Acute Management of Atrial Fibrillation

From Emergency Department to Cardiac Care Unit

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KEYWORDS

• Atrial fibrillation • Cardioversion • Rate control • Rhythm control • Stroke • Thromboembolism • Arrhythmia • Anticoagulation

KEY POINTS

- Atrial fibrillation is a complex disorder resulting from various causes that include reversible causes and progressive arrhythmic substrates that underlie initiation, recurrence, persistence, and progression of atrial fibrillation.
- Primary management goals include (1) accurate diagnosis, (2) clinical stabilization, (3) recognition and treatment of reversible causes and risk factors, (4) symptom management with rate and/or rhythm control, and (5) prevention of cardioembolic events.
- Atrial fibrillation may present with heterogeneous symptoms and severity that affect quality of life to varying degrees and may cloud initial evaluation.
- Restoration and maintenance of sinus rhythm have the primary goal of symptom control. This may not be required in all patients in the absence of mortality benefit but may improve quality of life.
- Multiple tools are available to stratify thromboembolic and hemorrhagic risks to guide optimal and safe methods of stroke prevention, which must be determined acutely and reassessed chronically.

INTRODUCTION

Atrial fibrillation (AF) has challenged physicians for more than 800 years since it was initially described by Maimonides in 1187.[1] Despite improved understanding of mechanism and therapy, optimal strategies to manage AF remain unclear.[2] Acute management goals include diagnosis, clinical stabilization, symptom control of rate and/or rhythm, thromboembolic stroke prevention, and treatment of reversible causes. Optimized and individualized therapy based on these goals allows smooth transition from acute to long-term AF care and risk modification.

Definition

AF is a supraventricular tachyarrhythmia characterized by rapid, chaotic atrial activity with fibrillatory or absent P waves on electrocardiography (ECG) that vary in amplitude and morphology, and with atrial rates that frequently exceed 300 beats per minute (bpm) (**Fig. 1**). In the presence of intact atrioventricular (AV) conduction, the

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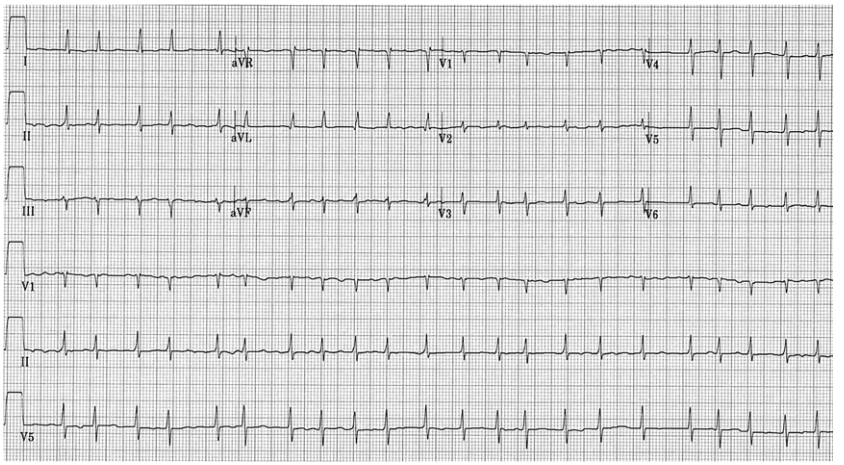

Fig. 1. AF with rapid ventricular response.

ventricular response rate is typically irregularly irregular with chaotic, rapid, and varying RR intervals. Abnormal AV conduction may blunt ventricular response rates. Atrial flutter (AFL) has been classified in multiple ways but is typically characterized by rapid, organized atrial activity at 250 to 350 bpm with negative sawtooth waves in the inferior ECG leads II, III, aVF and positive or biphasic waves in lead V1 (**Fig. 2**). Despite the organized nature of AFL, long-term complications and stroke risk are similar to those of AF.[3,4] Recommendations made in this article include AFL unless otherwise specified.

Epidemiology

AF is the most common arrhythmia, with estimated incidence of more than 75,000 and prevalence of more than 2.2 to 2.3 million in the United States and more than 6 million in the European Union

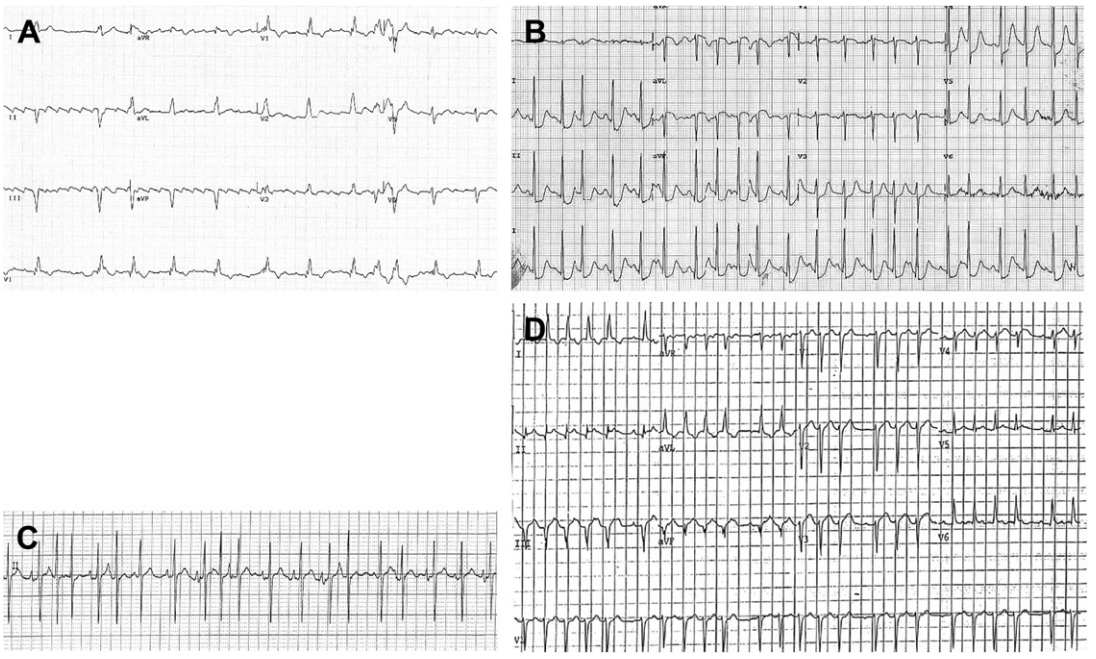

Fig. 2. Rhythms that may imitate AF. (*A*) Atrial flutter: typical negative sawtooth P waves in the inferior leads and positive P waves in V1 with variable atrioventricular block. (*B*) Sinus tachycardia with frequent atrial premature beats. (*C*) Multifocal atrial tachycardia: more than 3 discrete P wave morphologies are highlighted. (*D*) Atrial tachycardia with Mobitz I, second degree AV block (Wenckebach). (*Courtesy of* Stephen W. Smith, MD, Hennepin County Medical Center and University of Minnesota [*B*].)

(EU).[5–7] In the Medicare population, AF prevalence increased 5% per year between 1993 and 2007.[8] AF accounts for one-third of US hospitalizations with more than 529,000 annual discharges.[5,6] AF hospital admissions have increased 66% in the past 20 years.[9] Growth of the aging population and prevalent cardiopulmonary disorders, including hypertension, coronary artery disease (CAD), heart failure (HF), and valvular disease, contribute to increasing AF incidence (**Table 1**).[5,7] Systemic disorders including obesity, diabetes, and bronchopulmonary disease contribute to increasing AF prevalence, morbidity, and mortality, including HF and stroke.[10–14]

Approximately 15% to 20% of ischemic stroke is attributed to AF.[5,15,16] The ischemic stroke rate among patients with nonvalvular AF averages 5% per year, increases with age, and is 2 to 7 times the rate in patients without AF.[5,15,16]

AF is associated with increased overall and cardiovascular mortality.[17] Whether this is caused by AF or associated comorbid risks is unclear. However, interventions to maintain sinus rhythm (SR) once AF has occurred have not shown mortality benefit and highlight the importance of cardiovascular risk prevention.[18,19]

Causes and Pathophysiology

The pathophysiology of AF is multilayered and complex. Some reversible causes of AF include thyroid dysfunction, pain, and infection, and post-surgical states are associated with high rates of spontaneous conversion on correction of these conditions (see **Table 1**).[7,15] Approximately 50% of all AF in the emergency department (ED) spontaneously reverts to SR within 48 hours.[20] Whether this represents resolution of acute triggers or early events in AF natural history may be difficult to discriminate.

AF risk factors such as cardiopulmonary disease and aging initiate structural and electrophysiologic remodeling that underlie the recurrence, persistence, and progression of AF. AF begets further AF with progressive alterations in cardiomyocytes, cardiac fibroblasts, interstitial and microvascular architecture, systemic inflammatory state, cell coupling, left atrial (LA) dilatation, and

Table 1
Causes, risk factors, and associated conditions for AF

Reversible Conditions Associated with AF	Conditions Associated with Left Atrial Arrhythmic Substrate and AF
Alcohol intake (holiday heart syndrome)	Aging
Postoperative stress	Cardiovascular disease
Postcardiothoracic surgery (early)	• Hypertension
Pain	• Valvular disease
Infection	○ Mitral, aortic
Sepsis/systemic inflammatory response syndrome	• CAD
Myocardial infarction	• Heart failure
Pericarditis	○ Systolic, diastolic
Myocarditis	• Left ventricular hypertrophy
Pulmonary embolism	• Cardiomyopathy
Pneumonia	○ Hypertrophic
Asthma/chronic obstructive pulmonary disease exacerbation	○ Idiopathic/dilated
Hyperthyroidism	○ Primary electrical
Electrolyte abnormality	• Congenital heart disease
Autonomic tone	○ Atrial septal defect
Sympathetic	○ Other congenital defects
Parasympathetic (or vagal)	• Infiltrative disorders
Associated underlying arrhythmia:	○ Amyloidosis
• Atrial flutter	• Inflammatory sarcoidosis
• Wolff-Parkinson-White syndrome	Familial/genetic
• Atrioventricular node reentry tachycardia	Pulmonary
	• Chronic obstructive pulmonary disease
	• Obstructive sleep apnea
	Chronic kidney disease
	Systemic
	• Obesity
	• Diabetes mellitus

ion channels.[2,21] Atrial refractory properties, downregulation of L-type inward Ca^{2+} current, and upregulation of inward rectifier potassium (K^+) currents are altered within hours of AF onset.[7]

Classification

AF classifications presented in the 2006 American College of Cardiology (ACC)/American Heart Association (AHA)/European Society of Cardiology (ESC) and 2010 ESC Guidelines for AF are most commonly used because of their simplicity and clinical relevance (**Box 1**).[7,15] Asymptomatic AF episodes occur in patients with symptomatic AF.[22] Whether termination with antiarrhythmic therapy (AAT) or cardioversion alters paroxysmal or persistent AF designations varies with the 2006 or 2010 guidelines.[7,15] Long-standing persistent AF includes episodes of more than 1 year that frequently progress to permanent AF. Permanent AF has been unsuccessfully cardioverted or accepted within a long-term rate-control strategy.

