Atrial Fibrillation: How should it be treated?

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Historical Aspect
In 1827 Robert Adams was probably the first person to recognize Atrial Fibrillation (AF) clinically as a sign of mitral stenosis. Hope in 1839 identified irregular pulse in association with mitral stenosis. Etienne Marcy in 1863 published a tracing of atrial fibrillation from a patient with mitral stenosis. Arthur Cushney described it in 1899. Initially AF was termed as Delerium cordes.

Sir Thomas lewis at University college hospital, London recorded atrial fibrillation with electrocardiograph in 1909. In 1935 Bonillanad found that digitalis reduced ventricular rate dramatically even though irregularity of pulse persisted. In 1969, Lown recommended cardioversion of atrial fibrillation.

Introduction
The tachyarrhythmias are either supraventricular or ventricular. Atrial fibrillation is the most common supraventricular tachyarrhythmia encountered by the practicing physician. Atrial fibrillation can be dangerous in patients with short accessory pathways. The rapid fibrillatory waves are conducted along the accessory pathway when AV node is blocked by drugs like verapamil, beta-blockers or digoxin. The rapidly conducted fibrillatory waves across the accessory pathway may result into ventricular fibrillation and sudden death.

Usually 350-600 fibrillatory waves are produced in the atrium with a ventricular response of 100-160 per minute. The mechanism of fibrillatory wave production is believed to be re-entrant. All the fibrillatory waves cannot pass through the AV node resulting into reduced ventricular response. If the fibrillatory waves are 400 per minute and there is 4:1 AV block, the ventricular rate will be 100 per minute. Usually ventricles are protected by natural AV block until the number of fibrillatory waves are reduced to less than 256 per minute by drugs like quinidine and disopyramide. Once all the fibrillatory waves are allowed to pass through the AV node resulting into fast ventricular response. Quinidine and Disopyramide are known to convert atrial fibrillation into sinus rhythm by suppressing the fibrillatory waves. Because of the danger of causing fast ventricular response, drug like dizoxin is used to produce AV block before starting Quinidine or Disopyramide.

Presently the drug of choice in converting atrial fibrillation into sinus rhythm is amiodarone, which not only suppresses the fibrillatory waves but also blocks AV node. IV Ibutilide is another drug that can be used to convert AF into sinus rhythm. Atrial fibrillation in patients with pre-excitation can result into ventricular fibrillation and sudden death. In such a situation, if the patient is haemodynamically compromised, cardioversion should be done immediately. On the other hand, if the patient is haemodynamically stable, Amiodarone or Ibutilide can be given intravenously.

Epidemiology
1.0-1.5% of the general population is affected by AF. According to Miya Saka et al, 15.9 million people in the US are projected to have AF by 2050.

Aetiology
The following conditions are known to produce AF

1. Mitral valve disease
2. Coronary artery disease
3. Hypertensive heart disease
4. Cardiomyopathies
   4.1) Dilated cardiomyopathy
   4.2) Restrictive cardiomyopathy
   4.3) Hypertrophic cardiomyopathy
5. Constrictive pericarditis
6. Atrial septal defect
7. Cor pulmonale
8. Familial AF
9. Lone AF
10. Ventricular diastolic dysfunction
11. Congestive heart failure

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Reversible causes of AF
1. Excess alcohol consumption
2. Post cardiac surgery
3. Electric shock
4. Acute myocardial infarction
5. Acute periartitis.
6. Acute myocarditis
7. Pulmonary embolism
8. Hyperthyroidism

3 P classification
1. Paroxysmal – Terminates spontaneously or with intervention within 7 days.
2. Persistent- Persists more than 7 days.

In AF, warelets propagating in different directions with small irregular baseline undulations of variable amplitude and morphology are seen. Undulations may be coarse, medium and fine. Vagal induced AF is found during sleep and at rest after meal and responds to disopyramide. On the other hand, the adrenergic induced AF is seen during exercise or stress and responds to beta-blockers.

