EMERGENCY MEDICINE REPORTS

Practical, Evidence-Based Reviews in Emergency Care

APRIL 1, 2018 VOL. 39, NO. 7

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FINANCIAL DISCLOSURE

Dr. Farel (CME question reviewer) owns stock in Johnson & Johnson. Brian Hocum, PharmD, (pharmacist reviewer) is an employee of Braeburn Pharmaceuticals. Dr. Schneider (editor), Dr. Stapczynski (editor), Ms. Light (nurse planner), Dr. Matuskowitz (author), Dr. Abukhdeir (author), Dr. Weant (author), Dr. Calhoun (author), Dr. Domangue (author), Dr. Caporossi (author), Dr. Wilson (peer teviewer), Ms. Mark (executive editor), Ms. Coplin (executive editor), and Ms. Hatcher (editorial group manager) report no financial relationships with companies related to the field of study covered by this CME activity.

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Evidence-based Management of Atrial Fibrillation in the Emergency Department

As an emergency physician, how do you manage acute onset atrial fibrillation (AF) at your institution? Do you instinctively reach for beta- and calcium channel blockers, as many of us in the United States have been trained, or do you aggressively cardiovert recent-onset AF with electricity, procainamide, or yet another antiarrhythmic agent? While both are safe, the literature suggests that the decision to pursue rate vs. rhythm control should depend on the specific characteristics of the patient.

The following article provides an overview of AF and evidence-based guidance on controversial aspects of AF workup and management in the emergency department (ED). The evidence is provided to help safely reduce unnecessary testing and expand the emergency provider's management armamentarium to include electrical and pharmacologic conversion in recent-onset AF patients. Finally, the article integrates the evidence into a novel AF protocol, which in collaboration with cardiology and pharmacology stakeholders, may serve as a starting point for improving AF management at your institution.

Case Introductions

Case 1: A 45-year-old male presents to the ED with sudden onset palpitations and diaphoresis. Symptoms began suddenly five hours ago while at rest. He denies pain, describes the feeling as "uneasy" and constant since onset. The patient smokes 20 packs of cigarettes per year and drinks two to three beers per week but otherwise denies past medical history and has felt well until today. Triage vital signs are: 37.2˚C, 110 beats/min, 122/75 mmHg, 21 breaths/min, SpO2 100% on room air. The physical exam reveals tachycardia, no jugular venous distention, clear lung sounds, and no peripheral edema. What is in your differential diagnosis? What tests and/or imaging should you order? What are your options for treating this patient? What is this patient's disposition after treatment?

Case 2: A 68-year-old female presents with anxiety. She has associated palpitations, shortness of breath, and perioral tingling. Past medical history includes AF, well-controlled diabetes, and hypertension. Medications include sitagliptin, amlodipine, metoprolol, and apixaban. The patient was diagnosed with AF five years ago and has not felt her heart racing since she was placed on metoprolol and apixaban at that time. Triage vital signs: 37.0˚C, 160 beats/min, 140/90 mmHg, 24 breaths/min, 94% on room air. Physical exam reveals irregular tachycardia, clear lung sounds, and no peripheral edema. Her electrocardiogram (ECG) is shown in Figure 1. What is on your differential diagnosis? What other questions need to be answered to treat this patient? What tests and/or imaging should you order? What

EXECUTIVE SUMMARY

- The incidence of atrial fibrillation increases with age.
- Hypertension is the most common modifiable risk factor for atrial fibrillation.
- Rate or rhythm control approaches for patients with symptomatic atrial fibrillation yield equivalent short- and long-term clinical outcomes.
- Rhythm control in appropriate patients is associated with shorter ED lengths of stay and reduced hospital admission rates.
- All patients with atrial fibrillation should be evaluated for the need for anticoagulation to reduce the risk of stroke.

are your options for treating this patient?

Case 3: A 50-year-old male is brought in by EMS and appears acutely ill. Initially, the patient was alert and oriented with stable vital signs despite an irregular heart rhythm. However, upon arrival, he became diaphoretic and confused. The nurses have obtained IV access and placed the patient on the monitor. Vital signs are: 36.5°C, 270 beats/min, 85/40 mmHg, 12 breaths/min, 99% on 2 L NC. What are your first steps in managing this patient? What tests and/or imaging should you order? What is this patient's disposition after treatment?

Figure 1. Case 2 ECG

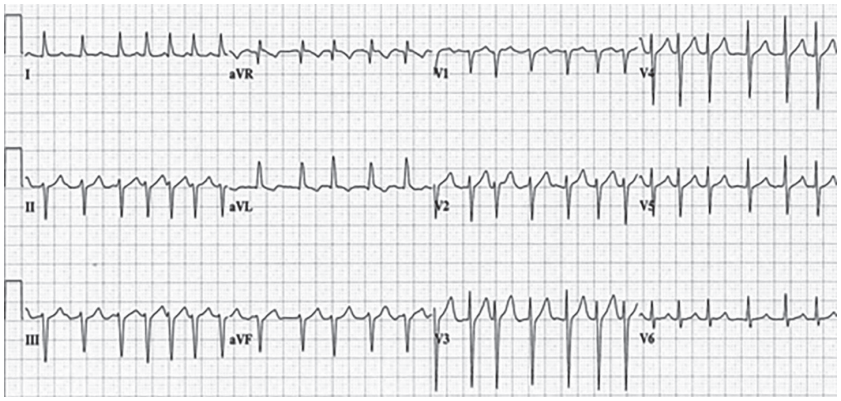


Figure used with permission from William J. Brady, MD.

Definition and Relevancy

AF, the most common supraventricular tachyarrhythmia, can lead to stroke, heart failure, and cardiac arrest if untreated. AF results from the excitation of multiple atrial foci that create excessive and poorly coordinated atrial activation and contraction.[1] ECG characteristics include "irregularly irregular" RR intervals without consistent or distinct P waves.[1] Decreased efficiency of blood flow through the atria can lead to atrial thrombus formation and results in a four- to five-fold increased risk of embolic stroke.[2] In fact, an estimated 20-30% of strokes may be secondary to AF.[3] Sustained, uncontrolled AF with rapid ventricular response (RVR) over the course of weeks can lead to tachycardia-related cardiomyopathy. While uncommon, even short-lived AF with very fast ventricular rates can cause hemodynamic instability and cardiac arrest.[4]

Epidemiology and Risk Factors

The incidence of AF increases with age, and it affects approximately one in four people during their lifetime. There are roughly 3 million people with AF in the United States alone,[5,6] and as life expectancy climbs, this number is expected to increase five-fold by 2050.[7] AF has been estimated to have a total incremental healthcare cost of $8,705 per patient per year, approximating to a $26 billion healthcare burden in the United States.[8] Consequently, cost-effective evidence-based management strategies are needed to limit escalating healthcare costs.

Many factors increase a patient's risk for AF. Age, the most predominant risk factor, increases AF's prevalence from 1% to 15% between the ages of 35 and 85 years.[9] Men are slightly more likely to develop AF than women, but women tend to live longer, so they represent half of the overall AF population.[10] Hypertension increases the risk of developing AF by more than 40%, and hypertension's enormous prevalence in the general populations makes it the most important modifiable risk factor.[11] Heart failure has a complex relationship with AF: The presence of one increases the likelihood of the other. As the severity of heart failure progresses, the prevalence of AF increases from < 5% to 50%.[12] Other risk factors for AF include coronary artery disease, valvulopathies, obesity, sleep apnea, and hypertrophic cardiomyopathy.[9]

Classification and Pathophysiology

AF typically is classified as paroxysmal, persistent, or permanent.[1,13] Paroxysmal AF is defined by atrial fibrillation that converts to sinus rhythm, either spontaneously or within seven days after intervention. Persistent AF lasts longer than seven days and usually requires cardioversion to convert to sinus rhythm. Permanent AF refers to individuals with persistent AF either refractory to cardioversion or where a decision has been made to no longer attempt to convert to sinus rhythm. New-onset AF refers to first-diagnosed or first-detected AF, and recent-onset refers to symptomatic AF that started within the last 48 hours. Finally, the term nonvalvular AF refers to atrial fibrillation in the absence of rheumatic disease, mitral stenosis, a prosthetic valve, or mitral valve repair.

