Clinical Spectrum of Acute or New-Onset Atrial Fibrillation

Parag Barwad¹, Mayank Singhal, Yashpal Sharma

Introduction

Atrial fibrillation (AF) is the most common sustained or new onset arrhythmia affecting 1–2% of the population, and this figure is likely to increase in the coming years.¹,² The prevalence of AF increases with age, from 0.5% at 40–50 years, to 5–15% at 80 years.³ ⁴ AF increases the risk of stroke 5-folds and one in five of all strokes can be attributed to it. Ischemic strokes in association with AF are often fatal, and in consequence, the risk of death from AF-related stroke is doubled and the cost of care is increased 1.5-fold.

In any patient, AF detected for the first time irrespective of its duration and symptom related to it, is called a new onset AF. In majority of patients there appears to be an inexorable progression of AF to persistent or permanent forms, associated with further development of the disease that may underlie the arrhythmia. Majority of recent research in relation to therapeutic intervention (drug or interventional) has been expended to slow or halt the progression of AF. The current review summarizes the epidemiology and clinical spectrum of new onset atrial fibrillation.

Classification

AF was historically defined as either acute or chronic AF, to describe the patient’s temporal profile. In due time as therapeutic modalities have evolved for AF with predominant focus on newer drugs and catheter based management, following classification has been proposed by the American College of Cardiology/American Heart Association/Heart rhythm society (ACC/AHA,HRS).⁶

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<td>Paroxysmal AF</td>
<td>• AF that terminates spontaneously or with intervention within 7 d of onset.</td>
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<td>• Episodes may recur with variable frequency.</td>
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<td>Persistent AF</td>
<td>• Continuous AF that is sustained &gt;7 d.</td>
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<td>Long-standing AF</td>
<td>• Continuous AF &gt;12 mo in duration.</td>
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<td>Permanent AF</td>
<td>• The term “permanent AF” is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm.</td>
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<td>• Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of AF.</td>
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<td>• Acceptance of AF may change as symptoms, efficacy of therapeutic interventions, and patient and clinician preferences evolve.</td>
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<tr>
<td>Nonvalvular AF</td>
<td>• AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.</td>
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Critical appraisal of this current classification shows its relevance and focus on rhythm based management, especially catheter based for patients with paroxysmal, persistent and long standing persistent atrial fibrillation. However an old term described in the previous classification given by European society of cardiology (ESC)⁷ is highly relevant even now and always, is new onset AF. New onset atrial fibrillation was defined as first time detected atrial fibrillation irrespective of duration of arrhythmia and symptom related to arrhythmia.⁷

Clinical Presentation

Most patients with new onset (first detected or diagnosed) AF present with symptoms related to the arrhythmia itself. These symptoms may include palpitations, tachycardia, feeling of weakness, fatigue, reduced exercise capacity, dizziness, light-headedness, frequency of micturation, or shortness of breath. Some may experience severe symptoms such as dyspnea at rest, angina, presyncope, or syncope. Others may present with an embolic event or the insidious onset of right-sided heart failure (in form of peripheral edema, weight gain, and ascites). As rapid ventricular rate per se is the most important cause of symptoms in new onset AF patients, slowing down the heart rate usually results in marked symptomatic improvement in majority of patients.

Epidemiology

AF is one of the commonest arrhythmias that any medical personnel deals in his day to day clinical practice. AF is uncommon in infants and children and is almost always associated with structural heart disease. Similarly healthy young adults are also at low risk; in one report, only five of over 122,000 routinely evaluated, healthy Air Force personnel had AF on a screening ECG.⁸

The prevalence of AF is much greater in elderly people. In the

¹Assistant Professor, Dept of Cardiology, PGIMER, Chandigarh
ATRIA study, for example, which studied 1.9 million subjects in a health maintenance organization in the United States it was demonstrated that the prevalence of AF ranged from 0.1 percent among adults less than 55 years of age to 9 percent in those ≥80 years of age. The prevalence was higher in men than women (1.1 versus 0.8 percent), a difference seen in every age group. Similar patterns were reported in a European population-based prospective cohort study of 6808 subject ≥55 years of age. The prevalence of AF was 5.5 percent, ranging from 0.7 percent in those aged 55 to 59 years and 17.8 percent for those ≥85 years of age. The prevalence was higher in men than women (6.0 versus 5.1 percent).

