Management of Acute Atrial Fibrillation

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Atrial fibrillation (AF) is a supraventricular tachyarrhythmia with uncoordinated atrial activation and consequently ineffective atrial contraction.\(^1\)\(^2\) It is characterized by uncoordinated atrial activity on the surface ECG, with fibrillary waves of varying shapes, amplitudes, and timing associated with an irregularly irregular ventricular response when atrioventricular (AV) conduction is intact. Acute AF is defined as a new onset or a first detectable episode of AF, whether symptomatic or not. Classification of AF begins with identifying a first episode, irrespective of whether it is symptomatic or asymptomatic. American College of Cardiology (ACC)/American Heart Association (AHA)/European Society of Cardiology (ESC) committee of experts on the treatment of patients with AF recommend classification of AF into the following patterns.\(^1\)\(^2\)\(^3\)\(^4\)

1. **Paroxysmal AF** – Episodes of AF that terminate spontaneously or with intervention within 7 days of onset (most episodes last less than 24 hours)
2. **Persistent AF** – Episodes of AF that last more than 7 days and may require either pharmacologic or electrical intervention to terminate
3. **Permanent AF** – AF that has persisted for more than 1 year, either because cardioversion has failed or because cardioversion has not been attempted and no further attempts for restoration of sinus rhythm is planned
4. **Nonvalvular AF** – AF in the absence of rheumatic mitral stenosis, a mechanical or bio prosthetic heart valve, or mitral valve repair.

This classification does not apply to AF secondary to correctable or reversible causes like thyrotoxicosis, electrolyte abnormalities, acute ethanol intoxication, fever, dehydration, acute myocardial infarction, presence of a central line, lung disease, cardiac surgery, pericarditis, sepsis, or pulmonary embolism. In these situations, AF is less likely to recur once the precipitating condition has been treated adequately and has resolved. The term “lone AF” had been used previously to describe AF in younger patients without structural heart disease, but no longer used now since the term was not a well-defined one.

**Clinical Approach to Treatment of Acute AF**

Most patients with acute AF present with rapid palpitations, heaviness in the chest, dizziness, or shortness of breath. Features of cardiac failure may be present. Some patients may present with stroke and embolic events. The onset of the first episode, its duration, and precipitating factors should be established.

**Step 1 – Detailed Clinical Examination**

The pulse should be assessed. An irregularly irregular pulse, both in the rhythm and volume, is characteristic. Accelerated hypertension can result in AF and should be corrected. Signs of the underlying cause of AF, such as elevated jugular venous pressure, basal rales (heart failure) or tremor, sweating, and thyroid swelling (hyperthyroidism), should be looked for. Patient should be carefully examined for fever, dehydration and any focus of infection. A central line in a post-surgical patient may the etiology of AF and should not be overlooked.

**Step 2 – Surface ECG**

Absent P waves that have been replaced by irregular fibrillary waves, and irregularly irregular QRS complexes will confirm the diagnosis of AF (Figure 1). Look for evidence of coronary ischemia, pulmonary embolism, electrolyte disturbances or structural heart disease in ECG.

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Fig. 1: Surface ECG showing atrial fibrillation

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Step 3 - Investigations for Etiology of AF and Reversible Factors

Blood biochemistry should be checked for abnormal potassium or magnesium levels. Liver function tests (LFTs) are useful to determine presence of a multisystem disorder affecting the liver. Furthermore, LFTs are useful to choose appropriate anti-arrhythmic agents and to monitor anti-arrhythmic drug therapy especially amiodarone. Cardiac biomarkers should be checked if patient has risk factors for developing CAD. Thyroid function testing should be part of the initial assessment, particularly in older people, as classic signs of thyrotoxicosis might not be obvious.