Figure 2. Atrial Fibrillation With Coarse Atrial Fibrillation Waves in Lead V1

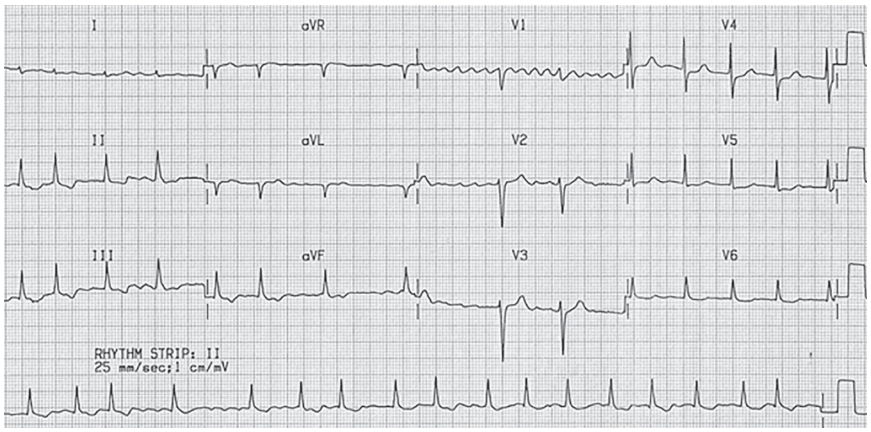
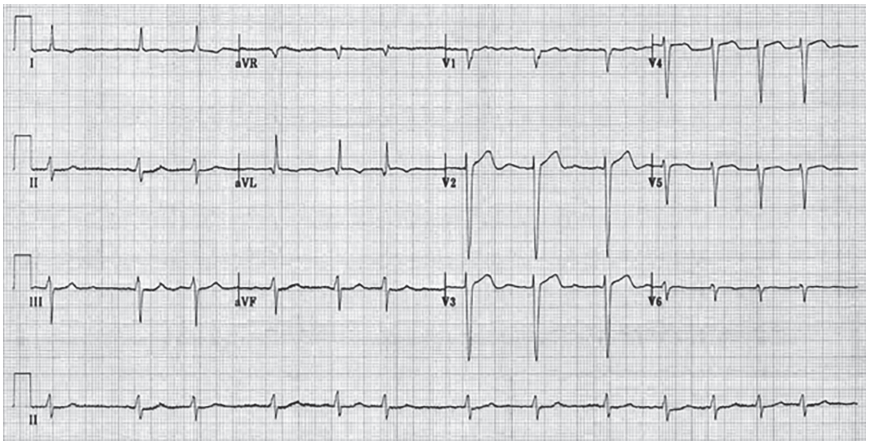


Figure used with permission from www.lifeinthefastlane.com.

Figure 3. Atrial Fibrillation With Fine Atrial Fibrillation Waves in Lead V1



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Various events may incite AF, including autonomic nervous system stimulation, bradycardia, atrial premature beats, atrial tachycardia, accessory AV pathways, acute atrial stretch, and ectopic foci in atrial tissue.[1,13,14] Repeated inciting events can lead to remodeling of the atria and the creation of multifocal reentrant loops, typically in the left atrium near the pulmonary veins.[13,15] As inciting events accumulate and remodeling continues, spontaneously returning to sinus rhythm, maintaining sinus rhythm, and successful cardioversion become more difficult.[13]

Clinical Features

AF is characterized on the ECG by an irregularly irregular ventricular rate and an absence of discernable P waves. (*See Figures 2–4.*) There also may be fine or coarse fibrillation waves that can be mistaken for P waves. Often, symptomatic patients present with an RVR, defined by a rate > 100 beats per minute (bpm). Symptoms typically include palpitations, shortness of breath, dizziness, fatigue, anxiety, and chest discomfort. Signs typically include an irregular heartbeat on auscultation and an irregular pulse on palpation.

Diagnostic Testing

Typical Workup

Despite the impulse to immediately correct this abnormal rhythm, be wary that AF with RVR often occurs in response to other acute disease processes. For instance, initiating rate control therapy in a septic patient whose RVR is attempting to maintain adequate tissue perfusion could trigger hypotension or cardiovascular collapse.[16] See Table 1 for a list of can't-miss pathologies that may present with AF.

History, physical exam, and knowledge of potential AF triggers dictate further testing. Initially, vital signs, complete blood count (CBC), and basic metabolic panel (BMP) usually are the laboratory tests required. Generally, there is no indication for liver transaminases and coagulation studies unless directed by history and physical. If a pulmonary embolism or deep venous thrombosis is a consideration, then D-dimer, venous duplex ultrasound, and/or CT angiography of the chest may be required. If overdose is a possibility, then some combination of ethanol level, urine drug screen, acetaminophen level, salicylate level, etc., may be required. Chest X-ray may be helpful to identify signs of heart failure, heart size, or pulmonary pathology.

Limited Indications for Echocardiogram

Formal echocardiogram generally is not indicated in the emergency setting when there is low suspicion for concomitant structural or functional heart anomalies. Exceptions include patients for whom flecainide or propafenone are being considered as treatment options. These two Class IC antiarrhythmic medications should be administered only in patients with structurally normal cardiac function, as discussed in the "Choosing the Right Rhythm Control Agent" section.[3,4,17] A transthoracic echocardiogram (TTE) can evaluate cardiac structure and function in these patients and is available in many EDs. A transesophageal echocardiogram (TEE) is required when a rhythm control strategy is being considered and duration of AF is unknown. Only TEE — not TTE — is sensitive enough to rule out atrial thrombi, but TEE requires conscious sedation and typically an inpatient admission.

Figure 4. Atrial Fibrillation With Rapid Ventricular Response

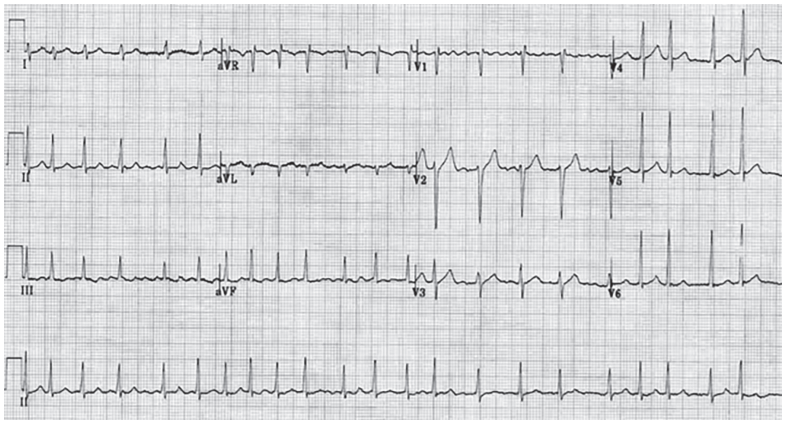
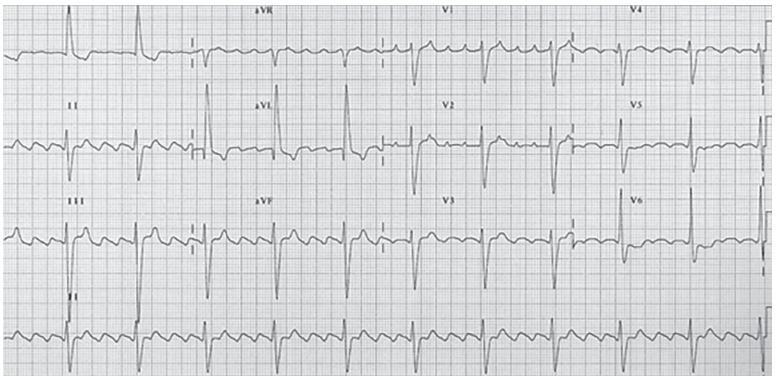


Figure used with permission from www.lifeinthefastlane.com.

Figure 5. Atrial Flutter



Atrial flutter with 4:1 AV condution. Note the deep, "saw-tooth" inteverted P waves in leads II, III, and aVF. Figure used with permission from www.lifeinthefastlane.com.

Limited Indications for Thyroid Stimulating Hormone Testing

Perhaps relatively low cost and decades of entrenched behavior have led many providers to order a thyroid-stimulating hormone (TSH) test indiscriminately for patients in AF with RVR. Evidence suggests that this approach is overkill. One retrospective study of nearly 2,000 patients with AF found low TSH indicative of hyperthyroidism in only 2% of patients, most commonly in those with new-onset AF or prior history of hyperthyroidism.[18] Other studies have reported similarly low yields of detecting thyroid disease.[19-21] Therefore, perform TSH testing only in patients with new-onset AF or hyperthyroidism for whom TSH testing has not occurred within the past three months.

Limited Indications for Troponin Testing and Importance of ST Segment Changes

Suspicion for acute coronary syndrome (ACS) causing or accompanying AF is an indication for cardiac biomarkers, but routine testing is unnecessary. Three studies investigating the causes of elevated troponin levels in the setting of tachyarrhythmias, including AF, found that troponin elevation was significantly more commonly associated with the rapid heart rate than ACS.[22-24] They concluded that elevated troponins in patients without definite clinical or electrocardiographic evidence of myocardial ischemia is not predictive of cardiovascular complications or death at one year.

