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Atrial Fibrillation- An Overview: Classification, Causes, Prognosis and Management

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Abstract:

Atrial fibrillation (AF) is one of the most common cardiac arrhythmias associated with serious morbidity and mortality. Prompt diagnosis and immediate management is important to avoid serious disability and complication such as stroke. AF can be classified based on timing and self-termination into first detected episode, recurrent episode or persistent. AF can further be classified into lone AF, nonvalvular AF or secondary AF based on patient's characteristics. There are multiple causes of AF. Failing to control AF may lead to thromboembolic events, dementia and even heart failure. Basic management approach includes the management and avoidance of

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precipitating factors, the rate-control approach to slow the ventricular rate and the rhythm-control approach to restore and maintain sinus rhythm. Restoring rhythm can be done through pharmacological conversion using antiarrhythmic drugs or electrical conversion. There are factors that favour a rate-control approach while others favour a rhythm-control approach. The treatment strategy is done on individual basis.

Key words: Atrial Fibrillation, AF, AF Classification, AF Treatment, AF diagnosis, AF prognosis

INTRODUCTION

Atrial fibrillation (AF/AFib) is the most common clinical cardiac arrhythmia in elderly [1] and a predisposing risk factor for stroke by five-fold [2] but still many patients are unaware of the severity. Atrial fibrillation is a type of supraventricular tachycardia whereby the atria beats irregularly and rapidly. [3] Palpitations, irregular heartbeat and anginal chest pain are the most common symptoms. Other symptoms include dizziness, fatigue, sweating, confusion, shortness of breath and anxiety. The main pathological change involved in AF is atrial fibrosis. Diagnosis of AF includes physical examination and a complete history, ECG test, complete blood count, thyroid function test and echocardiogram. Atrial fibrillation is associated with several serious complications and women are more associated with a worse outcome than men. [4] The prevalence of AF increases with age. [5,6] AF has become a major concerned and prompt diagnosis and prevention is very important to avoid related complications.

Classifications

AF can be defined based on episode timing and episode termination. Based on this concept, AF can be classified as being:

1. First detected episode of AF

It is uncertain about the duration and occurrences frequency of AF upon initial diagnosis. Thus, upon initial diagnosis, it is termed a first detected episode of AF irrespective of whether it is symptomatic or self-terminating.

2. Recurrent episode

When patients experience two or more episodes of AF, it is termed as recurrent AF. Based on whether episodes are self-terminating or duration of episodes, recurrent episode can be further divided into:

(1) Paroxysmal AF- when episodes of AF terminate spontaneously and usually last less than 7 days.

(2) Persistent AF- when the arrhythmia is not self-terminating and usually persists for more that 7 days.

3. Permanent AF

Permanent AF refers to AF that has been sustained for more than 1 year or cannot be cardioverted or any attempt to do so is inappropriate.

The above classification of AF is mainly based on the episode timing and termination of AF. About 50% of all AF cases accounts for permanent AF, 25% accounts for paroxysmal AF and the remaining 25% accounts for persistent AF. [7] Another classification of AF based on patient□s characteristics was defined by the ACC/AHA/ESC guidelines. [8]

1. Lone AF- usually structural heart abnormality causes AF. AF manifestation in the absence of abnormal echocardiographic findings of other underlying cardiovascular diseases and in those less than 60 years is termed as lone AF.

2. Nonvalvular AF- valve irregularities can lead to arrhythmias including that of AF. There is yet a standard definition of nonvalvular AF. However it can be defined as AF manifestation in the absence of rheumatic mitral valve disease, a prosthetic heart valve, or mitral valve repair.
3. Secondary AF several conditions can lead to the manifestation of AF. Secondary AF occurs in the setting of a primary condition such as acute myocardial infarction, cardiac surgery, pericarditis, myocarditis, hyperthyroidism, pulmonary embolism, pneumonia, or other acute pulmonary diseases.

