CME

Strategies for rate and rhythm control of atrial fibrillation in the ED

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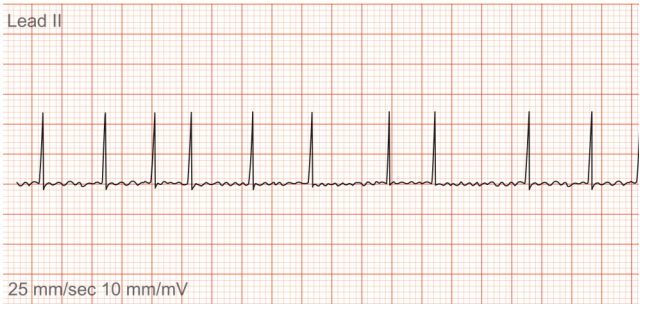
ABSTRACT

Atrial fibrillation (AF) is one of the most common dysrhythmias managed in the ED and accounts for more than half a million visits a year in the United States. More than 6 out of 10 of these visits result in admissions. As the prevalence of AF has continued to increase in recent years, so has the presentation of patients with AF to the ED. For these reasons, clinicians in emergency settings must be knowledgeable of evidence-based rate and rhythm control strategies for stabilizing patients and preventing complications. This article discusses options, indications, contraindications, and safe implementation of rate and rhythm control strategies for ED clinicians. Recent studies have suggested that early rhythm control may benefit newly diagnosed patients, reducing stroke risk, cardiovascular deaths, and disease progression.

Keywords: atrial fibrillation, ED, rate, rhythm, control, AF

Learning objectives

- Discuss rate control strategies for stabilization of patients with AF in the ED.
- Discuss rhythm control strategies for stabilization of patients with AF in the ED.
- Compare and contrast the potential benefits of rhythm and rate control strategies.



Atrial fibrillation (AF) is the most common dysrhythmia in the United States and globally.[1] As the global population ages, the prevalence of AF has doubled over the past 3 decades, reaching a prevalence of nearly 60 million cases, with 3 to 6 million of those patients living in the United States.[2,3] Over the past decade, incidence rates have increased 3% per year, with US cases predicted to reach 16 million in 2050.[3,4] In the United States, AF accounts for an estimated $8,705 additional healthcare cost per patient per year, resulting in a national incremental cost of about $26 billion annually.[5,6] AF's substantial cost, increasing prevalence, and increasing incidence present a growing global health burden with major public health implications.

AF is the most frequently encountered dysrhythmia in the ED, accounting for about 0.5% of visits, with an admission rate of 62% to 70%.[7-9] Prompt identification and intervention are required to minimize cardiovascular complications such as thrombosis and stroke. Patients with AF have a fivefold increased risk of stroke along with an increased risk of all-cause mortality (twofold in women and 1.5-fold in men).[6,10] Given the potential for complications, ED clinicians must be knowledgeable of evidence-based AF management strategies, because early diagnosis and intervention maximize positive patient outcomes.

Initial management of AF in the ED generally involves identifying AF as the primary problem; implementing rate or rhythm control strategies; and starting anticoagulation (if indicated) to prevent thromboembolism, slow disease progression, improve quality of life, and reduce AF-related symptoms.[11-13] Poorly controlled AF can progress to AF with a rapid ventricular response (RVR), which reduces myocardial blood flow as well as cardiac output; if sustained, RVR can cause myocardial damage.[9] Interventions are based on the patient's clinical presentation, medical history, and clinical pattern or duration of symptoms.[9,12] This article reviews rate and rhythm control strategies for

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Key points

- Beta-blockers are the most effective monotherapy for rate control in patients with AF, and reduce the risk of developing tachycardia-induced cardiomyopathy.
- The target heart rate for optimal rate control is 80 to 110 beats/minute.
- Rhythm control in a patient with new-onset AF can reduce stroke risk, cardiovascular death, and recurrence.
- Cardioversion may be beneficial in patients with new-onset AF if they have had symptoms for fewer than 48 hours, a CHA_2DS_2-VASc score less than 1, and no history of thromboembolism or left atrial appendage thrombus.

ED clinicians in conjunction with the recently updated American Heart Association Task Force, American College of Cardiology, Heart Rhythm Society, European Society of Cardiology, European Heart Rhythm Association, European Association for Cardio-Thoracic Surgery, Canadian Cardiovascular Society, and Canadian Heart Rhythm Society guidelines.[11-14]

RATE AND RHYTHM CONTROL STRATEGIES

Rate and rhythm control strategies are used to relieve symptoms, improve patient quality of life, and slow the progression of AF.[11-13] The choice of preferred intervention should be individualized to the patient, presentation, and clinical pattern of AF. Treatment regimens may change over time if symptoms change or previous interventions become ineffective.

