Atrial fibrillation: Overview and management of new-onset atrial fibrillation

Atrial fibrillation: Overview and management of new-onset atrial fibrillation

Author:

Kapil Kumar, MD

Section Editor:

Peter J Zimetbaum, MD

Deputy Editor:

Nisha Parikh, MD, MPH

INTRODUCTION

— Atrial fibrillation (AF) is the most commonly treated cardiac arrhythmia. AF is generally associated with an irregularly irregular ventricular

rhythm and absence of distinct P waves. This topic will provide a broad overview of the classification, clinical presentation, diagnosis, management, and sequelae of AF, including new-onset AF.

The initiation and maintenance of AF reflect electrophysiologic alterations in atrial myocardium. The pathophysiology of AF is discussed in detail elsewhere. (See "Mechanisms of atrial fibrillation".)

The epidemiology of AF including prevalence, risk factors, and associated chronic conditions is discussed in detail separately. (See "Epidemiology, risk factors, and prevention of atrial fibrillation".)

The following topics provide detail about specific types of AF and other management issues:

- (See "Atrial fibrillation in adults: Use of oral anticoagulants".)
- (See "Rhythm control versus rate control in atrial fibrillation".)
- (See "Control of ventricular rate in atrial fibrillation: Pharmacologic therapy".)

CLASSIFICATION AND TERMINOLOGY

— AF can be classified according to its duration and length of episodes; these were described in the 2014 American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines on AF management [1].

- **Paroxysmal (ie, self-terminating or intermittent) AF** – Paroxysmal AF is defined as AF that terminates spontaneously or with intervention within seven days of onset. Episodes may recur with variable frequency. (See "Paroxysmal atrial fibrillation".)

- **Persistent AF** – Persistent AF is defined as AF that fails to self-terminate within seven days. Episodes often require pharmacologic or electrical cardioversion to restore sinus rhythm. While a patient who has had persistent AF can have later episodes of paroxysmal AF, AF is generally considered a progressive disease.

- **Long-standing persistent AF** – Long-standing persistent AF refers to AF that has lasted for more than 12 months.

- **Permanent AF** – Permanent AF is a term

used to identify persistent AF for which a joint decision by the patient and clinician has been made to no longer pursue a rhythm control strategy. Acceptance of persistent AF may change as symptoms, therapeutic options, and patient and clinician preferences evolve [1].

While AF typically progresses from paroxysmal to persistent states, patients can present with both types throughout their lives.

AF can also be classified based by the way it presents or whether specific valvular conditions are present:

- **Subclinical or occult AF** – This refers to AF that is largely asymptomatic and only becomes apparent in the setting of a thromboembolic event, acute heart failure exacerbation, other medical illness, or upon routine electrocardiogram (ECG) done for other purposes. (See "Cryptogenic stroke and embolic stroke of undetermined source (ESUS)", section on 'Occult atrial fibrillation' and "Overview of the evaluation of stroke", section on 'Monitoring for subclinical atrial

fibrillation' and 'Common scenarios' below.)

Screening for AF is discussed separately. (See 'Screening' below.)

- **Valvular AF** – This refers to patients with moderate to severe mitral stenosis; these patients have a higher risk of stroke than patients without this condition.

- **Lone AF** – The term "lone AF" is a historical term that is now disfavored, as it may be confusing and does not enhance patient care [1,2]. The term lone AF has been used to describe AF in younger patients (eg, ≤60 years) with paroxysmal, persistent, or permanent AF who have no structural heart disease or cardiovascular risk factors. These characteristics identify a group of individuals with a CHA_2DS_2-VASc score of "0" and who are at lowest risk for thromboembolism from AF. (See "Atrial fibrillation in adults: Selection of candidates for anticoagulation", section on 'CHA2DS2-VASc score'.)

SCREENING

— We do not currently screen asymptomatic patients for AF. In a general population and among persons >65 years of age, screening has not been shown to be better than usual care (eg, pulse palpation on physical examination) for AF detection. Furthermore, screening showed modest to no benefit on reducing cardiovascular outcomes and death in one of two randomized studies. Screening may lead to more anticoagulation, but this has not been shown to be associated with robust protection from stroke or thromboembolic events [3-5]. The United States Preventive Services Task Force (USPSTF) also does not recommend screening for AF.

- **Effects on cardiovascular outcomes and death** – Two randomized studies of screening for AF (with either single-lead ECGs or implantable loop recorders) showed only a modest or no reduction in clinical events and are also limited in that they included a narrow patient population that may not be widely generalizable.

  A randomized, unmasked, parallel group study in Sweden (STROKESTOP) of 28,768

individuals aged 75 to 76 years compared outcomes (ie, a composite of ischemic or hemorrhagic stroke, systemic embolism, bleeding leading to hospitalization, and all-cause death) in patients who underwent two-week intermittent ECG screening with subsequent anticoagulation strategy versus those who received usual care [3]. After a median follow-up of 6.9 years, somewhat fewer outcomes occurred in the intervention group than in the control group (5.45 versus 5.68 events per 100 years; hazard ratio [HR] 0.96; 95% CI 0.92-1.00), but the overall risks and absolute benefit are very low.

In the LOOP study, 6004 individuals with stroke risk factors were randomly assigned to either implantable loop recorder monitoring (also called implantable cardiac monitor) or usual care [4]. Those in the implantable loop recorder group had three times the rates of AF detection and anticoagulation initiation but no change in rates of stroke or arterial embolization.

- **AF detection** – Data are mixed as to whether

screening for AF increases the number of new AF cases detected; however, the potential benefit appears to be small at best. The choice of test used to detect AF and population characteristics likely impacts these results.

In the VITAL-AF trial, 16 primary clinics were randomly assigned either to AF screening using a handheld single-lead ECG (AliveCor KardiaMobile) during vital sign assessments or to usual care [6]. More than 30,000 patients ≥65 years of age were followed for one year for the development of new-onset AF. New AF diagnosis in the screening and control groups was similar (1.72 versus 1.59 percent). In a prespecified subgroup analysis of persons aged ≥85 years, new AF diagnoses were more frequent in the screening versus control group (5.56 versus 3.76 percent).

In a meta-analysis of three cluster randomized studies (not including VITAL-AF), screening identified more cases of AF compared with no screening when using one-time approaches (pulse palpation, ECG, and/or Holter monitor [absolute risk difference range 0.06 to 0.60

percentage points; relative risk range 1.04 to 1.58]). However, this difference was small and statistically significant in only one of the studies in the meta-analysis [5].

The Apple Watch in combination with iPhone application was evaluated in over 400,000 individuals without a history of AF [7]. Irregular pulse notifications were sent to 2161 participants (0.52 percent). Of these, 450 participants were sent and returned an ECG patch and were not otherwise excluded per study protocol. AF was present in 34 percent of 450 patients. Among those who were notified of an irregular pulse on the watch while wearing the patch, 84 percent were concordant with AF. The Apple Watch study did not employ the gold standard reference of 12-lead ECG analyzed by two cardiologists, which limits interpretation of device accuracy for AF detection.

- **Accuracy of detection method** – The accuracies of specific AF detection tests were reviewed by the USPSTF [5]. In most studies, test accuracy was measured against the

reference of 12-lead ECG (interpreted by two cardiologists). Sensitivity and specificity were generally high for single-lead ECG and oscillometric blood pressure monitors. Implantable cardiac monitors are more sensitive than ECG and external monitoring [8].