Box 1
Classification of AF

First detected: no previously detected AF; duration and onset may be unknown.

Paroxysmal: recurrent episodes that self-terminate in less than 7 days.

Persistent: recurrent episodes that last more than 7 days

Long-standing persistent: persistent AF of more than 1 year's duration.

Permanent: ongoing long-term episodes accepted as part of a rate-control strategy or refractory to rhythm control.

Lone: AF in age less than 60 years in absence of clinical or echocardiographic findings of cardiopulmonary disease including hypertension. Prognosis in relation to mortality and thromboembolism is favorable.

Nonvalvular: episodes occur in absence of rheumatic mitral valve disease, a prosthetic heart valve, or mitral valve repair.

Secondary: episodes occur as a result of reversible causes such as acute myocardial ischemia, cardiac surgery, pericarditis, myocarditis, hyperthyroidism, or acute pulmonary disease.

Silent: asymptomatic episodes. Appreciation of subtle symptoms may develop. May also be paroxysmal, persistent, or permanent.

These terms typically apply to episodes of AF of more than 30 seconds in duration without reversible cause.

Classifications of AF are not mutually exclusive.

The natural history of AF typically includes clusters of initially brief, rare paroxysms that evolve to longer and more frequent episodes. Among patients without conditions that promote AF, the long-term risk of continued AF is 2% to 3%.[23] Over 25 years, ~31% of patients with paroxysmal or persistent AF progress to permanent AF.[23]

Socioeconomic Ramifications

AF is one of the most substantial economic burdens on the US health care system. Symptoms, sequelae, and psychological stress contribute to health care use, impaired quality of life, and likely loss of occupational productivity.[24,25] AF accounted for 276,000 ED and hospital outpatient visits in 2001.[26] Between 1996 and 2001, hospital discharges with a primary diagnosis of AF increased 34%.[5] In 2004, the estimated annual cost per patient was $3600.[27] Medicare expenditures related to AF have been estimated at $16 billion annually.[28]

Acute Evaluation in the ED

Successful transition of AF care depends on initial risk stratification and acute management. Initial AF assessment occurs in various inpatient or outpatient settings but often starts in the ED. Recommendations in this article are relevant to any site of initial AF management.

MANAGEMENT GOALS

Acute management of AF begins with accurate diagnosis, treatment of underlying causes and risks, acute stabilization, symptom control with rate and/or rhythm control, thromboembolic stroke risk stratification and modification, and transition to chronic management to prevent recurrence and complications of AF (**Fig. 3**).

Diagnosis

Focused but thorough history, including medical and procedural history, social and medication history, family history, physical examination, laboratory testing, and cardiac imaging, may elucidate AF patterns and causes.[7,15] Medication history identifies prior AF therapy and potential drug interactions. Family history increases AF risk 2-fold if any family member (and 4.7-fold if any family member aged <60 years) is affected by AF.[29] Physical examination frequently reveals an irregular pulse rate by palpation or auscultation. Essential examination features include signs of underlying causes, end-organ hypoperfusion, and HF.

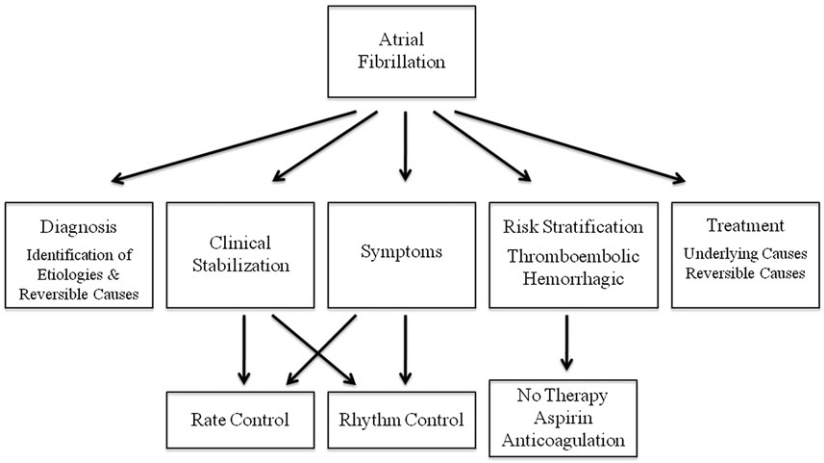

Fig. 3. Summary of acute management goals in AF.

AF presentations may vary with profound, subtle, or no symptoms. Initial manifestations may include hemodynamic instability, palpitations, cardiomyopathy, and stroke. More often, symptoms are subtle and nonspecific, including altered exercise tolerance, exertional dyspnea, and fatigue. AF may resolve before evaluation, and ambulatory cardiac rhythm monitoring may identify paroxysmal arrhythmias.

Diagnosis of AF requires high-quality ECG interpretation. AF frequently presents with rapid ventricular response (RVR) defined by ventricular rate more than 100 bpm (see **Fig. 1**). Other supraventricular tachyarrhythmias may mimic AF (see **Fig. 2**). Discriminating characteristics of these rhythms are reviewed in **Table 2**.

AF may present as wide complex tachycardia that may be challenging to differentiate from

Table 2
Discriminating characteristics of rhythms that imitate AF

	P Waves	Rhythm	Rate (bpm)
AF	Lack of organized or discernible P waves Coarse fibrillatory waves may mimic atrial flutter	Irregularly irregular QRS	Atrial: 300–600 Ventricular: normal, tachycardia, bradycardia
Multifocal atrial tachycardia	≥3 different P wave morphologies	Irregular Irregularly irregular	Atrial: >100–250 Ventricular: variable but often RVR rate
Sinus tachycardia with premature atrial complexes	Preservation of sinus P waves with intermittent PACs that may differ in P wave morphology	May seem irregular	Sinus P wave morphology and normal P wave axis >100 PACs with different coupling interval and morphology vs sinus
Atrial flutter	Counterclockwise or typical: (−) sawtooth pattern in inferior leads and (+) or biphasic in V1 Clockwise: opposite P wave findings Atypical: none of the waves listed earlier, usually with abnormal atrial substrate such as prior atrial ablation or cardiac surgery	P waves: regular QRS: regular or irregular	Atrial rate ~300 2:1 AV block frequently → ventricular rate ~150 (or multiples of atrial rate) Atrial rate and AV conduction may slow with AAT

Abbreviation: PAC, premature atrial contraction.

ventricular tachycardia. Preexisting bundle branch block (BBB), rate-related BBB, or aberrant conduction may manifest with wide complex tachycardia (**Fig. 4**). AAT or digoxin (Lanoxin) may regularize AF and require altered ECG sweep speed or duration for diagnosis.

On diagnosing AF, ECGs should be further reviewed for signs of predisposing factors, structural heart disease (SHD), or critical conditions that alter acute management. Some conditions apparent on ECG that predispose to AF risk include atrial enlargement, left ventricle (LV) hypertrophy, myocardial ischemia or myocardial infarction (MI), pulmonary conditions, pericardial disease, drug toxicity, hypothermia, and metabolic derangements (**Fig. 5**; see **Table 1**).

Assessment and Therapeutic Plan

Initial assessment includes determination of cardiopulmonary stability, symptom onset and severity, and thromboembolic versus hemorrhagic risk (see **Fig. 3**). Understanding AF causes, patterns, and stability stratifies patient risk and disposition. Detection of reversible or exacerbating causes allows rapid treatment and risk reduction (see **Table 1**). Evaluation for CAD is frequently initiated, but myocardial ischemia may contribute to, or result from, AF. Coronary evaluation should be tailored to CAD pretest probability based on signs and symptoms.

Echocardiography is an essential part of overall AF evaluation to determine cardiac structure and function. However, acute use of echocardiography is not recommended for AF alone and should be tailored to clinical suspicion of critical causes based on appropriateness guidelines.[30]

Acute Management of Patients with Symptoms or Hemodynamic Instability

Initial triage is determined by hemodynamic stability and symptoms. Myocardial ischemia, hypotension, angina, or HF prompts urgent therapy. Urgent electrical direct current cardioversion (DCC) is recommended in unstable scenarios while diagnostic assessment continues. If AF onset is within 48 hours, DCC may be performed without transesophageal echo (TEE) or systemic anticoagulation with stroke prevention directed by individualized risk stratification (**Fig. 6**; **Table 3**A–F). If onset is unknown or longer than 48 hours, TEE is recommended to evaluate for atrial thrombi. In the absence of anticoagulation, atrial thrombi are observed in 13% of patients, with 90% of thrombi found in the LA appendage.[31] If urgency of DCC precludes TEE, concurrent low-molecular-weight heparin (LMWH) or bolus intravenous (IV) heparin with infusion to achieve therapeutic activated partial thromboplastin time levels 2 times the upper limits of the reference range is recommended. Following cardioversion, atrial stunning, despite electrical systole, results in impaired atrial contraction in proportion to AF duration.[32] Atrial contractility usually improves within several days but may take 3 to 4 weeks.[15,32] Most thromboembolic events occur within 10 days, with 80% within 3 days.[33] Anticoagulation with vitamin K antagonism (VKA) to target International Normalized Ratio (INR) 2.0 to 3.0, direct thrombin inhibition, or factor Xa inhibition is recommended for at least 4 weeks during the highest thromboembolic risk period.[7,15]

