

Classification, Etiology and Clinical Evaluation of Atrial Fibrillation

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Introduction

Identification of Atrial Fibrillation

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation. On the ECG fibrillatory (f) waves (rapid oscillations with variable amplitude, shape and timing) replace normal P waves. Ventricular response becomes irregular and rapid depending on the intrinsic electrophysiological properties of the AV node and the balance between vagal and sympathetic tone.

The presence of an irregularly pulse is a clinical sign that can be quickly and reliably identified in any healthcare situation and indicates AF with a high sensitivity and specificity (95% and 75%, respectively). If the irregularity lasts for more than 20 seconds the specificity reaches 98%.²⁻⁴ Identification of AF can be done by using manual pulse palpation in those presenting with a variety of symptoms. It is desirable to check the blood pressure and pulse in all patients who present with breathlessness, dyspnea, palpitations, syncope, dizziness or chest discomfort. Furthermore, many patients presenting with an acute stroke are found to be in AF albeit asymptomatic with respect to non-neurologic complaints.

The finding of a sustained irregular wide QRS com-

plex tachycardia may be suspicious of AF conducted with bundle branch aberrancy over an accessory pathway, and in patients with A-V sequential pacemakers can reflect an inadequate configuration with ventricular tracking of sensed atrial activity.

Classification of Atrial Fibrillation¹

Although the pattern of AF can change over time, at the moment of diagnosis it may be helpful to characterize the arrhythmia. These are the different patterns: First-detected episode of AF. It can be self-limited or not and the symptoms can range from an ECG finding in absence of symptoms (up to 30%⁵) to the development of heart failure or syncope. In asymptomatic patients the uncertainty remains about the duration of the episode and the possibility of previous undetected episodes. The possibility of recurrent AF without significant symptoms must be taken into account and ruled out. Recurrent AF. After 2 or more episodes, AF is considered recurrent. When the arrhythmia terminates spontaneously, recurrent AF is designated paroxysmal; when sustained beyond 7 days, it is termed persistent. This last type includes those cases of long-standing AF, usually leading to permanent AF, in which cardioversion has failed to terminate AF. It has been suggested that in most patients paroxysmal AF represents an earlier stage of the disease and that its natural history in the absence of intervention is to progress to persistent/permanent types of AF.

Etiology of Atrial Fibrillation

Holter monitoring has shown that the majority of episodes of paroxysmal AF are triggered by atrial premature beats^{6,7} while a small number of episodes are preceded by typical atrial flutter or another supraventricular tachycardia.⁷ Ectopic foci are most often located near the PVs⁶, which is the most common origin of the AF triggers.

Atrial fibrillation in patients with cardiovascular disease

AF is frequently, but not uniformly, associated with underlying cardiovascular disease or echocardiographic characteristic features. The most important factors that may contribute to AF in the setting of cardiovascular diseases are included in

Table 1 Risk Factors for Stroke in Elderly Patients With Atrial Fibrillation

| |
|---------------------------------------------------------------------|
| Cardiovascular risk factors |
| Obesity (BMI > 30 Kg/m ²) ^{8,62} |
| Hypertension ** |
| Structural heart diseases |
| Valvular heart disease (most commonly mitral valve) ⁹ |
| Hypertensive heart disease ¹⁰ |
| Myocardial infarction ¹² |
| Hypertrophic cardiomyopathy ¹³ |
| Restrictive cardiomyopathy |
| Constrictive pericarditis |
| Congenital heart diseases ¹⁴ |
| Cardiac tumors |
| Chronic myocarditis (e.g. peripartum, lupus, etc) |
| Chronic pericarditis (e.g. idiopathic, uremic, etc) ¹⁵ |
| Cor pulmonale |
| Echocardiographic parameters |
| Left ventricle hypertrophy |
| Left atrium enlargement |
| Mitral valve prolapse/calcification of mitral annulus ¹⁶ |
| Other risk factors |
| Sleep apnea syndrome ¹⁷⁻²¹ |
| Age |

table 1.

Atrial Fibrillation in patients without cardiovascular disease

Up to 25-30% of cases of AF occur in young patients without demonstrable underlying disease.¹ This is the reason why this pattern of AF is usually called lone AF. Patients with lone AF often associate certain triggers with episodes of AF,²² and in up to 39% of them a family history of AF is present, suggesting that inheritance may be of great importance in lone AF. Table 2 shows the most important causes of AF in patients without known cardiovascular risk factors or structural heart disease.