ECG Changes of AF

Atrial Fibrillation has some key ECG features such as Irregularly irregular rhythm, absence of P waves, narrow QRS complexes < 120 ms unless there is presence of pre-existing bundle branch block, accessory pathway or aberrant conduction, absence of an isoelectric baseline, variable ventricular rate of 110-160 commonly. Ashmans's Phenomenon is the presence of aberrantly conducted beats, usually of RBBB morphology is also a feature of AF.

Slow AF is usually described as AF with a ventricular rate of <60 bpm and is termed as slow AF. Causes of slow AF include hypothermia, digoxin toxicity, sinus node dysfunction or medications.

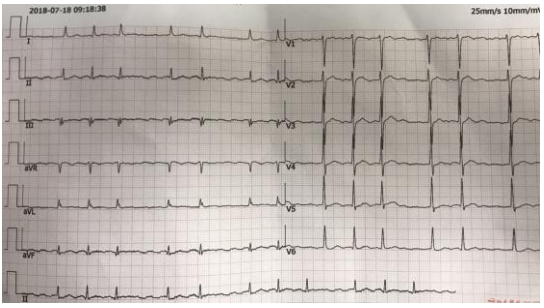

Figure 1: An ECG showing Atrial Fibrillation

Moreover, AF can occur in up to 11.5-39% of WPW patients. [9] The bundle of Kent, an accessory pathway present in WPW, provides an alternative pathway for electrical conduction to the ventricles bypassing the AV node. ECG features of AF in WPW are rate of greater than 200 bpm, wide QRS complexes, irregular rhythm and stable axis.

Causes

There are multiple causes of atrial fibrillation, including:

1. Genetics

Several genetic mutations can be accounted for AF. [10] The risk of AF increases by 1.85 fold if there is at least one parent suffering with AF. [11,12] There are mainly four types of genetic disorders that can leaf to AF. [13]

2. Hypertension

Hypertension is one of the most common risk factors associated with atrial fibrillation. [14] The pathophysiological link between hypertension and AF is still unclear. One plausible explanation could be due to the hemodynamic changes of the left atrium secondary to long-standing hypertension, resulting in left atrial enlargement. Moreover, the activation of renin-angiotensin-aldosterone system (RAAS) in hypertensive patients induces left atrial fibrosis. This in turns lead to conduction block in the left atrium, resulting in the development of AF.

3. Ischemic heart disease

Atrial ischemia secondary to coronary artery disease can lead to AF. Systolic heart failure secondary to coronary heart disease has been found to be a more important factor than that of atrial ischemia in causing atrial fibrillation. [15]

4. Hemodynamic stress

Mitral valve, tricuspid valve diseases and left heart failure can cause an increased of atrial pressure resulting in abnormal

electrical conductivity and remodelling of the atria, thus causing AF.

5. Inflammation

Inflammatory conditions such as pericarditis and myocarditis play an important role in the pathogenesis of AF, which have been confirmed by previous studies. [16,17] Inflammatory biomarkers such as C-reactive protein, high-sensitivity CRP (hs-CRP) and interleukin-6 are significantly increased in both paroxysmal and persistent AF. [18-20]

6. Alcohol and drug use

Stimulants, alcohol, and cocaine can trigger AF. Acute or chronic alcohol use has been found to be related to AF. Excessive chronic alcohol use and AF has been reported in previous studies with an association of increased risk of AF. [21]

7. Endocrine disorders

Low serum thyrotropin level is an independent risk factor for AF [22] and 10-15% of patients with hyperthyroidism suffer from AF. [23] Other disorders include pheochromocytoma and diabetes.

8. Advancing age

The prevalence of AF increases with age with 0.1% under 50 years old, 4% above 60 years old, and 14% over 80 years old. [24]

9. Others

A prospective cohort study found that anemia and chronic kidney disease carry an associated increased risk of AF onset. Patients with a combination of chronic kidney disease and anemia have a three fold more chance to experience AF. [25]

Prognosis

1.Thromboembolic events

Based on the Framingham heart study, AF carries a 1.5 to 1.9-fold higher risk of death, which is mainly due to

thromboembolic events. [26] Associated with risk of thromboembolic events, AF is associated with increased morbidity and mortality. Abnormal atrial electrical activity in AF leads to stagnant blood. This ultimately causes thrombus formation, most commonly in the left atrial appendage. An embolus is formed upon dislodgement and if travelled to the brain can cause an ischemic stroke of transient ischemic attack.