Multiple methods of thromboembolic and hemorrhagic risk stratification have been described

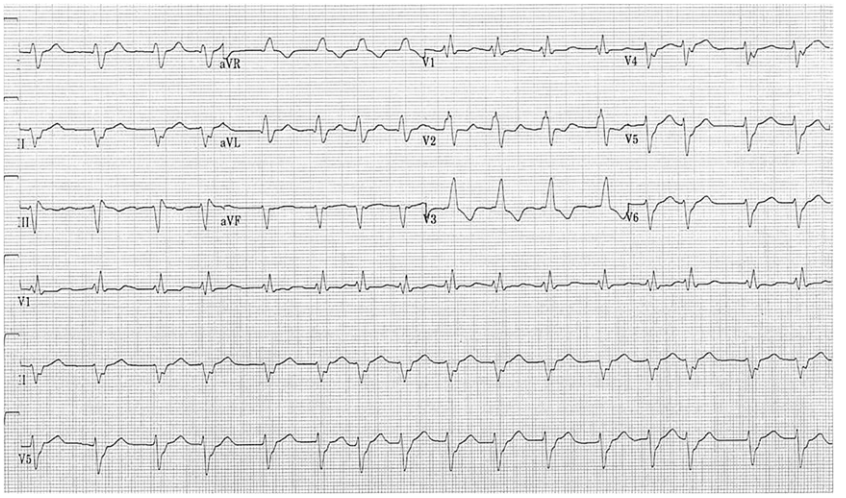

Fig. 4. AF with aberrancy presenting with wide complex rhythm.

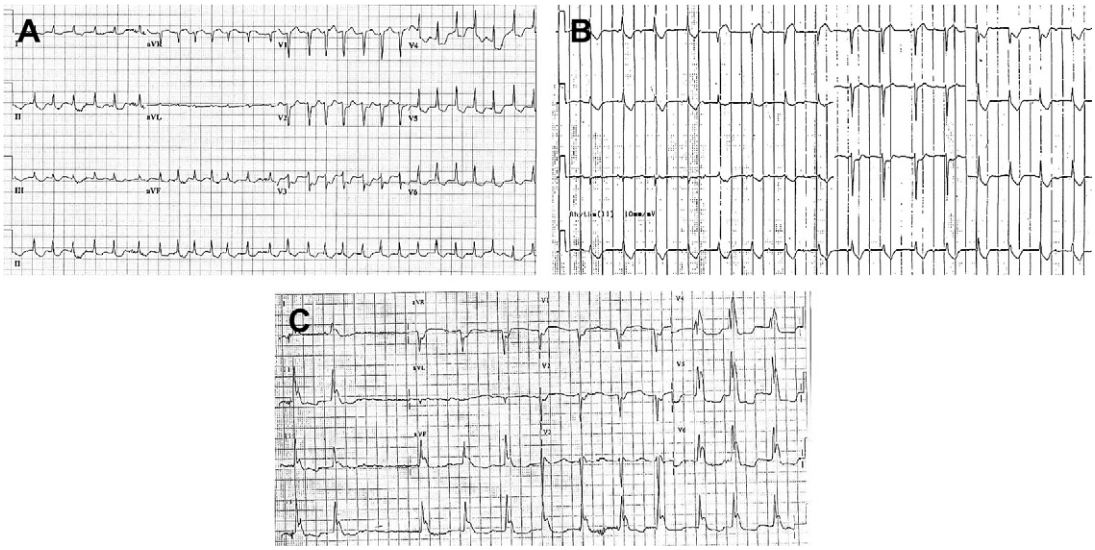

Fig. 5. Electrocardiographic clues to critical conditions coinciding with acute AF presentations. (*A*) Myocardial ischemia. (*B*) Digitalis toxicity: atrial tachycardia with AV block and repolarization abnormalities. (*C*) Hypothermia: AF, bradycardic ventricular response, and J or Osborne wave repolarization abnormalities. (*Courtesy of* Philip Podrid, MD, Boston University School of Medicine and West Roxbury Veteran's Affairs Medical Center [*B*, *C*].)

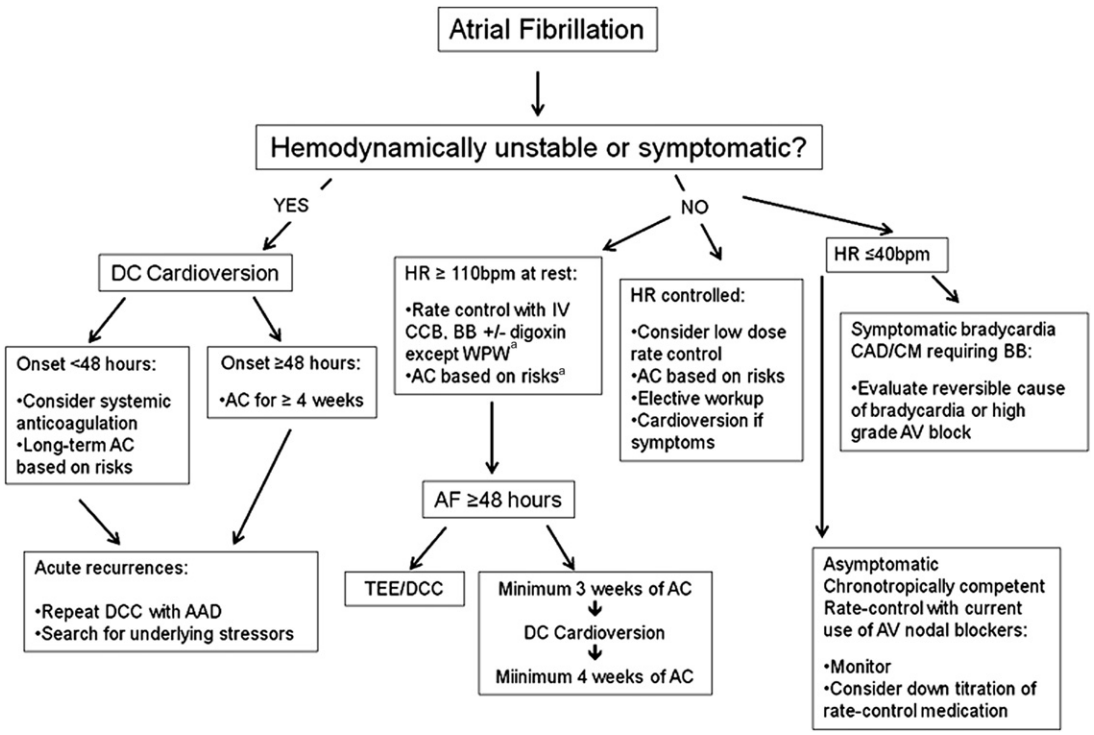

Fig. 6. Proposed approach to acute management of AF. Anticoagulation refers to vitamin K antagonists, direct thrombin inhibitors, or factor Xa inhibitors described in **Table 6**. Assumes identification and treatment of reversible causes and/or exacerbating risk factors highlighted in **Table 1** and **Fig. 3**. [a] Specific management goals in Wolff-Parkinson-White (WPW). AAD, antiarrhythmic drugs; AC, anticoagulation; BB, β-blocker; CCB, calcium channel blocker; CM, cardiomyopathy; HR, heart rate.

Table 3
Indices to stratify thromboembolic and hemorrhagic risks and associated thromboprophylaxis recommendations

(A) CHADS2 point system
(B) CHADS2 stroke risk
(C) CHADS-VASC point system
(D) CHADS-VASC stroke risk
(E) HAS-BLED score
(F) HAS-BLED hemorrhage risk

and validated. Among them, the CHADS2 (congestive heart failure, hypertension, age 75 years or older, diabetes mellitus, stroke or TIA or thromboembolism) and CHADS-VASC (vascular disease, age 65–74 years, sex category) scores (see **Table 3**A–F) are commonly used because of their simplicity and predictive value.[34,35] Thromboembolic and hemorrhagic risks must be balanced. HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly [>65 years], and concomitant drugs/alcohol) is a simple means of hemorrhagic risk stratification (see **Table 3**A–F).[36]

AF in the Stable Patient

Approximately 50% of all patients evaluated in the ED spontaneously convert from AF within 48 hours.[20] Among patients with spontaneous termination, 40% remained AF free for more than 5 years,[37] whereas others have described a 10% recurrence rate in the first year and 5% per year thereafter.[7] These findings may represent the resolution of reversible AF causes and/or early time points in AF natural history. In such settings, it is reasonable to monitor and rate-control patients while evaluation is initiated (see **Fig. 6**). Initial rate-control agents include β-blockers or nondihydropyridine calcium channel blockers (CCB). If these agents are contraindicated or inadequate, digoxin or amiodarone (Cordarone, Nexterone, Pacerone) may be considered in the absence of manifest preexcitation.[15] If rate control is refractory to multiple medications with continued symptoms or hemodynamic compromise, cardioversion is appropriate with concurrent cardioembolic risk modification.

In the presence of cardiovascular disease or persistent AF, AF recurrence rates are high after cardioversion. In the absence of mortality benefit from SR maintenance, initial rate control is appropriate unless patients are hemodynamically unstable or symptomatic. Patients refractory to or intolerant of AAT may benefit from electrophysiology consultation.

Table 3A
CHADS2 score

	CHADS2 Risk Factor	Score
C	Congestive HF	1
H	Hypertension	1
A	Age >75 y	1
D	Diabetes mellitus	1
S	Prior stroke or TIA[a]	2

[a] Systemic but noncerebrovascular thromboembolism included as stroke/TIA equivalent.

Abbreviation: TIA, transient ischemic attack.