Atrial fibrillation due to temporary causes

FAF can be related to temporary causes, including some of the conditions appearing in both tables above. In such cases, successful treatment of underlying condition often eliminates AF. Some examples are described below:

Sleep Apnea Syndrome (OSA)

Several lines of evidence support a possible causal relationship between OSA and AF. Observational studies have noted a significantly larger proportion of patients with OSA between patients in AF undergoing cardioversion compared with controls without AF referred for general cardiology evaluation (49% vs 32%).¹⁷ This observation has been prospectively confirmed in patients undergoing coronary artery bypass surgery, in whom preoperative sleep studies and postoperative AF incidence were assessed (39 % in OSA patients vs 18% in non-OSA patients).¹⁸

The risk of cardiac arrhythmias with OSA appears to be related to severity of the disease, such that the great majority of OSA patients presenting with significant arrhythmias have moderate or severe forms of the disease.²⁰ In a heart susceptible to atrial fibrillation, the presence of OSA would predispose to the subsequent development of atrial fibrillation. Furthermore, the frequent presence of atrial fibrillation in OSA may contribute to the increased risk for stroke and heart failure in this patient population.²¹ It has been speculated that factors directly related to OSA, such as repetitive hypoxemia, autonomic nervous system imbalance, systemic inflammation, fluctuations in intrathoracic hemo-

dynamic, and diastolic dysfunction may serve as a trigger for atrial fibrillation and may favor the perpetuation of the atrial arrhythmia by altering the atrial substrate. Finally patients receiving treatment with continuous positive pressure ventilation have a lower incidence of AF recurrence at 12 months (42 vs 82%).¹⁹

Hyperthyroidism

Patients with hyperthyroidism have an increased risk of developing AF,²⁸ and this risk is gender and age related. Thus AF due to hyperthyroidism is more likely to occur in men than in women (12.1 vs 7.6%) and in patients over age 60 (up to 10 to 20% of patients over age 60), while patients under age 40 have little or no increase in fold risk.²⁹ Even patients with subclinical hyperthyroidism (normal serum thyroid hormone –T4– concentrations and low serum thyroid stimulating hormone –TSH–)

represent a population with increased risk of AF, similar to patients with clinical hyperthyroidism.³⁰

Increased beta-adrenergic tone may be in part responsible for the development of AF in these patients, and certainly contribute to a rapid ventricular response. In addition, excess thyroid hormone increases the likelihood of AF in experimental animals.³¹ It has been hypothesized that ectopic beats initiating AF may be increased by enhanced automaticity or triggered activity.³²

Treatment consists of a beta-blocker to control the ventricular rate, and correction of the hyperthyroid state. Spontaneous reversion to sinus rhythm occurs within six weeks in patients under age 60 who are rendered euthyroid.²⁸ Older patients show a decline in the frequency of spontaneous reversion. Cardioversion, either electric or pharmacologic, is not indicated while the patient is thyrotoxic, since AF usually recurs.²⁸

Table 2

Risk factors for AF in patients without cardiovascular disease

| |
|---------------------------------------------------------------------------------------------------------------------------------------|
| Autonomic influenced AF |
| Vagal or sleeping related ^{23, 24} |
| Sympathetic or exercise related ^{23, 24} |
| Related to temporary causes AF |
| Alcohol intake ²⁵ |
| Other substances/medications (e.g. caffeine, theophylline, adenosine, digitalis) |
| Cardiac or thoracic postoperative period ²⁶ |
| Electrocution |
| Inflammation (elevated CRP) ²⁷ |
| Acute pericarditis |
| Myocarditis |
| Acute pulmonary diseases (e.g. pulmonary embolism) |
| Metabolic disorders (e.g. hyperthyroidism ²⁸⁻³²) |
| Familial AF |
| Polygenic inheritance ³³ |
| Monogenic inheritance –channelopathies– (e.g. KCNQ1, encoding IKs current ³⁴ ; SCN5A, encoding INa current ³⁵) |
| Supraventricular arrhythmias |
| Typical atrial flutter ³⁶ |
| Paroxysmal supraventricular tachycardias ³⁷ |

Clinical evaluation of Atrial Fibrillation

Etiologic diagnostic

A detailed history and clinical examination will provide helpful information. Other tests, including thyroid function and complete blood count, are routine.³⁸ A serum TSH should be measured as part of the initial evaluation in all patient with AF, whether there are symptoms suggestive of thyrotoxicosis or not. A transthoracic echocardiogram may provide useful information, identifying the presence of structural heart disease and an increased risk of thromboembolism³⁹ (e.g. significant left ventricular dysfunction, severe valvular disease or severe myocardial hypertrophy). Such information may influence subsequent therapeutic management including the need for anticoagulation treatment. In some of the patients transoesophageal echocardiography may be needed in order to rule out the presence of left atrial appendage thrombus, especially in those patients considering cardioversion without an adequate period of oral anticoagulation.