ECGs do not appear more effective than pulse palpation at AF detection. A USPSTF review of randomized trials and observational studies (17 studies and 135,300 patients age 65 years and older) found that systematic screening with ECG identified more cases of AF than no screening (absolute increase from 0.6 to 2.8 percent over 12 months) [9]. However, systematic screening with ECG did not detect more cases than a systematic approach using pulse palpation.

The role of evaluating patients with cryptogenic stroke for AF is discussed separately. (See "Cryptogenic stroke and embolic stroke of undetermined source (ESUS)", section on 'Occult atrial fibrillation'.)

CLINICAL PRESENTATION

Symptoms

— AF may or may not have associated symptoms, and the spectrum of symptoms is broad and nonspecific. Typical symptoms include the following:

- Palpitations
- Tachycardia
- Fatigue
- Weakness
- Dizziness
- Lightheadedness
- Reduced exercise capacity
- Increased urination
- Mild dyspnea.

Some patients have more severe symptoms. These include the following:

- Dyspnea at rest
- Angina
- Presyncope or rarely syncope
- Symptoms of stroke or other systemic embolic

event

- Symptoms of heart failure (eg, dyspnea on exertion, peripheral edema, weight gain, and abdominal swelling from ascites)

The severity and extent of symptoms are affected by the patient's underlying cardiac condition, age, presence of diabetes [10,11], and rapidity and regularity of the ventricular response. For example, one study of 2400 AF patients showed that the 420 patients with diabetes felt fewer AF-related symptoms (eg, palpitations, dizziness, exercise intolerance [odds ratio 0.74; 95% CI 0.59-0.92]), but had a worse quality of life (beta = -4.54; 95% CI -6.40 to -2.68) than those without diabetes [10]. Quality of life was measured on the 100-point European Quality of Life-5 Dimensions Questionnaire (EQ-5D).

The hemodynamic consequences of AF are discussed in detail separately. (See "Hemodynamic consequences of atrial fibrillation and cardioversion to sinus rhythm".)

Common scenarios

— A new diagnosis of AF may result from several

clinical scenarios that are described below:

- At the time of a routine examination, during which the patient complains of symptoms possibly due to AF or is being evaluated for another reason and is found to have an irregularly irregular pulse.

- On an ECG obtained for other reasons such as a preoperative evaluation. (See "The electrocardiogram in atrial fibrillation".)

- A patient with a stroke or other arterial thromboembolism can be found to have AF that had not been previously diagnosed [12]. In some cases, AF is detected during extended monitoring in an attempt to diagnose the cause for the stroke. (See "Stroke in patients with atrial fibrillation" and "Cryptogenic stroke and embolic stroke of undetermined source (ESUS)", section on 'Occult atrial fibrillation'.)

  Subclinical AF can be also detected by intracardiac, implantable, or wearable monitors [13]. Subclinical AF usually occurs in individuals without characteristic

symptoms of AF and without a prior diagnosis. Most of these individuals will have paroxysmal AF. A scientific statement from the American Heart Association on subclinical and cardiac implantable electronic device-detected AF was published in 2019 [13]. (See "Ambulatory ECG monitoring" and "Paroxysmal atrial fibrillation", section on 'Evaluation' and "Implantable cardioverter-defibrillators: Overview of indications, components, and functions", section on 'ECG monitoring and storage'.)

The ASSERT study of 2580 patients (65 years or older) with either a dual-chamber pacemaker or implantable cardioverter-defibrillator, hypertension, and no history of AF found that at three months, subclinical AF was detected in about 10 percent of patients [14]. Clinical AF developed in about 16 percent of patients with subclinical AF.

In a study of 590 individuals with stroke risk factors but without AF who underwent screening with an implantable loop recorder for an average of 40 months, 35 percent of

participants were found to have AF [8].

- During ECG monitoring with a 24-hour ambulatory monitor obtained for some other reason or during interrogation of an implanted cardiac rhythm device. (See "Ambulatory ECG monitoring" and "Implantable cardioverter-defibrillators: Overview of indications, components, and functions", section on 'ECG monitoring and storage'.)

- During hospitalization for another reason such as infection, recent myocardial infarction, thyrotoxicosis, pulmonary embolism, chronic obstructive pulmonary disease, myocarditis, and pericarditis, among others [15-18]. (See "Arrhythmias in COPD" and "Cardiovascular effects of hyperthyroidism" and "Pneumococcal pneumonia in patients requiring hospitalization", section on 'Cardiac events and other noninfectious complications'.)

- During or after cardiac or noncardiac surgery. (See "Atrial fibrillation in patients undergoing noncardiac surgery" and "Atrial fibrillation

and flutter after cardiac surgery" and "Arrhythmias during anesthesia", section on 'Atrial fibrillation'.)

- During recording from a patient-acquired recording device (eg, Apple watch, AliveCor KardiaMobile, etc). (See "The electrocardiogram in atrial fibrillation", section on 'Wearable consumer devices' and 'Screening' above.)

EVALUATION

History and physical examination

— Descriptions of any associated symptoms should include:

- Onset or date of discovery
- Possible precipitating factors
- Frequency and duration
- Severity of episodes and symptoms
- Qualitative characteristics
- Previous medical records of any prior supraventricular arrhythmias

A semi-quantitative method to classify symptoms

has been developed, but the clinical utility of such a system has not been demonstrated [19].

- **Associated conditions** – The presence and status of associated conditions such as other cardiovascular disease, cerebrovascular disease, diabetes, hypertension, chronic obstructive pulmonary disease, obstructive sleep apnea should be ascertained. (See "Epidemiology, risk factors, and prevention of atrial fibrillation" and "Arrhythmias in COPD", section on 'Atrial fibrillation' and "Obstructive sleep apnea and cardiovascular disease in adults", section on 'Atrial fibrillation'.)

The presence of potentially reversible causes should be assessed (eg, hyperthyroidism, unhealthy alcohol use). (See "Overview of the clinical manifestations of hyperthyroidism in adults" and "Diagnosis of hyperthyroidism" and "Risky drinking and alcohol use disorder: Epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis".)

- **Physical examination** – The physical examination should focus on the cardiovascular system and any associated

conditions. Abnormal findings may inform healthcare providers about associated conditions that might be contributing to the onset of AF and/or impacting the severity. Examples include heart murmurs or arterial pulse abnormalities indicative of mitral or aortic stenosis or regurgitation, hypertrophic cardiomyopathy, and signs and symptoms of heart failure. (See "Examination of the precordial pulsation" and "Auscultation of cardiac murmurs in adults" and "Examination of the jugular venous pulse" and "Examination of the arterial pulse".)

During AF with an irregularly irregular pulse, there is commonly a slight variation in the intensity of the first heart sound. S4 sounds are not heard, and jugular venous "a" waves are absent since atrial contraction is lost. (See "Auscultation of heart sounds", section on 'Clinical significance of S4'.)

An apical-radial pulse deficit is commonly observed in patients in AF. When one assesses the rates of the left ventricular apex and the radial pulse simultaneously, the radial heart

rate may be less than the apical heart rate. Since the heart rate is irregular, some ventricular contractions will occur, preceded by shorter periods of diastole in which there is a reduction in left ventricular filling. This results in ventricular beats with insufficient stroke volume to transmit the pressure wave to the arm. Variation in cuff blood pressure readings is also common during AF due to changes in the beat-to-beat cadence and changes in left ventricular filling and stroke volume. It is often necessary to measure the blood pressure multiple times and average these values to obtain a more accurate blood pressure reading.