The incidence of AF (new onset AF), like the prevalence, increases with advancing age and with the presence of cardiovascular disease. In a longitudinal study in which 3983 male Air Force recruits were followed for 44 years, 7.5 percent developed AF. The risk increased with advancing age (from 0.5 per 1000 person-years before age 50 to 9.7 per 1000 person years after age 70). Another study shows, in an age group of 45–64 years the incidence of new onset AF is 0.54/1000 person year. According to the multivariate analysis, male sex (OR 3.4), greater age (OR 1.29/decade), and cardiomegaly (OR 14.0) were the only independent predictors (p < 0.05) of new onset AF. Admission for new onset AF during 20 years of follow-up was 3.6% in men and 3.4% in women. Overall the independent predictors of new onset AF and hospitalization for AF were, age, angina, cardiomegaly, systolic blood pressure and body mass index (BMI).

Disease Associations

Heart failure: Several mechanisms operates in heart failure and predispose to AF by creating either a substrate or a trigger for this arrhythmia.

Though there is no exact estimate of incidence of new onset AF in patients of existing heart failure, AF constitutes a strong and independent risk factor for the development of heart failure, and both conditions frequently coexist, partly because of common risk factors. Development of AF in a patient with heart failure often leads to symptomatic deterioration, predisposes to episodes of worsening heart failure, increases the risk of thromboembolic episodes, and worsens long-term outcome.

Athletes: Physical activity has a U-shaped relationship with incident AF, indicating a positive antiarrhythmic effects of physical activity are partially negated when exercise is too strenuous. Data shows AF to be 2–10 times more prevalent in active or former competitive athletes and those performing intense recreational endurance sports. The reasons for this association is probably both functional (increased sympathetic activity, volume load during exercise, vagotonia at rest) and structural (atrial hypertrophy and dilatation). The role of performance-enhancing drugs on incident AF is not known.

Valvular Heart Disease: AF is frequently associated with valvular heart disease, especially mitral valve disease. LA distension and dilatation is an early manifestation of progressive mitral valve disease (mitral stenosis or mitral regurgitation), and the presence of paroxysmal or permanent AF is an accepted indication for early percutaneous or surgical mitral intervention. AF is also frequently seen in later stages of aortic valve disease when LV dilatation and elevated end-diastolic pressure exert secondary effects on LA function. As rheumatic heart disease is the commonest cause of valvular heart disease in India, it remains the most common cause of AF in India. It is well known that subclinical and transient AF.

Coronary Artery Disease: AF occurs transiently in 6 to 10 percent of patients with an acute myocardial infarction (MI), presumably due to atrial ischemia or atrial stretching secondary to heart failure. These patients have a worse prognosis that is mostly due to comorbidities such as older age and heart failure. Rarely AF has also been shown to be a sole manifestation of an acute Myocardial infarction or coronary ischemia per se in the absence of other signs or symptoms of CHD. On the other hand, incidence of AF is much lower in patients with chronic stable CHD. In the Coronary Artery Surgical Study (CASS), which included over 18,000 patients with angiographically documented coronary artery disease, AF was present in only 0.6 percent. These patients probably had chronic AF; the prevalence of paroxysmal AF may be higher. As in general population, AF in CAD patients was again associated with age greater than 60, male sex, mitral regurgitation, and heart failure; there was no association between AF and the number of coronary arteries involved. CASS and other studies also found that AF was an independent predictor of increased mortality in patients with stable CHD (relative risk 1.98).

Hypertension: The association between hypertension and AF was illustrated in the longitudinal study of male air crew recruits noted above: a history of hypertension increased the risk of developing AF 1.42-fold. Although this is a relatively small increase in risk, but hypertension being highly prevalent in the general population makes hypertensive heart disease on of the most common underlying disorder in patients with AF.

