

# Atrial Fibrillation: Causes, Investigations, and Treatment

Omar Elsaka<sup>1</sup>

1.Department of Cardiology, Mansoura University, Faculty of Medicine, Mansoura Manchester Medical Program (MMMP), Mansoura, Egypt.

Corresponding author: Omar Elsaka

Note: The name of the author should be written as (Omar Elsaka), don't write it as (Omar Mohamed Raouf Mohamed Ahmed Elsaka). please, just write it as (Omar Elsaka).

## Abstract

Background: Atrial fibrillation (AF) is a frequent progressive cardiac arrhythmia that worsens with age and the presence of comorbidities in the heart. A rapid and irregular heartbeat, known as atrial fibrillation, can go unnoticed or cause symptoms such as palpitations, shortness of breath, and dizziness. This disorder has been linked to more catastrophic consequences, such as an increased risk of stroke. Recent advances in the clinical epidemiology and management of AF have taught us something new about how we should approach the disease. This guidebook covers the epidemiology, techniques, and pathophysiology of AF, as well as diagnosis, testing, prevention, and therapy. Stroke prevention, quality control, and rhythm control are among the management options evaluated. We also discuss health-care quality and offer predictions for future developments and clinical trials to treat this prevalent cardiac arrhythmia.

Conclusion: AF was linked to a two-fold increase in the likelihood of VTE episodes. When those with PE other than DVT were excluded, the link was less, suggesting that the increased risk of VTE in patients with AF could be due to AF-related abnormalities or risk factors.

**Keywords:** *Atrial Fibrillation, Sinus Rhythm, Atrial Enlargement, Paroxysmal Atrial Fibrillation, Accessory Pathway*

## Introduction

Atrial fibrillation is an uncommon type of arrhythmia (rapid heartbeat) that can cause blood clots in the heart. Stroke, heart failure, and other cardiac disorders are all increased by atrial fibrillation. The upper chambers of the heart (atria) beat incorrectly and irregularly during atrial fibrillation, causing the bottom chambers (ventricles) of the heart to not align. AF can be asymptomatic in the majority of persons. Atrial fibrillation, on the other hand, might result in

a fast heartbeat, an elevated heart rate (heart rate), shortness of breath, or weakness. Atrial fibrillation episodes may resolve or remain. Although AF is rarely fatal, it is a medical emergency that necessitates prompt treatment to avoid a stroke. Medication, heart rate, and catheter techniques may be used to treat atrial fibrillation and prevent abnormal cardiac symptoms. A person with atrial fibrillation may also have atrial flutter, which is a heart condition. Although atrial flutter is another arrhythmia, the treatment is exactly the same as that for atrial fibrillation (1).

### **Causes and Risk Factors**

Coronary artery disease, heart attack, congenital heart disease, heart valve difficulties, hypertension, lung disease, physical stress following surgery, pneumonia, or other disease are some of the possible causes of arterial fibrosis. Heart surgery is used to treat heart illness (sick sinus syndrome), sleep aspiration, thyroid diseases such as hyperthyroidism and other metabolic imbalances, stimulant usage, drug-induced diseases, and diseases caused by particular medications, such as caffeine, tobacco, and alcohol. There are no documented heart abnormalities or damage in people who have atrial fibrillation (2).

Atrial fibrillation (A-fib) is caused by a number of factors, including: Age. A person's risk of atrial fibrillation increases with age. Heart disease is a serious condition. Atrial fibrillation is more likely among people who have heart valve abnormalities, congenital heart disease, severe heart failure, coronary artery disease, or who have had a heart attack or had heart surgery in the past. High blood pressure (hypertension): High blood pressure can raise the risk of atrial fibrillation, especially if it is not effectively controlled. Thyroid Illness Thyroid issues can induce arrhythmias, including atrial fibrillation, in certain persons. Other long-term health issues Atrial fibrillation is more likely to occur in those who have diabetes, metabolic syndrome, chronic renal disease, pneumonia, or a lack of sleep. Consumption of alcoholic beverages can result in an episode of atrial fibrillation in some people. Excessive drinking raises the risk. Obesity: Obese people have a higher risk of developing atrial fibrillation. Family history Some families have an increased risk of atrial fibrillation (3).

### **Mechanism of Atrial Fibrillation**

The most prevalent types of chronic AF are hypertensive, valvular, ischemic, and other types of cardiac disease, with AF alone accounting for 15% of AF disorders. AF is a well-defined family, despite the fact that it is now considered rare. The AF gene, which was originally found on chromosome 10 (10q22–q24), was responsible for families in which the arrhythmia was classed as a dominant autosomal component. Familial AF, on the other hand, appears to be a distinct illness. A family with a genetic mutation in the subunit of the cardiac channel IK on chromosome 11 experiences an increase in channel activity, with affected individuals having AF on a regular basis, possibly due to reflex deficiencies. Interactions between underlying causes, usually in the form of progressively ectopic foci that burst into one or more pulmonary arteries, and aberrant arterial tissue substrates capable of maintaining the arrhythmia, now play a role in the aetiology of AF. Although most AF patients acquire heart disease, the pathophysiology of AF in the heart appears to be common and little understood. Despite overcrowding, pulmonary arterial vasculature may have a significant role in younger

individuals with a normal heart and small paroxysms, but rare arterial tissue substrates may play a larger role in people with established heart disease and chronic or chronic AF (4).

A number of active replacement models have been proposed. According to the "lead circle" model, active recirculation loops should have the smallest loop size or wavelength possible. The contour size will be the lowest distance required to restore regenerated tissue at a particular operating speed (wavelength = mean conduction speed x refractory time). The size of the contour will not be less than the wavelength, as this will require the frontal **desolarizing depolarizing** wave to collide with the opposing tissue and extinguish itself: the front end of the circle cannot "bite its tail." (Figure 1) (5).