2. Dementia

The prevalence of dementia increases with age [27] just as that of AF. There is an association between AF and dementia [28], in patients after an acute stroke [29] or in patients who already had evidence of cognitive impairment. [30] Several mechanisms have been proposed including that of negative hemodynamic effects of AF resulting in reduced cardiac output and cerebral hypoperfusion [31] and silent small blood clots traveling to the brain resulting in small asymptomatic ischemic strokes [32]. These might predispose to the development of cognitive decline and dementia.

3. Heart Failure prediction

AF can lead to development of heart failure in patients suffering with valvular diseases and hypertensive heart diseases. Onset of AF is associated with a worse prognosis of heart failure according to the New York Heart Association (NYHA) classification. Heart failure can be classified as heart failure reduced ejection fraction (HFrEF) or as heart failure preserved ejection fraction (HFpEF). Based on a meta-analysis, HFrEF coupled with AF is associated with higher all-cause mortality than in patients with HFpEF. [33]

Management

Pharmacological approach

Treatment goals of AF include restoring circulatory stability and preventing thromboembolic events. This can be achieved by

(1) restoring normal heart rhythm (2) rate control (3) preventing thromboembolic events such as stroke (4) avoiding and managing risk factors, and (5) preventing heart failure. Clinical decision to use a rhythm-control drugs or rate-control drugs strategy depends on several factors, including degree of symptoms, previous unsuccessful cardioversion, presence of comorbidities, and candidacy for AF ablation. Deciding whether to use rate control or rhythm control option is based on several factors. (See Table 1)

Factors for rate control	Factors for rhythm control
Greater than 65 years	Less than 65 years
History if Ischemic Heart Disease	Symptomatic patients
	First AF presentation
	Lone AF
	AF secondary to stimulants
	Congestive Heart Failure

Table 1: Factors favouring rate or rhythm control

Rate control strategy is to prolong the AV nodal refractoriness. This can be achieved by the use of ß-adrenergic receptor blockers, nondihydropyridine calcium channel blockers, and digitalis glycosides. However, digoxin is not a first line agent anymore but it is the preferred choice for patients with coexisting heart failure. A retrospective study involving elderly population with nonvalvular AF showed that there is an increased risk of death of greater than 20% with the use of digoxin. [34} According to the AFFIRM study, rate control was better achieved by ß-blockers than calcium channel blockers (70% versus 54%, respectively) when used either alone or in combination with digitalis. [35]

Rhythm control may benefit most AF cases by improving symptoms and reducing risk of further structural remodeling caused by uncontrolled AF. [36]

Medications used for heart rhythm control include Sotalol (potassium channel blocker), Amiodarone (potassium

channel blocker), Flecainide (sodium channel blocker) and others (Procainamide, disopyramide, propafenone, quinidine). The CAST (Cardiac Arrhythmia Suppression Trial) studies found that the class IC agents (flecainide) increased mortality, especially in patients with episodes of acute ischaemia, and these class IC agents are therefore contraindicated in patients with structural heart disease. [37] Therefore, Amiodarone is used in AF patients with coexisting structural heart diseases and Flecanide is preferred in AF patients without structural heart diseases.

