



Atrial fibrillation (AF) is the most common sustained cardiac rhythm disturbance for which patients seek medical attention. AF has a heterogeneous clinical presentation, occurring in the presence or absence of detectable heart disease or related symptoms. Depending upon the duration and response to pharmacological and electrical cardioversion, AF can be classified as paroxysmal, persistent, or permanent. AF can be isolated or associated with other arrhythmias, often atrial flutter or atrial tachycardia. Minimum clinical evaluation of a patient with AF includes history, physical examination, and ECG documentation by at least single-lead ECG recording during the dysrhythmia. Additional investigation may include Holter monitoring, exercise testing, transesophageal echocardiography, and/or electrophysiological study.

Key words: arrhythmia, atrial fibrillation, Holter monitoring, atrial tachycardia

Atrial Fibrillation: Etiology, Diagnosis, and Initial Workup

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Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia.¹ Even in the absence of other cardiac abnormalities, the loss of effective atrial contraction and the inappropriately rapid ventricular rates during AF result in depressed cardiac function and promote the formation of intracardiac thrombi.² The incidence of AF is increasing, not only because the population is aging but also because more patients are surviving the acute phase of cardiac illness that formerly would have been fatal.²

According to population studies, the overall prevalence of AF is 0.4% or two million people in the United States,³ with most persons older than the age of 65.⁴ AF is a disease of older adults; its prevalence is low in children and young adults, but it becomes progressively more common in older age groups, reaching 3–5% in those over age 65⁵ and almost 9% in those over 80 years.⁶ The Manitoba Follow-up Study in Canada reported an incidence rate of two per 1,000 person years. The incidence of AF positively correlated with age, being less than 0.5 per 1,000 person years below the age of 50 and increasing to 2.3 per 1,000 person years by the age of 60.⁷

AF is an independent risk factor for cardiac mortality and morbidity as well as total mortality, with the risk increasing significantly with age.⁸ One of the

serious outcomes associated with AF is stroke, which occurs at an annual rate of 4.5%.^{5,9} AF is a powerful risk factor for thromboembolism, raising the risk of ischemic strokes five-fold. Because AF is common among older people, 14% of all strokes in United States are attributable to AF.⁵

Definition

Atrial fibrillation is an atrial tachyarrhythmia characterized by predominantly uncoordinated atrial activation with consequent deterioration of atrial mechanical function (Figure 1). On ECG, AF is indicated by the absence of consistent P waves; instead, there are rapid oscillations or fibrillatory waves that vary in size, shape, and timing, and are generally associated with an irregular ventricular response when atrioventricular conduction is intact.¹⁰ The ventricular response in AF depends on the electrophysiological properties of the AV node, the level of vagal and sympathetic tone, and drugs that affect AV nodal conduction.¹¹ However, regular RR intervals are possible in the presence of AV block or interference by ventricular or junctional tachycardia or drug therapy. A rapid, irregular, sustained wide QRS complex tachycardia should suggest AF with conduction over an accessory pathway or AF with bundle branch block. Extremely rapid rates (over 200 bpm) suggest the presence of an accessory pathway.¹²

Table 1: Classification of Atrial Fibrillation

| Terminology | Clinical Features | Arrhythmia Pattern |
|---|--|----------------------|
| Initial Event (first detected episode) | Symptomatic Asymptomatic (first detected) Onset unknown (first detected) | May or may not recur |
| Paroxysmal | Spontaneous termination <7days and most often <48hrs | Recurrent |
| Persistent | Not self-terminating Lasting >7days Or prior cardioversion | Recurrent |
| Permanent | Not terminated Terminated but relapsed No cardioversion attempt | Established |

Diagnosis and Clinical Classification

AF has a heterogeneous clinical presentation. It may occur in the presence or absence of detectable heart disease or related symptoms. An episode of AF may be self-terminating or may require medical intervention for termination. The clinician dealing with an episode of AF has to define the pattern over time, which includes the number as well as duration

of episodes, mode of onset, possible triggers, and response to therapy. Although the pattern of arrhythmia may change over time, it is of clinical value to characterize the arrhythmia at a given moment. Therefore, it appears necessary to classify various subsets of patients with AF in order to address properly the management of each patient subset.¹²

It is important for the clinician to ascertain whether an episode of AF is the

very first episode, that is, the initial event; whether it is symptomatic or not; and whether it is self-terminating or not. If the patient has had two or more episodes, AF is said to be recurrent. This terminology applies to episodes of AF lasting for more than 30 seconds. Depending upon the mode of presentation of these episodes, AF can be classified into the following groups (Table 1):¹²

Paroxysmal AF: The episodes of paroxysmal AF usually self-terminate within 48 hours and, by definition, in fewer than seven days.