A chest x-ray (CXR) should be performed to look for underlying structural heart disease, such as enlargement of the cardiac chambers or valvular calcification, and signs of heart failure. The CXR may also suggest a precipitating cause of AF, such as pneumonia. Following the initial assessment, patients should undergo echocardiography to evaluate cardiac chamber size and left ventricular function. This may also reveal an underlying cause such as valvular disease. A transesophageal echocardiogram (TEE) is essential in patients before cardioversion (unless they are already anticoagulated for sufficient duration) to rule out left atrial/appendage thrombus. Electrophysiological studies may be required to identify and treat arrhythmias such as Wolff-Parkinson-White syndrome, atrial flutter, or paroxysmal supraventricular tachycardia in selected patients.

Step 4 – Management of the Arrhythmia

The 3 elements in the management of acute AF are:

1. Ventricular rate control
2. Restoration and maintenance of sinus rhythm
3. Prevention of thromboembolic events.

Three modes of presentation of acute AF are:

A. AF - Haemodynamically unstable
B. AF-Haemodynamically stable and asymptomatic
C. AF-Hemodynamically stable and asymptomatic

Other factors to take into consideration in the management of acute AF are:

- If symptomatic, the onset of the symptoms (<48 hours, ≥48 hours, or unknown)
- The presence of thrombus on echo (TTE and TEE)
- If thrombus is absent on TTE and TEE, whether the patient has a high or low thromboembolic risk. Patients are considered at high risk of thromboembolic disease if their age is ≥75 years and/or ≥1 of the following risk factors are present: structural heart disease, diabetes, hypertension, rheumatic heart disease, prosthetic heart valves, history of prior thromboembolism, or left ventricular ejection fraction ≤35%.

A. Hemodynamically unstable AF

AF with a rapid ventricular rate causing ongoing chest pain, hypotension, shortness of breath, dizziness, or syncope requires immediate DC cardioversion. This is performed under adequate short-acting general anaesthesia and involves delivery of an electrical shock synchronised with the intrinsic activity of the heart. The energy output for successful termination of acute AF is at least 150 -200 J. Lower energy of 100 J may be used as the starting level when biphasic energy is used.

In a patient with structurally normal heart, AF seldom results in hemodynamic instability. But in persons with structural heart disease like severe aortic stenosis (AS), hypertrophic obstructive cardiomyopathy (HOCM) and mitral valve disease; especially rheumatic mitral stenosis, AF with fast ventricular response results in hemodynamic compromise and rapid clinical deterioration. Normally atrial contraction contributes to 20-25% of cardiac output, but in severe AS and HOCM, the atrial contribution to cardiac output may go up to 50% or more. Hence development of atrial fibrillation results in rapid decompensation and the patient presents with clinical heart failure and hypotension. Prompt restoration of sinus rhythm is vital in such situations.

Atrial fibrillation occurring in patients with Wolff-Parkinson-White (WPW) syndrome requires special attention. A rapidly conducting accessory pathway can transmit fibrillations occurring in atria to ventriciles, resulting in ventricular fibrillation and sudden cardiac death. Hence atrial fibrillation occurring in patients with pre excitation should be treated aggressively. Those patients presenting with fast ventricular rates (Figure 2) are better treated with DC version. It is important to note that drugs acting on AV node alone (Adenosine, Beta blockers, Calcium channel blockers, and Digoxin) are contra indicated in patients with pre-excited AF. They tend to block AV node and facilitate conduction through accessory pathway resulting in ventricular fibrillation. Class Ib drugs (eg, quinidine) and Class Ic drugs (eg, flecainide, propafenone) slow conduction velocity in the AP and prolong the AP refractory period in the bypass tract. Hence they are used along with an AV blocking drug until radiofrequency ablation of the accessory
pathway is carried out. Class III antiarrhythmic drugs like Amiodarone, dofetilide, and sotalol prolong refractoriness in myocardial tissue, including AV bypass tracts and are used to treat pre excited AF. Since class I drugs are not easily available and are approved for patients with structurally normal heart only; amiodarone remains the drug widely used in India for this indication.