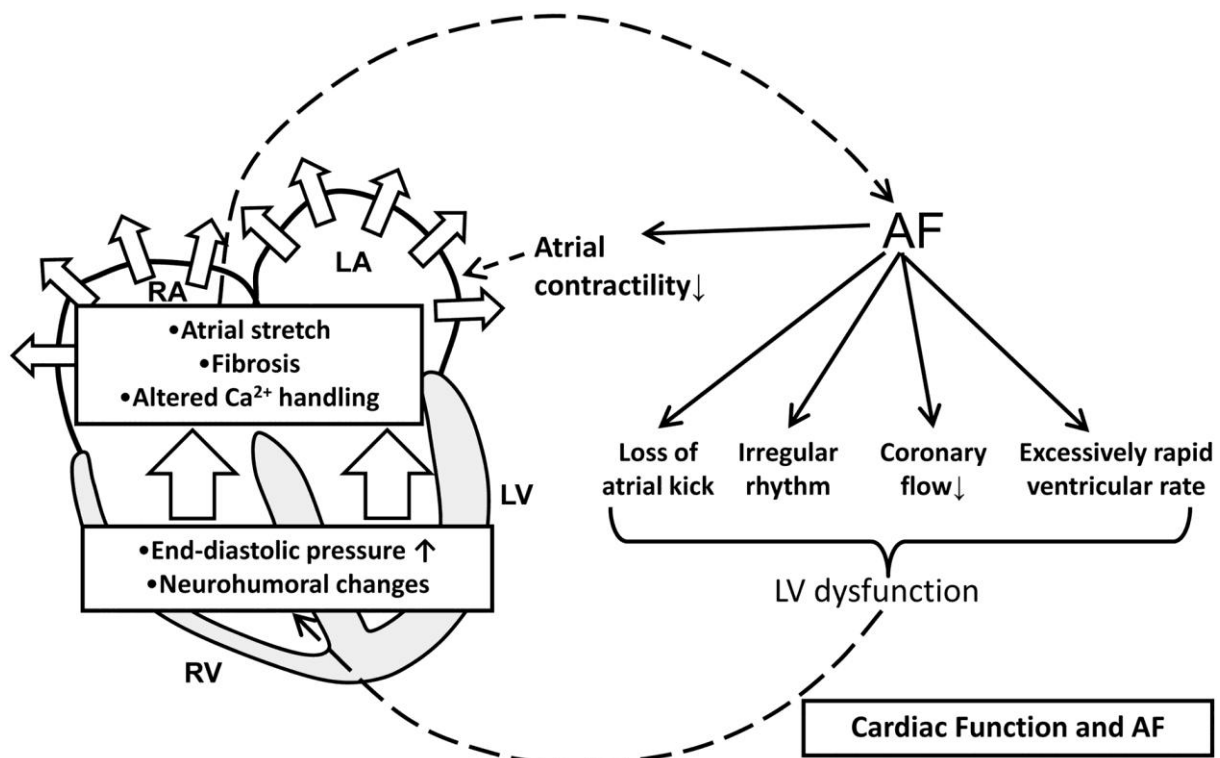
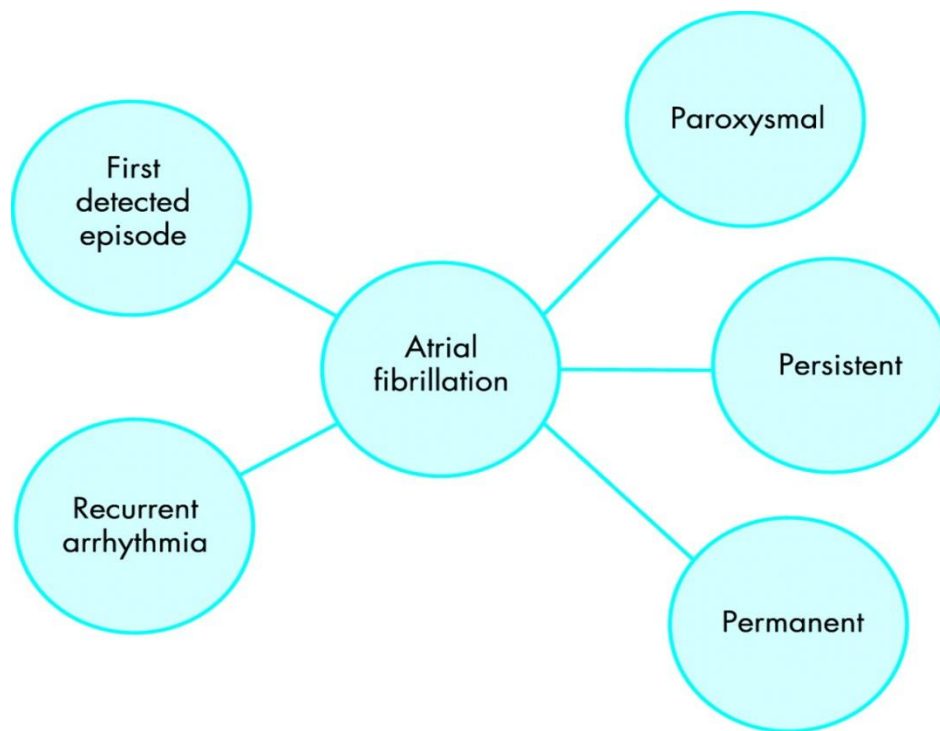


Figure 1 Mechanism of Atrial Fibrillation (5)

### Classification of Atrial Fibrillation (AF)

Separation of atrial fibrillation (AF) begins with the first apparent episode, whether symptomatic or limited. The American College of Cardiology (ACC)/American Heart Association (AHA)/Heart Rhythm Society (HRS) suggests categorising atrial fibrillation into three patterns in published guidelines for treating people with the condition: AF episodes in paroxysmal AF are usually over in 7 days (most episodes last less than 24 hours). Persistent AF is defined as AF episodes that continue longer than 7 days and necessitate medical or electrical intervention to resolve. Persistent AF occurs when an AF episode lasts longer than a year, either because cardioversion failed or because cardioversion was not attempted. After exchanging clinical decisions, both the patient and the physician decide to terminate any other treatment strategies (6).