Persistent AF: When an episode of AF has lasted longer than seven days, AF is designated as persistent. In that case, termination by pharmacological therapy or cardioversion may be required. The time frame of seven days, although arbitrary, represents the limit beyond which spontaneous cardioversion is unlikely to occur, and the success rate of pharmacological cardioversion is low. Persistent AF may be the first presentation of the arrhythmia or may be preceded by recurrent episodes of paroxysmal AF. When AF is persistent, termination by electrical cardioversion may be required.

Permanent or established AF: When AF is present for some time and fails to terminate using cardioversion, or is terminated but relapses within 24 hours, it is said to be permanent or established. Permanent AF may be the first presentation of a nonself-terminating arrhythmia, or be preceded by recurrent self-terminating episodes. Cases of longstanding AF in which cardioversion has not been indicated and/or attempted (e.g., not wanted by the patient) are also placed in this category.

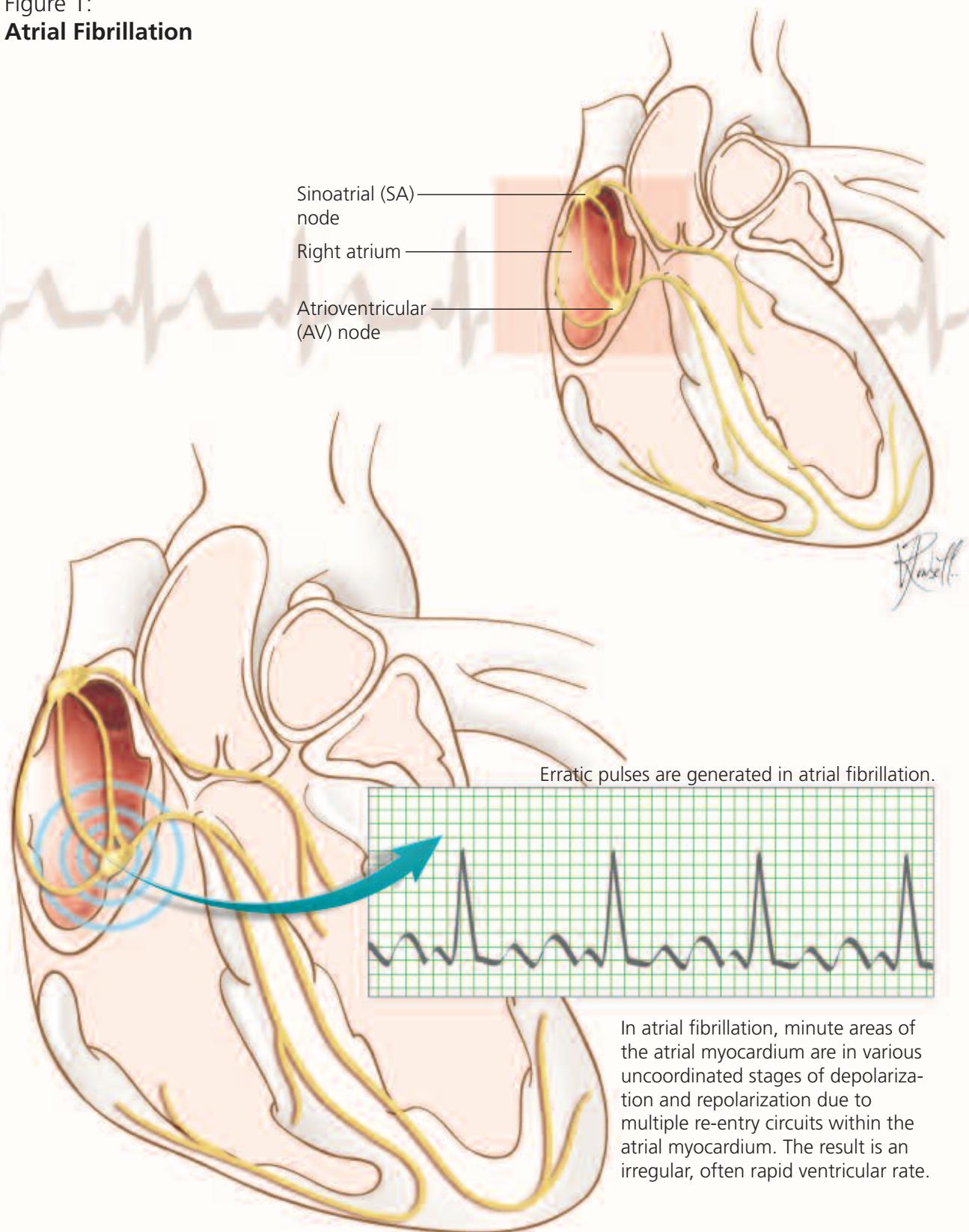
Etiopathophysiology

AF occurs far more commonly in patients with structural heart disease (Table 2). Approximately 25% of patients with AF have coronary artery disease as an antecedent diagnosis.¹ AF in the setting of acute myocardial infarction is uncommon, occurring in 11% of patients, but is associated with a 40% mortality.¹³ AF occurs in approximately one-third of

Table 2: Conditions Associated with Atrial Fibrillation

| Primary Cardiac Diseases | Primary Noncardiac Diseases |
|---|-----------------------------------|
| Coronary artery disease | Systemic hypertension |
| Dilated cardiomyopathy | Diabetes mellitus |
| Rheumatic valvular heart disease | Hyperthyroidism |
| Hypertrophic cardiomyopathy | Pulmonary diseases |
| Cardiac tumours | Chronic obstructive lung diseases |
| Nonrheumatic valvular diseases | Primary pulmonary hypertension |
| Pericarditis | Acute pulmonary embolism |
| Cardiac arrhythmias | Acute ethanol ingestion |
| Atrial tachycardia | |
| Atrial flutter | |
| Atrioventricular nodal re-entrant tachycardia | |
| Wolff-Parkinson White syndrome | |
| Sick sinus syndrome | |

Figure 1:
Atrial Fibrillation



