Atrial Fibrillation: Current Concepts

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Abstract:
Atrial fibrillation (AF) is the most common arrhythmia which is a focus of newer modalities of treatment, especially ablation techniques using innovative mapping techniques. Its incidence and prevalence increases with aging and presence of structural heart disease, the latter being less than 1% prior to age 40, rising to 8% at age 80. Concomittant morbidity and excessive mortality is related to the increased incidence of stroke and congestive heart failure. Once developed in a clinical setting, it tends to either persist or recur. Pharmacotherapy to control rate or rhythm tends to have a secondary failure, and therefore there is a growing interest in ablation techniques. The use of anticoagulation is also associated with bleeding risks and therefore the management of AF needs to be individualized in every patient. In this article, we shall be discussing clinical types of AF, etiology, the mechanism of genesis, symptoms, complications and approach to treatment in various clinical scenarios.

Keywords: Atrial fibrillation, Radiofrequency ablation, Pharmacology.

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Introduction

Rhythm characteristics and clinical classification

AF occurs when the normal sinus mechanism is replaced by a chaotic and a diffuse pattern of electrical activity in the atria with deterioration of mechanical function. It is characterized by disorganized atrial activity, irregularly irregular ventricular response and stasis of blood in atrium and its appendage resulting in thrombus formation and its propensity to embolisation. On the surface ECG, there is an absence of discernible P waves, which are replaced by fibrillatory waves that vary in amplitude, shape and timing. Rarely the ventricular response may be regular indicating concomitant third degree AV block (complete heart block).

According to a present classification [2], two or more episodes of AF are considered recurrent. Once it is determined to be recurrent, AF is described as paroxysmal (self-terminating), persistent (non-self-terminating), or permanent. Paroxysmal episodes terminate spontaneously, usually in less than seven days, although most terminate within 48 hours. Persistent AF can be the first episode of AF or the culmination of recurrent paroxysmal episodes. When cardioversion fails or it is not attempted, AF becomes permanent in most cases.

Etiology

Paroxysmal AF may be seen acutely during intense emotional stress, following cardiac surgery, sudden or unaccustomed exercise, acute alcoholic intoxication (Holiday heart syndrome), a prominent surge of vagal response (vasovagal activity), use of cocaine, amphetamine or other illicit drugs, acute hypoxia or hypercapnia, acute pneumonia, acute metabolic imbalance, theophylline use in COPD/asthma, hypertensive crisis, acute myocardial infarction, and septicemia [3].

Common clinical causes of persistent AF include: Hypertension, valvular heart disease—rheumatic and non-rheumatic (MS, MR, AS)—thyrotoxicosis, sick sinus syndrome (Tachycardia-bradycardia syndrome), chronic lung disease, cardiomyopathy, atrial septal defect, ischaemic heart disease, constrictive pericarditis, and congestive heart failure [4].

Epidemiology of AF

AF is the most common clinically significant arrhythmia, accounting for most of the hospitalizations related to cardiac rhythm disturbances. In USA, currently approximately 2.5 million Americans which are close to 1% of the total population have AF [5]. AF can be considered as a disease of aging, and with the projected increase in the elderly population in America, the prevalence is expected to be more than double by the year 2050. AF has a major impact on the elderly. It occurs in less than 1% of those between 60 and 65 years of age, but in 8-10% of those older than 80 years. The age-adjusted prevalence is higher in men than in women and higher in whites than in blacks. The prevalence of AF increases with the severity of heart failure and valvular heart disease [6].

Stroke Risk and Mortality

Several studies have demonstrated an increased mortality of a magnitude of approximately two-fold in patients with AF as compared to those in sinus rhythm [7]. One of the most important concerns about AF is the potential for thrombo-embolic events and stroke. The risk of stroke in persons with non-valvular AF is estimated at 5% per year, which is 2 to 7 times the rate for persons without AFib. The presence of AF is a stronger predictor of stroke than all other cardiovascular conditions. The risk factors for stroke in patients with AF have been identified and include prior embolic event or stroke, hypertension, advanced age, left ventricular dysfunction, coronary artery disease and diabetes mellitus. In persons younger than 60 years with no risk factors, the risk of stroke is low, and the risk increases incrementally with each risk factor. The risk of stroke in patients with paroxysmal versus permanent AF is similar [8].

Clinical Presentation and Evaluation

AF has a heterogeneous clinical presentation occurring in the presence or absence of detectable heart disease. Lone AF (in the absence of structural heart disease or obvious etiologic factors) has been reported in 4-35% of cases. Subtle disorders can cause AF and must be considered; in the elderly, these include sub clinical hyperthyroidism and undiagnosed hypertension. Familial AF is a genetically heterogeneous disorder. It is probably more common than previously thought; as many as 5-15% of AF patients have a family history [9]. A minimal initial evaluation of the patient

presenting with AF should include an EKG, chest radiograph, Tran thoracic echocardiogram, and thyroid function tests. The process of "ruling out" myocardial infarction is usually not necessary as AF rarely presents as myocardial infarction or vice versa.