ST segment elevations in concordant leads on any ECG should be evaluated for acute myocardial infarction (MI).[25,26] However, contrary to popular belief, transient ST segment depression during AF with RVR is not equivalent to a positive stress test. In one prospective cohort study in which 109 patients with AF and symptoms suggestive of ACS underwent a rule out MI protocol, only six (5.5%) suffered an MI.[26] The six patients with MI were more likely to have chest pain, new-onset AF, ST segment elevation, or ST segment depression > 2 mm than the 103 patients who did not have infarction. Either major ST segment depression (> 2 mm) or any ST segment elevation on the admission ECG had a sensitivity of 100% and a specificity of 99% for MI. Other studies similarly found that transient ST segment depression does not correlate with underlying coronary artery disease (CAD).[27,28] Therefore, in general for patients presenting with AF, ACS should be evaluated only when the patient specifically complains of chest discomfort or there is ST segment elevation or > 2 mm ST segment depression on the ECG.

Differential Diagnosis

AF can be mistaken for other arrhythmias, especially supraventricular tachycardia (SVT) and atrial flutter (AFL). SVT includes sinus tachycardia, atrioventricular nodal re-entry tachycardia (AVNRT), and atrioventricular reciprocating tachycardia (AVRT), all of which demonstrate regular RR intervals. Flutter waves, found in AFL, are characterized by large, inverted "saw tooth" P waves, typically in the inferior leads. In AFL, a re-entry circuit creates atrial impulses typically at a rate of 300 with varying degree of transmission through the atrioventricular (AV) node, resulting in 1:1, 2:1, 3:1, 4:1, or variable conduction ratios. (*See Figure 5.*)

Distinguishing AF from other types of tachycardia becomes increasingly difficult as heart rate increases. In cases of extreme SVT where AVNRT, AVRT, and AFL are at least as likely as AF, a transient AV node block via vagal maneuver or intravenous adenosine may help distinguish between or even resolve the tachyarrhythmia.

Table 1. Can't-miss Pathologies That May Present With Atrial Fibrillation

Disease Process	History, Signs, and Symptoms
Acute coronary syndrome (ACS)	Chest pressure, diaphoresis, ST elevation on ECG, positive biomarkers, dyspnea on exertion
Congestive heart failure (CHF)	Shortness of breath, S3, crackles on lung exam, jugular vein distension, hepatojugular reflex, bilateral lower extremity edema, and chest X-ray with edema
Pulmonary embolism (PE)	Pleuritic chest pain, unilateral extremity swelling, malignancy, prior deep vein thrombosis/pulmonary embolism, recent surgery or trauma, hemoptysis, oxygen saturation < 95%
Pericarditis/myocarditis	Chest pain, friction rub, PR depression, ST elevations, recent myocardial infarction/virus, positive troponin
Hyperthyroidism/thyroid storm	Hypertension, brisk reflexes, tremors, weight loss with normal appetite, heat intolerance
Valvular heart disease (e.g., mitral stenosis, regurgitation)	New murmur, recent ACS, history of CHF, syncope
Alcohol withdrawal	Tremors, anxiety
Sepsis	Quick sepsis related organ failure assessment (qSOFA) or systemic inflammatory response syndrome (SIRS) criteria
Drug overdose	History of drug use, toxidrome features
Gastrointestinal bleed	Positive fecal occult blood test, liver disease, peptic ulcer disease, melena, hematochezia, hematemesis

Special Consideration: Wolff-Parkinson-White Syndrome With Atrial Fibrillation

Wolff-Parkinson-White syndrome (WPW) with AF merits discussion because mistaking it for AF with RVR can have devastating consequences. WPW is characterized by an accessory pathway through which atrial impulses can bypass the AV node. ECG features of WPW during sinus rhythm include shortened PR-interval, slurring of the initial portion of the QRS complex (delta wave), slightly widened QRS complex, and T-wave inversions. (*See Figure 6.*) The most common tachyarrhythmia encountered in WPW is AVRT, which usually can be treated with vagal maneuvers or AV nodal blocking agents. However, administering AV nodal blocking agents in WPW with AF may promote unrestricted conduction through the accessory pathway, which can lead to rapid cardiovascular collapse.[29]

Although WPW is uncommon (< 0.3% of the population), AF comprises up to 40% of WPW tachyarrhythmias.[29] ECG characteristics of AF in WPW include wide, bizarre QRS complexes with significant beat-to-beat variations and variance in QRS width and amplitude, and may include slow QRS upstrokes — similar to delta waves — in the precordial leads. (*See Figure 7.*) *Diagnosis of WPW with AF should be suspected in any patient with wide complex AF on ECG.* ECGs of patients in AF with RVR and concomitant bundle branch blocks can be indistinguishable from WPW with AF, so reviewing prior ECGs is critical. Patients with WPW AF tend to be younger (usually < 50 years of age) with previous history of palpitations, syncope, or known WPW. Treatment of AF with WPW includes synchronized electrical cardioversion for unstable patients. If stable, chemical cardioversion may be attempted, provided electrical cardioversion is accessible immediately if the patient deteriorates. Procainamide often is considered the agent of choice, but both procainamide and ibutilide are reasonable.[29,30] Ibutilide confers a slightly higher risk of developing torsades de pointes, while procainamide causes hypotension more frequently. Amiodarone should be used with caution in WPW with AF, as degeneration into ventricular fibrillation can occur.[29]

ED Management

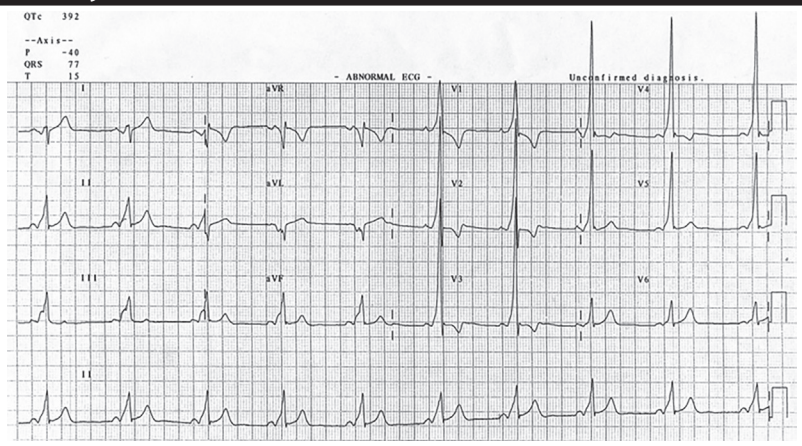
Standard Care for Every Patient With Atrial Fibrillation

In the acute setting, AF management focuses on stabilization, rate or rhythm control, and consideration for long-term anticoagulation therapy. AF requires an acute intervention when a patient is symptomatic, unstable, or demonstrates RVR.[31,32] All patients who are symptomatic, unstable, or have AF with RVR require a cardiac monitor, oxygen if hypoxic, appropriate IV access, frequent blood pressure monitoring, and application of defibrillation pads. Rapid sequence intubation equipment also should be available at the bedside in case the patient's clinical status deteriorates.

The Unstable Patient: Emergently Cardiovert and Consider Anticoagulation

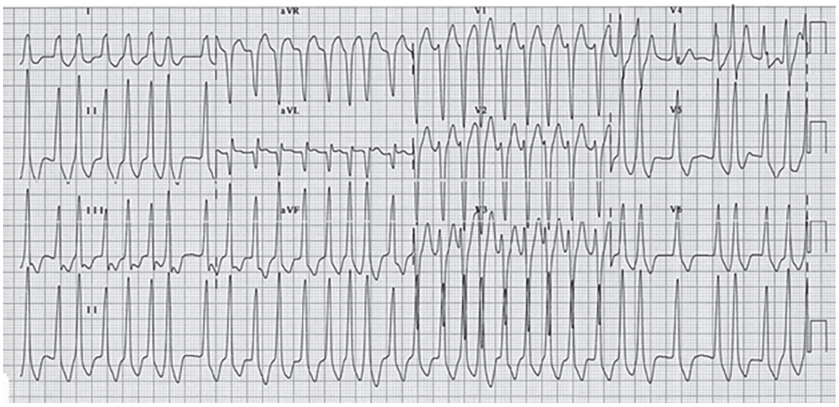
In patients with signs of hemodynamic instability, including active myocardial ischemia, acute heart failure, or significant hypotension attributable to RVR, perform immediate synchronized electrical cardioversion. Consider sedation/analgesia medications, but do

Figure 6. Wolff-Parkinson-White Syndrome in Normal Sinus Rhythm



Note the shortened PR-interval, delta wave, and slightly widened QRS complex. Figure used with permission from www.lifeinthefastlane.com.