The Elderly: The prevalence of AF is ~10% at the age of 80 years, and 18% in those aged ≥85 years. All patients aged ≥75 years with AF have an individual yearly risk of thrombo-embolism >4%

Hypertrophic Cardiomyopathy:
AF has been reported in 10 to 28 percent of patients with hypertrophic cardiomyopathy (HCM). The prognostic importance of AF in these patients is unclear, with some reports showing a worse prognosis and others no increase in mortality.

**Congenital Heart Diseases:** AF has been reported in approximately 20 percent of adults with an atrial septal defect. However, again the incidence of AF is related to age, ranging in one series from 15 percent for those aged 40 to 60, to 61 percent for those over the age of 60.

AF and/or flutter also occurs in other forms of congenital heart disease that affect the atria, including Ebstein's anomaly and patent ductus arteriosus, and after surgical correction of some other abnormalities, including ventricular septal defect, tetralogy of Fallot, pulmonic stenosis, and transposition of the great vessels.

**Other Cardiopulmonary Disorders:** AF is seen in 10 to 14 percent of patients with documented pulmonary embolism (PE). AF also occurs in chronic obstructive pulmonary disease, peripartum cardiomyopathy, lupus myocarditis, and both idiopathic and uremic pericarditis. There is also a possible causal relationship between obstructive sleep apnea (OSA) and AF. In a series of 39 patients diagnosed with both PAF and OSA, patients receiving treatment with continuous positive pressure ventilation had a lower incidence of AF recurrence at 12 months (42 percent, versus 82 percent for patients who were not treated).

**Diabetes Mellitus:** Diabetes and AF frequently co-exist because of associations such as coronary artery disease, hypertension, and LV dysfunction, and possibly as a result of autonomic dysfunction and ion channelopathy. Community studies demonstrate the presence of diabetes in 13% of patients with AF. Diabetes is an independent risk factor (RR 1.4–1.8) for incident AF. The presence of diabetes confers an adverse prognosis in AF with an increase in death and cardiovascular events.

**Metabolic Syndrome:** The presence of hypertension, diabetes, or obesity is associated with an increased likelihood of the development of AF. The potential relationship between the metabolic syndrome and the development of AF was evaluated in a prospective, observational cohort study of 28,449 Japanese citizens in which 4544 individuals with metabolic syndrome at baseline were followed-up for 4.5 years. During this period AF developed in 265 patients. The risk of developing AF was significantly greater in those individuals with the metabolic syndrome (hazard ratio 1.61, 95% CI 1.21-2.15), as well as in those with individual components of hypertension, obesity, low HDL cholesterol and impaired glucose tolerance, but not elevated triglycerides.

**Thyroid Disorders:** Patients with hyperthyroidism have also been found to have an increased risk of developing AF. In one population-based study of 40,628 patients with clinical hyperthyroidism, 8.3 percent had atrial fibrillation or flutter. Once again age was an important factor, with AF being present in 10 to 20 percent of patients over age 60 but in less than 1 percent of patients under age 40. Men were more likely to have AF than women (12.1 versus 7.6 percent). Interestingly patients with subclinical hyperthyroidism (low TSH in presence of normal T3 and T4) also have an increased risk of developing AF. The increase in risk was illustrated by a prospective study, in which 2007 subjects were followed for 10 years. The subsequent age-adjusted incidence of AF was significantly higher among those with a low serum TSH concentration compared to those with a normal value (28 versus 10 per 1000 person-years). In a review of 23,638 subjects, the prevalence of AF in those with clinical and subclinical hyperthyroidism was similar (14 and 13 percent, respectively) and higher than that in euthyroid subjects (2.3 percent).

