



Article 1
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Subclinical Atrial Fibrillation

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice. Global burden of disease study published in 2014 reported increasing prevalence of AF as we see some of the cardiovascular diseases are showing a decline in prevalence. Age adjusted prevalence of AF in year 1990 was 569.5 per 100,000 population in men which increased to 596.1 by year 2010. Similarly the prevalence increased in women from 359.9 to 373.1 per 100,000 population from 1990 to 2010¹. Similar trend is reported in South Asian Countries although the prevalence might be higher. Increase in prevalence is ascribed to increase in risk factors for AF (Aging, Hypertension, Coronary Heart Disease, Diabetes etc.)². There are no population-wide studies related to epidemiology and risk factors for AF in India. Knowing the increasing prevalence of hypertension, obesity and coronary heart disease we expect higher incidence and prevalence of AF in India compared to developed countries. Persistence of rheumatic heart disease in this region adds to this burden.

Risk Factors for AF

There are number of risk factors which increase the possibility of developing AF. These are clinical risk factors e.g. hypertension, valvular heart disease, heart failure, congenital heart disease, diabetes and metabolic syndrome, chronic kidney disease, sleep apnea syndrome and coronary heart disease³. Some reversible risk factors are hyperthyroidism overt as well as subclinical⁴, cardiopulmonary infections, air pollution⁵ and alcohol intake. Non modifiable risk factors are age and gender. Prevalence of AF increases with age¹ and prevalence is more in males⁶. Genetic factors are also responsible as 5% of patients have family history of AF⁷.

Classification

Classification of AF is based on recommendations by American Heart association and American College of Cardiology in Heart Rhythm Society Guidelines on AF management⁸. Various classes of AF patients are as follows.

1. *Paroxysmal (Intermittent and self terminating) AF*: Atrial Fibrillation that terminates spontaneously or with interventions within seven days of onset. Episodes are recurrent.
2. *Persistent AF*: AF that fails to self terminate within seven days. It needs pharmacological or electrical cardioversion. Patients might get episodes of paroxysmal AF on follow up and the disease is progressive.
3. *Longstanding persistent AF*: AF that has lasted for more than 12 months.
4. *Permanent AF*: Individuals who have persistent AF and there is joint decision by patient and clinician to no longer to pursue a rhythm control strategy.
5. *Lone AF*: AF seen in patients less than 60 year age with no structural heart disease. Embolic complications are very low that anticoagulation is not needed.

This classification includes only the patients who have clinically documented AF.

There are a number of patients who do get short episodes of AF but it is not documented clinically. They came to light only after we had devices used for long term monitoring. In a good number of patients who have risk factors for AF, long term monitoring reveals short episodes (at least 5 minutes) of AF. This has been termed as subclinical atrial fibrillation (SCAF). These patients are not included in above mentioned classification.

Subclinical Atrial Fibrillation (SCAF)

Atrial Fibrillation is a well known risk factor for ischemic stroke and systemic embolism, however, temporal relationship between two needs more understanding⁹. Logically, to prevent complication of AF, we should be able to detect AF early and implement preventive measures. Usually we correlate AF with embolic event when we document AF. But this is rather less common. We may be lucky enough to pick up AF during clinical visit of patient. We may take chance of prolonged observation of patient in hospital or clinic with bedside monitoring. The extension of this is short term monitoring in outpatient setting with use of electronic recording device (Holter Monitor). We may use extended Holter monitoring for few days to catch the culprit. Even then we are missing lot of patients with paroxysmal AF. Recently we have been using long term monitoring for weeks, months and even years to check for presence of arrhythmias which we have not been able to detect by short term monitoring. A subcutaneous device is used which is kept in place as long as we require. Device is called Internal Loop Recorder (ILR).

On behalf of ASSERT investigators, Michela Brambatti and others studied the temporal relationship between AF which was not documented clinically but was picked up on prolonged monitoring what they called Sub Clinical AF (SCAF)¹⁰.

They enrolled 2580 patients aged >65yr, with history of hypertension who underwent initial implantation of dual chamber pacemaker or implantable cardioverter-defibrillator. (ASSERT-I). Patients who had history of clinical AF or were on oral anticoagulants for any reason were excluded. Device was used in patients for 0.8-2.4 years. Episodes of AF for more than 5 minutes were labeled as Sub Clinical AF (SCAF).