Figure 7. Wolff-Parkinson-White Syndrome With Atrial Fibrillation



Note the irregular, widened QRS complexes and varying amplitude and width of the QRS complexes. Figure used with permission from www.lifeinthefastlane.com.

not delay cardioversion in an unstable patient.

Electrodes should be placed in the anterior-posterior (AP) or anterior-lateral (AL) positions; both are acceptable, but evidence suggests a slightly higher cardioversion success rate in the AP position.[33,34] For unstable patients, the Advanced Cardiac Life Support (ACLS) guidelines recommend immediately administering synchronized electrical cardioversion using biphasic direct current at 120-200 Joules (J).[35] The Canadian Cardiology Society (CCS) guidelines recommend starting at 150-200 J to increase likelihood of initial success.[4] For obese patients, consider administering 200 J; one randomized controlled study found that in patients with a BMI greater than 25, there was a 31% higher successful first-shock rate with 200 J compared to starting at a lower dose.[36]

Unstable patients with known duration greater than 48 hours, unknown duration, or an increased stroke risk additionally should receive a full venous thromboembolism dose of heparin before cardioversion or immediately afterward provided anticoagulation is not contraindicated. Such a patient should continue with anticoagulation for four weeks or longer post-cardioversion to reduce stroke risk.[4,37]

The Stable Patient

In a hemodynamically stable patient with symptomatic AF or RVR, rate or rhythm control should be initiated. While it is intuitive that restoring normal sinus rhythm would improve long-term outcomes, numerous studies have demonstrated no differences between rate and rhythm control in long-term risk of stroke, death, or any other major adverse outcome.[38-40] Therefore, the decision to pursue rate vs. rhythm control in the acute, stable patient depends on comorbidities, time of symptom onset, and shared decision-making with the patient.

Indications for Rate Control

Rate control is safe for most stable patients regardless of onset time. Rate control also should be used in patients with permanent AF, older patients with persistent AF, symptom onset greater than 48 hours or of unknown duration, recent transient ischemic attack (TIA)/stroke, and valvular disease.[4,16]

Rate Control: Metoprolol vs. Diltiazem

Both beta-blockers and calcium channel blocking agents slow AV conduction and prolong AV node refractoriness in acute AF. Metoprolol is the beta-blocker of choice because it selectively blocks beta-1 receptors in the heart, whereas nonselective agents also act on beta-2 receptors, increasing the risk of hypotension. Metoprolol is available in intravenous and oral formulations, making it an ideal rate-control agent while providing an easy transition to outpatient oral therapy.[1,4,41] In non-decompensated heart failure, a beta-blocker is the drug of choice because of the potential negative inotropic effect of calcium channel blockers.[1,3,4,41,42] Additionally, beta-blockers are the drugs of choice in the setting of AF secondary to an acute adrenergic surge or hyperthyroidism.

Although two classes of calcium channel blockers exist, only non-dihydropyridines calcium channel blockers (e.g., diltiazem, verapamil) are appropriate in symptomatic AF because of their negative chronotropic action. Like metoprolol, diltiazem is the drug of choice because of a wealth of supporting literature, decreased

Table 2. Rate Control Agent Summary

Primary Rate Control Agents				
Drug	**Acute Treatment in ED**	**Home Regimen**	**Side Effects**	**Comments**
Metoprolol	5 mg IV every 5 minutes until target heart rate achieved (max 15 mg)	Metoprolol tartrate (immediate release) 25 mg PO BID OR Metoprolol succinate (extended release) 50 mg PO daily	• Bradycardia, hypotension, potential activation of reactive airway disease	• If current home medication, increase to next available dosage form • Metoprolol tartrate less expensive than succinate form • Preferred in non-decompensated HF
Diltiazem	0.25 mg/kg IV once followed by a repeat dose of 0.35 mg/kg if target HR not achieved	Diltiazem IR 30 mg PO every six hours OR Diltiazem CD/LA/ER/XT 120 mg PO daily	• Bradycardia, hypotension • Avoid in heart failure	• If current home medication, increase to next available dosage form • Generally more expensive than metoprolol tartrate

Table 3. Characteristics Favoring Rate vs. Rhythm Control

Characteristics Favoring Rate Control	Characteristics Favoring Rhythm Control
• Age > 65 • Many comorbidities • Symptom onset > 48 hours or unknown • Longstanding or persistent AF • Recent TIA or stroke • Rheumatic heart disease • Mechanic heart valve	• Age < 65 • Few comorbidities • Symptom onset < 48 hours • Paroxysmal AF • Anticoagulated for ≥ 3 weeks or therapeutic INR

risk of negative inotropic and vasodilatory action, and availability as an oral and intravenous formulation.[1,3,4,41]

One study that randomized patients to receive diltiazem or metoprolol in patients with AF found that diltiazem was nearly 40% more successful at achieving a heart rate less than 100 bpm within five minutes than metoprolol, and approximately 50% more successful within 30 minutes. Adverse effects occurred equally in each group.[43] Therefore, while both agents are acceptable, diltiazem may be a more effective therapy in patients without heart failure.

Caution must be exercised when switching between IV beta- and calcium channel blockers. Several smaller studies have demonstrated symptomatic bradycardia and prolonged hypotension when these agents are combined.[44,45] Thus, it may be more prudent to initiate multiple doses of the same agent to achieve rate control rather than switching between beta- and calcium channel blockers. See Table 2 for a rate control medication summary.

Rhythm Control: Advantages in Recent-onset Atrial Fibrillation

While rate control is a time-honored, conservative approach to managing patients with symptomatic AF in the ED, rhythm control may have significant advantages when used in certain populations. Overcrowding, lack of hospital beds, and prolonged ED lengths of stay are common in many North American hospitals.[46] Many Canadian and a few U.S. institutions, therefore, have adopted a more aggressive rhythm control strategy, which has led to shorter ED stays and reduced admission rates. In the United States, approximately 30% of patients presenting with AF are discharged, but in Canada more than 60% are discharged.[47-49]

Rhythm control is ideal for patients with paroxysmal AF, especially those with new or recent-onset AF (less than 48 hours) or on anticoagulation for at least three weeks.[4,17] Rhythm control should be avoided if symptom onset is unknown, and patient-reported history is critical to determining symptom onset. Some clinicians feel uncomfortable relying on patient self-reported symptom onset. This concern has some merit. Two studies suggest that 35-37% of patients in AF do not perceive symptoms, although patients in these studies tended to be > 65 years old and had implantable cardiac devices suggesting diseased hearts at baseline.[50,51] In contrast, emergency medicine literature consistently supports that when known, patients' self-reporting of symptom onset is accurate and reliable.[46,52,53] When ED patients report < 48 hours of symptoms, rhythm control confers < 1% risk of stroke or death in the short- and long-term.[46,49,53]

History also is important in determining anticoagulation compliance. Patients on any of the direct oral anticoagulants (DOACs) need to be compliant on their medication for at least three weeks prior to attempting rhythm control.[37] If the patient is on warfarin, INR should be obtained first to determine if the patient is appropriately anticoagulated. Finally, rhythm control should be avoided in patients with permanent AF, older patients with persistent AF,