Electrocardiogram

— For all patients with suspected new-onset AF, we obtain a 12-lead ECG. On an ECG with AF, there are no discrete P waves but rapid, low-amplitude, continuously varying fibrillatory (f) waves are seen. The ventricular rhythm is generally irregularly irregular (lacking a repetitive pattern), although AF is uncommonly associated with a regular ventricular rate. The ECG in patients with

AF is described in detail separately (waveform 1). (See "The electrocardiogram in atrial fibrillation".)

There are a number of potential pitfalls in the ECG diagnosis of AF. Errors in the diagnosis of AF are especially common with computerized ECG interpretation and in patients who are continuously or intermittently paced. Hence, it is important that the automated ECG interpretation provided by the machine is confirmed by a skilled reader.

A baseline ECG, preferably in sinus rhythm, should also be evaluated for the following information:

- Markers of nonelectrical cardiac disease, such as left ventricular hypertrophy (possible hypertension) or Q waves (possible coronary artery disease).

- Markers of electrical heart disease, including the presence of ventricular pre-excitation or infranodal conduction disease (bundle branch block).

- The QT interval (to identify the potential risk of antiarrhythmic therapy)

- Evidence of severe bradycardia or sinus node

dysfunction

Echocardiogram

— We obtain a transthoracic echocardiogram (TTE) even if the physical examination is otherwise normal. The TTE does not need to be performed at the time of the first visit in stable patients. We obtain a TTE in order to evaluate the size of the right and left atria and the size and systolic function of the right and left ventricles; to detect possible valvular heart disease, left ventricular hypertrophy, diastolic dysfunction, and pericardial disease; and to assess peak right ventricular and right atrial pressures. The TTE may also identify left atrial thrombus, although the sensitivity is low. Transesophageal echocardiography is much more sensitive for identifying thrombi in the left atrium or left atrial appendage and can be used to determine the need for anticoagulation prior to any attempt at pharmacologic or electrical cardioversion. (See "Role of echocardiography in atrial fibrillation" and 'Anticoagulation' below.)

Additional cardiac testing

— We refer patients with signs or symptoms of ischemic heart disease for exercise testing. (See

"Exercise ECG testing: Performing the test and interpreting the ECG results" and "Stress testing for the diagnosis of obstructive coronary heart disease".)

Exercise testing is useful to help guide pharmacotherapy for AF, as some antiarrhythmic medications are contraindicated in patients with coronary artery disease. (See "Antiarrhythmic drugs to maintain sinus rhythm in patients with atrial fibrillation: Recommendations", section on 'Selecting an antiarrhythmic drug'.)

Ambulatory cardiac monitoring with event recorders, adhesive extended time event monitors, or insertable cardiac monitors (also sometimes referred to as implantable cardiac monitors or implantable loop recorders) can be used to identify the arrhythmia if it is intermittent and not captured on routine ECG. Ambulatory ECG monitoring can also be utilized to correlate symptoms to the arrhythmia along with assessment of the AF burden. Twenty-four- to 48-hour Holter monitoring mainly aids in the evaluation of overall ventricular response rates in individuals where a rate control strategy has been chosen and there is concern for

inadequate heart rate control or bradycardia. (See "Ambulatory ECG monitoring".)

Laboratory testing

— We obtain a complete blood count, serum electrolytes, and assessment of renal function, particularly in patients for whom a nonvitamin oral anticoagulant might be started. We do not order troponin unless acute ischemia is suspected. Clinical or subclinical hyperthyroidism is present in less than 5 percent of patients with AF [20]. A thyroid-stimulating hormone and free T4 levels should be obtained in all patients with a first episode of AF, or in those who develop an increase in AF frequency. (See "Epidemiology, risk factors, and prevention of atrial fibrillation", section on 'Hyperthyroidism'.)

Other important baseline tests include a complete blood count to assess for underlying anemia or sign of infection and evaluation for diabetes mellitus [21]. (See "Clinical presentation, diagnosis, and initial evaluation of diabetes mellitus in adults".)

Other tests

— A chest radiograph may be a useful diagnostic

test in selected patients with evidence of dyspnea and potential heart failure or risk of pneumonia. (See "Heart failure: Clinical manifestations and diagnosis in adults", section on 'Chest radiograph'.)

INITIAL MANAGEMENT

— A useful framework for the general care of AF patients (including those with new-onset as well as longstanding AF) is the ABC (Atrial Fibrillation Better Care) pathway [22,23].

- "A" can be considered for anticoagulation
- "B" for better symptom management
- "C" for cardiovascular risk factor and comorbid disease assessment and management.

Observational studies [24,25], a post-hoc analysis of the AFFIRM trial [26], and a prospective randomized trial using a mobile application [27] suggest that the implementation of such a framework of care for AF patients may have a salutary impact on adverse cardiovascular events and hospitalizations, while being cost saving for healthcare systems [28].

Management setting

- **Outpatient versus emergency department** – Whereas most patients with newly diagnosed AF can often be managed in an outpatient setting, some unstable patients require direct hospital admission or transfer to emergency department from an outpatient setting. Indications for transfer to a facility with emergency services include the following:

    - Hemodynamic instability and/or shock (manifested as hypotension, confusion, acute kidney injury, etc).

    - Suspected or confirmed myocardial ischemia/infarction.

    - Suspected or confirmed heart failure. (See "The management of atrial fibrillation in patients with heart failure".)

    - Evidence of pre-excitation (eg, Wolff-Parkinson-White syndrome) on the ECG.

    - Extreme, uncontrolled tachycardia.

- Bothersome symptoms that may require urgent rate or rhythm control.
- Hypotension for which AF is suspected to be causal or contributory and for which standard therapy to treat underlying causes and hypotension including intravenous fluids, attempts at rate control, potentially inotropic therapy, and other measures that have failed. Care must be given to other potentially inciting factors such as sepsis, fluid depletion, or vasodilation.

For patients whose AF is thought to be secondary to an initiating comorbidity such as pneumonia, treatment of the underlying cause of AF is important and may reduce the long-term risk of recurrent AF.

Finally, for those patients who require urgent management, we generally obtain the same baseline diagnostic tests as in stable patients unless other clinical characteristics suggest otherwise. In this case, the diagnostic approach should also include work-up for the suspected underlying condition (eg,

pneumonia, pulmonary embolus, etc).

- **Indications for hospitalization** – Many patients with new-onset AF who are evaluated in an emergency room may not need to be hospitalized. However, indications for hospitalization in these patients include:

    - Patients in whom ablation of an accessory pathway is being considered, particularly if the AF was highly symptomatic and associated with hemodynamic collapse and rapid ventricular response rate.

    - Severe bradycardia or prolonged pauses, including after cardioversion. (See "Sinus node dysfunction: Epidemiology, etiology, and natural history".)

    - Treatment of an associated medical problem, which is often the reason for the arrhythmia (eg, hypertension, infection, exacerbation of chronic obstructive pulmonary disease, pulmonary embolism, pericarditis, persistent myocardial ischemia). It

should be noted that AF alone is not an indication to rule out myocardial infarction.

- Further management of heart failure or hypotension after control of the rhythm or rate.
- Initiation of antiarrhythmic drug therapy (if patient and drug characteristics necessitate hospitalization).
- Difficult-to-control ventricular rates with evidence of ischemia, congestive heart failure symptoms or signs, and severe symptoms are indications for at least a 24-hour admission.

- **Referral to cardiologist** – AF is a common medical problem and can often be managed by primary care physicians without need for consultation with a cardiologist. We suggest patient referral when the physician is not comfortable with decision-making or when catheter ablation of AF is under consideration. Also, when cardioversion or

antiarrhythmic drugs are contemplated, cardiology consultation is advantageous.