Management of AF in Specific Scenarios

CAD and acute coronary syndrome

Dual antiplatelet therapy is recommended following acute coronary syndrome (ACS) and percutaneous coronary intervention (PCI). The prevalence of major bleeding with concurrent warfarin (Coumadin, Jantoven), aspirin, and clopidogrel (Plavix) is 2.6% to 4.6% at 30 days and 7.4% to 10.3% at 1 year.[7] Recent guidelines have recommended bare metal rather than drug eluting stents to allow short-term triple therapy if chronic anticoagulation is anticipated. Because warfarin and aspirin are similarly effective for secondary prevention of coronary events,[38,39] recent guidelines have recommended either anticoagulation alone for stable CAD or anticoagulation plus antiplatelet monotherapy following ACS and adequate time following PCI.[7] Development of AF during MI is associated with adverse short-term and long-term prognoses.[40]

AF and bradycardia

AF is typically associated with RVR, but AV conduction disease or AV nodal antagonists may result in slow ventricular rates. Distinguishing slow ventricular response from high-grade AV block may be challenging (**Fig. 7**). Regularized bradycardia with underlying AF and absence of AV nodal antagonists should prompt evaluation for high-grade AV block and potential pacing indications.

Tachy-brady syndrome describes sudden oscillations between paroxysmal AF and frequently associated sinus node dysfunction (SND). Tachy-brady syndrome may limit AF medication titration or result in symptomatic bradycardia, sinus pauses, or syncope (see **Fig. 7**).

Cardiac implantable electronic devices

Patients with implantable cardiac rhythm devices such as pacemakers or implantable cardioverter-defibrillators (ICD) may present with AF. Fibrillatory

Table 3B
Thromboembolic risk and treatment recommendations by CHADS2 score

CHADS2 Score	Adjusted Stroke Rate Per Year (%)	Thromboembolism Prevention AHA/ACC/ESC 2006	Thromboembolism Prevention ESC 2010
0	1.9	Aspirin 81–325 mg Consider no therapy	Aspirin or no therapy
1	2.8	Anticoagulation or aspirin: based on major risk factors Anticoagulation favored: (1) Female age >75 y; LVEF <35%	Age >75 y: Anticoagulation Age <75 y: Anticoagulation or aspirin
2	4.0	Anticoagulation	Anticoagulation
3	5.9	Anticoagulation	Anticoagulation
4+	8.5	Anticoagulation	Anticoagulation

Major risk factors: prior thromboembolic event; age >75 years in 2010 guidelines versus female age >75 years in 2006 guidelines.

2010 ESC guidelines have transitioned to a risk factor rather than risk score approach to thromboembolism prophylaxis.

Abbreviation: LVEF, left ventricular ejection fraction.

waves may be observed between ventricular paced complexes or with temporary pacing inhibition. Patients with ICDs may present with AF/RVR and inappropriate ICD therapy.[41] ICD shocks that effectively cardiovert or defibrillate ventricular arrhythmias may not cardiovert AF.

Ventricular preexcitation and Wolfe-Parkinson-White syndrome

Immediate DCC is recommended for preexcited AF with rapid tachycardia or hemodynamic instability (see **Fig. 6**; **Fig. 8**). RR intervals less than 250 milliseconds between consecutive preexcited QRS complexes suggest increased risk of preexcited AF degenerating to ventricular fibrillation and SCD.[42] because preexcitation reflects antegrade electrical fusion between decremental AV nodal and nondecremental accessory pathway conduction, AV nodal blockers including β-blockers, nondihydropyridine CCB, digoxin, and adenosine are contraindicated for preexcited AF.[15] If DCC is not immediately available, AATs that slow both accessory pathway and AV nodal conduction (including amiodarone, ibutilide, or procainamide) are reasonable.[15]

Pregnancy

AF is rare in pregnancy, but AF recurrence is common if previously diagnosed. Rate-control options include β-blockers, nondihydropyridine CCB, and digoxin, although first-trimester β-blocker use may be associated with growth retardation. Flecainide has been used for both pregnant and fetal arrhythmias. Amiodarone may have

Table 3C
CHADS-VASC score

	CHADS-VASC Risk Factor	Points	Thromboprophylaxis
C	Congestive heart failure/LV dysfunction	1	Risk Score
H	Hypertension	1	Risk Score
A	Age >75 y	2 (Major)	Anticoagulation
D	Diabetes mellitus	1	Risk Score
S	Stroke/TIA/TE	2 (Major)	Anticoagulation
V	Vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque)	1	Risk score
A	Age 65–74 y	1	Risk score
S C	Sex category (ie, female gender)	1	Risk score

Age >75 years and prior thromboembolic events are weighted major clinical risk factors for recurrent thromboembolism with recommendations for oral anticoagulation for thromboprophylaxis. Risk score refers to risk factor–based determination of thromboprophylaxis medication.

Abbreviation: TE, thromboembolism.

Table 3D
Thromboembolic risk and treatment recommendations by CHADS-VASC score

CHADS-VASC Score	Adjusted Stroke Rate (%/y)	Thromboprophylaxis Recommendations
0	0	Aspirin or no therapy
1	1.3	Anticoagulation preferred rather than aspirin Anticoagulation if >1 major risk factor[a]
2	2.2	Anticoagulation
3	3.2	Anticoagulation
4	4.0	Anticoagulation
5	6.7	Anticoagulation
6	9.8	Anticoagulation
7	9.6	Anticoagulation
8	6.7	Anticoagulation
9	15.2	Anticoagulation

[a] Major risk factors are: (1) age >75 years and (2) prior thromboembolic event.

negative fetal effects. DCC is recommended in unstable patients. Thromboembolism prophylaxis should be tailored to pregnancy stage and teratogenic and stroke risks.[7,15]

Rate-Control Targets

A randomized trial comparing lenient (<110 bpm) and strict (previously recommended <80 bpm at rest and <110 bpm with moderate exercise) heart rate control revealed noninferiority of lenient rate control in a primary outcome of cardiovascular death, HF and stroke hospitalization, systemic embolism, major bleeding, arrhythmic events, life-threatening adverse effects of rate-control drugs, and pacemaker or defibrillator implant.[43] Lenient rate control was easier to achieve.[43]

Consultation and Admission

Varying presentations, stability, and symptoms preclude unified recommendations for admission. First AF with stable hemodynamics and rate control absent symptoms or reversible causes may not require admission. Refractory tachycardia and hemodynamic instability may benefit from critical care evaluation. Critical coexisting issues or AF sequelae including MI pulmonary embolism, CVA, or sepsis may require critical care and cardiovascular specialty management.

Communication with primary care physicians and cardiologists is essential in overall AF management. Cardiac electrophysiologists provide subspecialty insight with particular attention to AAT or interventional therapy. Surgical or medical issues influence decisions regarding thromboembolic versus hemorrhagic risks. Drug interactions may result in significant morbidity, mortality, and rehospitalization (**Boxes 2** and **3**, **Table 4**).

Table 3E
HAS-BLED risk score

	HAS-BLED Risk Factor	Points
H	Hypertension	1
A	Abnormal liver and renal function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (eg, >65 y)	1
D	Drugs or alcohol (1 point each)	1 or 2

Abbreviation: INR, international normalization ratio.

Table 3F
HAS-BLED score and hemorrhagic risk

HAS-BLED Score	Bleeds Per 100 Patient-Years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.50
6	0.0
7	…
8	…
9	…
Any score	1.56

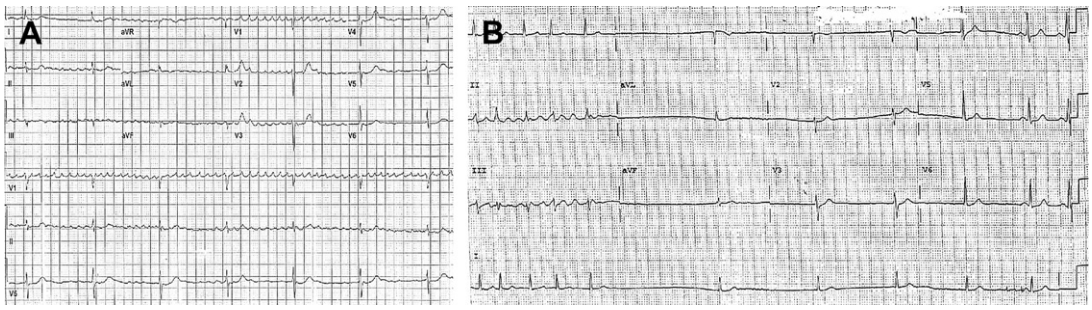

Fig. 7. AF associated with bradycardia. (*A*) AF with high-grade atrioventricular block and junctional escape rhythm. (*B*) Tachy-brady syndrome with paroxysmal AF termination and conversion pause before onset of sinus bradycardia. (*Courtesy of* P. Podrid, MD).

Atrial arrhythmias occur in 30% to 50% patients following cardiothoracic surgery. AF occurring late after cardiothoracic surgery suggests altered electroanatomic substrate that may benefit from arrhythmia consultation.[44] AF or AFL following cardiac transplant may represent rejection and should prompt evaluation by a transplant cardiologist.[45]

PHARMACOLOGIC STRATEGIES

Rate Control

Acute rate control may be achieved by IV or oral agents depending on desired time to onset, degree of tachycardia, symptoms, and hemodynamic stability. The optimal time over which to achieve rate control is unknown. β-Blockers, nondihydropyridine CCB, and digoxin are the mainstay of rate control (**Table 5**). Negative inotropy and chronotropy associated with β-blockers and CCB may precipitate HF, bradycardia, and AV block. Concurrent β-blocker and CCB administration is either not recommended or should be used cautiously.

β-Blockers

β-Blockers are first-line rate-control agents. In the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) study, β-blockers were superior to CCB in achieving rate targets.[22] β-Blockers differ in adrenergic receptor and receptor subtype selectivity. Patients with obstructive lung disease may tolerate β-blockade, but cautious monitoring is recommended regardless of selectivity. β-Blockers with concurrent α-blockade may precipitate vasodilation and hypotension. Esmolol is an IV β-blocker with rapid onset and offset that may be associated with large infusion volumes. Renal versus hepatic drug elimination may direct β-blocker selection. β-Blockers may aid treatment of AF in hyperadrenergic states.