Table 4. Rhythm Control Agent Summary

Drug	Class	Mechanism	Dose	Conversion Rate	Comments	Adverse and Side Effects
Procainamide	IA	• Blocks sodium channels	• 15-17 mg/kg IV over 60 min • Alternatively, 1,000 mg IV over 30 min	• 58.3% at 1 hr	• Safer in structural heart disease compared to Class IC agents	• Hypotension rate 5-8.5% • Bradycardia • Torsades de pointes
Propafenone	IC	• Blocks sodium channels • Weakly blocks potassium/calcium channels and beta receptors	• < 70 kg: 450 mg PO • > 70 kg: 600 mg PO	• 56-83%, typically within 2-3 hrs • Success dependent on AF duration	• Exclude in left ventricular dysfunction or heart failure, sick sinus syndrome, QRS duration ≥ 110 msec, and second- or third-degree AV block	• Transient arrhythmias and hypotension • Reversible QRS widening • Nausea • Metallic taste in mouth
Flecainide	IC	• Blocks sodium channels and slows conduction through the heart • Transiently decreases cardiac output and stroke volume	• < 70 kg: 200 mg PO • > 70 kg: 300 mg PO	• 51-72% within 8 hrs, typically within 3-5 hrs	• Great oral bioavailability (> 90%) • Minimal effects on blood pressure • Exclusions similar to propafenone	• Headache • Dizziness • Visual disturbances • Tremor
Ibutilide	III	• Prolongs action potential in cardiac tissue	• < 60 kg: 0.01 mg/kg IV over 10 min • > 60 kg: 1 mg IV over 10 min	• 27-40% in 60-90 min	• Some data suggest pretreatment with magnesium is warranted • Expensive • ECG monitoring for 4 hours afterward	• Hypotension • Bradycardia • Torsades de pointes (3%) risk
Amiodarone	III	• Prolongs phase 3 of cardiac action potential • Acts on multiple channels and nonselective inhibition of alpha and beta receptors	• Bolus of 5 mg/kg IV followed by an infusion of 1.2-1.8 gm over 24 hrs • 150 mg in 10 min followed by 1 mg/min for 6 hrs then 0.5 mg/min for 18 hrs	• Failed to show efficacy for the acute treatment of recent-onset AF	• Drug of choice for managing AF in setting of acute ischemia, acute MI, or LV dysfunction • Safe in structural heart disease • Not FDA approved for atrial fibrillation	• IV: phlebitis, hypotension • Chronic toxicities: - Photosensitivity - Hyperthyroidism - Hypothyroidism - Pulmonary fibrosis - Hepatotoxicty

symptom onset greater than 48 hours or of unknown duration, recent TIA/stroke, and valvular disease. See Table 3 for characteristics that favor rate vs. rhythm control.

Rhythm Control: Electrical vs. Pharmacologic Cardioversion

Choosing between electrical and pharmacologic cardioversion to restore sinus rhythm depends on the patient's blood pressure, risks of sedation, and patient and provider preference. There are some clear benefits to electrical compared to pharmacologic cardioversion. First, electrical cardioversion boasts significantly higher success rates of 89-96% compared to pharmacologic cardioversion success rates of 50-83%.[4,46,53,54] Second, once the patient is sedated, electrical cardioversion is instantaneous, whereas pharmacologic cardioversion may take several hours depending on the agent. Third, several antiarrhythmic agents cannot be used in patients with structural or functional heart disease, and none of them are safe in patients with low blood pressures.

Despite these advantages, the pharmacologic approach has an important role as well. When successful, rhythm control medications eliminate the need for procedural sedation and associated risks. Also, many hemodynamically stable patients are uncomfortable with the notion of electrical shock when another option is available. Therefore, clinicians should become comfortable with using several of the various antiarrhythmic agents. Note, pretreatment with rate control agents has not been shown to enhance the rate of cardioversion using antiarrythmics.[4]

Choosing the Right Rhythm Control Agent

The most commonly used antiarrhythmics include Class IA, IC, and III agents. Each has a unique set of advantages and disadvantages that must be

Table 5. CHA_2DS_2-VASc Score Calculation

	Condition	Points
C	Congestive heart failure (or left ventricular systolic dysfunction)	1
H	Hypertension: Blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	1
A_2	Age ≥ 75 years	2
D	Diabetes mellitus	1
S_2	Prior stroke, transient ischemic attack, or thromboembolism	2
V	Vascular disease (e.g., peripheral artery disease, myocardial infarction, aortic plaque)	1
A	Age 65-74 years	1
Sc	Sex category (i.e., female)	1

Table 6. Recommendations for Long-term Anticoagulation in Patients With Atrial Fibrillation

CHA_2DS_2-VASc Score	Adjusted Stroke Rate (per year)	Start Anticoagulation?
0	< 1%	No
1	1.3%	Consider aspirin vs. anticoagulation
≥ 2	2.2%	Yes

considered based on the comorbidities of the patient.

Procainamide, a Class IA antiarrhythmic, is an increasingly attractive option for rhythm control and has been used preferentially and safely in many Canadian EDs for years. A sodium channel blocking agent, procainamide has a 58-65% cardioversion rate for AF, often within one hour.[46,52,55] It boasts fewer side effects than Class IC agents, the most common being transient hypotension in 5-8% of cases. Unlike Class IC antiarrhythmics, procainamide can be used in patients with stable structural and functional heart disease.[4,54,56] In cases in which procainamide fails to restore normal sinus rhythm within one to two hours, electrical cardioversion can be initiated safely.[4]

For patients with paroxysmal AF, flecainide and propafenone are two of the most commonly prescribed antiarrhyhmics in the outpatient setting by cardiologists. Their use in the acute setting, however, remains less clear. Both are Class IC agents that block sodium channels, slow conduction through the heart, and exert a negative inotropic effect.[57] Acute treatment with flecainide is associated with a conversion rate of 51% at three hours and 72% at eight hours.[58] Similarly, propafenone effectively cardioverts patients 56-83% of the time, typically within three to four hours.[59,60] Monitoring patients for this length of time may not be tenable in many busy EDs. Additionally, these agents cannot be used in patients with structural or functional heart disease, including left ventricular dysfunction, heart failure, sick sinus syndrome, bundle branch blocks, or AV blocks.[37] Therefore, an echocardiogram should be obtained prior to administering these agents if not recently performed.

Ibutilide and amiodarone are Class III antiarrhythmics that primarily prolong action potential in cardiac tissue. The excessive cost and the lower rate of cardioversion makes ibutilide less favorable than procainamide. Ibutilide has demonstrated conversation rates of 40% at 90 minutes.[61] Furthermore, it is recommended that patients receiving ibutilide be monitored for at least four hours after administration, making its use in the ED cumbersome.[41,62-64] Amiodarone rarely is used in recent-onset AF because of significantly lower conversion rates and higher side effect profiles than the aforementioned agents.[65-67] However, amiodarone can be used in patients with acute ischemia, acute MI, and LV dysfunction.[68] See Table 4 for a rhythm control medication summary.

A Word on Digoxin and Magnesium

Digoxin, once the preferred agent in acute AF management, has fallen out of favor because of its delayed onset of action (up to six hours), complex impact on patients with heart failure, and poor cardioversion efficacy.[69-71] Its use may be best limited to patients with hypotension and heart failure, ideally in consultation with a cardiologist.[1,3,4,41]

While not a traditional rate control agent, magnesium is recommended as an adjunctive agent for AF patients in the acute setting because it may decrease conduction through the AV node and intra-arterial conduction times.[72,73] Many patients with arrhythmias have been shown to have intracellular magnesium deficiency.[74,75] Prophylactic magnesium use with ibutilide for chemical cardioversion has shown increased conversion rates and a decreased incidence of side effects from ibutilide.[75-77]

Disposition Considerations

Indications for admission of patients with AF include hemodynamic instability, serious alternative primary diseases, diagnostic uncertainty, and failure of symptomatic, rate, or rhythm control. Because of the risk of tachycardia-induced cardiomyopathy, a patient who remains in AF at a rate greater than 100 bpm at rest and 110 bpm with ambulation should not be discharged.[4,17] Even when rate or rhythm is well controlled but comorbidities abound, appropriate disposition may be unclear.

One clinical decision support tool that has shown promise in determining

Table 7. Comparison of Direct Oral Anticoagulants

Agent	Mechanism of Action	Dose	Dose Adjustments	Trials Comparing Direct Oral Anticoagulants to Warfarin
Dabigatran	Direct thrombin inhibitor	150 mg twice daily	Reduce dose to 75 mg BID if creatinine clearance (CrCl) 15-30 mL/min. No recommendations if CrCl < 15 mL/min or on dialysis	RE-LY: Lower rate of ICH and major GI bleeds; no reduction in major or fatal bleeds
Rivaroxaban	Factor Xa inhibition	20 mg daily with evening meal	Reduce dose to 15 mg once daily for CrCl 15-50 mL/min	ROCKET AF: Lower rate of ICH, fatal and major GI bleeds; no reduction in major bleeds
Apixaban	Factor Xa inhibition	5 mg twice daily	Serum creatinine ≥ 1.5 mg/dL and body weight ≤ 60 kg or age ≥ 80 years: Reduce dose to 2.5 mg twice daily	ARISTOTLE: Lower rate of ICH and major bleeds; no reduction in major GI bleeding
Edoxaban	Factor Xa inhibition	60 mg once daily	Reduce dose to 30 mg once daily if CrCl is 15-50 mL/min; CrCl < 15 mL/min or > 95 mL/min: not recommended	ENGAGE AF-TIMI: Lower rate of ICH, major, fatal, and major GI bleeds

which patients are safe for discharge is the Risk Estimator Decision Aid for AF (RED-AF).[78] A validation study of RED-AF has demonstrated that low-risk patients have less than 7% chance of having an adverse event including ED re-visits, rehospitalizations, cardiovascular complications, and death.[79]

Stroke Risk: Always Calculate CHA_2DS_2-VASc

Because patients with AF have an inherently increased stroke risk, estimating the patient-specific stroke risk is essential prior to discharge. That risk of stroke can be reduced by oral anticoagulation, but with an increased risk for bleeding. The challenge has been to identify patients for whom long-term anticoagulant therapy can reduce the risk of stroke with an acceptable risk for hemorrhage. The preferred risk-stratifying tool in patients with nonvalvular AF is the CHA_2DS_2-VASc score.[37,81,82] See Tables 5 and 6 for CHA_2DS_2-VASc score calculation and recommendations for long-term anticoagulation in patients with AF, respectively.