They found that although presence of SCAF was associated with increased risk of stroke and embolism compared to those who did not have SCAF, very few patients had SCAF in the month before their event.

Recently a study was published ahead of print in August 2017 by ASSERT 2 investigators. Study is named "Subclinical Atrial Fibrillation in Older patients"¹¹ 256 Enrolled patients were >65 yr old with no history of atrial fibrillation but were high risk patients with CHA2DS2-VASc score of equal to or greater than 2, some patients had sleep apnea, or BMI >30. Other eligibility criteria were left atrial enlargement (>4.4cm or volume >58ml) or increased serum NT-ProBNP (>290pg/ml). Patients were monitored for detection of AF episodes for 5 minutes or longer.

The conclusion of study was that SCAF is frequently detected by continuous electrocardiographic monitoring in older patients without any history of AF who are attending outpatient cardiology and neurology clinic but clinical significance is not clear as yet.

ASSERT studies highlight the importance of use of long term monitors to detect presence of atrial fibrillation especially in cryptogenic strokes and patients with clinically high risk for AF. ASSERT-I investigators established that SCAF is common in patients with implanted pacemakers and defibrillators and stroke risk was high in these patients.

Now the results of ASSERT-II demonstrate that SCAF is not unique to patients with implanted pacemakers and defibrillators, but is also seen in elderly patients aged 65 years or older, who have cardiovascular and stroke risk factors.

There is no doubt that AF is a strong risk factor for strokes and embolism. Equally clear is the fact that anticoagulants are highly effective in reducing number of strokes and embolic events in AF. Should we use anticoagulants in SCAF or for that matter in high risk patients to prevent these disabling complications? Will the use of anticoagulants be cost effective in these patients? These questions need answers and further studies are needed to make things clear.

Two studies are underway which might prove helpful to evaluate whether empiric anticoagulation will be helpful in high risk patients with cryptogenic strokes. These trials are:

Apixaban For Treatment of Embolic Stroke of Undetermined Source. (ATTICUS)

Rivaroxaban Versus Aspirin in Secondary Prevention of Stroke and Prevention of Systemic Embolism in Patients With Recent Embolic Stroke of Undetermined Source (NAVIGATE ESUS).

References:

1. Chugh SS, Havmoeller R, Naranan K, et al. Worldwide Epidemiology of Atrial Fibrillation: a Global Burden of Disease 2010 Study. *Circulation*. 2014; 129:837
2. Global Burden of Diseases 2013 Risk Factors Collaborators. Global, regional and national comparative risk assessment of 79 behavioral, environmental and occupational and metabolic risks or clusters of risks in 188 countries 1990-2013: a systematic analysis for GBD 2013. *Lancet*. 2015;386:2287
3. Narasimhan C, Verma JS, Kishore AGR et al. Cardiovascular risk profile and management of atrial fibrillation in India. Real world data from Realise-AF survey. *Indian Heart J*. 2016
4. Auer J, Scheibner P, Mische T et al. Subclinical Hyperthyroidism as a risk factor For atrial fibrillation. *Am. Heart J*. 2001;142:838
5. Link MS, Luttmann-Gibson H, Schwartz J, et al. Acute Exposure to air pollution triggers Atrial Fibrillation. *J. Am Coll Cardiol*. 2013;62:816
6. Go AS, Helen EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation adults: national implications for rhythm management and stroke prevention: Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study. *JAMA*. 2001;285:2370
7. Fox CS, Parish H, D'Agostino RB, et al. Parental Atrial Fibrillation as risk factor for atrial fibrillation in offspring. *JAMA*;291:2851
8. January CT, Wann LS, Alpert JS, et al Task Force Members. 2014 AHA/ACC/HRS guideline for management patients with atrial fibrillation: a report of American College of Cardiology/American Heart association Task Force on Practice Guidelines and Heart Rhythm society. *Circulation*. 2014;130(23): e199
9. Wolf PA, Abbot RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*. 1991;22:983
10. Brambatti M, Connolly SJ, Gold MR, et al. Temporal relationship between subclinical atrial fibrillation and embolic events. *Circulation*. 2014;129(21):2094
11. Healy JS, Alings M, Ha AC, et al. *Circulation*; 2017 Aug; Epub Ahead of Print.

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