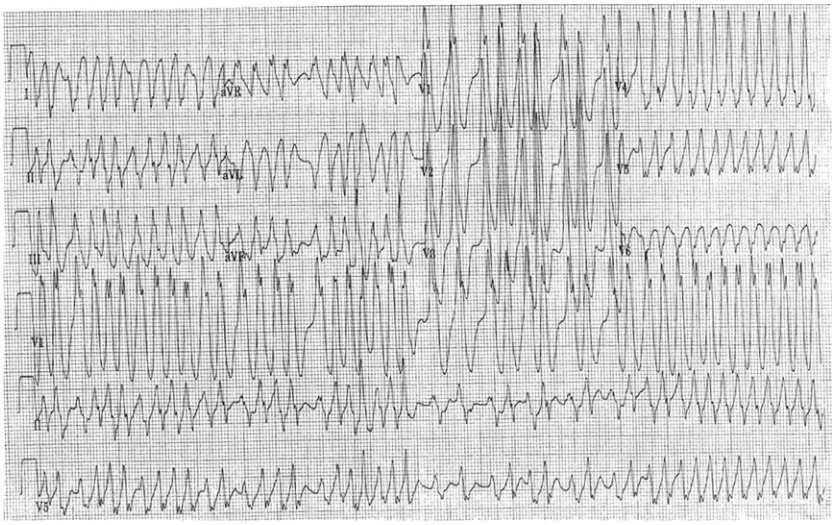

Fig. 8. Preexcited AF in the Wolff-Parkinson-White syndrome.

Box 2
Commonly used CYP450 inducers

Concurrent use increases bioavailability of each drug via the CYP450 system

Amiodarone
Coumadin
Digoxin
Procainamide
Flecainide
Quinidine
Simvastatin
Sildenafil
Theophylline

Calcium Channel Antagonists: Nondihydropyridine

Nondihydropyridine CCBs are effective for AF rate control. CCB may be preferred in patients with bronchospastic or obstructive pulmonary disease. CCB should be used with caution or avoided in HF with LV systolic dysfunction because of negative inotropic effects. Short-acting IV CCBs require continuous infusion that may influence disposition.

Box 3
Commonly used P-glycoprotein inhibitors and inducers

P-glycoprotein inhibitors (increase availability of other inhibitors)

Amiodarone
Cyclosporine
Digoxin
Diltiazem
Erythromycin
Indinavir
Itraconazole
Ketoconazole
Nicardipine
Quinidine
Ritonavir
Sirolimus
Tacrolimus
Verapamil

P- glycoprotein inducers (decrease availability of inhibitors)

Rifampin
St John's wort

Cardiac Glycosides

Digoxin is a purified cardiac glycoside that both inhibits the Na^+/K^+ ATPase and potentiates vagal tone, which slows AV node conduction. Positive inotropy without vasodilation makes digoxin useful in HF and hypotension. Benefits have been observed with concurrent β-blockers or CCB but not for digoxin monotherapy.

Narrow therapeutic window, renal clearance, and drug interactions (see **Boxes 2** and **3**, **Table 4**) via the cytochrome P450 system require cautious initiation and monitoring of digoxin. Digitalis toxic rhythms include delayed afterdepolarization-triggered ventricular arrhythmias and atrial tachycardia with complete AV block (see **Fig. 5**).[46] DCC is contraindicated in digitalis toxicity, because this may induce ventricular fibrillation that is particularly defibrillation resistant.[15]

Antiarrhythmic Medications in Rate Control

Amiodarone has multiple effects including antagonism of β-receptors and calcium, sodium, and potassium channels. Amiodarone may not effectively cardiovert AF but does augment rate control.

Pharmacologic Cardioversion

Pharmacologic cardioversion of AF is successful in ~30% to 50% of cases, in contrast with ~90% with DCC.[47] Pharmacologic cardioversion requires telemetry observation but no anesthesia. Oral or IV AAT available for cardioversion vary between the United States and EU (see **Table 5**). Prevention of thromboembolism, regardless of method, is reviewed later and in **Table 3**A–F.

Rhythm Control

The goal of maintaining SR is amelioration of AF symptoms. Rhythm control strategies have not shown reduction of mortality or complications.[18,19,22] Despite a history of multiple AAT used for AF rhythm control, currently recommended drugs are flecainide (Tambocor), propafenone (Rhythmol), dofetilide (Tikosyn), sotalol (Betapace, Sorine), amiodarone, and dronedarone (Multaq) (see **Table 5**).

Amiodarone

Amiodarone exerts multiple effects including sodium (I_{Na}), potassium (I_{Kr}, I_{Kur}, $I_{to,}$ I_{KAch}), calcium (I_{CaL}), funny current (I_f), and β-receptor blockade that vary between acute and chronic administration. Amiodarone is the most commonly

Table 4
Drug-drug interactions frequently encountered in AF management

Drugs	Drug Metabolism	Increased Effect	Decreased Effect
Antiarrhythmic Medications			
Amiodarone	CYP2C9 CYP2D6 CYP3A4[a] P-glycoprotein[b]	Digoxin Warfarin Dofetilide Flecainide Lidocaine (no effect if added) β-blockers Calcium channel blockers Fluoroquinolones Cyclosporine Protease inhibitors Theophylline Grapefruit juice	Bile acid sequestrant
Dofetilide	Renal cation transport system	QT prolonging drugs Megestrol Trimethoprim Verapamil Cisapride Cimetidine	—
Flecainide	CYP2D6	Amiodarone	—
Ibutilide	Hepatic Renal	Amiodarone Cisapride Class IA and III AAD QT prolonging drugs	—
Lidocaine	CYP1A2 CYP2B6 CYP3A4[a]	Nonselective β-blockers HIV protease inhibitors Amiodarone if added	CYP450 inducers (eg, rifampicin)
Propafenone	CYP1A2 CYP2D6 CYP3A4[a]	Digoxin (>80% patients) Warfarin	Rifampicin
Sotalol	Renal	Class IA and III AAD Digoxin QT prolonging drugs	Magnesium hydroxide Aluminum oxide
Rate-Control Agents			
Adenosine	Adenosine deaminase: Blood, tissue	AV nodal blockers Dipyridamole Carbamazepine	Caffeine products Theophylline
β-Blocker	Liver Renal	Other AV nodal blockers	β-Agonists
Calcium channel blocker	Verapamil: CYP3A4[a], P-glycoprotein Diltiazem: CYP3A4[a]	Other AV nodal blockers	β-Agonists
Digoxin	P-glycoprotein[b]	Amiodarone	—
Anticoagulants			
Warfarin	CYP2C9 *VKORC1* CYP3A4[a]	Digoxin Amiodarone Propafenone Verapamil	Vitamin K Diet and drugs Genetic variation ↓ or ↑

Grapefruit juice should be avoided in medications that involve the [a] CYP3A4 and [b] P-glycoprotein systems
Abbreviations: HIV, human immunodeficiency virus; VKORC1, vitamin K epoxide reductase complex.

Table 5
Pharmacologic therapy used in acute management of AF. Class definitions and Level of evidence (LOE) are based on those conventionally used in ACC/AHA/ESC guidelines

(A) Medical Therapy for Rate Control of AF

Drug Indication Class LOE	Loading Dose	Onset	Maintenance Dose	Major Side Effects
Esmolol Class I, LOE C	500 μg/kg IV more than 1 min	5 min	60–200 μg/kg/min IV	↓BP, HB, ↓HR, asthma, HF
Metoprolol Class I, LOE C	2.5–5 mg IV bolus over 2 min; up to 3 doses	5 min	NA	↓BP, HB, ↓HR, asthma, HF
Diltiazem Class I, LOE B	0.25 mg/kg IV over 2 min	2–7 min	5–15 mg/h IV	↓BP, HB, HF
Verapamil Class I, LOE B	0.075–0.15 mg/kg IV over 2 min	3–5 min	NA	↓BP, HB, HF
Amiodarone Class IIa, LOE C	150 mg over 10 min Oral loads may vary	Days	0.5–1 mg/min IV 200 mg daily (may vary)	↓BP, HB, pulmonary toxicity, skin discoloration, hypothyroidism, hyperthyroidism, corneal deposits, optic neuropathy, warfarin interaction, sinus bradycardia, conduction defects, phlebitis, drug-drug interactions (see **Table 4**)
Digoxin Class I, LOE B	0.25 mg IV each 2 h, up to 1.5 mg	60 min or more	0.125–0.375 mg daily IV or oral	Digitalis toxicity, HB, ↓HR Not recommended as monotherapy

(B) Medical Therapy for Cardioversion of AF and/or Maintenance of SR

Drugs Indication Class Level of Evidence	Dosing	Major Adverse Effects
Amiodarone Class IIA, LOE A	Intravenous or oral Refer to Table 5A for details	Drug-drug interactions CYP450 P-glycoprotein Higher risk of ventricular proarrhythmia with: Prolonged QT SHD Depressed LV function Bradycardia

		Electrolytes: hypokalemia, hypomagnesemia Addition of diuretics, QT prolonging drugs Renal dysfunction Rapid dose increase Female gender Excessive QT increase after initiation of drug Previous proarrhythmia
Ibutilide Class I (IIA for persistent), LOE A	IV 1 mg over 10 min If AF/AFL persists after 10 min, an additional 1 mg infusion may be considered	Torsades de pointes (not dose dependent) Stop infusion if arrhythmia terminates, ventricular arrhythmias, or significant ↑ QTc No concurrent class III AAT for at least 4 h after or within 5 half-lives
Sotalol (for SR maintenance, not cardioversion)	Oral 80, 120, 160 mg	Torsades de pointes Monitor with renal failure May be used but with caution in heart failure
Dofetilide Class I, LOE A	Registered prescribers CrCl-based dosing 500, 250, 125 μg oral BID	Torsades des pointes No HR slowing or bradycardia effects
Flecainide, Propafenone Class I, LOE A	Oral (United States) Oral or IV (United States or EU)	Higher risk of ventricular proarrhythmia with: QRS >120 ms Structural heart disease Depressed LV function Concomitant VT Rapid ventricular rate Rapid dose increase Addition of negative inotropes Excessive QRS widening >150%

Abbreviations: BID, twice daily; CrCl, creatinine clearance; HB, heart block; HR, heart rate; HF, heart failure.

prescribed AAT for AF despite not being approved by the US Food and Drug Administration for AF. Data are conflicting regarding rates of cardioversion (IV ~52%; oral ~28%) at 24 hours.[7,15] Time to cardioversion is delayed versus class IC agents.