Unrelated situations caused by AF deterioration are resolved by this rating software (e.g., thyrotoxicosis, abnormal electrolytes, ethanol). Acute myocardial infarction, cardiac surgery, pericarditis, sepsis, pulmonary embolism, or severe lung illness are all considered causes of atrial fibrillation in contemporary clinical **practice practise**. This is because it is believed that once the seizure problem has been adequately treated and resolved, the chances of AF recurrence are low. The Framingham Heart Study, on the other hand, found that more than 60% of participants with secondary AF acquire reflex AF within 15 years of follow-up. Furthermore, participants without additional stimuli and those with other diseases had the same long-term risks of stroke and the underlying cause of death. As a result, long-term AF screening measures in these patients, as well as the present rate of cryptogenic stroke patients, may be examined (figure 2) (7).



**Figure 2 Classification of Atrial Fibrillation (AF) (7)**

### **Symptoms**

Atrial fibrillation (A-fib) affects some people without causing any symptoms. Rapid heartbeat, palpitations, or heartbeat (heartbeat), chest pain, dizziness, weariness, vertigo, lack of ability to exercise, and shortness of breath are all signs and symptoms of atrial fibrillation. A lack of pain, weakness, and atrial fibrillation are all symptoms of atrial fibrillation. It's possible: On rare occasions (paroxysmal atrial fibrillation). A-fib symptoms might last anywhere from a few minutes to several hours. The symptoms may last for a week or more, and the bouts may reoccur. It's possible that the symptoms will go gone on their own. Some patients with A-fib require treatment on a regular basis. Persistence The heartbeat does not return to normal in this type of atrial fibrillation. Cardioversion or medication may be used to restore and sustain a person's heartbeat if they have A-fib symptoms. It has a limited shelf life. Atrial fibrillation of this type is persistent and lasts for more than a year. Abnormal heart rate

cannot always be restored in this type of atrial fibrillation. Medication is needed to control the heartbeat and prevent blood clots (8).

### **Complications**

A severe risk factor for atrial fibrillation, which can lead to stroke, is blood clots. An irregular heart rhythm called atrial fibrillation can cause blood to pool in the heart's upper chambers (atria) and produce clots. A blood clot that forms in the upper left chamber (left atrium) of the heart can go to the brain and cause a stroke. Atrial fibrillation increases the risk of stroke as people get older. High blood pressure, diabetes, heart failure, heart abnormalities, and blood clots and stroke in persons with atrial fibrillation are all factors that can enhance the risk of stroke caused by A-fib (9).

### **Prevention**

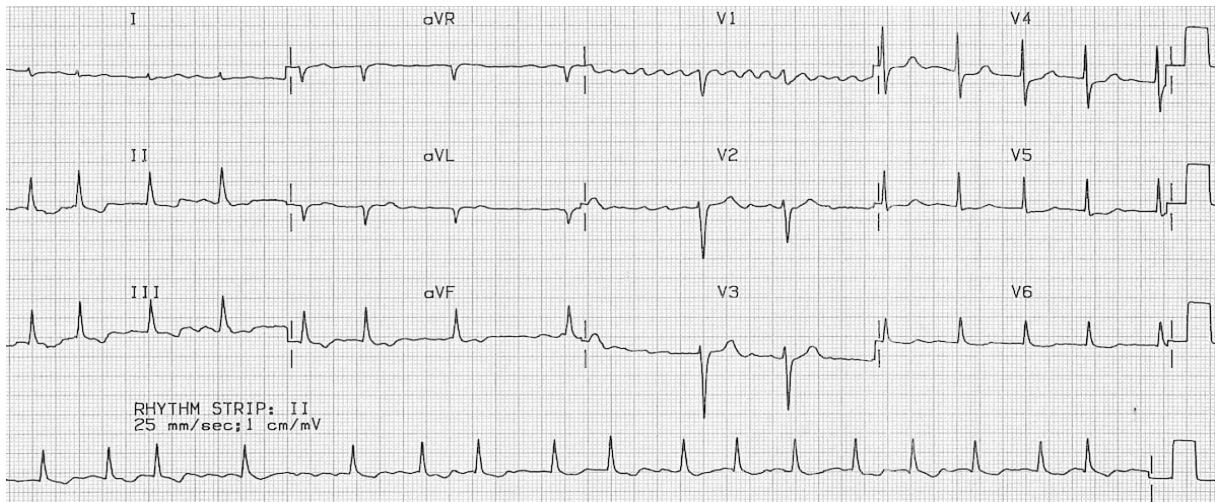
A healthy lifestyle can help prevent atrial fibrillation and minimise the risk of heart disease. Here are some crucial aspects to consider when it comes to heart health: Eat a balanced diet, exercise regularly, and keep a healthy weight, don't smoke, avoid or limit alcohol and caffeine, and manage stress, as too much stress and anger can trigger heart rhythm problems (10).

### **Investigations**

Some people are oblivious to the fact that they have A-fib. When doctors ask for a heart using a stethoscope during a physical examination for other reasons, A-Fib can occur. To diagnose A-Fib or rule out other illnesses that cause similar symptoms, doctors may perform various tests. One or more of the following may be included in the test (11):

#### **Electrocardiogram (ECG or EKG)**

This painless and rapid test assesses cardiovascular activity. On the chest, as well as the arms and legs, adhesive patches (electrodes) are applied. The electrodes are connected to the computer, which shows the test results, through connections. The ECG shows if the heart is beating quickly, slowly, or not at all. The electrocardiogram (ECG) is the most common test for atrial fibrillation (figure 3) (12).