Anticoagulation in AF

A meta-analysis of several randomized studies showed that adjusted-dose oral anticoagulation with warfarin is effective in preventing strokes in patients with non-valvular AF, with a risk reduction of just over 60% compared with placebo [10]. Patients with valvular AF were not included in this meta-analysis, as it is known that this group is at high risk for stroke and should always be treated with full anticoagulation. The target intensity for anticoagulation is an INR between 2 and 3, a range that provides the best balance between efficacy and bleeding risk. Aspirin offers only modest protection, showing less consistency in its benefit compared to warfarin probably because atrial clots are not platelet-rich.

The current American College of Cardiology / American Heart Association / European Society of Cardiology (ACC/AHA/ESC) guidelines on the management of AF mandate that unless there is a contraindication, warfarin should be administered to all patients with AF and risk factors for stroke [11]. In order to simplify the determination of stroke risk in patients with AF and to spare patients the risks and inconvenience of unnecessary anticoagulation therapy, the CHADS2 risk stratification scheme was designed and tested [12]. The CHADS2 acronym is derived from the individual stroke risk factors: Congestive heart failure, hypertension, age >75 years, diabetes mellitus, and prior stroke or transient ischemic attack (TIA). Patients are assigned two points for a previous stroke or TIA and one point for each of the other risk factors. The calculated CHADS2 stroke rate per 100 patient-years increases by a factor of approximately 1.5 for each point increase in CHADS2 score. In patients with a CHADS2 score of 0, the risk of stroke is low. Those with a CHADS2 score of 3 or more and those with a prior TIA or stroke are at high risk. For patients at intermediate risk, the risks and benefits of warfarin therapy should be assessed on an individual basis, including consideration of co-morbidities, risk of major hemorrhage, and patient preference.

In patients with uncomplicated AF who are undergoing procedures that carry a risk of bleeding, anticoagulation can be interrupted for up to one week without the need for heparin. In high-risk patients, such as those with AF and mechanical valves, those with prior stroke or TIA, or when a series of procedures require an interruption for longer than one week, bridging with heparin therapy is recommended, either unfractionated or low-molecular-weight heparin.

Decisions about anticoagulation in the very elderly are more difficult because there is a reported 3-4% risk of major hemorrhage per year in this population. Therefore, the risk factors for stroke should be estimated and weighed against the risk for hemorrhage. Although the ACC/AHA/ESC guidelines recommend lower-intensity anticoagulation (INR range, 1.6-2.5) in patients older than 75 years, a more recent case-control study [13] found that the risk of intracranial hemorrhage was not reduced at INR below 2.0. Therefore, once the decision has been made to treat with anticoagulation, the target INR in elderly patients should be between 2 and 3. INR above 3.5 should be avoided in this age group.

Acute Management of Fib

The acute management of atrial fibrillation depends on associated symptoms, hemodynamic stability, and the accuracy with which onset can be determined. Often, patients cannot reliably tell when atrial fibrillation started because their symptoms are non-specific like fatigue. When symptoms have been present for longer than 48 hours or the duration is uncertain, the anticoagulation therapy must be administered. When the ventricular response is fast, rate control can be achieved with intravenous β-blockers or calcium channel blockers; efficacy is similar for both classes of drugs in the acute setting. A combination of drugs might be necessary, and careful dose titration is important. Cardioversion might be required in hemodynamically unstable patients [14]. Approximately 50% of patients who are presented to the emergency department with atrial fibrillation convert spontaneously within 24 hours.

When atrial fibrillation is persistent, a decision must be made whether to attempt to restore sinus rhythm or not. In those with atrial fibrillation of more than 48 hours' duration, there are two approaches for preventing stroke after

cardioversion. One approach is to treat the patient with rate-controlling drugs and perform the cardioversion after three weeks of adequate anticoagulation with warfarin. The second approach is to perform a Tran esophageal echocardiogram to look for blood clots in the left atrial appendage. If no clot is seen, cardioversion is performed. Both strategies are comparable in terms of stroke risk, death, major bleeding and cardioversion success; the clinical benefit of the latter approach is limited to the relative promptness of the cardioversion. Both approaches require full anticoagulation for at least four weeks following cardioversion. Low-molecular-weight heparin can be used as a bridge to full anticoagulation with warfarin [15].