Amiodarone effectively maintains SR (>60% over 16 months).[7,15,24] It is tolerated in the presence of SHD.

Adverse effects and intolerance are common (15%–20%) with amiodarone.[48] QT prolongation is frequent, but torsades de pointes (TDP) is uncommon.[49] SB and AV conduction abnormalities are common. Metabolism via the CYP3A4, CYP2C9, and P-glycoprotein pathways results in multiple drug interactions with verapamil (Calan, Covera, Isoptin, Verelan), digoxin, statins, and warfarin (see **Boxes 2** and **3**, **Table 4**).[46] Long-term adverse effects depend on dose and duration and include corneal deposits; photosensitivity; and pulmonary, thyroid, and liver toxicity. Phlebitis and hypotension are common with IV administration. Amiodarone-AAT interactions increase proarrhythmia risk; cessation of class I or III AAT for at least 3 to 5 half-lives is recommended. Amiodarone cessation for at least 3 months is recommended before initiation of dofetilide.

Class III antiarrhythmic therapy

Ibutilide Ibutilide is a class III AAT with predominant I_{Kr} antagonism approved for acute IV administration to convert AF or AFL with estimated rates of 44% over 90 minutes.[50] Minimal changes in sinus rate, PR interval, or QRS duration are observed. TDP occurs in 3% to 5% of cases independent of dose.[51] Telemetry observation is recommended for at least 4 hours.[46,52] Class IA and III AAT are contraindicated within 4 hours of ibutilide infusion.

Dofetilide Dofetilide is effective for the conversion to and maintenance of SR in populations with and without HF. Estimated conversion rates are ~87% within 30 hours with 58% to 79% suppression of AF at 1 year. Dose-dependent QTc prolongation and TDP risks require inpatient loading by certified prescribers in the United States. Renal impairment and prolonged QTc limit dofetilide use.

Sotalol Sotalol is effective at maintaining SR with rates of ~37% at 1 year, but is ineffective for cardioversion.[7,15] QTc prolongation and TDP are significant adverse effects that require ECG monitoring at initiation. Renal insufficiency, bronchospasm, QT prolongation, and HF require cautious initiation.

Dronedarone Dronedarone is a deiodinated designed molecule resembling amiodarone. Dronedarone is less effective than amiodarone for SR maintenance but reduces AF hospitalizations and recurrence. It is contraindicated in decompensated or recent decompensated HF and permanent AF because of increased mortality. Adverse effects include bradycardia and gastrointestinal intolerance. Concerns regarding liver toxicity and cardiovascular events in ischemic heart disease have surfaced, but so far without specific recommendations.

Class IC antiarrhythmic medications

Oral flecainide and propafenone have estimated net conversion rates of 38%.[7,15] Both maintain SR at ~30% to 35% over 1 year with reduced AF recurrence and duration. These drugs are contraindicated in the context of MI, CAD, and SHD based on increased sudden death in the Cardiac Arrhythmia Suppression Trial (CAST).[53] Both are sodium channel blockers that exhibit use dependence with QRS prolongation at increased heart rates. Propafenone and flecainide may slow and organize AF to AFL leading to 1:1 AFL that is often poorly tolerated (**Fig. 9**). Concurrent AV nodal blockade is recommended; propafenone has mild β-blocker activity.[46] Both are ineffective for termination of persistent AF or AFL. Adverse effects include neurologic effects, hypotension, and bradycardia.

Flecainide A single oral dose of flecainide 300 mg has cardioversion rates of 75% to 91% at 8 hours. In Europe, IV flecainide cardioversion rates are 67% to 92%. QRS widening more than 25% may portend increased proarrhythmia risk; some advocate exercise testing for QRS duration.[54]

Propafenone Propafenone conversion rates are ~56% at 2 to 6 hours with a single 600-mg oral dose. IV propafenone is available in Europe with termination rates of 40% to 90%.

Quinidine

Quinidine was one of the earliest AAT to show efficacy in maintaining SR. Its use is limited by increased mortality attributed to proarrhythmia based on meta-analysis.

Vernakalent

Vernakalent is a multichannel blocker with predominant blockade of atrial potassium (I_{to}, I_{KAch}, I_{Kur}) and late sodium (I_{NaL}) currents. IV vernakalent is approved in the EU but pending in the United States for acute AF conversion. Oral vernakalent is initiating phase II testing. No proarrhythmia has been described thus far.

Thromboembolic Risk Reduction

Current oral anticoagulation options are vitamin K antagonists (warfarin), direct thrombin inhibitors

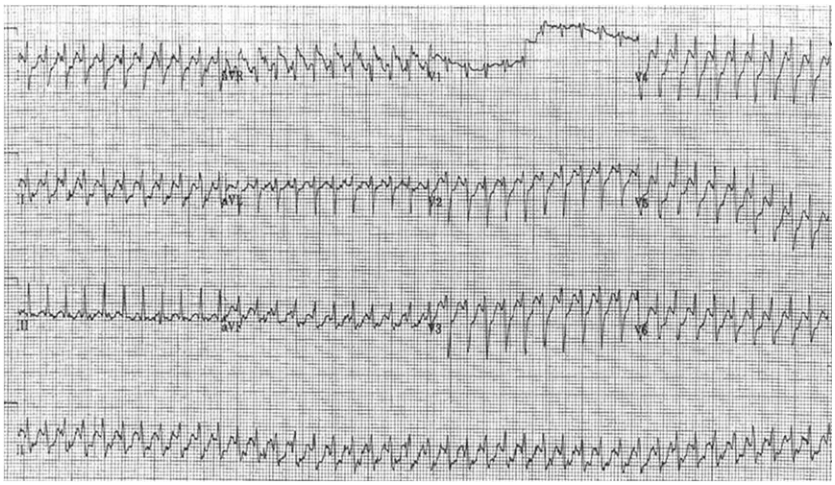

Fig. 9. Atrial flutter with 1:1 atrioventricular conduction.

(dabigatran; Pradaxa) or factor Xa inhibitors (rivaroxaban; Xarelto) (**Table 6**). Two factor Xa inhibitors are pending US Food and drug Administration (FDA) approval (apixaban) or further phase III data (edoxaban). Antiplatelet therapy is less effective than anticoagulation but may be considered in low-risk patients without SHD. CHADS2 or CHADS-VASC risk scores help determine thromboembolic risk and appropriate prophylaxis (see **Table 3**A–F). Anticoagulation risk with VKA may be acceptable and underused in elder adults.[55] Suboptimal real-world time in therapeutic range (TTR) and inconvenience of monitoring limit the usefulness of VKA. In contrast, disadvantages of newer agents include costs, lack of antidote, lack of assay, and limited long-term data regarding adverse effects. Enthusiasm surrounded the direct thrombin inhibitor, ximeligatran, until escalating short-term liver toxicity forced its market withdrawal. Whether VKA or newer oral anticoagulants should be used as first line remains controversial.[56,57]

Table 6
Approved antithrombotic medical therapy for prevention of thromboembolic events

Anticoagulant	Mechanism	Dosing	Pros	Cons
Warfarin (Coumadin)	Vitamin K antagonist	Dosing by INR 2.0–3.0	Cost Experience Long-term data Monitoring: INR Reversibility	INR monitoring and costs Variable dose response Drug interactions Food interactions
Dabigatran (Pradaxa)	Direct thrombin inhibitor	150 mg orally BID CrCl 15–30 mL: 75 mg BID CrCl <15 mL: not recommended	Monitoring: none Diet: no restrictions	Caution with renal dysfunction, elderly No monitoring or antidote
Rivaroxaban (Xarelto)	Factor Xa inhibitor	20 mg orally daily CrCl 30–50 mL: caution CrCl <30 mL: not recommended Child-Pugh class B or C liver failure: avoid	Once-daily dosing Monitoring: none Diet: no restrictions	Caution with renal/hepatic dysfunction, elderly Bridging: ↑ thromboembolic events on drug cessation

Abbreviation: BID, twice daily; CrCl, creatinine clearance.

Vitamin K antagonists

VKA have established relative risk reduction (RRR) of stroke (~64%) and mortality (~26%) versus control and ~39% RRR of stroke versus aspirin.[7,15,58] Hemorrhagic risks are a major concern but may be reduced to less than 1% per year with appropriate monitoring targeting INR of 2 to 3.[7] Drug interactions, diet and lifestyle, genetic variation, and adherence influence dose response and TTR. Recent randomized trials of anticoagulants have described a ~60% rate of TTR.[59–61]

Direct thrombin/factor II inhibitors

Dabigatran is an oral, direct thrombin inhibitor approved by the FDA in 2010 for thromboembolism prophylaxis in nonvalvular AF. Dabigatran is not recommended in patients with valvular disease, prosthetic valves, severe renal insufficiency (glomerular filtration rate [GFR] <15 mL/min), advanced liver disease with impaired clotting function, and advanced age.[59,62]

Factor Xa inhibitors

Novel oral factor Xa inhibitors (rivaroxaban, apixaban) have emerged as noninferior alternatives to warfarin in nonvalvular AF. Rivaroxaban is FDA approved for prevention of thromboembolic events in nonvalvular AF with once-daily dosing. However, anticoagulant bridging is recommended because of increased thromboembolism rates on rivaroxaban withdrawal.[61,63] Rivaroxaban is not recommended in patients with valvular disease or impaired renal or hepatic function.

FDA review of apixaban for prevention of AF embolic events is pending.

Antiplatelet therapy

Anticoagulant therapy with VKA is superior to dual antiplatelet therapy with aspirin plus clopidogrel for thromboprophylaxis.[64] Although aspirin plus clopidogrel reduced stroke in patients with AF not amenable to anticoagulation, a significantly increased risk of bleeding was observed compared with aspirin alone.[65] Anticoagulation has been prominently recommended rather than antiplatelet therapy between the 2006 ACC/AHA/ESC and 2010 ESC guidelines.[7,15]

AF Prevention

Upstream therapies including antagonism of the renin-angiotensin-aldosterone axis, statins, and polyunsaturated fatty acids may delay development or progression of AF but have no benefit in acute AF.