**Chronic Kidney Disease:** CKD increases the risk of the development of AF. The relationship between CKD and AF was evaluated in a report of 10,328 individuals free of AF participating in the Atherosclerosis Risk in Communities (ARIC) study. Compared to individuals with eGFR $\geq$ 90 mL/min/m² (estimated glomerular filtration rate), the multivariable hazard ratios for the development of AF were significantly increased at 1.3, 1.6, and 3.2 in those with eGFR of 60-89, 30-59, and 15-29 mL/min/m² respectively during a median follow-up of 10.1 years suggesting a significant increase in incidence of AF with worsening GFR. In addition, macroalbuminuria and microalbuminuria were also significantly associated with higher AF risk.

**Surgery:** Atrial fibrillation occurs in relation to a variety of different types of surgery, with the incidence is greatest in patients undergoing coronary artery bypass graft (CABG) or cardiac valve surgery. AF has been reported in up to 30 to 40 percent of patients in the early postoperative period following CABG, in 37 to 50 percent after valve surgery, and in as many as 60 percent undergoing valve replacement plus CABG. AF has been described in 10 to 24 percent of patients with a denervated transplanted heart, often in the absence of significant rejection. Most episodes occur within the first two weeks, while AF developing after two weeks may be associated with an increased risk of subsequent death. AF is less common after noncardiac compared to cardiac surgery. The largest experience comes from a review of 4181 patients over the age of 50 who were in sinus rhythm...
prior to major noncardiac surgery.\textsuperscript{48} The incidence of perioperative AF was 4.1 percent; most episodes occurred within the first three days after surgery. The risk was greatest with intrathoracic surgery (odds ratio 9.2).

**Alcohol:** Alcohol intake has a very interesting relationship with AF. Atrial fibrillation occurs in up to 60 percent of binge drinkers with or without an underlying alcoholic cardiomyopathy.\textsuperscript{49} Hence, most cases have been reported during and following weekends or holidays when alcohol intake is increased, a phenomenon that has been termed “the holiday heart syndrome.” However, even modest amounts of alcohol can trigger AF in some patients. Although, moderate, long-term alcohol consumption does not appear to be a risk factor for AF, but on the other hand, heavy alcohol consumption is associated with an increased incidence of AF. Two large cohort studies, evaluating men with heavy alcohol consumption, found an increased incidence of AF among such people (hazard ratio 1.45 in both).\textsuperscript{50,51} Neither study found a correlation between heavy alcohol use and AF in women, but the ability to detect such a correlation was limited by the small numbers of women with alcohol consumption in this range. Another study evaluating 1055 cases of AF occurring during long term follow up found an increased risk (relative risk 1.34, 95% CI 1.01-1.78) with consumption of more than 36 grams per day (approximately >3 drinks/day).\textsuperscript{52}

**Medications:** Certain medications can cause or contribute to the development of AF.\textsuperscript{53} These include theophylline,\textsuperscript{54} adenosine,\textsuperscript{55} and, since increased vagal tone can induce AF,\textsuperscript{56} drugs that enhance vagal tone, such as digitalis.

**Other Factors:** The presence of AF in a first-degree relative, particularly a parent, has long been associated with an increase in risk, independent of standard risk factors such as age, sex, hypertension, diabetes, or clinically overt heart disease.\textsuperscript{57} In an analysis of over 4400 individuals in the Framingham Heart Study, the occurrence of AF in a first degree relative was associated with a significantly increased risk of incident AF (multivariable-adjusted hazard ratio 1.40, 95% CI 1.13-1.74).\textsuperscript{58} The strength of this relationship was greater when only first-degree relatives with premature onset (age ≤65 years) were considered. The heritability of AF is complex. For the majority of patients, genetic susceptibility, if present, is probably a polygenic phenomenon, meaning that it is due to the combined effects of a number of genes. Polygenic inheritance can explain why some diseases cluster in families, but do not demonstrate the classic Mendelian inheritance patterns of monogenic disorders. However, a small number of families demonstrate monogenic inheritance characteristics. Some families have been identified in which AF inheritance follows more typical Mendelian patterns, consistent with a single disease-causing gene. Both autosomal dominant and autosomal recessive forms have been identified. Genetic linkage analysis has identified loci at 10q22-q24, 11p15.5, 6q14-16, 3p22-p25, and 4q25.\textsuperscript{59-63}

**References**