B. Hemodynamically stable AF (Symptomatic)

They don’t require emergency cardioversion and are given rate-control therapy until cardioversion is carried out electively. If there is no evidence of heart failure, beta-blockers (intravenous esmolol, propranolol, metoprolol tartrate, or oral atenolol, metoprolol succinate, nadolol, propranolol, bisoprolol, carvedilol) or non-dihydropyridine calcium-channel blockers (diltiazem, verapamil) are the preferred choice. If rate control is inadequate with monotherapy, a combination of a beta-blocker and calcium-channel blockers may be used. Digoxin is the next drug to consider especially if there is heart failure. Patient should be carefully monitored to prevent excess AV nodal blockade. If there is evidence of systolic heart failure, non dihydropyridine calcium channel blockers should be avoided.

Patients presenting with acute AF of <48 hours’ duration or those with no evidence of LA thrombus on TEE should have DC or pharmacological cardioversion. DC cardioversion is fast, safe and reliable. Pharmacological cardioversion must be used with caution as they may cause bradycardia or ventricular tachyarrhythmias. Anti-arrhythmic agents with efficacy for cardioversion of acute AF include flecainide, propafenone, ibutilide, vernakalant,7,8 dronedarone,9,10 and amiodarone. Class III agents (including amiodarone and ibutilide) are less efficacious than class IC agents (flecainide and propafenone) in conversion to sinus rhythm. In Europe, dronedarone is approved for the maintenance of sinus rhythm. In Europe, dronedarone is approved for the maintenance of sinus rhythm. However, use of dronedarone may be associated with an elevated risk of heart failure and liver toxicity.

Intravenous vernakalant has demonstrated superior efficacy to amiodarone for acute conversion of recent-onset AF and oral vernakalant appears to be effective in preventing AF recurrence post-cardioversion.11 However amiodarone remains the most commonly used drug in India and remains the only approved drug available in India when the patient has structural heart disease. Flecainide is now an option for those with structurally normal heart, but has to be initiated at a hospital as an “in-patient” drug only. Once safety is demonstrated by monitoring ECG, flecainide can be given as OP drug for long term rhythm control strategy as a “pill in the pocket” strategy. Ibutilide, is a good alternative to electrical cardioversion and will be available in India in the near future. Ibutilide has a conversion rate of up to 75% to 80% in recent-onset atrial fibrillation and flutter; the conversion rate is higher for atrial flutter than for atrial fibrillation. It is also safe in the conversion of chronic atrial fibrillation/flutter among patients receiving oral amiodarone therapy. However it is available only as intravenous preparation and requires close monitoring for QT prolongation by ECG in the initial 4-6 hours of treatment.

C. Hemodynamically stable AF (Asymptomatic)

Most cases of acute AF revert to sinus rhythm spontaneously, usually in the first 24 hours. All reversible causes of AF should be addressed and corrected. If AF does not resolve spontaneously, rate-
control therapy is required until cardioversion is successful. Cardioversion can be attempted by DC shock or using antiarrhythmic drugs. AF lasting less than 48 hours in a structurally normal heart does not require long-term anticoagulation. But if cardioversion was required either electrically or chemically, it requires anticoagulation for 4 weeks. This is due to atrial stunning, which is a function of duration of AF and predispose to thrombus formation in LA.

**Anticoagulation in patients presenting with acute AF lasting <48 hours (Hemodynamically stable)**

If the thromboembolic risk is low, no anticoagulation is required in a structurally normal heart. If the thromboembolic risk is high, IV heparin (aPTT of 45-60 seconds) or subcutaneous low molecular weight heparin (1mg/kg twice daily) should be started before cardioversion. Once sinus rhythm is restored, the patients should be started on warfarin and heparin continued until the warfarin levels are therapeutic (INR 2-3). In selected patients warfarin may be substituted with newer novel oral anticoagulants such as dabigatran, rivaroxaban, or apixaban. Dabigatran should not be used in patients with marked renal insufficiency or in those who have mechanical prosthetic valves. The concomitant use of rivaroxaban, apixaban, or dabigatran with heparin (including low molecular weight heparin), heparin derivatives, or warfarin is contraindicated. Anticoagulation is continued for at least 4 weeks after cardioversion, and may be required for longer in some patients.