Anticoagulation

— Every patient with AF should be evaluated for the need for antithrombotic therapy to prevent systemic embolization even for the first AF episode. This is accomplished by use of a risk-scoring system for incident stroke called the CHA_2DS_2-VASc score (table 1). Patients who require antithrombotic therapy include those in whom cardioversion (whether electrically or pharmacologically) to sinus rhythm is being considered (regardless of the CHA_2DS_2-VASc score or method of cardioversion [electrical or pharmacologic]) and those who meet criteria for long-term anticoagulation. All patients whose risk of embolization exceeds the risk of bleeding are candidates for long-term antithrombotic therapy. These issues are discussed in detail elsewhere.

- (Related Pathway(s): Atrial fibrillation: Anticoagulation for adults with atrial fibrillation.)

Triggers

— In some cases, onset of AF is triggered by another acute medical diagnosis: hyperthyroidism, acute pulmonary embolism, myopericarditis, pneumonia, and after cardiac surgery. Treatment of specific triggers may lead to years or even a lifetime without further episodes of AF.

The treatment of a suspected precipitating cause may result in reversion to sinus rhythm.

For patients with severe hyperthyroidism, the main goal of therapy initially is rate control, anticoagulation, treatment of hyperthyroidism, and restoration of sinus rhythm once they are euthyroid. (See "Graves' hyperthyroidism in nonpregnant adults: Overview of treatment", section on 'Therapeutic approach'.)

Treatment of AF in patients with heart failure and/or chronic obstructive pulmonary disease should generally be undertaken simultaneously with treatment of their other condition. (See "The management of atrial fibrillation in patients with heart failure", section on 'Correction of reversible causes'.)

Cardiovascular risk factors — Identifying and

treating risk factors and comorbidities may help with AF symptoms and burden. Common risk factors and comorbidities that can lead to the development of AF include advanced age, hypertension, diabetes, obstructive sleep apnea, heart failure, and obesity. For most identified risk factors, we believe that treating the risk factor may reduce but not eliminate the likelihood of subsequent episodes of AF. A comprehensive description of risk factors for AF is discussed separately. (See "Epidemiology, risk factors, and prevention of atrial fibrillation", section on 'Chronic disease associations' and "Overview of established risk factors for cardiovascular disease".)

Symptom and hemodynamic management

Unstable patients

— In some hemodynamically unstable patients who manifest with signs or symptoms such as hypotension, altered mental status, or heart failure, we attempt ventricular rate control. Slowing of the ventricular rate will sometimes lead to spontaneous reversion to sinus rhythm. Rate control is usually performed with a beta blocker or calcium channel

blocker (verapamil or diltiazem). This is discussed in detail separately. (See "Control of ventricular rate in atrial fibrillation: Pharmacologic therapy".)

For patients with AF and heart failure, ventricular rate control strategies are discussed separately. (See "The management of atrial fibrillation in patients with heart failure", section on 'Rate control in heart failure with reduced ejection fraction'.)

If the patient remains hemodynamically unstable, emergency cardioversion should be performed, particularly if the hemodynamic compromise is due to an uncontrolled rapid ventricular rate and/or we believe that the lack of atrial contraction is impairing cardiac output. Emergent therapy with rate control and/or cardioversion for unstable patients is discussed separately. (See "Atrial fibrillation: Cardioversion", section on 'Unstable patients' and "Control of ventricular rate in atrial fibrillation: Pharmacologic therapy".)

Unless AF reverts spontaneously, a decision is made whether, when, and how cardioversion will be performed. Management of thromboembolic risk is a key consideration when cardioversion is considered. (See "Atrial fibrillation: Cardioversion"

and "Prevention of embolization prior to and after restoration of sinus rhythm in atrial fibrillation".)

If we decide to perform emergency cardioversion, the risk for a thromboembolic event needs to be considered. Most patients who will undergo cardioversion should be anticoagulated as soon as the decision is made to cardiovert or after assessment of their clinical thromboembolic risk based on their CHA_2DS_2-VASc score. Issues related to anticoagulation around the time of cardioversion are discussed in detail separately. (See "Prevention of embolization prior to and after restoration of sinus rhythm in atrial fibrillation", section on 'AF duration less than 48 hours' and "Atrial fibrillation: Cardioversion" and "Prevention of embolization prior to and after restoration of sinus rhythm in atrial fibrillation".)

Once the patient becomes hemodynamically stable, the remainder of the acute and long-term management is similar to that of stable patients.

Stable patients

— For **stable** patients with new-onset AF who do not meet the above criteria for emergency

management and in whom we have performed an evaluation, we try to accomplish the following in the outpatient setting:

- Evaluate the need to slow the ventricular rate.

- Discuss the possible need for cardioversion with the patient. If the patient is highly symptomatic or if there is new-onset AF even in the absence of symptoms, we usually attempt cardioversion. Among patients with new-onset AF, even if cardioversion is contemplated, it usually does not need to be performed urgently; the majority of these patients will spontaneously convert to sinus rhythm within 48 to 72 hours [29]. Among 1822 patients admitted to the hospital because of AF, 356 had an arrhythmia duration less than 72 hours. Sixty-eight percent of the patients with this short AF duration spontaneously reverted to sinus rhythm [29]. Two-thirds of those with spontaneous reversion had AF duration of less than 24 hours; AF duration less than 24 hours was the only predictor of spontaneous

reversion.

A detailed discussion of cardioversion, including reasons to not cardiovert, is found elsewhere. (See "Atrial fibrillation: Cardioversion" and "Rhythm control versus rate control in atrial fibrillation", section on 'Summary and recommendations'.)

The choice of electrical or pharmacologic cardioversion requires consideration of the efficacy and safety of the approach, comorbidities, stability, preferences of the patient, and comfort of the clinician to use one or the other approach. This issue is discussed in detail elsewhere. (See "Atrial fibrillation: Cardioversion", section on 'Electrical versus pharmacologic cardioversion'.)

- Determine the need for acute and long-term anticoagulant therapy.
- Discuss the cause (if known) and natural history of AF. (See 'Sequelae' below.)
- Consider consultation with a cardiologist. Reasons to consult a cardiologist include the

need for cardioversion or the need to treat with antiarrhythmic drugs or catheter ablation. (See 'Management setting' above.)

- Schedule follow-up. (See 'Long-term management' below.)

LONG-TERM MANAGEMENT

Early follow-up

— Follow-up after an episode of acute AF is necessary to evaluate the safety and efficacy of rate or rhythm control, patient adherence with anticoagulant and antiarrhythmic therapy, need for continued therapies for AF, to discuss any strategies to reduce AF recurrence, and to assess the functional status of the patient.

For many patients, a one-week follow-up visit, or as soon as possible if one week is not realistic for a particular patient, is a reasonable strategy. This early return is particularly important for patients started on antiarrhythmic drug therapy to assess safety, efficacy, and side effects that can be specific to their therapy. (See "Antiarrhythmic drugs to maintain sinus rhythm in patients with atrial fibrillation: Recommendations".)

Prevention of thromboembolism

— Following initial pre- and postcardioversion anticoagulation, the decision to continue long-term anticoagulation following a single reversible incident is debatable, and the decision is highly individualized based on the presumed future risk of recurrent AF in that individual (vis a vis CHA_2DS_2-VASc score). It is also reasonable to take an observational approach following a reversible cause of AF involving clinical follow-up of symptoms and ambulatory monitoring for surveillance for possible recurrence. (See "Atrial fibrillation in adults: Selection of candidates for anticoagulation".)