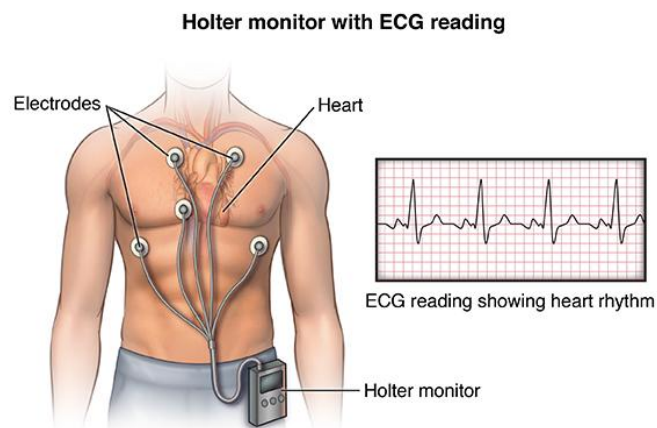
**Figure 3 Electrocardiogram of Atrial Fibrillation (12)**

### Blood tests

This helps the doctor diagnose thyroid problems or to detect other substances in the blood that may lead to A-fib (13).

### Holter Monitor

This small, portable ECG device can be carried in a pocket, shoulder strap or shoulder strap during normal daily activities. It records the heart rate continuously for 24 hours or more (figure 4) (14).



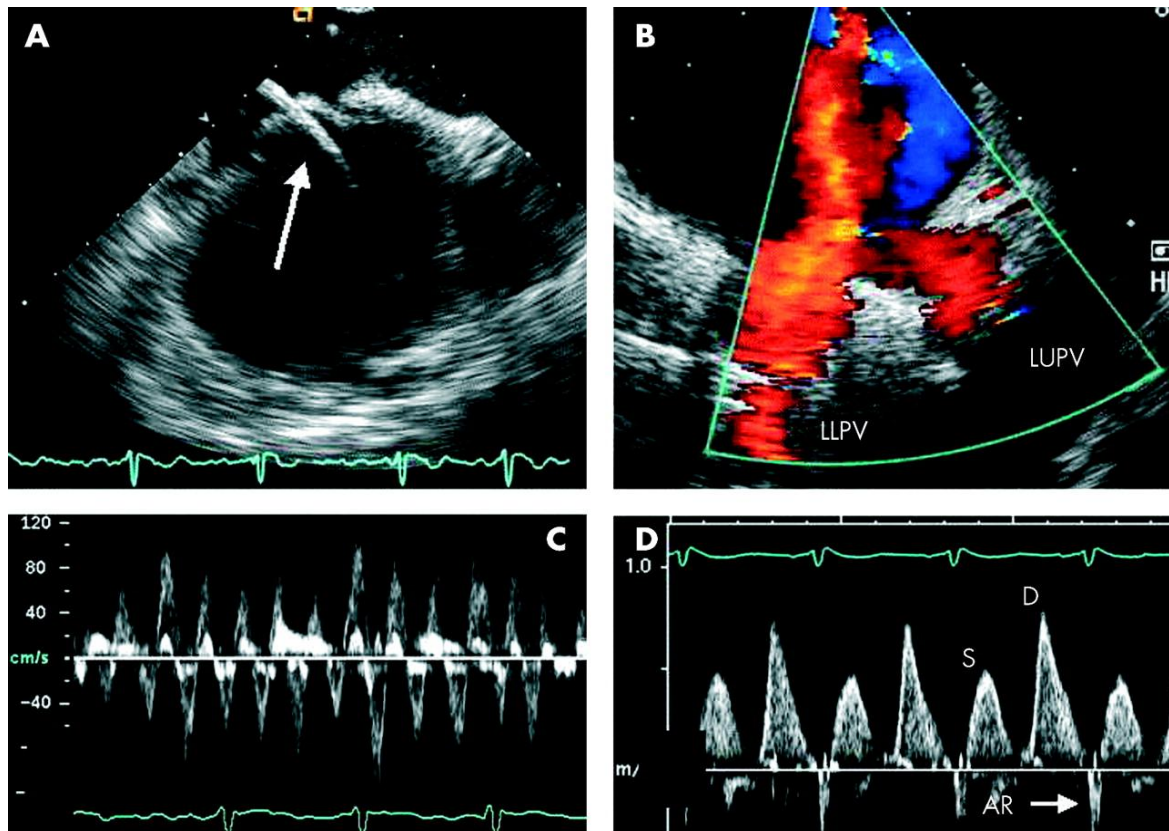
**Figure 4 Holter Monitor (14)**

### Event Recorder

This device looks like a Holter monitor, however it only records for a few minutes. Wearing a Holter monitor for a longer period of time, usually 30 days. Patients frequently hit the button when they hear symptoms. Some technologies can detect irregular heartbeats automatically (15).

## Echocardiogram

This non-invasive experiment uses sound waves to create images of heart size, shape, and movement (figure 5) (16).