If anticoagulation is necessary, the choice is between a low molecular-weight heparin bridge with warfarin or one of the newer DOACs. Each DOAC is superior to or as effective in reducing stroke as warfarin in nonvalvular AF. In fact, all DOACs demonstrated lower rates of intracranial hemorrhage (ICH), the most feared bleeding complication, and lower or similar rates of fatal and major bleeds.[83] Moreover, DOACs do not require INR monitoring, a not-to-be overlooked benefit to the patient.

While all DOACs effectively prevent stroke, compliance and cost are important considerations. For instance, it may be much easier for patients to remember to take medications that require once-daily dosing compared to twice-daily dosing. Additionally, it is a disservice to the patient to prescribe a medication that he or she cannot afford. For instance, the authors of this article inquired into the cost of one of the most commonly used DOACs and learned that even with Medicare coverage, the monthly cost without additional coverage benefits approaches $300 monthly, an unaffordable price for many Americans. Fortunately, all DOACs have patient assistance or prescription vouchers available through the manufacturers. ED and inpatient pharmacists are great resources for this assistance. See Table 7 for a comparison of DOAC agents.

Outpatient Medication Recommendations: Keep It Simple

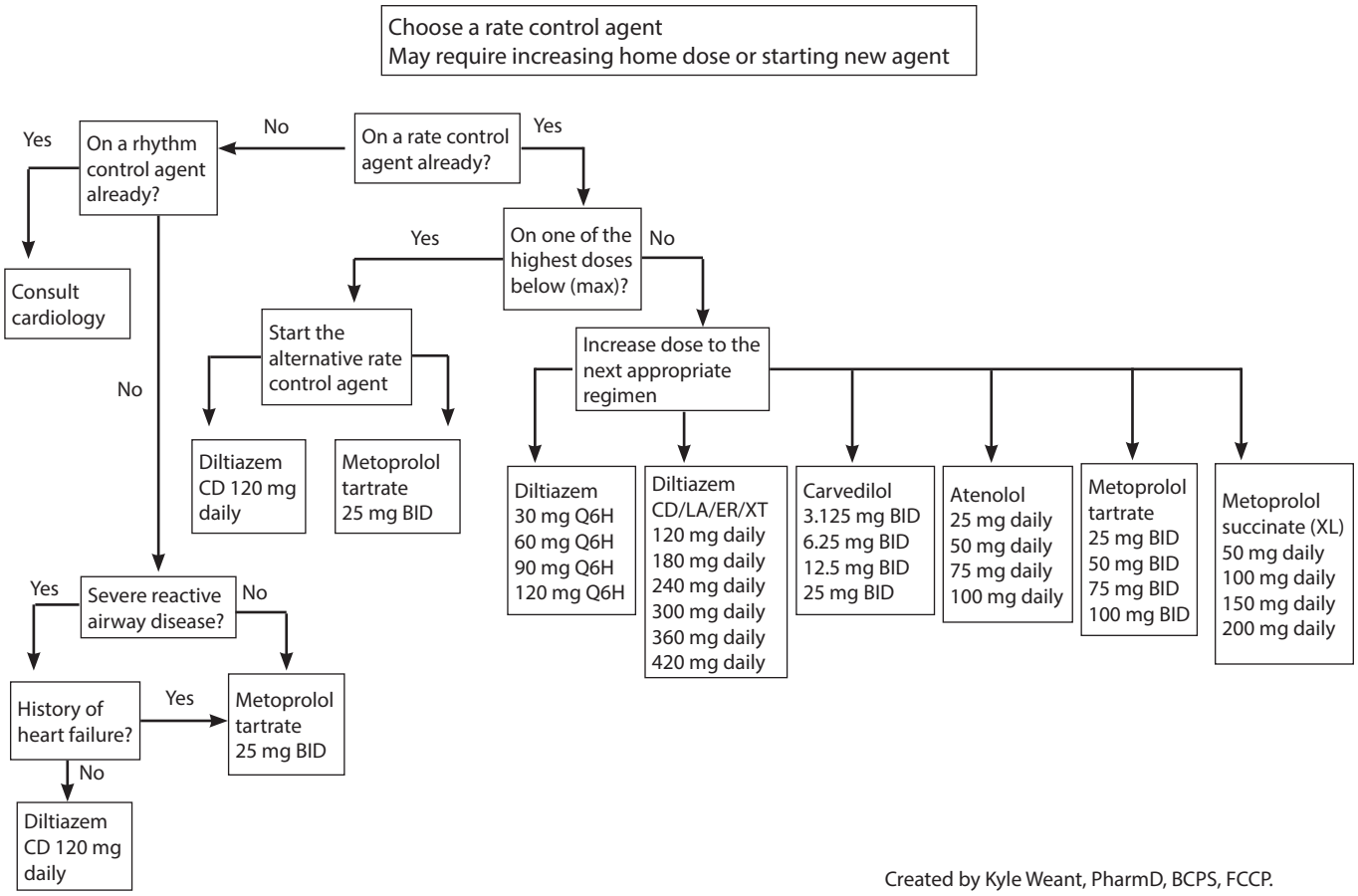
When rhythm control agents are used in the acute setting, prescribing rate control agents in the outpatient setting may provide distinct advantages and more optimal side-effect profiles. For new or recent-onset AF, consider prescribing a beta- or a calcium channel blocker (depending on the patient's history), or simply increase the patient's baseline home dose. If initiating a new medication upon ED discharge, provide adequate counseling, including monitoring parameters and possible adverse effects, and ensure patients have an opportunity to ask questions. When increasing the dose of a patient's existing medication, it is recommended to provide a new prescription with the updated dosing regimen to ensure the patient takes the correct amount. See Figure 8 for medication recommendations in the outpatient setting.

Summary

Workup and management of AF depends on the patient presentation. TSH testing is not indicated except in new-onset AF or in a patient with hyperthyroidism who has not had TSH checked recently. Troponin testing generally is not indicated unless the patient endorses angina symptoms. ST segment elevation and ST segment depression > 2 mm in AF with RVR are concerning for ACS, but transient ST segment depression < 2 mm is not.

Unstable patients require immediate synchronized cardioversion, and anticoagulation should be administered if symptom onset is greater than 48 hours or of unknown duration, or if the patient has an increased stroke risk. Stable patients who reliably can confirm AF onset time of less than 48

Figure 8. Medication Recommendations for AF Post-ED Discharge



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hours, or those who have been anticoagulated consistently for three weeks can safely be cardioverted pharmacologically or electrically. Rate control also is reasonable in these patients provided that a slower rate improves their symptoms.

For patients with an alternative primary diagnosis, such as sepsis or acute decompensated heart failure, treat the primary diagnosis first; treating AF in these cases with rate control or cardioversion either is unlikely to be successful or could worsen clinical status.

In patients who are appropriate for discharge, calculating the CHA_2DS_2-VASc score determines whether long-term anticoagulation is necessary. Newer DOACs are at least as safe as warfarin and do not require monitoring. However, because of their high cost, ask the inpatient or ED pharmacists to contact the manufacturers to secure free vouchers and set up long-term plans to ensure patients can access these potentially lifesaving medications. See Figure 9 for an evidence-based suggested AF workflow.

Case Conclusions

Case 1: *Differential Diagnosis:* AF with RVR, AFL, SVT, PE, and hyperthyroidism

Tests/Imaging: CBC, BMP, and TSH (since new-onset AF). The ECG confirms AF with RVR.

Treatment options include rate control or rhythm control.

A CHA_2DS_2-VASc score should be calculated to determine the need for anticoagulation. The patient should have a follow-up appointment with a cardiologist and an outpatient echocardiogram.

Case 2: *Differential Diagnosis:* AF with RVR, AFL, SVT, and PE. This patient's symptoms and ECG suggest low likelihood of ACS. Consider PE if shortness of breath does not resolve with intervention.