**Anticoagulation in patients presenting with acute AF lasting >48 hours or unknown duration (Hemodynamically stable)**

If the onset of symptoms is >48 hours or unknown and there is no evidence of LA/LA appendage thrombus on TEE, patients should have DCor pharmacological cardioversion, but the cardioversion should not be attempted until the patient is established on anticoagulation. If TEE is not available or not technically feasible, patient should be anticoagulated for 3-4 weeks with target INR 2-3 before cardioversion is done. The risk of thromboembolic events is greatest when AF has been present for longer than 48 hours and the risk of thromboembolism is similar in patients undergoing either pharmacologic or electrical cardioversion. Acute cardioversion for AF carries a risk of thromboembolism up to 7% unless anticoagulation therapy is initiated prior to the procedure and continued post procedure. Cardioversion is most successful when initiated within 7 days after onset of AF. Anticoagulation is continued for at least 4 weeks after cardioversion, and may be required for longer in some patients. (See step 5 below for details on long term anticoagulation)

If there is evidence of LA thrombus on TTE/TEE, concomitant heparin and warfarin therapy should be started, and heparin continued until the warfarin levels are therapeutic (INR 2-3). Anticoagulation with warfarin at the target INR should be established for 3 to 4 weeks before cardioversion is attempted. Newer novel oral anticoagulants such as dabigatran, rivaroxaban, and apixaban may be used as an alternative to warfarin in selected patients and are associated with an overall increase in clinical benefit compared with warfarin. Anticoagulation is continued for at least 4 weeks after cardioversion, and may be required for longer in some patients.

**Post-cardioversion management**

Patients with a newly detected first episode of acute AF converted to sinus rhythm are not continued on rhythm maintenance therapy as the risks of antiarrhythmic therapy outweigh the benefits. They are generally treated by rate control medications; usually a beta blocker. Those with chronic AF with significant symptoms or with structurally abnormal heart may be treated with antiarrhythmic drugs or catheter ablation. Medical therapies aimed at rhythm control offered no survival advantage over rate control and anticoagulation; according to the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial13. Patients presenting within 48 hours of the onset of symptoms and have low thromboembolic risk do not require long-term aspirin or anticoagulation. Long-term anticoagulation is required for patients with identified high risk for thromboembolism even after sinus rhythm has been restored.

**Step 5 - Assessment of Need for Long Term Anticoagulation (Risk of Thromboembolism as well as Risk of Bleeding to be Assessed)**

**Estimation of risk of stroke**

The new European Society of Cardiology4 guidelines for the management of AF recommend CHA2DS2-VASc score for risk stratification and to decide on chronic anticoagulation therapy. The CHA2DS2-VASc score is a clinical prediction rule for estimating the risk of stroke in patients with nonvalvular AF.14 It is used to determine whether or not treatment is required with anticoagulation therapy or antiplatelet therapy. A high CHA2DS2-VASc score corresponds to a greater risk of stroke, while a low CHA2DS2-VASc score corresponds to a lower risk of stroke. The CHA2DS2-VASc score is shown in Tables 1 and 2. In this system, 2 points are assigned for a history of stroke or transient ischemic attack; 2 points for age ≥75 years; and 1 point each for age 65 to 74 years, history of hypertension, diabetes, recent cardiac failure, vascular disease (MI, complex aortic plaque, and peripheral arterial disease) and female sex. Based on the ESC guidelines on AF, oral anticoagulation is recommended or preferred for
The renin-angiotensin-aldosterone system has emerged as an important hormonal system in the initiation and pathogenesis of AF. Therefore, ACE inhibitors and angiotensin receptor blockers are emerging as upstream therapy for the prevention of AF. However, they may not be used as primary or sole anti-arrhythmic therapy in patients with AF.16