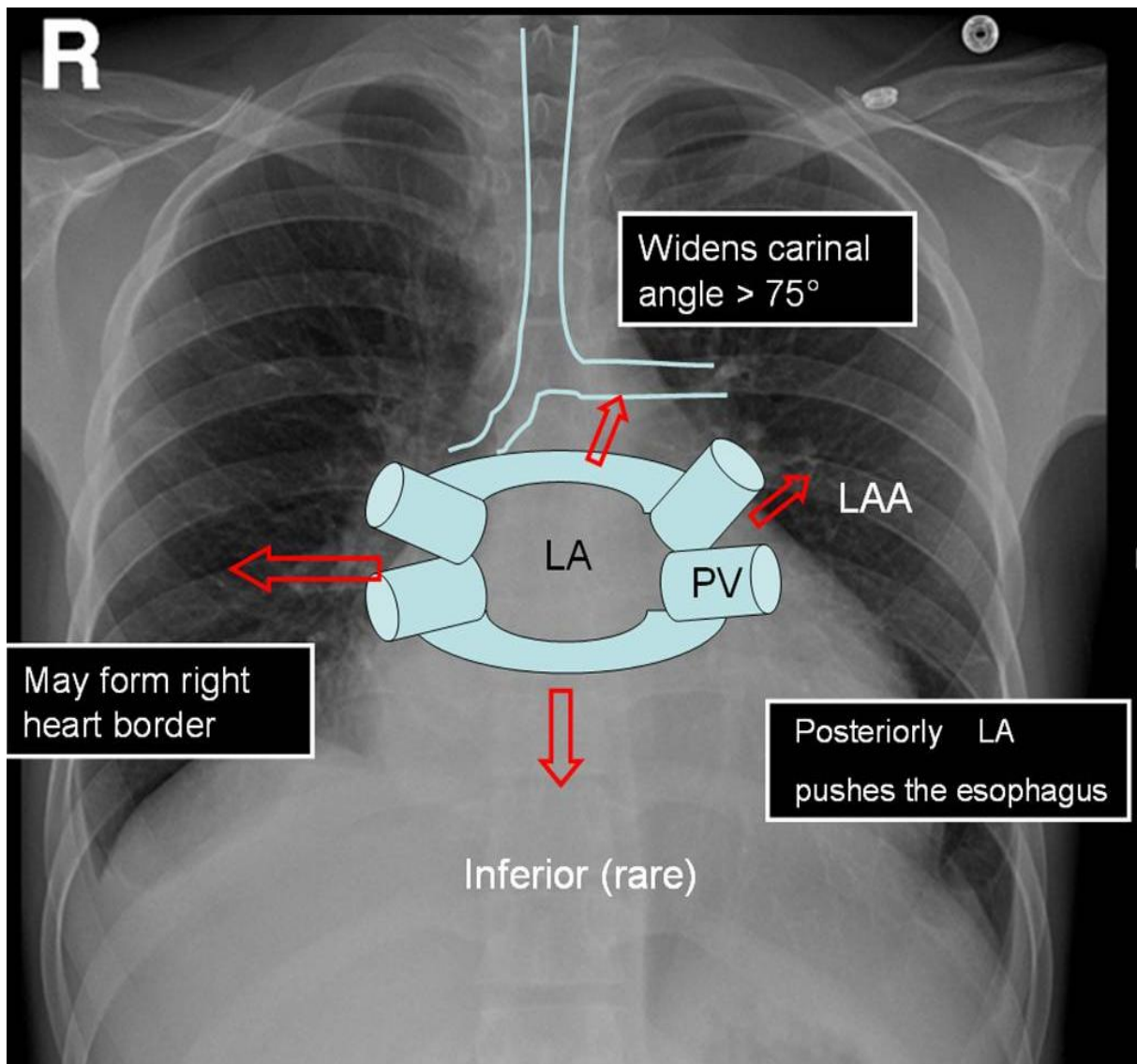
**Figure 5** Intracardiac echocardiography (ICE) images. (A) Transeptal piercing with a catheter (arrow) from the right atrium to the left. (B) Color block diagram showing the combination of upper and lower extremity pulmonary arteries (LUPV and LLPV). (C) LAA pulse-wave Doppler indicating constant velocity in a patient with AF. (D) Pulse Doppler for LUPV, which shows a decrease in systolic (S) blood flow compared to diastolic flow (D) and heart rate followed by atrial reversal systolic reversal (AR) conversion in the same patient (16).

## Stress Test

Also called a physical exam, a stress test involves a heart test while exercising on a treadmill or standing bike (17).

## Chest X-ray

X-rays help the doctor to see the condition of the lungs and heart (figure 6) (18).



**Figure 6 Modes of Left Atrial Enlargement in Case of Atrial Fibrillation (18)**

### **Treatment**

Treatment for atrial fibrillation is determined by the length of time the patient has had the condition, the severity of the symptoms, and the underlying reason of the heart disease. Treatment objectives include restoring heartbeat, controlling heartbeat, preventing blood clots that can cause stroke, and treating the underlying cause, if recognised. Medications, cardiopulmonary treatment, surgery, or catheter procedures may all be used to treat atrial fibrillation. The optimal treatment option will be discussed with the doctor. It's critical to stick to your atrial fibrillation treatment regimen. Misdiagnosis of atrial fibrillation can lead to complications like stroke and heart failure (19).

Medications: The patient may be given medication to help control and normalise the heart rate. Blood clots, a significant condition for A-fib patients, are also treated with medications. The following medications are used to treat atrial fibrillation: Beta-blockers are a type of medication that prevents the body At rest and during exercise, these drugs can help slow

down the heartbeat. Calcium channel blockers are drugs that prevent calcium from entering the body. These medications regulate heart rate, but patients with heart problems or low blood pressure should avoid them. Digoxin: This drug can lower your heart rate when you're not exercising, but not when you're working out. The majority of people require additional or alternative drugs, such as calcium channel blockers and beta blockers. Anti-arrhythmic medicines are used to keep a normal cardiac rhythm rather than only control heart rate. Anti-arrhythmics are used less frequently than heart-regulating medications because they have more dangerous side effects. Clots in the blood. The doctor may prescribe an anticoagulant to lower the risk of stroke or other issues caused by blood clots. Warfarin, apixaban, dabigatran, edoxaban, and rivaroxaban are all blood thinners. Patients who are taking warfarin will require regular blood tests to monitor the medication's effects (20).

### **Cardioversion Therapy**

If symptoms of A-fib are severe or if it is the first stage of atrial fibrillation, doctors may try to reset the heartbeat (sinus rhythm) using a procedure called cardioversion. Cardioversion can be done in two ways (21):

#### **Electrical Cardioversion**

This process of resetting the heart rate is done by sending electrical shock to the heart through paddles or patches (electrodes) placed on the chest (22).

#### **Drug Cardioversion**

To restore the heart's rhythm, medicines are given intravenously or orally. The cardiac version is normally performed in a hospital setting, although it can also be performed in an emergency situation. To lower the risk of blood clots and stroke, warfarin or other anticoagulants may be administered weeks before the procedure. Arrhythmic medications may be prescribed indefinitely after cardioversion to prevent further occurrences of atrial fibrillation. A second episode of atrial fibrillation can occur even if the patients are taking the medication (figure 7) (23).