NONPHARMACOLOGIC STRATEGIES

Cardioversion

Electrical cardioversion is a widely available and highly successful method of restoring SR in up to 90% of patients.[47] The benefit of rhythm control for death, stroke, and HF remain absent,[50] but cardioversion may be necessary for symptomatic and unstable AF.

Electrical cardioversion uses direct current energy. Biphasic waveforms use less energy and reduce tissue injury. Synchronization to the QRS complex is critical to avoid inadvertent T wave shock and ventricular fibrillation induction.

Review of the procedure, anticoagulation plan, and informed consent are required. Adequate skin preparation improves electrode contact. Anterolateral or anteroposterior (AP) positions maximize energy vectors through the LA. Dedicated airway, hemodynamic, and rhythm monitoring is required. Applied pressure with electrically inert material may improve electrode contact. Advanced cardiac life support recommendations for first shock are 120 to 360 J.

Unsuccessful DCC may occur for various reasons at any interface between the defibrillator and the patient (**Table 7**). Immediate or early recurrence of AF may be confused with unsuccessful DCC. Patch or paddle position, contact, and connections must be confirmed. Increased energy output may be used; many practitioners initially cardiovert at higher energy. AP patch repositioning may improve shock vectors. Addition of AAT can be considered. Although acute success of cardioversion is high, recurrence rates relate to arrhythmic substrate including LA size, AF duration, and valvular dysfunction.

Ablation of AF for Rhythm Control

AF ablation may be performed using various catheter-based or surgical techniques to electrically isolate AF triggers or modify atrial substrate to maintain SR for symptomatic relief. This typically involves electrical pulmonary vein isolation (PVI), because the most common electrophysiologic AF triggers emanate from sites of automaticity in the LA–pulmonary vein junctions.[66] Although definitions of recurrence, follow-up, and methods vary, studies indicate freedom from recurrent atrial arrhythmia in the range of 39% to 79.4% after 3-year to 6-year follow-up.[67–72] AF ablation is recommended to candidates with symptomatic, recurrent AF refractory to, or intolerant of, at least 1 AAT; AF ablation may be considered before AAT for paroxysmal AF.[71]

Although ablation is performed electively for long-term AF management, acute recurrence and complications (**Table 8**) may require expedited acute evaluation. Death and atrioesophageal fistula occur in less than 1%. Cerebrovascular events (1%–2%), cardiac tamponade (1%–6%), major or

Table 7
DCC: troubleshooting and complications

Issues	Management
Cardioversion: unsuccessful	Unsuccessful vs immediate/early recurrence of AF? Patch position Patch contact Apply pressure during shock with electrically inert material Check connections Antiarrhythmic medication Repeat shock Repeat shock with higher energy
Ventricular fibrillation	Avoidance: synchronize shock to QRS Defibrillation: switch shock to asynchronous
Bradycardia Asystole Pulseless electrical activity	Transcutaneous pacing Confirm ventricular capture Advanced cardiac life support
Immediate or early recurrence of AF	Frequent cause of failed cardioversion Repeat cardioversion Antiarrhythmic medication

minor hemorrhage (~5%), and pulmonary vein stenosis (0%–10%) estimates vary.[69,70,73,74] Iatrogenic atypical atrial flutter may occur in 2% to 14%.[74]

Recurrent arrhythmias including AF, atrial tachycardia, and atypical AFL are common within the first 3 months of ablation and may not predict success. Many electrophysiologists recommend rhythm control in this period, although this practice is of unclear benefit.[75] Patients having AF ablation are typically anticoagulated for at least several months.

Ablation of Atrial Flutter for Rhythm Control

AFL typically involves a macroreentrant circuit between the tricuspid annulus, inferior vena cava, and crista terminalis. Rate control of AFL may be more challenging. The cavotricuspid flutter isthmus is frequently amenable to ablation with favorable acute and long-term success at low complication rates; AFL ablation may be considered as first-line therapy.

Ablation for Rate Control of AF

AV junction ablation may be considered for patients intolerant of, or unable to achieve, adequate AF rate control and are not optimal AF ablation candidates. AV junction ablation is ~90% effective for symptom relief but requires acceptance of heart block and pacemaker implant.[76] Because AF remains present, thromboembolic risks remain unmodified after this procedure. Heightened TDP risk observed immediately following AV junction ablation is ameliorated by short-term increased pacing rates.[76]

Left Atrial Appendage Occlusion for Prevention of Thromboembolism

LA appendage occlusion devices have emerged and may be considered for nonacute thromboembolism risk reduction when anticoagulation is contraindicated.

Self-management Strategies

Education, understanding of signs and symptoms, and adherence to medication, lifestyle modification, and follow-up may reduce ED visits for AF. Risk modification including trigger avoidance, weight reduction, and treatment of underlying conditions must be reinforced.

Pill-in-pocket antiarrhythmic therapy

Some patients are appropriate candidates for ambulatory cardioversion using oral flecainide or propafenone as discussed earlier (see **Table 5**).[77] This strategy should be initiated in a monitored setting.[15]

Anticoagulation monitoring

Some patients with appropriate compliance and stable warfarin dosing may perform point-of-care home INR monitoring.

Evaluation and Reassessment

Regardless of treatment strategy, reevaluation of symptoms, hemodynamics, comorbidities, and

Table 8
AF ablation: complications, evaluation, and management

Complications	Presentation	Management
Cerebrovascular event TIA vs stroke	Altered mental status and focal deficits; diagnosis may be delayed until recovery	Neurologic consultation Head CT, MRI, and MRA of the brain Anticoagulation, thrombolysis, or intervention May be embolism caused by thrombus or air
Vascular complications Arteriovenous fistula Pseudoaneurysm Hematoma	Within 1 d to 1 wk May be asymptomatic Groin swelling, pain, thrills, pop Retroperitoneal bleed: back pain	Serial examinations, blood counts. Transfusion if appropriate Femoral ultrasound. CT scan for retroperitoneal bleed Anticoagulation management varies with severity Interventional vascular/vascular surgery consultation
Pericardial effusion Cardiac tamponade	During procedure or within days: dyspnea, hypotension, shock	Hemodynamic monitoring; cardiac silhouette on fluoroscopy Echocardiography (intracardiac, transthoracic, transesophageal) Reversal of anticoagulation Pericardiocentesis: may require surgical repair
Pulmonary vein stenosis	Rapid or insidious: weeks -months Variable symptoms including dyspnea, hemoptysis, bronchitis	CT angiography to evaluate pulmonary veins Possible balloon dilation/stent placement
Atrial-esophageal fistula Esophageal injury	Insidious: 1–5 wk after ablation Fever, malaise, neurologic symptoms, gastrointestinal bleed, hemoptysis, hematemesis Requires high index of suspicion	CT scan or MRI Surgery for fistula Endoscopy: may exacerbate fistula Esophageal temperature probe Esophageal barium swallow Proton pump inhibitors
Phrenic nerve palsy	Usually periprocedural Dyspnea, cough, hiccup, effort intolerance, diaphragmatic increase	Favorable prognosis: frequently recovers without intervention
Atrial arrhythmias AF Atypical atrial flutter Atrial tachycardia	AF: may be common in first 3 mo without impact on long-term outcome AT/atypical AFL: may be challenging to control with AAT or rate control	Rhythm monitor: transtelephonic, Holter, implantable Contact electrophysiology Cardioversion Antiarrhythmic drug Electrophysiology study/ablation

Abbreviations: CT, computed tomography; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging.

stroke risk is essential both acutely and chronically. Communication among primary care physicians, cardiologists, and electrophysiologists facilitates successful long-term care. Reassessment of underlying conditions and adequate rate control aids treatment of symptoms.

SUMMARY

Key goals of acute AF management include accurate diagnosis, clinical stabilization, modification of underlying causes and risks, amelioration of symptoms by rate or rhythm control, and stratification and prevention of thromboembolic stroke. Because clinical manifestations of AF vary greatly, management must be individualized. Evolving methods of risk assessment and therapy may augment therapeutic options to prevent and reduce AF and associated sequelae. Appropriate selection of AF management tools and strategies benefits from collaboration among emergency, primary, cardiovascular, and cardiac rhythm physicians.

REFERENCES

1. Rosner F. Maimonides' medical writing. Translated and annotated by Fred Rosner, MD. Haifa (Israel): The Maimonides Research Institute; 1989.
2. Prystowsky EN. The history of atrial fibrillation: the last 100 years. J Cardiovasc Electrophysiol 2008; 19(6):575–82.
3. Seidl K, Hauer B, Schwick PA, et al. Risk of thromboembolic events in patients with atrial flutter. Am J Cardiol 1998;82:580–3.
4. LeLorier P, Humphries KH, Krahn A, et al. Prognostic differences between atrial fibrillation and atrial flutter. Am J Cardiol 2004;93(5):647–9.
5. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics-2011 update: a report from the American Heart Association. Circulation 2011;123(4):e18–209.
6. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study. JAMA 2001;285:2370–5.
7. Camm AJ, Kirchhof P, Lip GY, 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(19):2369–429.
8. Piccini JP, Hammill BG, Sinner MF, et al. Incidence and prevalence of atrial fibrillation and associated mortality among Medicare beneficiaries, 1993-2007. Circ Cardiovasc Qual Outcomes 2012;5:85–93.
9. Friberg J, Buch P, Scharling H, et al. Rising rates of hospital admissions for atrial fibrillation. Epidemiology 2003;14:666–72.
10. Levy S, Maarek M, Coumel P, et al. Characterization of different subsets of atrial fibrillation in general practice in France: the ALFA study. Circulation 1999;99:3028–35.
11. Gami AS, Pressman G, Caples SM, et al. Association of atrial fibrillation and obstructive sleep apnea. Circulation 2004;110:364–7.
12. Wanahita N, Messerli FH, Bangalore S, et al. Atrial fibrillation and obesity-results of a meta-analysis. Am Heart J 2008;155(2):310–5.
13. Krahn AD, Manfreda J, Tate RB, et al. The natural history of atrial fibrillation: incidence, risk factors, and prognosis in the Manitoba Follow-Up Study. Am J Med 1995;98:476–84.
14. Maggioni AP, Latini R, Carson PE, et al. Valsartan reduces the incidence of atrial fibrillation in patients with heart failure: results from the Valsartan Heart Failure Trial. Am Heart J 2005;149:548–57.
15. Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines 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 European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients with Atrial Fibrillation). Circulation 2006;114:e257–354.
16. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke 1991;22:983–8.
17. 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(10):946–52.
18. Van Gelder IC, Hagens VE, Bosker HA, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. N Engl J Med 2002;347:1834–40.
19. Roy D, Talajic M, Nattel S, et al. Rhythm control versus rate control for atrial fibrillation and heart failure. N Engl J Med 2008;358:2667–77.
20. Dell'Orfano JT, Patel H, Wobrette DL, et al. Acute treatment of atrial fibrillation: spontaneous conversion rate and cost of care. Am J Cardiol 1999;83:788–90.
21. Davies MJ, Pomerance A. Pathology of atrial fibrillation in man. Br Heart J 1972;34:520–5.
22. Wyse DG, Waldo AL, DiMarco JP, et al, Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med 2002;347:1825–33.
23. Jahangir A, Lee V, Friedman PA, et al. Long-term progression and outcomes with aging in patients with lone atrial fibrillation: a 30-year follow-up study. Circulation 2007;115(24):3050–6.

