Atrial fibillation in diabetes: Need for cardiovigilance
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Abstract
Atrial fibillation (AF), the commonest arrhythmia in clinical practice, is also the commonest arrhythmia for which hospitalization is required. AF is associated with a 5 fold increase in stroke, a 2 fold increase in all-cause mortality, and a higher risk of heart failure. Hence, it is imperative to focus on the risk factors and clinical features of this condition, so that it can be prevented and managed in a timely manner. AF is linked with multiple metabolic and endocrine morbidities. This implies that the endocrinologist has an important role to play in AF detection and referral. This review, the first of a two part series, encourages preventive cardiovigilance, and especially electro-cardiovigilance, in diabetes practice.

Keywords: Atrial fibrillation, type 2 diabetes, prevention of atrial fibrillation, cardiovigilance.

Definition
Atrial fibillation (AF) is a supraventricular arrhythmia which presents with low-amplitude baseline oscillations (fibrillatory or f waves from fibrillating atria), and an irregularly irregular ventricular rhythm. The f waves vary in amplitude, shape and timing, and usually beat at a frequency of 300 to 600/minute1. It must be differentially diagnosed from other atrial tachyarrhythmias.

Classification
AF can be classified according to its temporal profile, or according to the autonomic environment it occurs in2. The various types of AF are listed in Table 1.

Table 1: Classification of Atrial Fibrillation (AF)
- **Paroxysmal AF**: terminates spontaneously within 7 days
- **Persistent AF**: presents continuously for more than 7 days
- **Long standing persistent AF**: persists for longer than 1 year
- **Permanent AF**: AF refractory to cardioversion
- **Lone AF**: AF in persons younger than 60 years without hypertension or evidence of structural heart disease.
- **Vagotonic AF**: AF is initiated in a setting of high vagal tone (evening; during relaxation/sleep).
- **Adrenergic AF**: AF is initiated in a high sympathetic setting (strenuous exertion).
- **Tachycardia-induced AF**: due to tachycardia e.g., AV nodal reentrant tachycardia, WPW (Wolff-Parkinson-White) syndrome.
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Table 2: Risk Factors For Atrial Fibrillation
- **Non-modifiable**
  - Age
  - Gender
  - Familial AF (mutations)
- **Vasculo-metabolic**
  - Hypertension
  - Obesity
    - Atrial dilation
    - Systemic inflammation
    - Epicardial fat deposition
      - Adipocyte infiltration in to atrial muscle
      - Atrial fibrosis due to adipokines
      - Local secretion of pro-inflammatory factors
  - Diabetes
    - Macrovascular complications of diabetes
    - Microvascular complications of diabetes
  - Obstructive sleep apnoea
    - Hypoxia
    - Surge in autonomic tone
    - Hypertension
- **Cardiac**
  - Left atrial enlargement
  - Valvular disease
    - Aortic
    - Mitral
  - Cardiomyopathy
    - Hypertrophic
    - Dilated
    - Restrictive
      - amyloidosis
  - Constrictive pericarditis
  - Cardiac tumours
  - Severe pulmonary hypertension
- **Others**
  - Thyrotoxicosis
  - Psoriasis
  - Alcohol intake (holiday heart)

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Risk Factors

Multiple risk factors are associated with AF. We classify these from an endocrine perspective (Table 2). The ORBIT-AF registry shows that persons with diabetes form a significant (29.5%) proportion of all patients with AF. They are likely to be younger, have hypertension, chronic kidney disease, heart failure, coronary heart disease and stroke. They also have a poorer quality of life, and are more likely to receive anticoagulation. They experience a higher morbidity and mortality risk, including cardiovascular hospitalization, hospitalization, cardiovascular death, sudden cause death, and non-cardiovascular death. However, no difference in risk of thromboembolic events, bleeding-related hospitalization, new-onset heart failure, and atrial fibrillation progression. Thyrotoxicosis is the most common correctable cause of AF.

Mechanisms

AF is a complex arrhythmia, which can occur due to a variety of mechanisms. These are unique in different individuals. Mechanisms for triggering AF are separate from those which maintain it. Rapid discharges from the pulmonary veins are the most frequent triggers of AF, and also contribute to maintenance. Discharges from the atria, especially in a fibrotic atrium, perpetuate AF as well.

Familial AF may occur due to polymorphisms in genes related to potassium and sodium channels, sarcoplasm, renin-angiotensin system, connexin-40, endothelial nitric oxide synthase, and interleukin-40 These lead to abnormalities in calcium handling, fibrosis, conduction and inflammation.

Symptoms

AF presents with a variety of complaints, ranging from none to disability. Symptoms include palpitations, breathlessness, effort intolerance, easy fatigability and lightheadedness. Concomitant release of atrial natriuretic peptide may cause polyuria. A long sinus pause on termination of AF can lead to syncope in some patients. Neurocardiogenic or vasodepressor syncope can also occur due to ventricular tachycardia associated with severe drop in blood pressure.