AF's clinical patterns are categorized by duration and are used to tailor patient treatment.[9,11,12]

- *Paroxysmal AF* lasts fewer than 7 days.
- *Persistent AF* lasts more than 7 days.
- *Longstanding persistent AF* lasts more than 12 months.
- *Permanent AF* occurs when no treatment can return the patient to sinus rhythm.

RATE CONTROL STRATEGIES

Rate control generally is considered the first line in AF management to curtail the pathologic progression of AF and prevent development of tachycardia-induced cardiomyopathy (**Table 1**).[13] Suboptimal rate control can lead to AF with RVR, resulting in eventual poor hemodynamic consequences, disease progression, and poorer prognosis.[11,13] Although the optimal target heart rate for initial onset of AF is unclear, the general consensus is between 80 and 110 beats/minute.[11-14] In the RACE and Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trials, no clinical difference was found between a strict target heart rate of less than 80 beats/minute and a lenient heart rate of 110 beats/minute.[11-13,15-18]

Beta-adrenergic receptor blockers, non-dihydropyridine calcium channel blockers, and (to a limited extent) digitalis glycosides such as digoxin are used to achieve rate control by slowing conduction across the atrioventricular (AV) node.[12] Amiodarone has dual rate and rhythm control properties and can be useful as an alternative to beta-blockers or non-dihydropyridine calcium channel blockers in select patients.[12] These AV nodal blocking agents are contraindicated in patients with concurrent preexcitation pathologies such as Wolff-Parkinson-White syndrome or Lown-Ganong-Levine syndrome, because they can precipitate ventricular fibrillation; cardioversion is indicated for patients in AF who have RVR and preexcitation.[9,11-13,19] Choice of rate control agent is determined by patient comorbidities and clinical circumstances.[11-14]

Oral or IV medications can be used in rate control strategies.[12] Oral administration is appropriate unless urgent rate or rhythm control is required.[12-14] Should IV routes be used as the initial therapy, coadministration of oral rate control agents is recommended to avoid rebound tachycardia.[12] Use caution if coadministration of a beta-blocker or non-dihydropyridine calcium channel blocker with digoxin or amiodarone is necessary—these drugs have synergistic negative chronotropic and inotropic properties,

TABLE 1. Common rate control strategies[11-14]

Guidelines for rate control dosing calculations, indications, contraindications, and considerations must be rechecked and drugs administered in conjunction with appropriate clinical judgment.

Class	Drug	Route	Half-life	Considerations
Beta-blockers	Metoprolol	Oral, IV	3-7 hours	• Cautioned: decompensated heart failure, hypotension, asthma, chronic obstructive pulmonary disease with history of severe bronchospasm • May induce hypotension, bronchospasms
	Esmolol	IV	9 minutes	
Non-dihydropyridine calcium channel blockers	Diltiazem	Oral, IV	3-9 hours	• Cautioned: decompensated heart failure, hypotension, left ventricular dysfunction • May induce hypotension, dysrhythmias in preexcitation etiologies
Digitalis glycosides	Digoxin	Oral, IV	1.5-2 days	• Consider obtaining renal function prior to starting for renally adjusted dosing • May induce bradycardia, AV blocks, ventricular arrhythmias

and concomitant use may increase the risk of hypotension, bradycardia, or heart block.[11,13,20-22]

Beta-blockers As the most effective monotherapy for rate control, beta-1 selective blockers, such as metoprolol, are considered first-line agents in the acute setting and are the most commonly used class of medication for rate control.[9,13] By blocking sympathetic tone, beta-blockers achieve rate control, improve left ventricular (LV) function in patients with chronic heart failure, and reduce myocardial oxygen demand in patients with concurrent acute coronary syndrome (ACS) and AF.[12-14] Beta-blocker use can reduce the rate of hospitalizations and lead to more favorable long-term outcomes in patients with concurrent chronic heart failure, LV dysfunction, or concurrent ACS.[11-14,23,24] Nonselective beta-blockers, such as propranolol, labetalol, and carvedilol, should be used with caution in patients with chronic lung diseases because of the potential risk for bronchospasm.[14,25] Beta-blockers and non-dihydropyridine calcium channel blockers should not be used in patients with signs of acute heart failure, hemodynamic instability, or hypotension, because their negative chronotropic and inotropic effects can cause excess bradycardia.[9,12-14]