Use of ECG monitoring to detect AF

Noninvasive ECG monitoring is used to detect AF⁴⁰ and to identify its characteristic pattern during the initial diagnosis. Such monitor may be important to assess the control of the rhythm and rate during

the follow up in patients under pharmacological treatment or after an ablation procedure. Extended ECG monitoring will also help document asymptomatic AF episodes and will help quantify the burden of AF. When symptoms are frequent a 24-h or 48-h Holter monitor may yield a diagnosis but with less frequent episodes, a 7-days Holter or an event recorder, which is either patient-triggered or auto-triggered, may be needed to document the arrhythmia. Implantable loop recorders and pacemakers can record continuous data over prolonged periods. All monitoring modalities have limitations. Non-invasive ECG monitoring may provide useful information in only 10-40% of cases, even with prolonged recordings.⁴¹⁻⁴³

The current American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the use of Ambulatory ECG Monitoring establish the following indications for Holter monitoring in the setting of AF:

Therefore in patients with suspected paroxysmal atrial fibrillation undetected by standard ECG, a 24-h ambulatory ECG monitor should be used in those with suspected AF episodes less than 24 hours apart. In patients with symptomatic episodes more than 24 h apart an event-recorder ECG should be used.

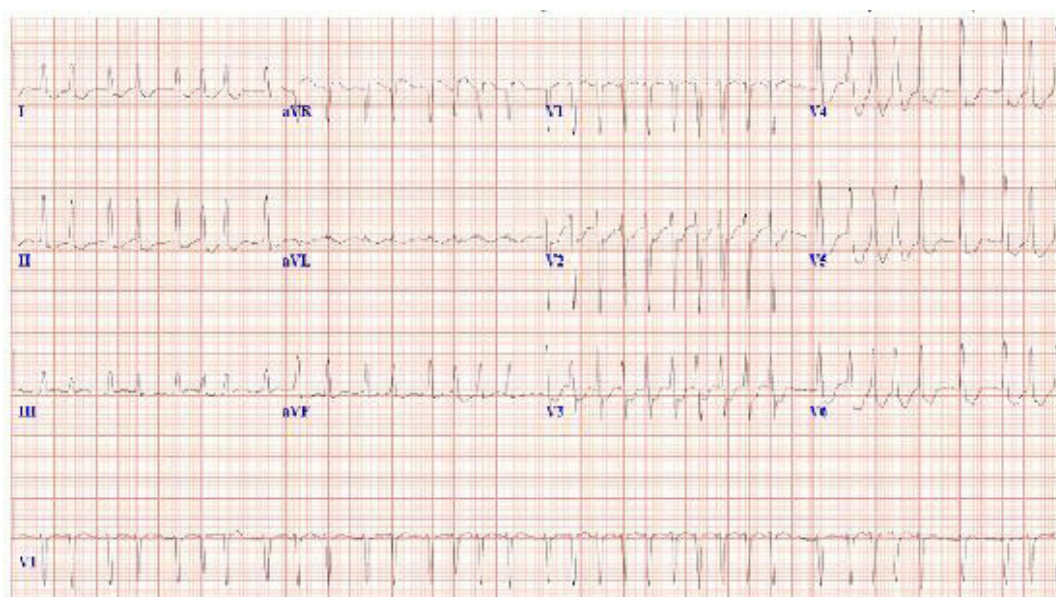
Monitoring can also help with embolism prevention. It is important to note that a 24 to 48-hour

Holter monitoring identifies AF in 1 to 5% of patients with previous stroke and undetected asymptomatic AF by initial basal ECG assessment⁴⁴. Increased duration of monitoring appears to be associated with increased rates of detection of AF. Certainly patients with risk factors for stroke with AF should undergo more extensive monitoring to exclude the presence of asymptomatic AF. We routinely encourage patient participation in monitoring with frequent pulse taking to supplement ECG recording efforts.

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Figure 1: Twelve-lead ECG showing an atrial fibrillation with rapid ventricular response in relation to an hyperthyroid state.



Class I

- To assess antiarrhythmic drug response in individuals in whom baseline frequency of arrhythmia has been well characterized as reproducible and of sufficient frequency to permit analysis.

Class IIA

- To detect proarrhythmic response to antiarrhythmic therapy in high-risk patients.

Class IIB

- To assess rate control during atrial fibrillation.
- To document recurrent symptomatic or asymptomatic non-sustained arrhythmias during therapy in the outpatient setting.

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