At least 25% of all AF patients are asymptomatic, and history taking alone does not suffice in screening. Partly because of this, AF may present directly with a thromboembolic event or florid congestive cardiac failure.

Physical examination reveals an irregularly irregular pulse, a pulse deficit (apical rate > peripheral pulse rate) irregular jugular venous pulsations, and variable intensity of first heart sound. The pulse deficit occurs as short R-R intervals do not allow left ventricular diastolic filling to occur, thus causing a low stroke volume.

Diagnosis

In persons with complaints or signs suggestive of AF, ambulatory monitoring must be done. Depending upon the frequency of symptoms, a 24 hour Holter or 2-4 week long monitor may be warranted.

History taking should explore the precipitating factors, settings, timing and frequency of symptoms, as well as factors which lead to resolution. One should also search for correctible causes such as hyperthyroidism, alcohol intake, structural heart disease and diabetes. Laboratory testing should focus on exclusion or identification of these causes as well Echocardiography, chest radiography and stress test must be performed as required.

Prevention

Primary Prevention

Primary prevention of AF aims to prevent the condition in persons in whom risk factors are present. This will include, from an endocrine perspective, strategies to prevent and manage obesity, obstructive sleep apnoea and hyperthyroidism, as well as limit complication of diabetes.

Secondary Prevention

Once AF has occurred, a major aim of intervention is to prevent thromboembolic events (e.g.; stroke). Such secondary prevention may be done using aspirin, warfarin, low molecular weight heparin or novel oral anticoagulants (NOACs). Risk stratification helps in calculating risk benefit ratio and informing choice of anticoagulant therapy. One must quantify risk of a thromboembolic event, and balance it against potential risk of iatrogenic bleeding with anticoagulant therapy.

The strongest predictors of stroke in AF are previous history of stroke, diabetes, hypertension, heart failure and age ≥70 years. The CHADS2 score helps stratify risk of patients according to presence of risk factors (cardiac failure, hypertension, age diabetes, and stroke). Though CHADS 2 is simple to use, it is unable to distinguish low risk from intermediate risk patients. This can be done using CHA2DS2-VASc scoring. Cardiac failure, hypertension, diabetes, vascular disease, age 65-74 years, and female gender are given a score of 1 point each, while 2 points are allotted to age ≥75 years and prior stroke or transient ischaemic event.

Apart from the predictors listed in CHA2DS2-VASc, renal failure (both non end stage and end stage) is an
independent risk factor for AF\(^9\). Renal function should therefore be assessed while stratifying risk and planning anticoagulant prophylaxis.

The burden of thromboembolic complications seems to be similar in persistent and paroxysmal AF, and guidelines do not differentiate between the two.

Risk of bleeding informs risk benefit calculations for AF secondary prevention as well. This can be quantified objectively using the HAS-BLED score\(^{10}\). This index scores 1 point for each of hypertension, abnormal renal/hepatic function, stroke, bleeding history or predisposition, labile international normalized ratio(INR), elderly(>75 years), and concomitant drug (anti platelet agent or non-steroidal anti-inflammatory drug) or alcohol use. The higher the score, the more the risk of bleeding.

One must individualize the decision to anticoagulate with warfarin, direct thrombin inhibitors or factor X inhibitors. Aspirin is useful as mono therapy only in persons with CHA\(_2\)DS\(_2\)-VASc score of 0. Even aspirin can be omitted if non valvular AF is associated with a CHA\(_2\)DS\(_2\)-VASc score of 0. At score 1, the choice is between aspirin, oral anticoagulant or no therapy. This is based upon risk of bleeding. Aspirin and clopidogrel combination can be used in patients with score>1 and intolerance to warfarin or NOACs\(^1,2\).

**Tertiary Prevention**

AF management retains its relevance even if a thromboembolic event has occurred. The most important predictor of occurrence of stroke is history of prior stroke. Thus persons with history of stroke must receive prophylactic anticoagulant therapy. This, along with post-stroke rehabilitation, forms the crux of tertiary prevention. The acute management of AF complicated by stroke is also a part of tertiary prevention.

**Quaternary Prevention**

The philosophy of quaternary prevention\(^{11}\) enjoins us to avoid over diagnosis, over labelling and overtreatment. Scrupulous adherence to guidelines for screening, diagnosis, treatment of AF, and prevention of its complications is mandatory. Anticoagulation should be prescribed based upon risk stratification. Safer drugs such as NOACs must be preferred to reduce the risk of iatrogenic complications such as bleeding.

**Summary**

AF is a significant cause of morbidity and mortality. Its epidemiologic risk factors are such that there is great overlap between AF and diabetes. Endocrinologists must keep a high index of clinical suspicion for AF in their patients. Timely screening, diagnosis and referral can help early institution of therapy and prevent potentially life-threatening complications.

**References**

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