Non-dihydropyridine calcium channel blockers Rate control also can be achieved with non-dihydropyridine calcium channel blockers such as diltiazem or verapamil, which act directly on the AV node's L-type calcium channels.[11,13] In a multicenter study of 1,639 patients, non-dihydropyridine calcium channel blockers were used more often for acute rate control in the ED, although beta-blockers were more successful: Beta-blockers successfully achieved rate control 70.9% of the time, compared with 66.1% for non-dihydropyridine calcium channel blockers.[23] Although slightly less effective than beta-blockers, non-dihydropyridine calcium channel blockers demonstrate comparable outcomes in achieving rate control in acute settings, with no significant difference in complications or worsening of chronic heart failure.[11-13] Unlike beta-blockers, non-dihydropyridine calcium channel blockers may be used in patients with chronic lung disease because they do not carry the same risks for bronchospasm. Otherwise, non-dihydropyridine calcium channel blockers carry similar safety concerns as beta-blockers and should be used cautiously in patients with LV systolic dysfunction or decompensated heart failure.

Digitalis glycosides Although not an optimal first-line agent for rapid rate control, digoxin may be beneficial in patients with AF and RVR that is refractory to beta-blockers and non-dihydropyridine calcium channel blockers, or in patients with ongoing hypotension, LV dysfunction, or decompensated heart failure.[11-14] The positive inotropic properties of digoxin are most effective in patients with hypotension or those with known LV dysfunction or decompensated heart failure.[12-14] However, appropriate titration and close monitoring are important because digoxin is associated with a 17% increase in all-cause mortality in general and a 23% increase in all-cause mortality in patients with AF specifically.[26] Monitoring is particularly important in patients with reduced renal function because of the pharmacokinetic and pharmacodynamic properties of digoxin: the drug has a long half-life (36 hours), a narrow therapeutic window, and relies on the kidneys for excretion, putting patients with reduced renal function at a higher risk of developing increased serum levels of digoxin and toxicity that is associated with higher risk of mortality.[12,26] Abnormal levels of serum potassium may affect digoxin's interaction with cardiac cells, even at therapeutic levels, increasing the risk for AV blocks and ventricular dysrhythmias.[11-14,26]

Amiodarone Although not a first-line agent, amiodarone may be considered in patients with AF refractory to beta-blocker and non-dihydropyridine calcium channel blocker therapy; however, it must be used with caution in patients at risk for hypotension because IV formulations may have negative inotropic effects.[11-14] In patients with moderate to severe AF, digoxin is preferred.[11-14]

The dual rate and rhythm control properties of amiodarone make it the most effective antiarrhythmic drug for maintenance therapy in patients with paroxysmal or persistent AF, and a useful alternative to facilitate a delayed conversion to sinus rhythm in select patients who qualify for acute rhythm control.[11-14] Amiodarone is not a first-line agent because of its risk for bradycardia, QT prolongation, photosensitivity, and extracardiac toxicities such as thyroid dysfunction, hepatic injury, pulmonary fibrosis, neurotoxicity, and optic neuropathy.[11-13]

RHYTHM CONTROL STRATEGIES

Pharmacologic and electrical cardioversion can be used in the ED to achieve rhythm control (**Table 2**).[11-13] The primary indication for elective rhythm control is to reduce symptoms, improve quality of life, reduce recurrence, and slow AF progression.[27] Patients on rhythm control strategies have significantly lower rates of AF progression than those only on rate control.[11,12] Unstable patients or those with medication-refractory tachycardia, new-onset AF (less than 48 hours of persistent symptoms), younger patients, those with tachycardia-mediated cardiomyopathy, or those with AF precipitated by an acute illness also may benefit from rhythm control.[11-13,28]

Cardioversion in stable patients Rhythm control can be achieved pharmacologically or electrically and requires cardiac monitoring during cardioversion attempts.[11,12] Electrical cardioversion is achieved through synchronized direct current and is considered safer and more effective at achieving return to sinus rhythm. In the Electrical versus Pharmacological Cardioversion for Emergency Department Patients with Acute Atrial Fibrillation (RAFF2) trial, cardioversion of AF to sinus rhythm was achieved in 92% of patients with electrical cardioversion, compared with 52% via pharmacologic cardioversion.[29] Although more effec-

TABLE 2. Drugs for pharmaceutical cardioversion[11-14]

Guidelines for antiarrhythmic dosing calculations, indications, contraindications, and considerations must be rechecked and drugs administered in conjunction with appropriate clinical judgment.