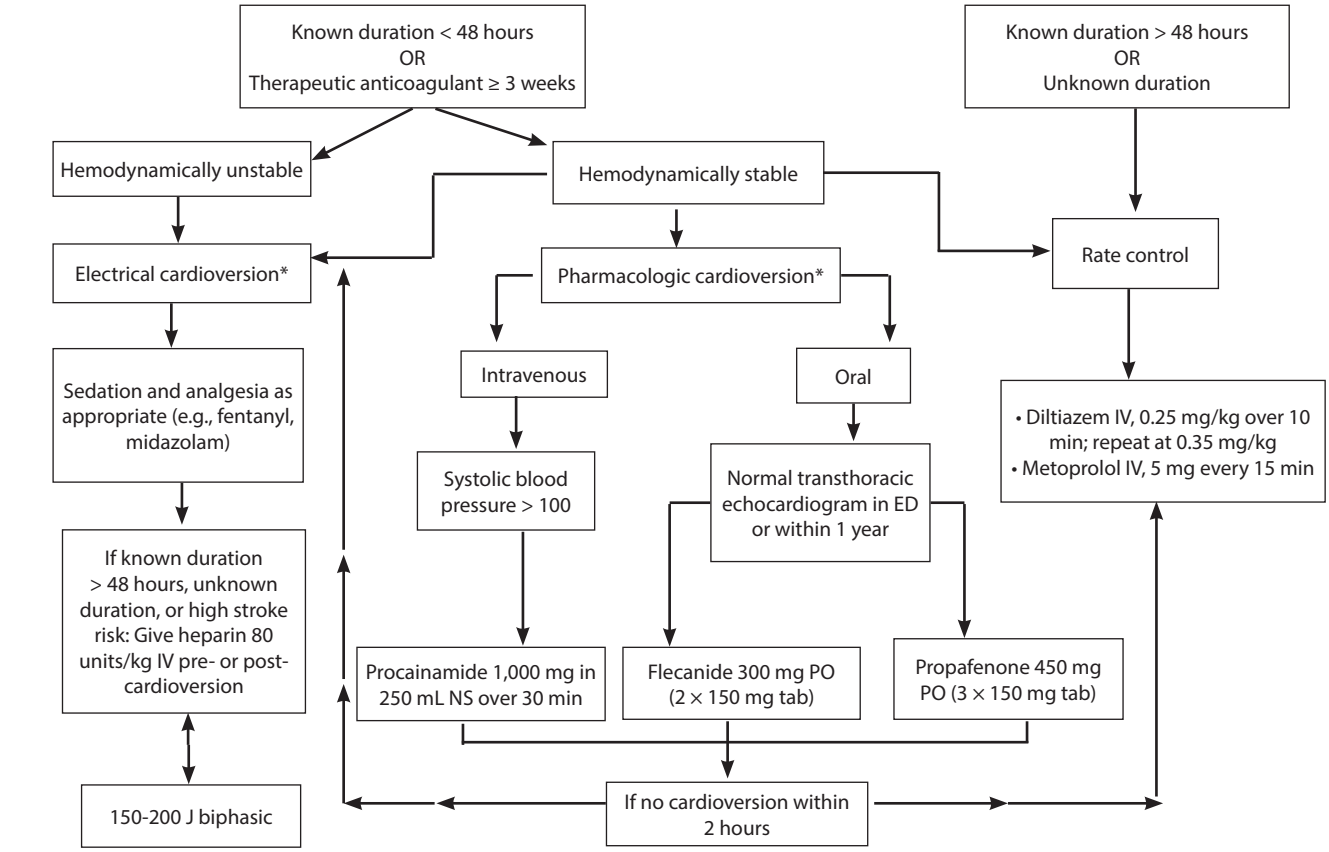
Important questions to ask: 1) Has she missed any apixaban doses in the past three weeks? 2) Does she remember the exact onset time?

Tests/Imaging: ECG, BMP, and CBC. ECG confirms the diagnosis of AF with RVR.

Treatment: If the patient has been taking apixaban consistently for at least three weeks without missing doses, and if she is confident that her AF started within the past 48 hours, then either rhythm or rate control are appropriate options. If she reports that she has missed doses in the past three weeks or is not certain of onset time, then her only option is rate control. If stable for discharge, then she should follow up with her cardiologist. Either her beta- or calcium channel blocker should be increased if possible.

Case 3: This patient is hemodynamically unstable and requires immediate synchronized electrical cardioversion. Place defibrillator pads on the patient in the anterior-posterior positions and

Figure 9. An Evidence-based Atrial Fibrillation Workflow



Disposition

1. All patients with symptomatic AF:
- Increase home rate control agent or start new agent
- Assess CHA_2DS_2-VASc score
- ED referral to cardiology

2. Safe for discharge home if:
- Conversion to sinus rhythm with stable vitals

OR
- AF/flutter with HR < 100 at rest or < 110 after ambulation PLUS symptomatic improvement

3. For new-onset AF:
- Order outpatient transthoracic echocardiogram

Note: If emergently electrocardioverted in ED and known duration > 48 hours, unknown duration, or high risk for stroke:
- Prescribe 4 weeks of anticoagulation

Factors Favoring Rate Control	Factors Favoring Rhythm Control
• Age > 65	• Age < 65
• Many comorbidities	• Few comorbidities
• Onset > 48 hours or unknown duration	• Onset < 48 hours
• Recent TIA/stroke	• Anticoagulated ≥ 3 weeks or therapeutic INR
• Rheumatic heart disease	
• Mechanical heart valve	

* Exclusions to electrical or chemical cardioversion:
- Permanent AF (chronic, persistent, or longstanding)
- Symptoms > 48 hours or unknown duration (unless therapeutically anticoagulated with warfarin for ≥ 3 weeks)
- Mechanical heart valve
- Rheumatic heart disease
- Recent TIA/stroke
- Unstable cardiac ischemia, severe congestive heart failure, hypotension
- Additional primary diagnosis necessitating admission

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obtain IV access if possible, but do not delay cardioversion. The patient should receive at least 120 J and up to 200 J if obese.

Once the patient is stabilized, a thorough history should be obtained regarding symptom onset, recent medical history, possible AF triggers, and past medical history. His answers will dictate the appropriate tests to order. If he has no history of hyperthyroidism and no prior symptoms concerning for ACS, then TSH and troponins should not be ordered. If the patient remains stable after cardioversion and workup, then discharge home may be reasonable. He should be started on a rate control agent or increased dose if he is already taking a rate control agent. A CHA_2DS_2-VASc score should be calculated to determine the need for long-term anticoagulation. The patient should have a follow-up appointment with cardiology and an outpatient echocardiogram if he has not had one recently.

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CME/CE Questions

1. Where do the ectopic foci of atrial fibrillation originate?
   a. Pulmonary arteries
   b. Bronchiole arteries
   c. Sinoatrial node
   d. Pulmonary veins
2. What is the most important ECG characteristic to make the diagnosis of atrial fibrillation?
   a. Fine or course fibrillations
   b. Irregularly irregular rhythm
   c. Lack of P waves
   d. Lack of an isoelectric baseline
3. Which of the following is the most predominant risk factor in atrial fibrillation?
   a. Smoking
   b. Age
   c. Obesity
   d. Coronary artery disease
4. Which of the following is the best test to diagnose atrial fibrillation?
   a. Echocardiogram
   b. Stress electrocardiogram
   c. Electrocardiogram
   d. Physical exam
5. In a patient with unknown duration of AF, how long must he or she be anticoagulated to be a candidate for rhythm control?
   a. 1 week
   b. 2 weeks
   c. 3 weeks
   d. 4 weeks
6. What are the options for treating atrial fibrillation with rapid ventricular response?
   a. Beta blockade, calcium channel blockade, vagal maneuvers, adenosine
   b. Rate control, synchronized electrical cardioversion, chemical cardioversion
   c. Transvenous pacing, transcutaneous pacing, atropine, vasopressor drip
   d. Rate control, unsynchronized electrical cardioversion, chemical cardioversion
7. What minimum level of energy and setting is recommended to electrically cardiovert atrial fibrillation?
   a. 120 J, asynchronous
   b. 120 J, synchronous
   c. 150 J, asynchronous
   d. 200 J, synchronous
8. Which of the following class of medications is the most appropriate for atrial fibrillation with rapid ventricular rate in a patient with stable heart failure?
   a. Beta-blockers
   b. Calcium channel blockers
   c. Class IC antiarrhythmics
   d. Benzodiazepines
9. To safely use flecainide or propafenone as rhythm control agents, which of the following tests should be obtained?
   a. Echocardiogram
   b. Electrocardiogram
   c. Electrocardiogram stress test
   d. Cardiac MRI
10. Which of the following is recommended by the 2014 American Heart Association guidelines to determine whether anticoagulation is necessary in patients with atrial fibrillation?
    a. $CHADS_2$
    b. CHA_2DS_2-VASc
    c. RED-AF
    d. HAS-BLED

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EMERGENCY MEDICINE REPORTS™
(ISSN 0746-2506) is published 24 times annually by AHC Media, a Relias Learning company, 111 Corning Road, Suite 250, Cary, NC 27518-9238. Telephone: (800) 688-2421.