Among patients with AF, thrombus in the left atrial appendage is the primary source for thromboemboli. (See "Hemodynamic consequences of atrial fibrillation and cardioversion to sinus rhythm", section on 'Atrial stunning'.)

A subset of patients who require long-term anticoagulation may be unable to take it due to high bleeding risk or poor adherence. In such patients, occlusion of the left atrial appendage may be considered. After left atrial appendage

occlusion, patients are required to be on short-term anticoagulation. Left atrial appendage occlusion is described in detail separately. (See "Atrial fibrillation: Left atrial appendage occlusion".)

AF recurrence

— Continuous cardiac monitoring studies have shown that approximately 90 percent of patients with AF have recurrent episodes of AF [30]. However, up to 90 percent of episodes are not recognized by the patient [31], and asymptomatic episodes lasting more than 48 hours are not

uncommon, occurring in 17 percent of patients in a study that used continuous ECG monitoring to detect AF [30]. The latter study also showed that 40 percent of patients had episodes of AF-like symptoms in the absence of AF. (See "Paroxysmal atrial fibrillation", section on 'Natural history'.)

Some methods to reduce AF recurrence and/or burden including the following:

- **Alcohol reduction** – Alcohol is a modifiable risk factor for AF, and among people who consume an excessive amount of alcohol, reduction and abstinence appear to decrease

the risk of recurrent AF and time in AF. (See "Epidemiology, risk factors, and prevention of atrial fibrillation", section on 'Alcohol'.)

In one study, 140 symptomatic patients with paroxysmal or persistent AF who were in sinus rhythm at baseline and who consumed 10 or more standard drinks per week (about 120 g of pure alcohol) were randomly assigned to alcohol abstention or usual alcohol consumption [32]. After six months, patients underwent comprehensive rhythm monitoring.

Patients assigned to abstinence had:

- Greater reduction in their alcohol intake from 16.8 to 2.1 standard drinks per week, while those in the usual consumption group reduced their consumption from 16.4 to 13.2 per week.

- Lower rates of recurrent AF (53 versus 73 percent of the two groups). Recurrence of AF was also delayed in the abstinence group, and the AF

burden was significantly lower.

- **Weight loss and physical activity** – Among patients with AF, both of these measures can lead to healthy cardiac remodeling [33] and reduce AF burden [33,34] and cardiovascular mortality [35,36]:

    - In one study, 150 patients with symptomatic AF and a body mass index in the overweight or greater range ($\geq$ 25 kg/m^2) were randomized to a weight management intervention or general lifestyle advice [33]. After 15 months, participants assigned the intervention showed a greater reduction in weight compared with the general lifestyle advice group (14.3 versus 3.6 kg). The intervention group also had a greater reduction in AF symptom burden (11.8 versus 2.6 points), symptom severity scores (8.4 versus 1.7 points), number of AF episodes (2.5 fewer versus no change), and cumulative AF duration (692-minute decline versus 419-minute increase). Echocardiographic cardiac

remodeling parameters also improved in the intervention versus control group (ie, reduction in interventricular septal thickness [1.1 and 0.6 mm] and reduction in left atrial area [3.5 and 1.9 cm^2]).

- In a nonrandomized intervention study, 149 patients undergoing a catheter ablation for symptomatic AF were offered a three-month cardiovascular risk factor management program [34]. Patients had a body mass index of ≥ 27 kg/m^2 plus at least one additional cardiovascular risk factor. Sixty-one patients opted for the risk factor management intervention and 88 did not (the control group). On follow-up, patients who chose the intervention lost weight, whereas the control group gained weight (-13.2 versus +1.5 kg). The intervention group had a mean systolic blood pressure reduction, whereas the control group had a blood pressure increase (-34.1 versus 20.6).

Control of dyslipidemia was higher in the intervention compared with control group (46 versus 17 percent). More patients in the control group experienced AF recurrence (32.9 versus 9.7 percent; hazard ratio [HR] 2.6; 95 %CI, 1.7-4.0) compared with the intervention group.

- Among patients with AF, physical activity may lower cardiovascular mortality [35,36]. (See 'Benefit of physical activity' below.)

Rate or rhythm control

— Once ventricular rate control is achieved, a decision regarding the long-term management (rhythm versus rate control) of AF should be made; this decision depends on many factors. These are discussed in detail separately. (See "Rhythm control versus rate control in atrial fibrillation".)

The following points should be kept in mind irrespective of the strategy chosen:

- Both strategies can fail in the short and long term. Consequently, many patients need to be

reconsidered for the alternate strategy as the natural history of their disease progresses.

- All patients with AF, irrespective of strategy chosen/rhythm, should have their thromboembolic risk assessed and be managed accordingly. (See "Atrial fibrillation in adults: Selection of candidates for anticoagulation".)

- For patients who are managed with a rhythm-control strategy, rate control is necessary due to the possibility of recurrence of AF.

The advantages and disadvantages of rhythm and rate control, and subgroups of patients for whom one or the other is preferred, are discussed in greater detail separately. (See "Rhythm control versus rate control in atrial fibrillation".)

A rhythm-control strategy uses either antiarrhythmic drug therapy, percutaneous catheter ablation, and/or a surgical procedure. Electrical cardioversion may be necessary to restore sinus rhythm. Antiarrhythmic medications are generally started before cardioversion and continued to maintain sinus rhythm (in the event

of AF recurrence). (See "Atrial fibrillation: Surgical ablation", section on 'Maze procedure' and "Atrial fibrillation: Catheter ablation", section on 'Efficacy'.)

The decision regarding which of the above rhythm-control methods to pursue is discussed in detail separately. (See "Maintenance of sinus rhythm in atrial fibrillation: Catheter ablation versus antiarrhythmic drug therapy".)

Among patients undergoing cardiac surgery for another reason (eg, mitral valve or coronary artery bypass surgery), surgical ablation to control refractory AF can be done during the same procedure. Several surgical techniques have been developed for the control of refractory AF and maintenance of sinus rhythm. These surgical procedures appear effective at eliminating or reducing the frequency of AF in a high percentage of patients. For patients who are at high risk for stroke, long-term anticoagulation is still continued. This is discussed in detail separately. (See "Atrial fibrillation: Surgical ablation".)

A rate-control strategy generally uses drugs that slow conduction across the atrioventricular node

such as beta blockers, nondihydropyridine calcium channel blockers, or digoxin. Atrioventricular junction ablation with pacemaker placement is used in patients with persistent tachycardia, hemodynamic instability, and poorly tolerated and/or highly symptomatic AF, in whom rate control has not been successful. These approaches to ventricular rate control in AF are discussed in detail separately. (See "Control of ventricular rate in atrial fibrillation: Pharmacologic therapy" and "Atrial fibrillation: Atrioventricular node ablation".)

Most patients who present with AF will require slowing of the ventricular rate to improve symptoms. (See "Control of ventricular rate in atrial fibrillation: Pharmacologic therapy".)

Long-term follow-up

— Patients with paroxysmal, persistent, longstanding persistent, or permanent AF will need periodic care and occasional urgent evaluation during the natural history of their disease. (See 'Classification and terminology' above.)

We suggest routine follow-up every 12 months in stable patients and sooner if there are changes in

symptoms. Patients on high-risk antiarrhythmic therapy, such as dofetilide or sotalol, are often seen every six months. These patients may need to be under the care of a cardiologist and/or electrophysiology specialist for management of antiarrhythmic medications.

From time to time, patients should be monitored for the following:

- Efficacy and safety of antithrombotic therapy (international normalized ratio for patients on warfarin and creatinine clearance for patients on antiarrhythmic therapy and other newer anticoagulants).