patients undergoing coronary artery bypass surgery.¹⁴ The onset is within the first three days postoperatively, and the arrhythmia mostly self-terminates within the first week. Postoperatively, AF adds significantly to the hospital stay and cost, and attempts to restore sinus rhythm in this setting are usually met with limited success.¹⁴

Rheumatic valvular heart disease increases the risk of having atrial fibrillation by 14-fold and increases the risk of having a thromboembolic complication by four-fold.¹⁵ AF can occur postoperatively in as many as 60% of patients having valvular surgery.¹⁶

Approximately 19% of patients with left ventricular dysfunction have AF.¹⁷

Cardiac tumours such as atrial myxomas can also be associated with AF.¹⁸

AF can occur as a cardiac sequel of other noncardiac diseases. Systemic hypertension is present in about 45% of patients with AF.¹ Diabetes mellitus is found in about 10% of patients with AF.¹ Thyroid disease is an unusual and sometimes overlooked cause of AF, occurring in about 2% of patients.¹⁹ AF is found in about 3% of patients with chronic obstructive pulmonary disease and is associated with increased mortality. Acute pulmonary embolism can present as a new-onset atrial fibrillation.

Other cardiac arrhythmias have a strong association with atrial fibrillation. Patients with atrial tachycardias, atrioventricular nodal reentrant tachycardia, and sick sinus syndrome can develop atrial fibrillation.²⁰ Approximately 10% of patients with Wolff-Parkinson-White syndrome may have AF; removal of the accessory pathway eliminates AF in over 90% of patients.²¹

Approximately 3% of patients with atrial fibrillation have no identifiable cause. Known as lone atrial fibrillation, this entity does not carry a high thromboembolic risk in younger patients, but the risk may increase in patients afflicted at an older age or in the presence of systemic hypertension.²²

Initial Workup

History and physical examination constitute an important part of the initial assessment of patients with AF. Many patients first presenting with AF have palpitations, exertional fatigue, or lightheadedness. History and physical examination should be directed towards establishing the degree of clinical compromise caused by AF and establishing the risk of complications (Table 3). Patients with uncontrolled ventricular rates may present with features of congestive cardiac failure or myocardial ischemia.