Clinical Features
1. Palpitation
2. Features of thromboembolism
4. Worsening of heart failure

The following physical findings have been described in AF
1. Absence of a wave in JVP
2. Pulse deficit
3. Irregularly irregular ventricular response
4. Slight variation in the intensity of first heart sound.

Investigations
1. Thyroid function test
2. X-ray chest
3. Electrocardiogram
4. Echocardiogram
5. Holter monitoring: 7 day holter or event recorder: Patient triggered or ECG triggered.
6. Electrophysiological study if associated with WPW syndrome

Electrocardiography in AF
- Absent P waves
- Presence of fibrillatory waves
- Irregularly irregular ventricular response.
- Aberrant conduction: Ashman phenomenon.

Aberrant conduction in AF should be differentiation from ventricular extra systole. The characteristics of aberrant conduction in AV are as follows.
1. Initial vector same as conducted beat
2. Absence of compensatory pause
3. Follows long short interval and is known as Ashman Phenomenon.
4. Variable coupling intervals with little tendency to bigeminy.

Ventricular extra systoles may be present in patients with AF. The characteristics of ventricular extra systole in AF are as follows.
1. Monophasic or diphasic QRS in V1
2. Presence of fixed coupling intervals
3. Long cycle ending in anomalous beat
4. LBBB pattern with beginning
5. Presence of compensatory pause.

Management
1. Rhythm control
2. Rate control
3. Prevention of thromboembolism
4. Radio frequency ablation
5. Surgery

Rate Control Versus rhythm control
Control of rate versus Rhythm in Rheumatic Atrial Fibrillation Trial (CRRAFT) from Mumbai in young people has reported an advantage of rhythm control with amiodarone over rate control with regards to exercise to tolerance and quality of life.

In persistent atrial fibrillation, rhythm control can be achieved either by drugs or by cardioversion. Patients with atrial fibrillation converted into sinus rhythm relapse in approximately 50% at 12 months. After the conversion of atrial fibrillation into sinus rhythm, long term antiarrhythmic drugs are advised. Besides amiodarone, fast action IV betablocker esmolol or IV Ibutilide is also effective in converting AF into sinus rhythm. Dizoxin is ineffective in this respect.

Atrial contraction contributes between 20% and 40% of the total stroke volume. The heart rate in AF should be faster than that in sinus rhythm to maintain cardiac output. In AF, ventricular rate between 60-80 beats/min at rest and between 90 and 115 beats/min
during moderate exercise have been recommended by Fuster V and his colleagues, Betablockers or Calcium channel antagonists are commonly used with or without dizoxin in controlling heart rate in AF.

The Atrial Fibrillation Follow up investigation of Rhythm Management (AFFIRM) study has shown no noticeable mortality difference with either a rate-control or a rhythm control strategy. The rhythm control strategy has been shown to be associated with a slightly higher incidence of stroke (7.3% V 5.7%).

The Rate Control Versus Electrical Cardioversion (RACE) trial has reported a non-significant trend towards more end points in the rhythm control arms (22.6% V 17.2%) in patients with hypertension. This relationship has been found to be reversed (12.5% V 17.7%) in normotensive patients.

Strategies of Treatment of Atrial Fibrillation (STAF) study did not show significant difference in primary end point between rate-control and rhythm control. Pharmacological Intervention in Atrial Fibrillation (PIAF) study has shown better exercise performance in the rhythm control strategy but did not show effect on symptoms or quality of life. How to Treat Chronic Atrial Fibrillation (HOTCAFE) study did not show any difference in the primary end point but there was greater incidence of hospitalization in the rhythm control arm.

Use of ACE inhibitors have been shown to be associated with lower incidence of AF and mortality benefit. Patients with AF and Pulmonary disease are advised to take diltiazem or verapamil to control the heart rate AF associated with thyrotoxicosis should be treated with betablocker. AF associated with pregnancy is treated with Dizoxin, betablocker or calcium antagonist.