- Functional status, including change in symptoms (history).

- Efficacy and safety of antiarrhythmic drug therapy (eg, ECG, assessment of renal and hepatic function). (See "Antiarrhythmic drugs to maintain sinus rhythm in patients with atrial fibrillation: Recommendations".)

- Efficacy of rate control (history, ECG, and extended Holter monitoring if variability in heart rate is suspected). (See "Control of

ventricular rate in atrial fibrillation: Pharmacologic therapy".)

In active patients with AF, we use stress testing to gauge adequacy of heart rate control in AF during exercise. Insufficient heart rate control in AF is a major factor for exercise intolerance in AF. (See "Ambulatory ECG monitoring".)

Laboratory testing

— We obtain a complete blood count, serum electrolytes, and assessment of renal function, particularly in patients for whom a nonvitamin oral anticoagulant might be started. We do not order troponin unless acute ischemia is suspected. Clinical or subclinical hyperthyroidism is present in less than 5 percent of patients with AF [20]. A thyroid-stimulating hormone and free T4 levels should be obtained in all patients with a first episode of AF, or in those who develop an increase in AF frequency. (See "Epidemiology, risk factors, and prevention of atrial fibrillation", section on 'Hyperthyroidism'.)

SEQUELAE

Myocardial infarction

— Myocardial infarction has been shown to occur as a result of a coronary artery thromboembolism resulting from AF [37,38]. However, large studies of this sequelae of AF are lacking.

Also, myocardial infarction from demand ischemia (also called type 2 myocardial infarction) can also result from AF, usually in the setting of a rapid ventricular rate. (See "Diagnosis of acute myocardial infarction", section on 'Comparing type 1 and 2 myocardial infarction'.)

Whereas tachyarrhythmias have been shown to account for about 25 percent of type 2 myocardial infarction [39], studies specifically studying AF and type 2 myocardial infarction are lacking.

In patients with a recent myocardial infarction, the subsequent development of AF increases mortality [40,41]. This effect is primarily due to associated risk factors such as heart failure and cardiogenic shock and not due to AF itself [41,42].

Mortality

AF and mortality

— AF is an independent risk factor for mortality across a wide age range and in both males and females, but the evidence is insufficient to establish AF as a cause of excess mortality rather than just a marker of high risk [43].

Rhythm-control trials among patients with AF suggest that those in sinus rhythm had lower mortality compared with those in AF [44,45]. In a secondary analysis of the randomized controlled AFFIRM trial of rhythm versus rate control in AF, the presence of sinus rhythm was associated with a significant reduction in mortality (hazard ratio [HR] 0.54; 95% CI 0.42-0.70) [44]. A similar benefit from being in sinus rhythm (relative risk 0.44; 95% CI 0.4-0.64) was noted in a separate trial of dofetilide in patients with reduced left ventricular function [45].

- **Strength of association** – Observational cohort studies have also shown that AF is associated with increased mortality [46-49]. In a post-hoc analysis of the Women's Health Study of 34,772 women with a median age of 53 who were free of AF, 2.9 percent developed AF at a median follow-up of 15.4

years [46]. New-onset AF was associated with a significantly increased adjusted risk of all-cause, cardiovascular, and noncardiovascular mortality (HR 2.14, 95% CI 1.64-2.77; HR 4.18, 95% CI 2.69-6.51; and HR 1.66, 95% CI 1.19-2.30, respectively). Adjustment for nonfatal cardiovascular events such as myocardial infarction, stroke, or heart failure lowered these risks, but incident AF remained significantly associated with all types of mortality (HR 1.7, HR 2.57, HR and 1.42, respectively).

- **Sex difference** – Several observational studies have suggested that the association between AF and death is greater in women with AF compared with men [47,48]. In a retrospective study of 272,186 patients with incidental AF at the time of hospitalization and 544,344 matched AF-free controls, the adjusted relative risk of death with AF was higher in females compared with males across all age categories (2.15 versus 1.76 for those <65 years, 1.72 versus 1.36 for those ages 65 to 74 years, and 1.44 versus 1.24 for those 75 to 85 years) [47]. In 621 participants in the

Framingham Heart Study, having AF led to an almost doubling of the risk of death in both men and women (adjusted odds ratio 1.9 for women and 1.5 for men) (figure 1) [48]. This sex difference in the association between AF and mortality was also shown in a separate study of 15,000 men and women [49].

- **Cause of excess mortality** – In participants with AF in the Framingham Heart Study, both heart failure and stroke contributed to the excess mortality [48]. In addition, in an observational study of over 20,000 individuals in two cohorts, incident AF was associated with an increased risk of sudden cardiac death (HR 2.47; 95% CI 1.95-3.13) as well as nonsudden cardiac death (HR 2.98; 95% CI 2.52-3.53) [50]. The specific causes of death, as well as their frequency and predictors, were evaluated using follow-up data from the RE-LY trial comparing dabigatran with warfarin [51]. Among 18,113 randomized patients with a median follow-up of two years, the annual mortality rate was 3.84 percent. Cardiac deaths (sudden cardiac death and progressive heart failure)

accounted for 37.4 percent of these; stroke and hemorrhagic death accounted for 9.9 percent.

- **Predictors of mortality in patients with AF** – In the RE-LY trial , the strongest independent clinical predictors of cardiac death were heart failure, intraventricular conduction delay on an ECG, and prior myocardial infarction [51]. In a post-hoc analysis of the RACE II trial, the risk of cardiovascular morbidity and mortality was highest in those with the greatest symptom burden as assessed with the Toronto AF Severity Scale [52]. This finding was driven by the increased rate of heart failure hospitalizations.

Benefit of physical activity

— As in the general population, among patients with AF, physical activity can significantly reduce cardiovascular mortality [35,36]. (See "The benefits and risks of aerobic exercise", section on 'Mortality'.)

In a prospective Danish study of over 1100 individuals with AF, metabolic equivalents were

used to estimate cardiorespiratory fitness, and patients were followed for up to nine years for mortality outcomes. This study observed that each one-metabolic equivalent task higher was associated with a lower risk of all-cause mortality (HR 0.88; 95% CI 0.81-0.95) and cardiovascular disease mortality (HR 0.85; 95% CI 0.76-0.95) [35]. Patients meeting European Society of Cardiology physical activity recommendations had a lower risk of cardiovascular mortality compared with inactive patients (HR 0.54; 95% CI 0.34-0.86) [36].

Stroke and silent cerebral ischemia

- **Stroke** – Stroke is the most frequent major complication of AF; this topic is discussed in detail separately. (See "Atrial fibrillation in adults: Use of oral anticoagulants" and "Atrial fibrillation in adults: Selection of candidates for anticoagulation".) (Related Pathway(s): Atrial fibrillation: Anticoagulation for adults with atrial fibrillation.)

- **Silent cerebral ischemia** – Silent cerebral ischemia occurs in a patient who has specific lesions on imaging studies in the absence of

clinical complaints or findings. Among patients with AF, these lesions are relatively common; this is discussed in detail separately. (See "Stroke in patients with atrial fibrillation", section on 'Silent cerebral infarction'.)

Cognitive impairment and dementia

— AF increases the risk of cognitive impairment, all-cause dementia, vascular dementia, and Alzheimer's disease [53,54]. It is uncertain whether anticoagulation protects against dementia [54,55]. This is discussed in detail separately. (See "Risk factors for cognitive decline and dementia", section on 'Atrial fibrillation'.)

Heart failure

— AF is a risk factor for new-onset heart failure. This is discussed separately. (See "The management of atrial fibrillation in patients with heart failure", section on 'Epidemiology'.)