ECG remains the main tool for the diagnosis of AF. A 12-lead ECG can establish the diagnosis most accurately and determine the ventricular rate as well as evidence of cardiac ischemia or ventricu-

Table 3: Clinical Evaluation of Patients with Atrial Fibrillation

Minimum Evaluation

1. History and physical examination, to define

- The presence and nature of symptoms associated with AF
- The clinical type of AF (first episode, paroxysmal, persistent, or permanent)
- The onset of the first symptomatic attack or date of discovery of AF
- The frequency, duration, precipitating factor, and modes of termination of AF
- The response to any pharmacological agents that have been administered
- The presence of any underlying heart disease or other reversible conditions (such as hyperthyroidism or alcohol consumption)

2. Electrocardiogram, to identify

- Rhythm (to verify AF)
- LV hypertrophy
- P-wave duration and morphology or fibrillatory waves
- Pre-excitation
- Bundle-branch block
- Prior MI
- Other atrial arrhythmias
- To measure and follow the RR, QRS, and QT intervals in conjunction with antiarrhythmic drug therapy

3. Chest radiograph, to evaluate

- The lung parenchyma, when clinical findings suggest an abnormality
- The pulmonary vasculature, when clinical findings suggest an abnormality

4. Echocardiogram to identify

- Valvular heart disease
- Left and right atrial size
- LV size and function
- Peak RV pressure (pulmonary hypertension)
- LV hypertrophy
- LA thrombus
- Pericardial disease

5. Blood tests of thyroid function

- For the first episode of AF
- When the ventricular rate is difficult to control
- When AF recurs unexpectedly after cardioversion

lar pre-excitation. If the ECG reveals a slow, regular ventricular response in the setting of atrial fibrillation, suspicion of digitalis toxicity or complete heart block should be raised.

ECG is easy to perform and inexpensive; however, the paroxysmal (and frequently asymptomatic) nature of AF in most patients limits the value of usual 12-lead ECG as a screening test for AF. A negative single ECG, therefore, has limited sensitivity, which may be improved by ECG monitoring. The diagnosis of AF requires ECG documentation by at least a single ECG lead recorded during the arrhythmia, which may be facilitated by review of emergency department records, Holter monitoring, or transtelephonic or telemetric recordings. A portable ECG recording tool may help establish the diagnosis in cases of paroxysmal AF and provide a permanent ECG record of the dysrhythmia. If episodes are frequent, a 24-hour Holter monitor can be used. If episodes are infrequent, then an event recorder, which allows the patient to transmit the ECG to a recording facility when the arrhythmia occurs, may be more useful.²³

In patients with implanted pacemakers, there is a unique possibility of monitoring of the intra-atrial electrograms.^{24,25} Morphological and functional information on the atria, ventricles, and valves can be obtained with two-dimensional, colour flow, and Doppler echocardiography. Exercise testing can be considered in the patients in whom ischemia or an increased risk for coronary artery disease is suspected. Thyroid function tests should be checked because hyperthyroidism represents a potentially reversible cause for AF (Table 4).¹⁵

Chest radiography can identify the abnormalities in cardiac silhouette or evidence of pulmonary congestion. Patients with longstanding hypertension, coronary artery disease, decreased left ventricular function, valvular abnormalities, and ECG abnormalities compatible with left ventricular hypertrophy might benefit from aggressive screening for AF, though such an approach has yet to be shown to be beneficial. Educating the public to recognize cardiac arrhythmia can help in early detection of patients with AF.

Patients can identify an irregular heartbeat by monitoring their wrist pulse for one minute. The Research Centre for Stroke and Heart Disease (www.stroke-heart.org) has initiated a campaign called "take your pulse for life." During this project, people, particularly those older than 55 years, are asked to monitor their pulse for one minute the first day of every month. This can help in early detection of AF in this group of patients.

Summary

In summary, AF is the most common chronic tachycardia, affecting 5% of people over the age of 65. Several cardiac and noncardiac disorders predispose to AF, though AF can occur in the absence of any disease. The clinical classification divides AF into paroxysmal, persistent, and permanent forms and helps the clinician in selecting the correct therapeutic option. The clinical evaluation of AF requires history, physical examination, ECG documentation of the episode of arrhythmia, and investigations to evaluate the cardiac status and associated disease states. ♦