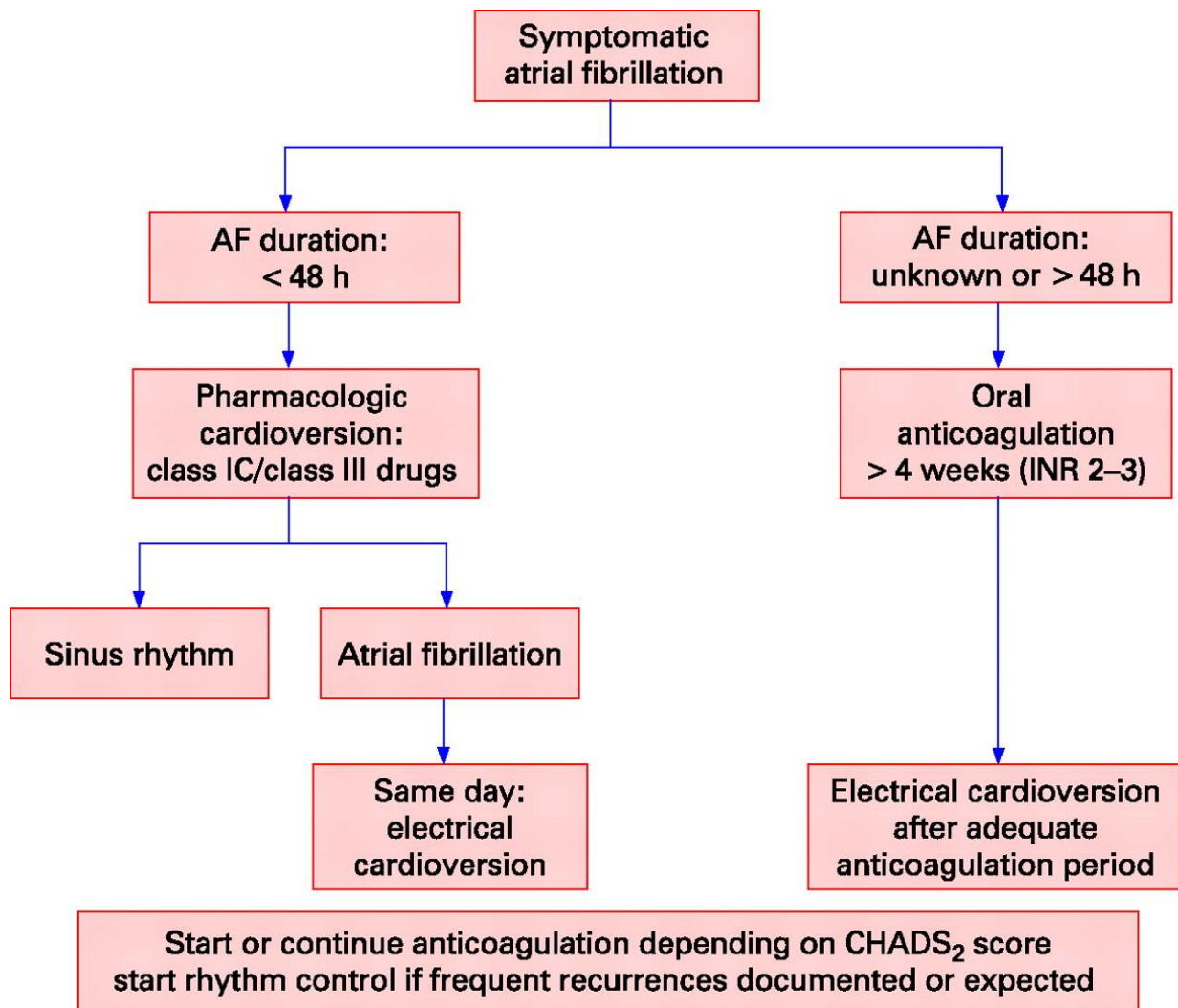


Figure 7 Cardioversion Therapy Decisions (23)

### Surgery or Catheter Procedures

If medicine or other treatments fail to alleviate A-fib, a doctor may consider cardiac ablation. For some patients, ablation is the first line of defense. Cardiac ablation creates scars in the heart, blocks aberrant electrical signals, and restores a normal heartbeat using heat (radio frequency energy) or cryoablation. A flexible catheter is inserted into the bloodstream, generally the lungs and heart. It's possible to utilize more than one catheter. Cold or heat energy is used in the veins at the catheter's tip. During open heart surgery, ablation is rarely done with a knife. Different forms of cardiac output exist. The type of treatment for atrial fibrillation will be determined by the patient's symptoms, length of life, and whether or not the patient will undergo additional heart surgery. The following are some examples of cardiac output that could be employed to treat atrial fibrillation (24):

### Atrioventricular (AV) Node Ablation

Heat or cold power is applied to the heart muscle in the AV node to damage the electrical signal connection. After the release of the AV node, a pacemaker is required for life (25).

## Maze Procedure

Doctors use heat or cold energy or scalpel to create a pattern of red tissue in the upper chambers of the heart. Because red tissue does not send electrical signals, the maze interferes with lost heart signals and causes atrial fibrillation. If a scalpel is used to create a maze, open heart surgery is required. This is called surgical complication. It is the preferred method of treating atrial fibrillation for those who need other heart surgeries, such as coronary artery bypass surgery or coronary heart valve repair. Atrial fibrillation may return after cardiac arrest. In this case, another heart transplant or other heart therapy may be recommended. After a heart attack, life-long blood transfusions may be required to prevent paralysis. If a person with A-Fib is unable to take anticoagulants, the doctor may recommend a catheterization procedure to close the small appendix of the upper left ventricle (appendage), where multiple A-Fib-related clots are formed. This process is called closure of the left atrial appendage. The closing device is slowly passed through the catheter into the bag. Once the device is installed, the catheter is removed. The device will stay in place forever. Surgery to close the left atrial appendage is an option for some people who already have heart surgery (figure 8) (26).

