



Non-Valvular Atrial Fibrillation: A Systematic Review

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Abstract



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Non-Valvular atrial fibrillation is defined as the one which develops in the absence of moderate to severe rheumatic mitral stenosis, a mechanical or bioprosthetic valve or mitral valve repair. Atrial fibrillation is the most common pathological cardiac arrhythmia and major cause of ischemic stroke. There are many major risk factors for development of atrial fibrillation. Among these advanced age, hypertension, ischemic heart disease, chronic lung disease and consumption of alcohol are the major causes. Aim of treatment is to control the rate, rhythm and anticoagulation so as to prevent tachycardia induced cardiomyopathy, heart failure and stroke. This review article gives a comprehensive and systematic approach for the management of Non-valvular atrial fibrillation.

Keywords: Atrial fibrillation (AF), Stroke, Anticoagulation.

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Introduction:

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated electrical activity of the atria resulting in ineffective contraction of atria, associated with irregularly irregular ventricular rhythm with absence of distinct P waves on electrocardiogram. It is the most commonly treated arrhythmia. Thromboembolism and heart failure are some of the complications associated with atrial fibrillation¹⁻⁴. There is also an increased risk of mortality in patients with atrial fibrillation.

Etiology:

Cardiac diseases, as well as many non-cardiac conditions are associated with AF⁵. Most common conditions include hypertension, coronary artery disease, and myocardial infarction⁶. Some conditions that occur in resource poor settings include congestive heart failure, hypertension, and rheumatic valvular disease^{7,8}.

Other cardiac causes include:

- Diastolic and systolic heart failure^{6,9}.
- Atrial and ventricular dilation or hypertrophy
- Sick sinus syndrome
- Congenital heart disease
- Cardiac benign or malignant primary or metastatic tumours
- Inflammatory or infiltrative disease (e.g. pericarditis, amyloidosis, myocarditis)
- Age related atrial and ventricular fibrosis.

Non-cardiac conditions that can also lead to AF include:

- Thyroid disease
- Autonomic neuronal dysfunction
- Alcohol and caffeine abuse
- Pulmonary hypertension
- Infections.
- Familial or genetic (Laminin A and C associated heart disease) and other familial cardiomyopathies¹⁰.

Pathophysiology:

AF is usually associated with underlying heart diseases that result in an abnormal atria anatomically and histologically. Fibrosis and inflammation along with the dilation of the atria lead to difference in refractory periods within the atrial tissue which in turn lead to electrical re-entry that results in AF. Arrhythmias, such as atrial tachycardia, atrial flutter, or atrioventricular (AV) nodal re-entrant tachycardia and AV re-entrant tachycardia are other conditions that can cause AF. The latter is due to concealed or manifest accessory bypass tracts.^{11,12,13}. Other diseases such as hypertension, congestive heart failure, and coronary artery disease which can cause myocardial stretch and fibrosis together with the cellular and electrical remodeling eventually lead to atrial fibrillation^{14,15,16}.

Classification:

According to the American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines AF is classified into following types ¹⁷⁻²¹.

- Paroxysmal AF: Defined as recurrent AF with each episode lasting ≥ 30 seconds and which terminates spontaneously or with intervention within 7 days.
- Persistent AF: AF that is sustained and is continuous beyond 7 days, including episodes terminated by cardioversion after 7 days or longer.
- Long-standing persistent AF: Continuous AF >1 year duration
- Permanent AF: The one which is refractory to cardioversion or accepted as a final rhythm and restoration of sinus rhythm by any means, including catheter or surgical ablation is either not attempted or attempts have been tried but failed.
- Chronic AF may be paroxysmal, persistent, long-standing persistent, or permanent.
- Acute AF is a new-onset, or a first detectable symptomatic or asymptomatic episode of AF.

'Lone AF' is used in those patients <60 years of age without echocardiographic or clinical evidence of cardiac, pulmonary, or circulatory disease. However, the term Lone AF should not be used because definitions are variable, and all patients with AF have some form of pathophysiological basis that lead to AF ^{19, 21}.

Approach:

Clinical presentation: Most commonly patients usually present with symptoms of palpitations, shortness of breath, fatigue, chest pain, dizziness, and stroke related symptoms ⁵. ²². AF can also cause symptoms of CHF due to tachycardia-induced cardiomyopathy. In some cases, cerebral hypoperfusion can result in presyncope or syncope which is due to rapid ventricular response. AF may also be detected incidentally during a routine health checkup or following an acute complication such as stroke in asymptomatic patients. Cardiovascular disease, cerebrovascular disease, diabetes, hypertension, chronic obstructive pulmonary disease, obstructive sleep apnea, hyperthyroidism, and alcohol abuse are some conditions associated with AF and should be ascertained on appropriate history taking.

Modified European Heart Rhythm Association Symptom Scale

- Class 1: Asymptomatic (AF does not cause any symptoms)
- Class 2a (mild): Symptoms related to AF do not affect normal daily activity
- Class 2b (moderate): Symptoms related to AF do not affect normal daily activity but symptoms cause some trouble to patients.
- Class 3 (severe): Symptoms related to AF affect normal daily activities.
- Class 4 (disabling): Patients can't perform normal daily activities.

There is an association between AF and increased risk of cognitive impairment and dementia as demonstrated by several studies ^{23, 24}. However exact mechanism leading to this is not known so far.