24. Singh BN, Singh SN, Reda DJ, et al. Amiodarone versus sotalol for atrial fibrillation. N Engl J Med 2005;352:1861–72.
25. Rohrbacker NJ, Kleinman NL, White SA, et al. The burden of atrial fibrillation and other cardiac arrhythmias in an employed population: associated costs, absences, and objective productivity loss. J Occup Environ Med 2010;52(4):383–91.
26. Coyne KS, Paramore C, Grandy SG, et al. Assessing the direct costs of treating nonvalvular atrial fibrillation in the United States. Value Health 2005;9(5):348–56.
27. Le Heuzey JY, Paziaud O, Piot O, et al. Cost of care distribution in atrial fibrillation patients: the COCAF study. Am Heart J 2004;147:121–6.
28. Lee WC, Lamas GA, Balu S, et al. Direct treatment cost of atrial fibrillation in the elderly American population: a Medicare perspective. J Med Econ 2008; 11:281–98.
29. Fox CS, Parise H, D'Agostino RB Sr, et al. Parental atrial fibrillation as a risk factor for atrial fibrillation in offspring. JAMA 2004;291(23):2851–5.
30. Douglas PS, Garcia MJ, Haines DE, et al. ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 appropriate use criteria for echocardiography: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol 2010. http://dx.doi.org/10.1016/j.jacc.2010.11.002. published online before print November 19, 2010.
31. Manning WJ, Silverman DI, Katz SE, et al. Impaired left atrial mechanical function after cardioversion: relation to the duration of atrial fibrillation. J Am Coll Cardiol 1994;23(7):1535–40.
32. Khan IA. Atrial stunning: determinants and cellular mechanisms. Am Heart J 2003;145:787–94.
33. Berger M, Schweitzer P. Timing of thromboembolic events after electrical cardioversion of atrial fibrillation or flutter: a retrospective analysis. Am J Cardiol 1998;82:1545–7.
34. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA 2001;285(22):2864–70.
35. Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on Atrial Fibrillation. Chest 2010;137(2):263–72.
36. Pisters R, Lane DA, Nieuwlaat R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest 2010;138(5):1093–100.
37. Kerr R, Humphries KH, Talajic M, et al. Progression to chronic atrial fibrillation after initial diagnosis of paroxysmal atrial fibrillation: results from the Canadian Registry of Atrial Fibrillation. Am Heart J 2005; 149:489–96.
38. Smith P, Arnesen H, Holme I. The effect of warfarin on mortality and reinfarction after myocardial infarction. N Engl J Med 1990;323(3):147–52.
39. Hurlen M, Abdelnoor M, Smith P, et al. Warfarin, aspirin, or both after myocardial infarction. N Engl J Med 2002;347:969–74.
40. Lopes RD, Pieper KS, Horton JR, et al. Short- and long-term outcomes following atrial fibrillation in patients with acute coronary syndromes with or without ST-segment elevation. Heart 2008;94(7): 867–73.
41. Van Rees JB, Borleffs CJ, de Bie MK, et al. Inappropriate implantable cardioverter-defibrillator shocks: incidence, predictors, and impact on mortality. J Am Coll Cardiol 2011;57(5):556–62.
42. Klein GJ, Bashore TM, Sellers TD. Ventricular fibrillation in the Wolff-Parkinson-White syndrome. N Engl J Med 1979;301:1080–5.
43. Van Gelder IC, Groenveld HF, Crijns HJ, et al. Lenient versus strict rate control in patients with atrial fibrillation. N Engl J Med 2010;362(15):1363–73.
44. See VY, Roberts-Thompson KC, Stevenson WG, et al. Atrial arrhythmias after lung transplantation: epidemiology, mechanisms at electrophysiology study, and outcomes. Circ Arrhythm Electrophysiol 2009;2(5):737–41.
45. Dasari TW, Pavlovic-Surjance B, Patel N, et al. Incidence, risk factors, and clinical outcomes of atrial fibrillation and atrial flutter after heart transplantation. Am J Cardiol 2010;106(5):737–41.
46. Zipes DP, Jalife J. Cardiac electrophysiology. Philadelphia: Saunders; 2009.
47. Kirchhof P, Monnig G, Wasmer K, et al. A trial of self-adhesive patch electrodes and hand-held paddle electrodes for external cardioversion of atrial fibrillation. Eur Heart J 2005;26:1292–7.
48. Goldschlager N, Epstein AE, Naccarelli GV, et al. A practical guide for clinicians who treat patients with amiodarone: 2007. Heart Rhythm 2007;4(9):1250–9.
49. Hohnloser SH, Klingenheben T, Singh BN. Amiodarone-associated proarrhythmic effects. A review with special reference to torsade de pointes tachycardia. Ann Intern Med 1994;121(7):529.
50. Wyse DG. Cardioversion of atrial fibrillation for maintenance of sinus rhythm: a road to nowhere. Circulation 2009;120:1444–52.
51. Li H, Easley A, Barrington W, et al. Evaluation and management of atrial fibrillation in the emergency department. Emerg Med Clin North Am 1998;16: 389–403.

52. Pfizer. Ibutilide (Corvert) [package insert]. [Online]; 2006. Available at: http://www.pfizer.com/files/products/uspi_corvert.pdf. Accessed March 29, 2012.
53. Echt DS, Liebson PR, Mitchell LB, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo - the Cardiac Arrhythmia Suppression Trial. N Engl J Med 1991;324:781–8.
54. Zimetbaum P. Antiarrhythmic drug therapy for atrial fibrillation. Circulation 2012;125:381–9.
55. Hylek EM, Evans-Molina C, Shea C, et al. Major hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. Circulation 2007;115(21):2689–96.
56. Ansell J. New oral anticoagulants should not be used as first-line agents to prevent thromboembolism in patients with atrial fibrillation. Circulation 2012;125:165–70.
57. Granger CB, Armaganijan LV. New oral anticoagulants should be used as first-line agents to prevent thromboembolism in patients with atrial fibrillation. Circulation 2012;125:159–64.
58. Hart RG, Pearce LA, Aguilar MI, et al. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007;146:857–67.
59. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139–51.
60. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2011;365(11):981–92.
61. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011;365(10):883–91.
62. Wann LS, Curtis AB, Ellenbogen KA, et al. 2011 ACCF/AHA/HRS Focused update on the management of patients with atrial fibrillation (update on dabigatran). J Am Coll Cardiol 2011;57:1330–7.
63. Jannsen Pharmaceuticals. Rivaroxaban (Xarelto) [package insert]. [Online] 12/2011. Available at: http://www.xareltohcp.com/sites/default/files/pdf/xarelto_0.pdf#zoom=100. Accessed March 29, 2012.
64. Connolly S, Pogue J, Hart R, et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. Lancet 2006; 367(9526):1903–12.
65. Connolly SJ, Pogue J, Hart RG, et al. Effect of clopidogrel added to aspirin in patients with atrial fibrillation. N Engl J Med 2009;360:2066–78.
66. Haïssaguerre M, Jaïs P, Dipen C, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998; 339:659–66.
67. Weerasooriy R, Khairy P, Litalien J, et al. Catheter ablation for atrial fibrillation: are results maintained at 5 years of follow-up? J Am Coll Cardiol 2011;57: 160–6.
68. Gaita F, Caponi D, Scaglione M, et al. Long-term clinical results of 2 different ablation strategies in patients with paroxysmal and persistent atrial fibrillation. Circ Arrhythm Electrophysiol 2008;1: 269–75.
69. Hussein AA, Saliba WI, Martin DO, et al. Natural history and long-term outcomes of ablated atrial fibrillation. Circ Arrhythm Electrophysiol 2011;4:271–8.
70. Sorgente A, Tung P, Wylie J, et al. Six year follow-up after catheter ablation of atrial fibrillation: a palliation more than a true cure. Am J Cardiol 2012; 109:1179–86.
71. Calkins H, Brugada J, Packer DL, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow up. Europace 2007;9:335–79.
72. Calkins H, Brugada J, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) task force on catheter and surgical ablation of atrial fibrillation. Europace 2012;9:632–96.
73. Holmes DR, Monahan KH, Packer D, et al. Pulmonary vein stenosis complicating ablation for atrial fibrillation. JACC Cardiovasc Interv 2009;2:267–76.
74. Wazni O, Wilkoff B, Saliba W. Catheter ablation for atrial fibrillation. N Engl J Med 2011;365:2296–304.
75. Leong-Sit P, Roux JF, Zado E, et al. Antiarrhythmics after ablation of atrial fibrillation (5A study): six-month follow-up study. Circ Arrhythm Electrophysiol 2011;4(1):11–4.
76. Betts TR. Atrioventricular junction ablation and pacemaker implant for atrial fibrillation: still a valid treatment in appropriately selected patients. Europace 2008;10:425–32.
77. Alboni P, Botto GL, Baldi N, et al. Outpatient treatment of recent-onset atrial fibrillation with the "pill-in-the-pocket" approach. N Engl J Med 2004;351: 2384–91.