroke, but also imperative from a human perspective, many patients with AF are not diagnosed until an often devastating thromboembolic event occurs. This underscores the importance of early diagnosis and preventative strategies as a priority for AF-patients. Cardiologists around the world are therefore urging Primary Care Providers to adopt screening programmes for the detection of AF.

Screening for AF in the over 65s has been recommended by the European Society of Cardiologists (ESC) on the basis of several studies showing increased detection rates of silent AF, which then leads to an increased number of patients receiving crucial anticoagulation therapy. A recent systematic review study ascertained that screening can identify 1.4% of the population aged 65 with previously undiagnosed AF. The recommended strategy for screening is by pulse palpation, followed by a 12-lead electrocardiogram (ECG) by a trained clinician if an irregular pulse is detected. Systematic population screening with this technique is expensive and time consuming. However, recent research has indicated that opportunistic screening in patients over 65 yielded similar detection rates of new AF cases as systematic screening. Seasonal influenza vaccination clinics have been suggested as a good opportunity for screening the target population. Although one study that examined the effectiveness of screening at flu clinics concluded that this was ineffective, this was not due to the screening method as such, but rather due to the poor uptake of ECGs following pulse palpation.

This is the point where new technologies can offer encouraging alternative screening strategies. Hand-placement ECG devices are quick and simple to use and cost little to administer. It is likely that they would be more cost effective than pulse palpation followed by 12-lead ECG, as higher specificity may reduce the number of false positive confirmatory 12-lead ECGs generated.

In the UK, the National Screening Committee (NSC) has yet to recommend screening for atrial fibrillation in the over 65 year old population, thereby explicitly contravening the recommendation for screening by the ESC, British Heart Foundation, Arrhythmia Alliance, AF Association, All Party Parliamentary Group for AF and the Royal College of Physicians of Edinburgh.

The German Society for Cardiology (DGK) endorses the ESC recommendations in their guidelines and urges doctors actively to pursue the detection of Atrial Fibrillation in all patients over 65 by pulse palpation. Additionally, two German statutory health insurers have included a software-assisted ECG approach for the recommended strategy for screening by the ESC. British Heart Foundation, Arrhythmia Alliance, AF Association, All Party Parliamentary Group for AF and the Royal College of Physicians of Edinburgh.

As cost-effectiveness is one of the driving factors in the decision on national screening programmes, the development of new cost-saving technologies that afford fast and direct ECG acquisition coupled with computer-assisted diagnosing techniques might change the parameters in favour of a national screening programme in the UK, in line with other European countries. In addition, technology that combines ECG recording with blood pressure readings would have the potential to integrate AF screening with hypertension screening – which is recommended by NICE – at no extra time or cost.

Conclusion

In summary, AF is a major cardiovascular challenge in modern society with immense medical, social and economic implications. Apart from devastating consequences for patients and their families, it is associated with substantial costs from diagnostics, interventions, treatments and inpatient care. Economic models of the benefits of screening and preventive measures, such as anticoagulation treatment, have to weigh up the costs of these measures against the costs of treating acute ischaemic trauma, such as strokes.

In the UK, the population of over 65-year-olds is about 11.5 million, according to the Office for National Statistics. If, as research suggests, screening can identify 1.4% of people in this age range with previously undetected AF, this would be approximately 160,000 cases. Even if, in reality, only 50% of cases were detected and only 50% of these would go on to take up anti-coagulation treatment, this could potentially reduce the risk for 40,000 people from the devastating consequences of a stroke. Treatment with NOACs would cost approximately £32 million, but this stands in stark contrast to the acute cost of stroke of £490 million in year one alone. However, we must consider that the cost of strokes is higher than their direct burden on healthcare budgets. Most stroke survivors require long-term care and more often than not, this care is provided informally in family settings. This is often overlooked, yet it also comes with a tremendous cost to society. Finally, there is the human cost, which is incalculable.

As the evidence mounts from both medical and health economic research, we cannot ignore the fact that comprehensive screening for AF in the over 65 population is not only cost-efficient, but also imperative from a human perspective.

About Cardiocity

Cardiocity was formed to take the “know-how” of telemetry systems from Formula 1 motorsport and adapt them for use in healthcare. Utilising new sensor technologies coupled with design innovation has led to the development of award winning new “med-tech” devices.

Working with our partners, our ambition is to create novel health systems that not only provide more acceptable patient experiences, but also generate meaningful human physiological data for clinicians and patients the world over.

We want to help move the world to proactive healthcare, providing new tools that allow human performance monitoring. You take your car for a diagnostic service more frequently than you take your body, we want to change this model, putting the human first, worrying about the car second.

Cardiocity

engine monitoring for the heart

Cardiocity RhythmPad screens for AF in 30 seconds.

About Cardiocity

Cardiocity was formed to take the “know-how” of telemetry systems from Formula 1 motorsport and adapt them for use in healthcare. Utilising new sensor technologies coupled with design innovation has led to the development of award winning new “med-tech” devices.

Working with our partners, our ambition is to create novel health systems that not only provide more acceptable patient experiences, but also generate meaningful human physiological data for clinicians and patients the world over.

We want to help move the world to proactive healthcare, providing new tools that allow human performance monitoring. You take your car for a diagnostic service more frequently than you take your body, we want to change this model, putting the human first, worrying about the car second.