SOCIETY GUIDELINE LINKS

— Links to society and government-sponsored guidelines from selected countries and regions

around the world are provided separately. (See "Society guideline links: Atrial fibrillation" and "Society guideline links: Arrhythmias in adults".)

INFORMATION FOR PATIENTS

— UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the

keyword(s) of interest.)

- Basics topics (see "Patient education: Atrial fibrillation (The Basics)" and "Patient education: Medicines for atrial fibrillation (The Basics)" and "Patient education: Coping with high drug prices (The Basics)" and "Patient education: Heart failure and atrial fibrillation (The Basics)")

- Beyond the Basics topics (see "Patient education: Atrial fibrillation (Beyond the Basics)" and "Patient education: Coping with high prescription drug prices in the United States (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Background** – Atrial fibrillation (AF) is the most common cardiac arrhythmia that can have adverse consequences related to a reduction in cardiac output (symptoms) and atrial and atrial appendage thrombus formation (stroke and peripheral embolization) (waveform 1).

- **Classification** – Patients are classified as having paroxysmal, persistent, longstanding persistent, or permanent AR. Other classifications include subclinical or occult AF. (See 'Classification and terminology' above.)

- **Screening** – We do not screen asymptomatic patients for AF. There is no sufficient evidence that screening for AF will substantially detect more AF or protect against cardiac events. Electrocardiograms (ECGs) do not appear more effective than pulse palpation at AF detection. (See 'Screening' above.)

- **Presentation and Evaluation** – A new diagnosis of AF can present in a variety of ways; sometimes the patient has symptoms of AF and other times it is picked up incidentally. (See 'Common scenarios' above.)

  Essential information from the patient's symptoms and past medical history, physical examination, electrocardiogram (ECG), and a transthoracic echocardiogram (TTE) should be obtained at the time of diagnosis and

periodically during the course of the disease. Additional laboratory testing, such as thyroid stimulating hormone assay, and ambulatory ECG monitoring may be necessary. (See 'History and physical examination' above and 'Laboratory testing' above.)

- **Initial steps in all patients**

    - It is important to decide whether the patient should be managed as an outpatient or in the emergency room or acute hospital setting. When deciding, we take the patient's presentation, symptom burden, and associated conditions into consideration. (See 'Management setting' above.)

    - Other initial steps for all patients include consideration of antithrombotic therapy, treatment of potentially reversible triggers of AF, and cardiovascular risk factor management. (See 'Initial management' above.)

        - (Related Pathway(s): Atrial fibrillation: Anticoagulation for

adults with atrial fibrillation.)

- **Acute symptom management** – Symptom management starts with rate control of acute AF episodes and early decision-making regarding the need for cardioversion.

    - **Unstable patients** – In some hemodynamically unstable patients, ventricular rate control can be attempted; slowing of the ventricular rate sometimes leads to spontaneous reversion to sinus rhythm. If rate control does not work and the patient remains hemodynamically unstable, we pursue cardioversion; if we decide to perform emergency cardioversion, the risk for a thromboembolic event needs to be considered. (See "Prevention of embolization prior to and after restoration of sinus rhythm in atrial fibrillation", section on 'AF duration less than 48 hours'.)

    - **Stable patients** – For stable patients, usually in the nonacute care setting, we discuss the need for possible

cardioversion, need for acute and long-term anticoagulant therapy, the cause (if known), and natural history of AF. (See 'Sequelae' above.)

We consider consultation with a cardiologist. Reasons to consult a cardiologist include the need for cardioversion or the need to treat with antiarrhythmic drugs or catheter ablation. (See 'Management setting' above.)

- **Long-term management** – Follow-up after an episode of acute AF is necessary to evaluate the safety and efficacy of rate or rhythm control, patient adherence with anticoagulant and antiarrhythmic therapy, need for continued therapies for AF, to discuss any strategies to reduce AF recurrence, and to assess the functional status of the patient. Lifestyle modification with reducing alcohol consumption, weight reduction, and increasing physical activity can reduce AF burden and decrease recurrence. (See 'Long-term management'

above.)

- **Sequelae** – In the absence of a reversible precipitant, AF is typically recurrent. AF is associated with increased risk of mortality, stroke, silent cerebral ischemia, cognitive impairment, dementia, and heart failure. Physical activity and higher cardiorespiratory fitness may protect against mortality in AF. (See 'Sequelae' above.)

ACKNOWLEDGMENT

— The UpToDate editorial staff acknowledges Alan Cheng, MD, who contributed to an earlier version of this topic review.

REFERENCES

1. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation 2014; 130:e199.

2. Wyse DG, Van Gelder IC, Ellinor PT, et al. Lone atrial fibrillation: does it exist? J Am Coll Cardiol 2014; 63:1715.
3. Svennberg E, Friberg L, Frykman V, et al. Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial. Lancet 2021; 398:1498.
4. Svendsen JH, Diederichsen SZ, Højberg S, et al. Implantable loop recorder detection of atrial fibrillation to prevent stroke (The LOOP Study): a randomised controlled trial. Lancet 2021; 398:1507.
5. US Preventive Services Task Force, Davidson KW, Barry MJ, et al. Screening for Atrial Fibrillation: US Preventive Services Task Force Recommendation Statement. JAMA 2022; 327:360.
6. Lubitz SA, Atlas SJ, Ashburner JM, et al. Screening for Atrial Fibrillation in Older Adults at Primary Care Visits: VITAL-AF Randomized Controlled Trial. Circulation 2022; 145:946.
7. Perez MV, Mahaffey KW, Hedlin H, et al.

Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation. N Engl J Med 2019; 381:1909.
8. Diederichsen SZ, Haugan KJ, Kronborg C, et al. Comprehensive Evaluation of Rhythm Monitoring Strategies in Screening for Atrial Fibrillation: Insights From Patients at Risk Monitored Long Term With an Implantable Loop Recorder. Circulation 2020; 141:1510.
9. Jonas DE, Kahwati LC, Yun JDY, et al. Screening for Atrial Fibrillation With Electrocardiography: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2018; 320:485.
10. Bano A, Rodondi N, Beer JH, et al. Association of Diabetes With Atrial Fibrillation Phenotype and Cardiac and Neurological Comorbidities: Insights From the Swiss-AF Study. J Am Heart Assoc 2021; 10:e021800.
11. Echouffo-Tcheugui JB, Shrader P, Thomas L, et al. Care Patterns and Outcomes in Atrial Fibrillation Patients With and Without Diabetes: ORBIT-AF Registry. J Am Coll Cardiol 2017; 70:1325.