Newer Anticoagulants

New drugs for oral anticoagulation include the direct thrombin inhibitor dabigatran as well as the factor Xa inhibitors rivaroxaban, apixaban, and edoxaban. They are faster in onset of action and have a wide therapeutic window, little interaction with food intake, and other drugs compared to vitamin K antagonists. The cumbersome monitoring of the anticoagulation effect associated with vitamin K antagonists is

Table 4: HAS-BLED score

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
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<tbody>
<tr>
<td>H</td>
<td>Hypertension</td>
</tr>
<tr>
<td>D</td>
<td>Abnormal renal function</td>
</tr>
<tr>
<td>A</td>
<td>and liver function (1 point each)</td>
</tr>
<tr>
<td>S</td>
<td>Stroke</td>
</tr>
<tr>
<td>B</td>
<td>Bleeding</td>
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<tr>
<td>L</td>
<td>Labile INRs</td>
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<tr>
<td>E</td>
<td>Elderly (Age ≥ 65 years)</td>
</tr>
<tr>
<td>D</td>
<td>Drugs or alcohol (1 point each)</td>
</tr>
<tr>
<td>Maximum 9 points</td>
<td></td>
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(Hypertension: Systolic blood pressure >160 mmHg. Abnormal kidney function: chronic dialysis or renal transplantation or creatinine ≥ 200 mmol/L. Abnormal liver function: chronic hepatic disease (e.g., cirrhosis) or biochemical evidence of significant hepatic derangement e.g., bilirubin >2x upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/ alkaline phosphatase >3x upper limit of normal). Bleeding: previous bleeding history and/or predisposition to bleeding, for example, bleeding diathesis, anemia. Labile INRs: unstable/high INRs or poor time in therapeutic range (e.g., <60%). Drugs/alcohol use: concomitant use of drugs, such as antiplatelet agents, nonsteroidal anti-inflammatory drugs, or alcohol abuse)
thus not necessary anymore in patients receiving these new drugs. Possible disadvantages of these new molecules include the lack of antidotes, difficulties in effect monitoring, and the short half-life that might pose a problem in patients with low compliance. At present, newer anticoagulants are significantly more expensive than conventional anticoagulants though they avoid the need for frequent prothrombin time monitoring. They are not widely available in India and the indications of their use are only evolving. Moreover they are not approved for valvular AF, in coronary heart disease and in the presence of prosthetic valves. Further studies may find newer anticoagulants to be useful in these conditions as well and with the availability of generic molecules in the future, cost may also come down.

Follow up and Prognosis

Patients presenting with acute AF, whether they have paroxysmal, persistent, or permanent AF need long-term follow-up. Depending on the nature of the underlying cause of AF (CAD, valvular heart disease, or heart failure), patients should have regular cardiac evaluation. Patients who are taking anti-arrhythmic agents need frequent follow-up for ECG monitoring. Exercise stress testing is recommended to assess for risk of ventricular tachycardia in patients taking long term flecainide or propafenone. Patients on amiodarone will require frequent monitoring of thyroid function (once in 3 months) and respiratory function (once in 6 months).

A regular follow-up (monthly) to monitor INR is mandatory for those patients who are taking warfarin for anticoagulation. They should be educated regarding the dietary modifications to be made while on vitamin K antagonists. Routine monitoring of digoxin levels is not required but levels can be checked if toxicity or inadequate dosing is suspected. Patients, who have known triggers to AF, such as alcohol, stimulants, caffeine, or nicotine, should be advised to avoid them to prevent recurrences.

The prognosis of acute AF depends on several factors, such as the precipitating event, underlying cardiac status, risk of thromboembolism, and whether the nature of the AF is paroxysmal, persistent, or permanent. In young patients with no structural cardiac abnormalities who have an episode of acute AF following alcohol binging, prognosis is excellent if further alcohol intake is avoided. In contrast, prognosis for patients presenting with new onset AF with heart failure following myocardial infarction (MI) is poor. Patients with prior AF or new-onset AF following MI need close clinical follow-up.

References