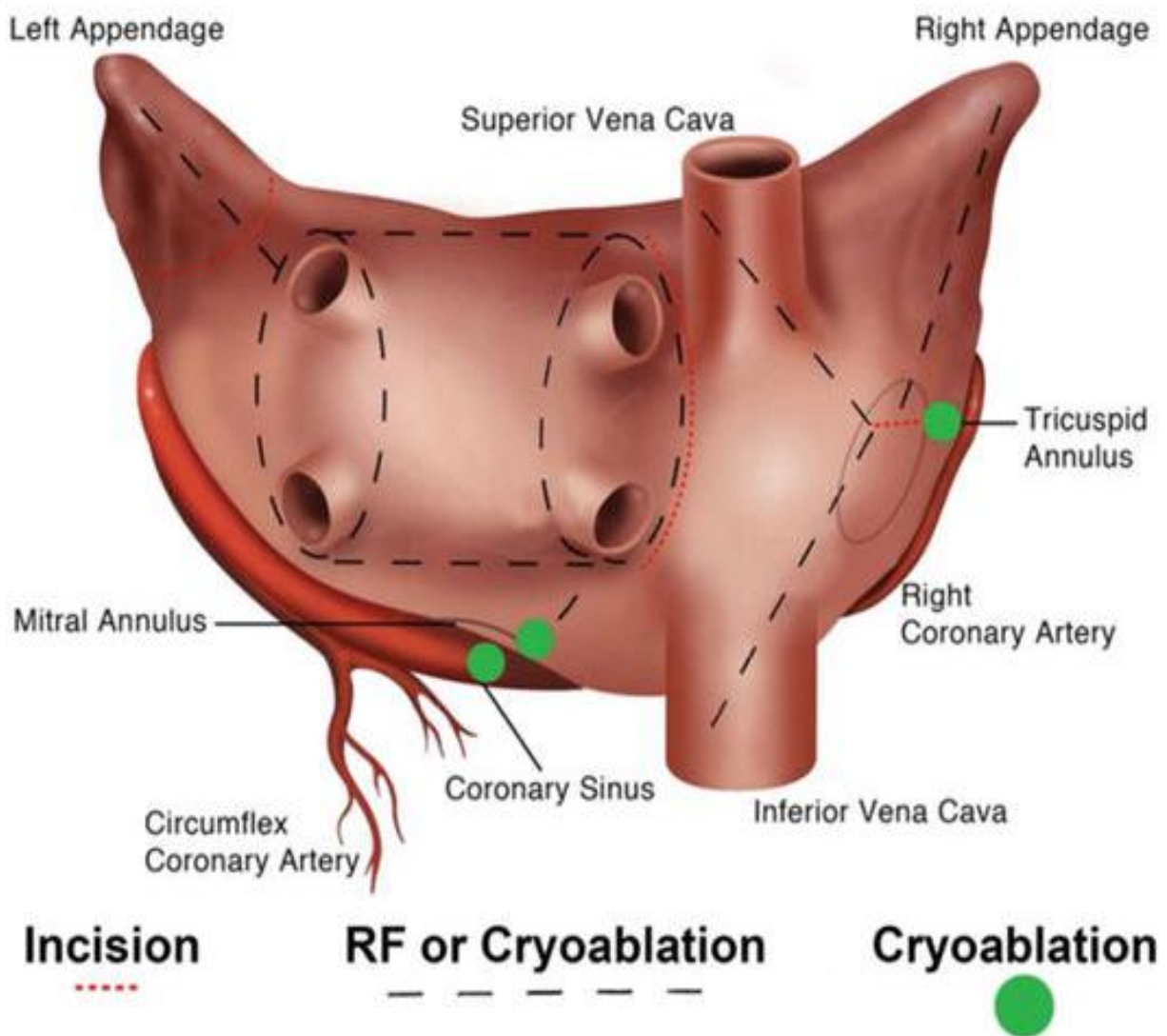


Figure 8 Maze Procedure (26)

## **Discussion**

In most cases of atrial fibrillation, the arrhythmia's symptoms hide the conditions that allow it to be diagnosed. As a result, patients with stroke, thyrotoxicosis, or pulmonary edoema due to severe mitral stenosis can develop atrial fibrillation. Atrial fibrillation, on the other hand, may be completely undetectable and only identified during a routine public electrocardiographic check. In patients with paroxysmal atrial fibrillation, long-term recordings may indicate multiple brief bouts of atrial fibrillation that go unreported. Few people, however, are aware of arrhythmias that occur during atrial fibrillation, with anxiety, palpitations, early malaise, shortness of breath, and dizziness being the most typical symptoms. Orthostatic stress tolerance is better in patients with atrial fibrillation, and they are less prone to suffer orthostatic hypotension. In patients with atrial fibrillation and a ventricular stance, syncope, or near syncope, may suggest heart blockage and reverse circulation after 2–3 seconds (27).

## **Conclusion**

Most early strokes have no recognised cause (ESUS). AF: Stroke and transient ischemic attack (TIA) may be the cause, however they are difficult to diagnose. The existence of undetected AF may increase the likelihood of recurrence, hence proper diagnosis and treatment of AF may lower the risk of recurrence and stroke death. Using Ambulatory Holders, MCOTs, ELRs, and ILRs, outpatient cardiac monitoring can detect more AF than hospital monitoring alone. Although these findings are consistent with earlier systematic reviews that show that long-term follow-up improves the diagnostic utility of AF, comparison data are insufficient to determine which devices are optimal for long-term monitoring of a patient's heart. Duration. Long-term surveillance. For patients with ESUS, general evidence suggests that ambulatory cardiac monitoring of AF is reasonable. Interpretation of clinical data is limited by the significant number of different patients, the duration of follow-up, and the significant clinical variation between subjects in terms of definitions of AF. Therefore, more research is needed with well-designed RCTs.

## **Conflict of Interest**

There is nothing to disclose

## **Disclaimer regarding Consent and Ethical Approval:**

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors

## **References**

- 1) Culebras A, Messe SR, Chaturvedi S, Kase CS, Gronseth G. Summary of evidence-based guideline update: prevention of stroke in nonvalvular atrial fibrillation: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2014 Feb 25. 82 (8):716-24.