**Antithrombotic Treatment**

Long term anticoagulation with rate control is safe and effective treatment for non-rheumatic atrial fibrillation. Increased levels of plasma Von Willebrand factor, an index of endothelial damage and soluble P-selection, and index of platelet activation have been reported as indices of prothrombotic state in both non-valvular atrial fibrillation and hypertension separately. Hypertension does not seem to have an independent additive effect on prothrombotic state in atrial fibrillation.

In valvular atrial fibrillation, the incidence of thromboembolism is reported in 9-20% of patients. The risk of stroke and thromboembolism is five fold in non-valvular AF. Annual rate of major bleeding with anticoagulant treatment is 1.3% compared to 1% in control patients. Risk of stroke is reduced by 25% with aspirin. Patients with AF should be treated with anticoagulants and should be started two weeks after the onset of ischaemic stroke due to thromboembolism.

The Prevalence of AF is strongly age dependent affecting 5% of people older than 65 years and nearly 10% of those > 80 years. AF increases the risk of stroke four to five fold accounting for 10-15% of all ischaemic strokes and nearly a quarter of strokes in people > 80 years. Patients with stroke due to AF have a worse outcome. Absence of symptoms does not do confer a more favorable prognosis.

Patients aged >75 years with lone AF are at a high risk of thromboembolism and need thrombophylaxis. Long term anticoagulation treatment of patients with non-valvular atrial fibrillation can reduce the annual risk of stroke by two thirds. Suboptimal anticoagulation has been found to be associated with poor clinical outcomes.

Met analysis of 13 trials has shown significant reduction in ischaemic stroke in patients treated with warfarin. Metaanalysis of six randomized trials has shown significant risk reduction of stroke by 22%. According to Lip and Edwards, warfarin has been found to be superior to aspirin in reducing the risk of ischaemic stroke.

Copenhagen Atrial Fibrillation Aspirin and Anticoagulation Study (AFASAK I), Stroke Prevention in Atrial Fibrillation (SPAF II), European Atrial Fibrillation Trial (EAFT), AFASAK II and Primary Prevention of Atrial Fibrillatiion (PATAF) studies have shown 35% risk reduction of stroke by warfarin compared to aspirin. Patients with high risk of stroke (Previous TIA, Ischaemic CVA, Thromboembolism, Age > 75years with diabetes, Valve disease, Heart failure, or Impaired LV function) should be treated with warfarin. Patients with low risk of stroke (Age < 65years with no history of embolism) may be treated with aspirin.

Data from the Stroke Prevention using the Oral Thrombin inhibitors in Patients with NVAF (SPORTIF III and V studies) have shown promising results in stroke reduction in AF with the use of oral direct thrombin inhibitor, Ximelagatran, which can be used unfixed dosing and monitoring is not needed. Ximelagatran is known to produce abnormal liver function test in 6% of patients.

Patients with AF, who cannot take oral anticoagulant should be given aspirin and clopidogrel.
Radio Frequency Ablation
Catheter ablation for AF was first reported in 1994. According to Bourke and colleagues, following AF ablation of Pulmonary valve, 55% of patients with persistent AF remain in sinus rhythm without the use of antiarrhythmic drugs at 6 month follow up. In Paroxysmal AF, 70% success rate has been reported.16 Macro re-entry circuit in the right atrium has been found in patients with worse atrial fibrillation. Right atrium has been found to be reactivated by break through from the left atrium through the septum in fine atrial fibrillation. Tricuspid anulus – Inferior venacava isthmus (TV-IVC) ablation has been found to have no advantages over electrical cardioversion for the management of coarse atrial fibrillation.17 Patients with infrequent and brief Paroxysms may be suitable for the pill in the pocket approach. Amiodarone is more effective than sotalol and propaferone.

Surgical Ablation
The maze procedure of multiple atrial incisions has recently been modified. Cut and sew techniques, which isolate Pulmonary veins, are carried out. Linear incisions in left atrium connecting to the mitral valve anulus create barriers to conduction eliminating macro reentran t circuits. Usually such procedure is carried out at the time of valve surgery.5

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