12. Sanna T, Diener HC, Passman RS, et al. Cryptogenic stroke and underlying atrial fibrillation. N Engl J Med 2014; 370:2478.
13. Noseworthy PA, Kaufman ES, Chen LY, et al. Subclinical and Device-Detected Atrial Fibrillation: Pondering the Knowledge Gap: A Scientific Statement From the American Heart Association. Circulation 2019; 140:e944.
14. Healey JS, Connolly SJ, Gold MR, et al. Subclinical atrial fibrillation and the risk of stroke. N Engl J Med 2012; 366:120.
15. Walkey AJ, Benjamin EJ, Lubitz SA. New-onset atrial fibrillation during hospitalization. J Am Coll Cardiol 2014; 64:2432.
16. Tung P, Levitzky YS, Wang R, et al. Obstructive and Central Sleep Apnea and the Risk of Incident Atrial Fibrillation in a Community Cohort of Men and Women. J Am Heart Assoc 2017; 6.
17. Lavie CJ, Pandey A, Lau DH, et al. Obesity and Atrial Fibrillation Prevalence, Pathogenesis, and Prognosis: Effects of Weight Loss and Exercise. J Am Coll Cardiol

2017; 70:2022.
18. Wang TJ, Parise H, Levy D, et al. Obesity and the risk of new-onset atrial fibrillation. JAMA 2004; 292:2471.
19. Wynn GJ, Todd DM, Webber M, et al. The European Heart Rhythm Association symptom classification for atrial fibrillation: validation and improvement through a simple modification. Europace 2014; 16:965.
20. Krahn AD, Klein GJ, Kerr CR, et al. How useful is thyroid function testing in patients with recent-onset atrial fibrillation? The Canadian Registry of Atrial Fibrillation Investigators. Arch Intern Med 1996; 156:2221.
21. European Heart Rhythm Association, European Association for Cardio-Thoracic Surgery, Camm AJ, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J 2010; 31:2369.
22. Lip GYH. The ABC pathway: an integrated

approach to improve AF management. Nat Rev Cardiol 2017; 14:627.
23. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J 2021; 42:373.
24. Yoon M, Yang PS, Jang E, et al. Improved Population-Based Clinical Outcomes of Patients with Atrial Fibrillation by Compliance with the Simple ABC (Atrial Fibrillation Better Care) Pathway for Integrated Care Management: A Nationwide Cohort Study. Thromb Haemost 2019; 119:1695.
25. Pastori D, Pignatelli P, Menichelli D, et al. Integrated Care Management of Patients With Atrial Fibrillation and Risk of

Cardiovascular Events: The ABC (Atrial fibrillation Better Care) Pathway in the ATHERO-AF Study Cohort. Mayo Clin Proc 2019; 94:1261.
26. Proietti M, Romiti GF, Olshansky B, et al. Improved Outcomes by Integrated Care of Anticoagulated Patients with Atrial Fibrillation Using the Simple ABC (Atrial Fibrillation Better Care) Pathway. Am J Med 2018; 131:1359.
27. Guo Y, Lane DA, Wang L, et al. Mobile Health Technology to Improve Care for Patients With Atrial Fibrillation. J Am Coll Cardiol 2020; 75:1523.
28. Pastori D, Farcomeni A, Pignatelli P, et al. ABC (Atrial fibrillation Better Care) Pathway and Healthcare Costs in Atrial Fibrillation: The ATHERO-AF Study. Am J Med 2019; 132:856.
29. Danias PG, Caulfield TA, Weigner MJ, et al. Likelihood of spontaneous conversion of atrial fibrillation to sinus rhythm. J Am Coll Cardiol 1998; 31:588.
30. Israel CW, Grönefeld G, Ehrlich JR, et al. Long-term risk of recurrent atrial fibrillation

as documented by an implantable monitoring device: implications for optimal patient care. J Am Coll Cardiol 2004; 43:47.
31. Page RL, Wilkinson WE, Clair WK, et al. Asymptomatic arrhythmias in patients with symptomatic paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia. Circulation 1994; 89:224.
32. Voskoboinik A, Kalman JM, De Silva A, et al. Alcohol Abstinence in Drinkers with Atrial Fibrillation. N Engl J Med 2020; 382:20.
33. Abed HS, Wittert GA, Leong DP, et al. Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation: a randomized clinical trial. JAMA 2013; 310:2050.
34. Pathak RK, Middeldorp ME, Lau DH, et al. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the ARREST-AF cohort study. J Am Coll Cardiol 2014; 64:2222.
35. Garnvik LE, Malmo V, Janszky I, et al. Physical activity, cardiorespiratory fitness,

and cardiovascular outcomes in individuals with atrial fibrillation: the HUNT study. Eur Heart J 2020; 41:1467.

36. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2016; 37:2315.
37. Schmitt J, Duray G, Gersh BJ, Hohnloser SH. Atrial fibrillation in acute myocardial infarction: a systematic review of the incidence, clinical features and prognostic implications. Eur Heart J 2009; 30:1038.
38. Garg RK, Jolly N. Acute myocardial infarction secondary to thromboembolism in a patient with atrial fibrillation. Int J Cardiol 2007; 123:e18.
39. Belkouche A, Yao H, Putot A, et al. The

Multifaceted Interplay between Atrial Fibrillation and Myocardial Infarction: A Review. J Clin Med 2021; 10.

40. Crenshaw BS, Ward SR, Granger CB, et al. Atrial fibrillation in the setting of acute myocardial infarction: the GUSTO-I experience. Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries. J Am Coll Cardiol 1997; 30:406.
41. Eldar M, Canetti M, Rotstein Z, et al. Significance of paroxysmal atrial fibrillation complicating acute myocardial infarction in the thrombolytic era. SPRINT and Thrombolytic Survey Groups. Circulation 1998; 97:965.
42. Goldberg RJ, Seeley D, Becker RC, et al. Impact of atrial fibrillation on the in-hospital and long-term survival of patients with acute myocardial infarction: a community-wide perspective. Am Heart J 1990; 119:996.
43. Leong DP, Eikelboom JW, Healey JS, Connolly SJ. Atrial fibrillation is associated with increased mortality: causation or

association? Eur Heart J 2013; 34:1027.
44. Corley SD, Epstein AE, DiMarco JP, et al. Relationships between sinus rhythm, treatment, and survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study. Circulation 2004; 109:1509.
45. Pedersen OD, Bagger H, Keller N, et al. Efficacy of dofetilide in the treatment of atrial fibrillation-flutter in patients with reduced left ventricular function: a Danish investigations of arrhythmia and mortality on dofetilide (diamond) substudy. Circulation 2001; 104:292.
46. Conen D, Chae CU, Glynn RJ, et al. Risk of death and cardiovascular events in initially healthy women with new-onset atrial fibrillation. JAMA 2011; 305:2080.
47. Andersson T, Magnuson A, Bryngelsson IL, et al. All-cause mortality in 272,186 patients hospitalized with incident atrial fibrillation 1995-2008: a Swedish nationwide long-term case-control study. Eur Heart J 2013; 34:1061.
48. 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.
49. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. Am J Med 2002; 113:359.
50. Chen LY, Sotoodehnia N, Bůžková P, et al. Atrial fibrillation and the risk of sudden cardiac death: the atherosclerosis risk in communities study and cardiovascular health study. JAMA Intern Med 2013; 173:29.
51. Marijon E, Le Heuzey JY, Connolly S, et al. Causes of death and influencing factors in patients with atrial fibrillation: a competing-risk analysis from the randomized evaluation of long-term anticoagulant therapy study. Circulation 2013; 128:2192.
52. Vermond RA, Crijns HJ, Tijssen JG, et al. Symptom severity is associated with cardiovascular outcome in patients with permanent atrial fibrillation in the RACE II study. Europace 2014; 16:1417.

53. Papanastasiou CA, Theochari CA, Zareifopoulos N, et al. Atrial Fibrillation Is Associated with Cognitive Impairment, All-Cause Dementia, Vascular Dementia, and Alzheimer's Disease: a Systematic Review and Meta-Analysis. J Gen Intern Med 2021; 36:3122.
54. Kim D, Yang PS, Yu HT, et al. Risk of dementia in stroke-free patients diagnosed with atrial fibrillation: data from a population-based cohort. Eur Heart J 2019; 40:2313.
55. Moffitt P, Lane DA, Park H, et al. Thromboprophylaxis in atrial fibrillation and association with cognitive decline: systematic review. Age Ageing 2016; 45:767.

Topic 1022 Version 81.0