- 2) Connolly SJ, Eikelboom J, Joyner C, et al, for the AVERROES Steering Committee and Investigators. Apixaban in patients with atrial fibrillation. *N Engl J Med*. 2011 Mar 3. 364 (9):806-17.
- 3) Connolly SJ, Ezekowitz MD, Yusuf S, et al, for the RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009 Sep 17. 361 (12):1139-51.
- 4) Deftereos S, Giannopoulos G, Kossyvakis C, et al. Colchicine for prevention of early atrial fibrillation recurrence after pulmonary vein isolation: a randomized controlled study. *J Am Coll Cardiol*. 2012 Oct 30. 60 (18):1790-6.
- 5) Doyle JF, Ho KM. Benefits and risks of long-term amiodarone therapy for persistent atrial fibrillation: a meta-analysis. *Mayo Clin Proc*. 2009 Mar. 84 (3):234-42.
- 6) Fang MC, Go AS, Chang Y, et al. Thirty-day mortality after ischemic stroke and intracranial hemorrhage in patients with atrial fibrillation on and off anticoagulants. *Stroke*. 2012 Jul. 43 (7):1795-9.
- 7) Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. *Eur Heart J*. 2012 Jun. 33 (12):1500-10.
- 8) Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF). *Am Heart J*. 2006 Mar. 151 (3):713-9.
- 9) Gerds E, Wachtell K, Omvik P, et al. Left atrial size and risk of major cardiovascular events during antihypertensive treatment: losartan intervention for endpoint reduction in hypertension trial. *Hypertension*. 2007 Feb. 49 (2):311-6.
- 10) Giugliano RP, Ruff CT, Braunwald E, et al, for the ENGAGE AF-TIMI 48 Investigators. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2013 Nov 28. 369 (22):2093-104.
- 11) Granger CB, Alexander JH, McMurray JJ, et al, for the ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2011 Sep 15. 365 (11):981-92.
- 12) Hagens VE, Ranchor AV, Van Sonderen E, et al, for the RACE Study Group. Effect of rate or rhythm control on quality of life in persistent atrial fibrillation. Results from the Rate Control Versus Electrical Cardioversion (RACE) Study. *J Am Coll Cardiol*. 2004 Jan 21. 43 (2):241-7.
- 13) Hansen ML, Sorensen R, Clausen MT, et al. Risk of bleeding with single, dual, or triple therapy with warfarin, aspirin, and clopidogrel in patients with atrial fibrillation. *Arch Intern Med*. 2010 Sep 13. 170 (16):1433-41.
- 14) Imazio M, Brucato A, Ferrazzi P, et al, for the COPPS Investigators. Colchicine reduces postoperative atrial fibrillation: results of the Colchicine for the Prevention of the Postpericardiotomy Syndrome (COPPS) atrial fibrillation substudy. *Circulation*. 2011 Nov 22. 124 (21):2290-5.
- 15) Kowey PR, Reiffel JA, Ellenbogen KA, Naccarelli GV, Pratt CM. Efficacy and safety of prescription omega-3 fatty acids for the prevention of recurrent symptomatic atrial fibrillation: a randomized controlled trial. *JAMA*. 2010 Dec 1. 304 (21):2363-72.

- 16) Larsen TB, Lip GY. Warfarin or novel oral anticoagulants for atrial fibrillation?. *Lancet*. 2014 Mar 15. 383 (9921):931-3.
- 17) Lip GY, Skjoth F, Nielsen PB, Larsen TB. Non-valvular atrial fibrillation patients with none or one additional risk factor of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score. A comprehensive net clinical benefit analysis for warfarin, aspirin, or no therapy. *Thromb Haemost*. 2015 Oct. 114 (4):826-34.
- 18) Liu T, Korantzopoulos P, Shehata M, Li G, Wang X, Kaul S. Prevention of atrial fibrillation with omega-3 fatty acids: a meta-analysis of randomised clinical trials. *Heart*. 2011 Jul. 97 (13):1034-40.
- 19) Lopes RD, Al-Khatib SM, Wallentin L, et al. Efficacy and safety of apixaban compared with warfarin according to patient risk of stroke and of bleeding in atrial fibrillation: a secondary analysis of a randomised controlled trial. *Lancet*. 2012 Nov 17. 380 (9855):1749-58.
- 20) Majeed A, Hwang HG, Connolly SJ, et al. Management and outcomes of major bleeding during treatment with dabigatran or warfarin. *Circulation*. 2013 Nov 19. 128 (21):2325-32.
- 21) McNamara RL, Tamariz LJ, Segal JB, Bass EB. Management of atrial fibrillation: review of the evidence for the role of pharmacologic therapy, electrical cardioversion, and echocardiography. *Ann Intern Med*. 2003 Dec 16. 139 (12):1018-33.
- 22) Moreno I, Caballero R, Gonzalez T, et al. Effects of irbesartan on cloned potassium channels involved in human cardiac repolarization. *J Pharmacol Exp Ther*. 2003 Feb. 304 (2):862-73.
- 23) O'Shea SI, Arcasoy MO, Samsa G, et al. Direct-to-patient expert system and home INR monitoring improves control of oral anticoagulation. *J Thromb Thrombolysis*. 2008 Aug. 26 (1):14-21.
- 24) Patel MR, Mahaffey KW, Garg J, et al, for the ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011 Sep 8. 365 (10):883-91.
- 25) Piccini JP, Hasselblad V, Peterson ED, Washam JB, Califf RM, Kong DF. Comparative efficacy of dronedarone and amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation. *J Am Coll Cardiol*. 2009 Sep 15. 54 (12):1089-95.
- 26) Roy D, Talajic M, Dorian P, et al, for the Canadian Trial of Atrial Fibrillation Investigators. Amiodarone to prevent recurrence of atrial fibrillation. *N Engl J Med*. 2000 Mar 30. 342 (13):913-20.
- 27) Shi Y, Li D, Tardif JC, Nattel S. Enalapril effects on atrial remodeling and atrial fibrillation in experimental congestive heart failure. *Cardiovasc Res*. 2002 May. 54 (2):456-61.