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Editorial Group Manager: Terrey L. Hatcher

Senior Accreditations Officer: Lee Landenberger

GST Registration No.: R128870672

Periodicals Postage Paid at Cary, NC, and additional mailing offices.

POSTMASTER: Send address changes to ***Emergency Medicine Reports,*** Relias Learning, 111 Corning Road, Suite 250, Cary, NC 27518-9238.

Back issues: $30. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

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EMERGENCY MEDICINE **REPORTS**

Evidence-based Management of Atrial Fibrillation in the Emergency Department

Table 1. Can't-miss Pathologies That May Present With Atrial Fibrillation

Disease Process	History, Signs, and Symptoms
Acute coronary syndrome (ACS)	Chest pressure, diaphoresis, ST elevation on ECG, positive biomarkers, dyspnea on exertion
Congestive heart failure (CHF)	Shortness of breath, S3, crackles on lung exam, jugular vein distension, hepatojugular reflex, bilateral lower extremity edema, and chest X-ray with edema
Pulmonary embolism (PE)	Pleuritic chest pain, unilateral extremity swelling, malignancy, prior deep vein thrombosis/pulmonary embolism, recent surgery or trauma, hemoptysis, oxygen saturation < 95%
Pericarditis/myocarditis	Chest pain, friction rub, PR depression, ST elevations, recent myocardial infarction/virus, positive troponin
Hyperthyroidism/thyroid storm	Hypertension, brisk reflexes, tremors, weight loss with normal appetite, heat intolerance
Valvular heart disease (e.g., mitral stenosis, regurgitation)	New murmur, recent ACS, history of CHF, syncope
Alcohol withdrawal	Tremors, anxiety
Sepsis	Quick sepsis related organ failure assessment (qSOFA) or systemic inflammatory response syndrome (SIRS) criteria
Drug overdose	History of drug use, toxidrome features
Gastrointestinal bleed	Positive fecal occult blood test, liver disease, peptic ulcer disease, melena, hematochezia, hematemesis

Table 2. Rate Control Agent Summary

Primary Rate Control Agents

Drug	Acute Treatment in ED	Home Regimen	Side Effects	Comments
Metoprolol	5 mg IV every 5 minutes until target heart rate achieved (max 15 mg)	Metoprolol tartrate (immediate release) 25 mg PO BID OR Metoprolol succinate (extended release) 50 mg PO daily	• Bradycardia, hypotension, potential activation of reactive airway disease	• If current home medication, increase to next available dosage form • Metoprolol tartrate less expensive than succinate form • Preferred in non-decompensated HF
Diltiazem	0.25 mg/kg IV once followed by a repeat dose of 0.35 mg/kg if target HR not achieved	Diltiazem IR 30 mg PO every six hours OR Diltiazem CD/LA/ER/XT 120 mg PO daily	• Bradycardia, hypotension • Avoid in heart failure	• If current home medication, increase to next available dosage form • Generally more expensive than metoprolol tartrate

Table 3. Characteristics Favoring Rate vs. Rhythm Control

Characteristics Favoring Rate Control	Characteristics Favoring Rhythm Control
• Age > 65 • Many comorbidities • Symptom onset > 48 hours or unknown • Longstanding or persistent AF • Recent TIA or stroke • Rheumatic heart disease • Mechanic heart valve	• Age < 65 • Few comorbidities • Symptom onset < 48 hours • Paroxysmal AF • Anticoagulated for ≥ 3 weeks or therapeutic INR

Table 4. Rhythm Control Agent Summary

Drug	Class	Mechanism	Dose	Conversion Rate	Comments	Adverse and Side Effects
Procainamide	IA	• Blocks sodium channels	• 15-17 mg/kg IV over 60 min • Alternatively, 1,000 mg IV over 30 min	• 58.3% at 1 hr	• Safer in structural heart disease compared to Class IC agents	• Hypotension rate 5-8.5% • Bradycardia • Torsades de pointes
Propafenone	IC	• Blocks sodium channels • Weakly blocks potassium/calcium channels and beta receptors	• < 70 kg: 450 mg PO • > 70 kg: 600 mg PO	• 56-83%, typically within 2-3 hrs • Success dependent on AF duration	• Exclude in left ventricular dysfunction or heart failure, sick sinus syndrome, QRS duration ≥ 110 msec, and second- or third-degree AV block	• Transient arrhythmias and hypotension • Reversible QRS widening • Nausea • Metallic taste in mouth
Flecainide	IC	• Blocks sodium channels and slows conduction through the heart • Transiently decreases cardiac output and stroke volume	• < 70 kg: 200 mg PO • > 70 kg: 300 mg PO	• 51-72% within 8 hrs, typically within 3-5 hrs	• Great oral bioavailability (> 90%) • Minimal effects on blood pressure • Exclusions similar to propafenone	• Headache • Dizziness • Visual disturbances • Tremor
Ibutilide	III	• Prolongs action potential in cardiac tissue	• < 60 kg: 0.01 mg/kg IV over 10 min • > 60 kg: 1 mg IV over 10 min	• 27-40% in 60-90 min	• Some data suggest pretreatment with magnesium is warranted • Expensive • ECG monitoring for 4 hours afterward	• Hypotension • Bradycardia • Torsades de pointes (3%) risk
Amiodarone	III	• Prolongs phase 3 of cardiac action potential • Acts on multiple channels and nonselective inhibition of alpha and beta receptors	• Bolus of 5 mg/kg IV followed by an infusion of 1.2-1.8 gm over 24 hrs • 150 mg in 10 min followed by 1 mg/min for 6 hrs then 0.5 mg/min for 18 hrs	• Failed to show efficacy for the acute treatment of recent-onset AF	• Drug of choice for managing AF in setting of acute ischemia, acute MI, or LV dysfunction • Safe in structural heart disease • Not FDA approved for atrial fibrillation	• IV: phlebitis, hypotension • Chronic toxicities: - Photosensitivity - Hyperthyroidism - Hypothyroidism - Pulmonary fibrosis - Hepatotoxicty

Table 5. CHA_2DS_2-VASc Score Calculation

	Condition	Points
C	Congestive heart failure (or left ventricular systolic dysfunction)	1
H	Hypertension: Blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	1
A_2	Age ≥ 75 years	2
D	Diabetes mellitus	1
S_2	Prior stroke, transient ischemic attack, or thromboembolism	2
V	Vascular disease (e.g., peripheral artery disease, myocardial infarction, aortic plaque)	1
A	Age 65-74 years	1
Sc	Sex category (i.e., female)	1

Table 6. Recommendations for Long-term Anticoagulation in Patients With Atrial Fibrillation

CHA_2DS_2-VASc Score	Adjusted Stroke Rate (per year)	Start Anticoagulation?
0	< 1%	No
1	1.3%	Consider aspirin vs. anticoagulation
≥ 2	2.2%	Yes

Table 7. Comparison of Direct Oral Anticoagulants

Agent	Mechanism of Action	Dose	Dose Adjustments	Trials Comparing Direct Oral Anticoagulants to Warfarin
Dabigatran	Direct thrombin inhibitor	150 mg twice daily	Reduce dose to 75 mg BID if creatinine clearance (CrCl) 15-30 mL/min. No recommendations if CrCl < 15 mL/min or on dialysis	RE-LY: Lower rate of ICH and major GI bleeds; no reduction in major or fatal bleeds
Rivaroxaban	Factor Xa inhibition	20 mg daily with evening meal	Reduce dose to 15 mg once daily for CrCl 15-50 mL/min	ROCKET AF: Lower rate of ICH, fatal and major GI bleeds; no reduction in major bleeds
Apixaban	Factor Xa inhibition	5 mg twice daily	Serum creatinine ≥ 1.5 mg/dL and body weight ≤ 60 kg or age ≥ 80 years: Reduce dose to 2.5 mg twice daily	ARISTOTLE: Lower rate of ICH and major bleeds; no reduction in major GI bleeding
Edoxaban	Factor Xa inhibition	60 mg once daily	Reduce dose to 30 mg once daily if CrCl is 15-50 mL/min; CrCl < 15 mL/min or > 95 mL/min: not recommended	ENGAGE AF-TIMI: Lower rate of ICH, major, fatal, and major GI bleeds

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