Electrical cardioversion is performed in the fasting state and under adequate anesthesia. Pharmacologic cardio version is an option when anesthesia is difficult, although electrical conversion is generally preferred because the success rate is much higher. Ibutilide, a class III antiarrhythmic agent, is the only intravenous drug approved for cardioversion by the U.S. Food and Drug Administration (FDA). The main side effect of this drug is a small incidence of polymorphic ventricular tachycardia–torsades de pointes; it should therefore be administered under close cardiac monitoring. The risk of torsades de pointes is higher during the first 30 minutes, but the patient must remain under cardiac monitoring for four hours after administration. The efficacy of pharmacologic cardioversion is not as high as that of electrical cardioversion, and it is more effective in patients whose AF is of short duration. Anticoagulation guidelines following pharmacologic cardioversion are the same as for electrical cardioversion, i.e. for one month [16].

For AF of very recent onset (hours), a bolus of either oral propafenone (600 mg) or flecainide (300 mg) is highly effective for acute cardioversion. This method called as “Pill in Pocket” should be considered only in patients with structurally normal hearts [17].

Long-term management

In patients who tolerate atrial fibrillation well or who are minimally symptomatic, attempt at restoration of normal sinus rhythm is not necessary. In the landmark AFFIRM trial [18], the strategies of rate control and rhythm control resulted in similar clinical results with respect to symptoms, mortality, and stroke risk. More hospitalizations and adverse drug reactions occurred in the rhythm control arm, and the majority of strokes were related to the discontinuation of warfarin or sub therapeutic INR, even in patients in whom sinus rhythm was restored. Thus, this study is the basis for the current recommendation that antiarrhythmic drug therapy and attempts at restoring sinus rhythm should be reserved for patients who are symptomatic and who do not tolerate the rhythm well, whereas rate control alone is a reasonable alternative for those with minimal symptoms. The study also emphasizes that all patients with risk factors for stroke should be treated with warfarin indefinitely, even if they appear to remain in normal sinus rhythm.

Rhythm Control

For highly symptomatic patients, prophylactic therapy with antiarrhythmic agents is often necessary to improve the likelihood of remaining in normal sinus rhythm [19]. The goal is to reduce arrhythmia burden, not to eliminate the arrhythmia; occasional recurrences should not be considered treatment failure. The choice of antiarrhythmic agent is based on safety. Patients with heart disease have a higher risk of adverse events with the use of antiarrhythmic agents, and therapy must be tailored to the type of heart disease present and safety data. The use of these agents requires experience and knowledge of the side effects and drug interactions, and the referral to an electro physiologist is necessary. The potential side effects of antiarrhythmic agents include torsade de pointes, liver and lung toxicity, thyroid gland disorder, gastrointestinal discomfort, and neurological abnormalities. Some drugs, such as sotalol and dofetilide, mandate inpatient initiation. Type IC antiarrhythmic agents are contraindicated in patients with prior myocardial infarction.

Rate Control

Of the oral medications for rate control, β-blockers appear to be marginally superior to calcium channel blockers although both drug types are effective [20]. Digoxin is not extremely effective when used alone, but it is helpful when combined with a calcium channel blocker or a β-blocker, as it enhances the effects of both classes of drugs. The heart rate is considered controlled when the resting average rate is 60-80/min and 90-115/ min during moderate physical activity. In patients

with permanent AF in whom the rate cannot be controlled pharmacologically, the ablation of the AV node with pacemaker implantation can be considered [21]. This procedure is highly effective at improving symptoms in patients with rapid AF, but must be considered as a last resort because it produces irreversible complete heart block.

Newer Therapies

The most important emerging therapy for AF is catheter ablation around the pulmonary veins, which offers the prospect of cure to atrial fibrillation patients [22]. This procedure developed from the recognition that ectopic beats originating from the sleeves of muscles within the pulmonary veins are often triggers of atrial fibrillation. The initial method was aimed at electrically isolating the pulmonary veins. Since then, several strategies have been used to improve the success rate of the procedure; left atrial ablation [23] is a more recently developed strategy that involves isolating a large part of the left atrium near the pulmonary veins, without isolating the pulmonary veins individually. A success rate of 88% at six months was reported in patients with paroxysmal AF who underwent left atrial ablation.

Because the technique for catheter ablation is still in evolution, its role for the general AF population remains unclear. Patients who are considered potential candidates should be referred to experienced centers. The best results are seen in patients with paroxysmal AF and preserved left ventricular function. Serious complications, although rare, can occur and include pulmonary vein stenosis, left atrial flutter, and stroke. Because the long-term effects of the procedure are unknown, it should be limited to patients with refractory AF and disabling symptoms. As this technique is refined, it will increasingly become more available to patients with Fib.

The surgical maze procedure can offer the potential for curing AF, but requires open heart surgery [24]. Therefore, the best candidates are patients with AF undergoing heart surgery for other reasons, such as valve replacement. Less invasive surgical procedures called “mini-maze” are under development, and in early reports, show great promise [25].

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