Table 4: Clinical Evaluation of Patients with Atrial Fibrillation

| Additional Testing | No competing financial interests declared. |
|---|--|
| One or several of the following may be necessary: | |
| 1. Exercise testing | |
| <ul style="list-style-type: none"> – If the adequacy of rate control is in question (permanent AF) – To reproduce exercise-induced AF – To exclude ischemia before treatment of selected patients with type IC antiarrhythmic drug | |
| 2. Holter monitoring or event recording | |
| <ul style="list-style-type: none"> – If diagnosis of the type of arrhythmia is in question – As a means of evaluating rate control | |
| 3. Transesophageal echocardiography | |
| <ul style="list-style-type: none"> – To identify LA thrombus (in the LA appendage) – To guide cardioversion | |
| 4. Electrophysiological Study | |
| <ul style="list-style-type: none"> – To clarify the mechanism of wide-QRS-complex tachycardia – To identify a predisposing arrhythmia such as atrial flutter or PSVT – Seeking sites for curative ablation or AV conduction block/modification | |
| References | |
| <ol style="list-style-type: none"> 1. Kannel WB, Abbott RD, Savage DD, et al. Epidemiological features of chronic atrial fibrillation: the Framingham study. <i>N Engl J Med</i> 1982;306:1018-22. 2. Gosselink ATM, Crijns HJGM, Van Den Berg MP, et al. Functional capacity before and after cardioversion of atrial fibrillation: a controlled study. <i>Br Heart J</i> 1994;72:161-6. 3. Domanski MJ. The epidemiology of atrial fibrillation. <i>Coron Artery Dis</i> 1995;6:95-100. 4. Psalty BM, Manolio TA, Kuller LH, et al. Incidence and risk factors for atrial fibrillation in older adults. <i>Circulation</i> 1997;96:2455-61. 5. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. <i>Stroke</i> 1991;22:983-8. 6. Kannel WB, Wolf PA, Benjamin EJ, et al. Prevalence, incidence, prognosis and predisposing conditions for atrial fibrillation: population based estimates. <i>Am J Cardiol</i> 1998;82:2-9N. 7. Krahn AD, Manfreda J, Tate RB, et al. The natural history of atrial fibrillation: incidence, risk factors, and prognosis in the | |

Atrial Fibrillation

Manitoba follow-up study. *Am J Med* 1995;98:476-84.

- 8. Benjamin EJ, Wolf PA, D'Agostino RB, et al. Impact of atrial fibrillation on the risk of death: the Framingham heart study. *Circulation* 1998;98:946-52.
- 9. Leckey R, Aguirre EJ, Phillips SJ. Atrial fibrillation and the use of warfarin in patients admitted to an acute stroke unit. *Can J Cardiol* 2000;16:481-5.
- 10. Ballet S. Clinical disorders of the heart beat. Philadelphia: Lea and Fibiger, 1971: 223-33.
- 11. Prystowsky E, Katz A. Atrial fibrillation. In Topol EJ, ed: *Textbook of cardiovascular medicine*. Philadelphia: Lippincott-Raven, 1998: 1661-89.
- 12. Levy S, Camm AJ, Saksena S, et al. International consensus on nomenclature and classification of atrial fibrillation. *J Cardiovasc Electrophys* 2003;14:443-5.
- 13. Skata K, Kurihara H, Iwamori K, et al. Clinical and prognostic significance of atrial fibrillation in acute myocardial infarction. *Am J Cardiol* 1997;80:1522-7.
- 14. Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. *Circulation* 1996;94:390-7.
- 15. Pelosi F, Morady F. Evaluation and management of atrial fibrillation. *Med Clin North Am* 2001;85:225-44.
- 16. Creswell LL, Schuessler RB, Rosenbloom M, et al. Hazards of postoperative atrial arrhythmias. *Ann Thorac Surg* 1993;36:253-61.
- 17. Middlekauff HR, Stevenson WG, Stevenson LW. Prognostic significance of atrial fibrillation in advanced heart failure: a study of 390 patients. *Circulation* 1991;84:40-8.
- 18. Levy S. Factors predisposing to the development of atrial fibrillation. *Pacing Clin Electrophysiol* 1997;20:2670-4.
- 19. Krahn AD, Klein GJ, Kerr CR, et al. How useful is thyroid function testing in patients with recent onset atrial fibrillation? *Arch Intern Med* 1996;156:2221-4.
- 20. Rubenstein JJ, Schulman CL, Yurchak PM, et al. Clinical spectrum of the sick sinus syndrome. *Circulation* 1972;46:5-13.
- 21. Haissaguerre M, Fischer B, Labbe T, et al. Frequency of recurrent atrial fibrillation after catheter ablation of overt accessory pathways. *Am J Cardiol* 1992;69:493-7.
- 22. Brand FN, Abbott RD, Kannel WB, et al. Characteristics and prognosis of lone atrial fibrillation: 30-year follow up in the Framingham study. *JAMA* 1985;254:3449-53.
- 23. American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients with Atrial fibrillation). ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary. *J Am Coll Cardiol* 2001;38:1231-66.
- 24. Savelieva I, Camm AJ. Clinical relevance of silent atrial fibrillation: prevalence, prognosis, quality of life, and management. *Interv Card Electrophys* 2000;4:369-82.
- 25. Crystal E, Connolly SJ. Atrial fibrillation: guiding lessons from epidemiology. *Cardiol Clin* 2004;22:1-8.