Physical examination:

The pulse may be irregularly irregular and other findings may include irregular jugular venous pulsations with absent a wave

in the jugular venous tracing, variation in the intensity of the first heart sound. Palpation of the carotids or auscultation may be necessary.

Physical findings consistent with an underlying cause of AF, such as features of heart failure, stroke, or an endocrine problem such as hyperthyroidism is also seen in these patients.

Diagnosis:

ECG: An ECG should be performed in all patients with possible AF. Rapid fibrillatory waves replace normal P waves and definite P waves are absent. In patients with COPD multifocal atrial tachycardia may be observed and may mimic AF.

Echocardiography:

Trans thoracic echocardiogram (TTE) is important to exclude valvular, pericardial and other cardiomyopathies and other risk factors for persistent AF ^{14, 23}. It is necessary to perform a Trans-oesophageal echocardiogram (TEE) to rule out left atrial thrombus because this test is more accurate at detecting left atrial thrombi than TTE.

Laboratory tests:

Thyroid function tests should be done in all patients presenting with chronic AF. Hyperthyroidism can be diagnosed with laboratory work and treated appropriately with medicine, radioablative therapy, or surgery. Other important baseline tests include a complete blood count, a serum creatinine, serum urea and electrolytes including serum magnesium levels and liver transaminases should be ordered to assess for the presence of other comorbid conditions, and a test for diabetes mellitus ²⁵.

Treatment:

In general, ABC (Atrial Fibrillation Better Care) pathway is used for the care of patients with atrial fibrillation ^{21, 26}. The "A" for anticoagulation, "B" for better symptom management, and "C" for cardiovascular risk factor and comorbid disease assessment and management. The risk of stroke is reduced with the long-term use of oral anticoagulants. Rate control (either as a monotherapy or combination of two out of three is used among the following medications: beta blockers, Non dihydropyridine calcium channel blockers and digoxin) are used as the first line in the management of patients with AF, and then with the rhythm control (either pharmacological or electrical cardioversion) for the longer term. Finally, identifying and treating risk factors and comorbidities, is equally important in the management. Before elective electrical or pharmacological cardioversion anticoagulation should be started immediately either with oral anticoagulants or heparins, and continue for a minimum of 3 weeks before performing cardioversion ^{22, 27}.

After cardioversion oral anticoagulation should be continued for at least 4 weeks in all patients with AF duration of more than 24 hours ²⁷. DOACs are preferred nowadays (Apixaban, Edoxaban, Rivaroxaban or Dabigatran) as compared to conventional oral anticoagulants in view of lesser bleeding risks and monitoring for coagulogram is not required. Beyond 4 weeks, whether to continue long-term anticoagulation or not should be assessed as per the patient's CHADS₂ score.

Stroke risk:

Use the CHA₂DS₂-VASC (CHF 1 point, Hypertension 1 point, Age ≥ 75 , Diabetes mellitus 1 point, Stroke/TIA/Thromboembolic event 2 points, Vascular disease 1 point, Age 65 to 74 years 1 point, Sex category i.e female 1 point) score to calculate stroke risk in all patients presenting with AF ^{22, 27}. In men with a CHA₂DS₂-VASC score of 1 or more and women

with a score of 2 or more consider oral anticoagulation for the prevention of stroke ^{22,27}. Anticoagulation to be continued on long term in these patients ²⁷.

Bleeding risk:

Use the ORBIT score (Table 1), or the HASBLED score (Table 2) when considering a patient for anticoagulation to assess the risk of major bleed ^{22, 27, 29, 30}.

- Identify modifiable risk factors for bleeding, such as uncontrolled hypertension, alcohol abuse, deranged international normalised ratio, use of medication (including antiplatelets, selective serotonin reuptake inhibitors, and non-steroidal anti-inflammatory drugs) and causes of anemia (reversible).

- High bleeding risk patients for early review and follow-up.

Table 1: Depicting ORBIT score to assess bleeding risk.

ORBIT SCORE	
O=older age ≥75 years	1 point
R: reduced haemoglobin/haematocrit/anaemia	2 points
B: bleeding history	2 points
I: insufficient kidney function	1 point
T: treatment with antiplatelets	1 point
A score 0-2 represents low risk, a score of 3 represents medium risk, and a score 4-7 represents high risk).	

Table 2: Depicting HASBLED score.

HASBLED Score	
Hypertension (H)	1 point
Abnormal renal or hepatic function (A)	1 point
Stroke (S)	1 point
Bleeding or its risks (B),	1 point
Labile international normalised ratios (L),	1 point
Elderly age group (>65 years) (E),	1 point
Drugs such as antiplatelets (D) Alcohol	1 point
The risk of major bleeding is increased when HASBLED score is ≥3	

Conclusion:

Several factors, such as the precipitating cause, underlying cardiovascular status, risk of thromboembolism etc affect the prognosis of the patients. Prognosis is poor for patients presenting with new onset AF and its relation to heart failure following myocardial infarction (MI). In Swedish cohort study it has been found that there is 30% higher risk of cardiovascular events (i.e., all-cause mortality, MI, and ischaemic stroke) among those presenting with AF compared with those in sinus rhythm in patients hospitalized for MI ²⁸. There is increased risk of stroke and mortality in patients with asymptomatic AF compared with symptomatic AF ²³. A close clinical follow-up is important for the patients with MI who also present with AF.

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