Cardioversion Approach

Cardioversion can be done either by pharmacological approach or by electrical or direct current (DC) conversion. The timing and method of cardioversion is important. Clinically, Class Ia, Ic and III antiarrhythmic drugs are used for pharmacological cardioversion. [38] However, in the presence of electrolytes disturbances or structural heart disease, there is considerate risk of proarrhythmia. [39,40]

If the onset of AF is less than 48 hours, patients should be heparinised. Life long anticoagulation therapy is indicated for those having risk factors for ischemic stroke. Pharmacological conversion using amiodarone (if structural heart disease) of flecainice (in those without structural heart disease) can be used. Electrical, or direct current cardioversion can also be used under anaesthesia and is very effective in most AF cases. [41] External, monophasic DC cardioversion is successful in 80% of cases, although the rate of conversion varies with joules used. [42] Alternatively, using a percutaneous catheter in the right atrium for DC cardioversion is mostly 100% effective but highly invasive. [43] On the other hand, the cardioversion approach is different if patient has been in AF for more than 48 hours. The risk of thromboembolic events is a major concern with either DC or pharmacological

cardioversion [44], which may lead to thrombus formation [45] and therefore anticoagulation therapy is needed to reduce the risk of stroke. The ACC/AHA/ESC guidelines proposed to give anticoagulation to a therapeutic International Normalized Ratio (INR) to patients with AF of more than 48 hours or an unknown duration for at least 3 weeks before and continued for 4 weeks after cardioversion. However, in those who are hemodynamic unstable, heparin should be given and cardioversion should be done, followed by warfarin.

Alternatively, another strategy is to perform a trans-esophageal echo (TEE) to exclude an atrial appendage (LAA) thrombus. With a negative result, patients may be heparinized and cardioverted immediately. The safety and efficacy of this approach was confirmed by the ACUTE I (Assessment of Cardioversion Using Tran-esophageal Echocardiograph) trial. [46] Previous cardioversion failure or AF recurrence carry a high risk or cardioversion failure. Hence, it is recommended that amiodarone or satolol be given for at least 4 weeks prior to cardioversion. Following electrical cardioversion, anticoagulation is still required for 4 weeks post-procedure. After this time, decision about anticoagulation should be assessed individually for thromboembolic risk by the CHADS2 or CHA_2DS_2-VASc scoring system. [47]

Anticoagulation

Stroke is the most serious complication in AF patients and can be observed in 5% patients every year who do not use anticoagulation treatment, especially in the elder population. [48,49] Stroke is a major cause of mortality affecting almost 800,000 patients in USA. [50] Therefore, AF is a life threatening condition, and stroke prophylaxis is thus essential for AF patients. Warfarin or new oral anticoagulation agents has become the therapy of choice for either primary or secondary stroke prevention. The CHA_2DS_2-VASc score, an

updated version of CHADS2 score, are clinical risk factors for predicting the risk of stroke in those with non-rheumatic atrial fibrillation.

$CHADS_2$		$CHAD_2SVAS_C$	
Risk Factors	Points	Risk Factors	Points
CHF	1	CHF	1
HTN	1	HTN	1
Age≥75	1	Age≥75	2
Diabetes Mellitus	1	Diabetes Mellitus	1
Prior Stroke/TIA/embolism	2	Prior Stroke/TIA/embolism	2
		Vascular Diseases	1
		Age 64-74	1
		Sex category	1

Table 2: Comparison between $CHADS_2$ and $CHAD_2SVAS_C$

Score	Anticoagulation
0	No treatment
1	Males: Consider anticoagulation Females: No treatment
2 or more	Offer anticoagulation

Table 3: Anticoagulation strategy based on risk score.

CONCLUSIONS

Atrial fibrillation is the most common cardiac arrhythmia which impairs cardiac function and increases the risk of stroke. The incidence of atrial fibrillation increases with age. AF can be classified based on timing and self-termination into first detected episode, recurrent episode or persistent. AF can further be classified into lone AF, nonvalvular AF or secondary AF based on patient's characteristics. Treatment strategies include restoring normal sinus rhythm, controlling heart rate, and preventing thromboembolism. Rate control is the preferred management option in most patients. Rhythm control is an option for patients in whom rate control cannot be achieved or who have persistent symptoms despite rate control. Anticoagulation therapy is needed with rate control and

rhythm control to prevent stroke. Clinical tools that predict the risk of stroke ($CHADS_2$ and $CHAD_2SVAS_C$) and the risk of bleeding (HASBLED scoring system) are helpful in making decisions about anticoagulation therapy.

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