Class	Drug	Route	Half-life	Considerations
Ic	Flecainide	Oral, IV	20 hours	• Contraindications: atrial flutter cardioversion, ischemic heart disease, significant structural heart disease • May induce hypotension, atrial flutter, QRS complex widening
Ic	Propafenone	Oral, IV	2-10 hours	
Ia	Procainamide	IV	3-4 hours	• Contraindications: hypotension, Brugada syndrome, AV blocks, prolonged QT • May induce premature ventricular contractions, ventricular tachycardia, QRS widening, hypotension
III	Amiodarone	IV	58 days	• May induce hypotension, bradycardia, AV block, QT prolongation, phlebitis
III	Ibutilide	IV	6 hours	• Contraindications: prolonged QT, LV hypertrophy, low LV ejection fraction • May induce QT prolongation, polymorphic ventricular tachycardia

tive, electrical cardioversion requires procedural sedation. Pharmacologic cardioversion does not require procedural sedation, and may be a beneficial alternative.[11,12] Indications for anticoagulation before pharmaceutical or electrical cardioversion depend on the patient's thromboembolic risk as measured with evidence-based tools such as the CHA_2DS_2-VASc score, symptom onset timing, and shared medical decision-making with the patient.[11-14] Anticoagulation is required during but not before cardioversion in patients who have had symptoms for fewer than 48 hours, a CHA_2DS_2-VASc score less than 1, and no history of thromboembolism or evidence of left atrial thrombus.[9,11,13,30] Elective cardioversion within 48 hours of symptom onset is effective and safe with a 0.7% risk of thrombotic complications overall and 1.1% risk within 12 to 48 hours of symptom onset.[31] The risk of thromboembolic complications is further reduced to 0.3% or less if cardioversion is performed within the first 12 hours.[11,12,14,31] Patients who do not meet this criterion or have unknown onset of AF symptoms require anticoagulation for 3 to 4 weeks before elective cardioversion, to reduce stroke risk to 0.3% to 0.8%.[11-13,30] Elective cardioversion is less effective at preventing AF recurrence in patients with structural heart disease, enlarged left atrium, heart failure, or older age.[11]

Following cardioversion, patients will continue with rhythm or rate control therapy and discuss short-term 4-week anticoagulation postcardioversion if their CHA_2DS_2-VASc score is less than 1 (**Table 3**).[11-14] Additional or long-term anticoagulation is based on weighing thromboembolic risk against anticoagulation-related bleeding, resulting in an individual approach for all patients.[13,14,30]

Cardioversion in unstable patients Cardioversion is indicated in hemodynamically unstable patients who are in shock or have severe hypotension, pulmonary edema, ongoing myocardial infarction, ischemia, decompensated heart failure, or AF with preexcitation.[11-14] Should cardioversion be pursued, electrical cardioversion is preferred because it is 90% effective at immediately restoring sinus rhythm, compared with a 60% efficacy for pharmacologic cardioversion.[9,11,13] Before cardioversion, patients should have periprocedural anticoagulation with heparin, low-molecular-weight heparin, or a direct oral anticoagulant (DOAC).[12,13] The need for long-term anticoagulation postcardioversion is determined by balancing each patient's stroke risk profile against bleeding risk.[11,13,14,30]

In critically ill patients with AF, clinicians must keep in mind that concomitant pathologies often contribute to patients' hemodynamic status. In a recent single-arm study of 66 electrical cardioversions performed on hemodynamically unstable patients, 51% relapsed into AF 6 hours later.[32] Furthermore, 50% of patients were considered still hemodynamically unstable despite cardioversion, suggesting additional contributing factors that must be considered during patient management.[32]

ANTICOAGULATION

Indications for long-term anticoagulation are based on an individualized approach using evidence-based tools such as the CHA_2DS_2-VASc and HAS-BLED scores, which predict patient risk for thromboembolic stroke and bleeding, respectively (**Table 4**).[13,14] Anticoagulation is recommended

TABLE 3. CHA_2DS_2-VASc score[11,13,14]

Men with a score of 2 or greater and women with a score of 3 or greater should have anticoagulation for stroke prevention. Calculations must be rechecked and should not be used alone to guide patient care, nor should they substitute for clinical judgment.

Criteria		No	Yes
C	Heart failure	0	+1
H	Hypertension	0	+1
A_2	Age 75 years or older	0	+2
D	Diabetes	0	+1
S_2	History of stroke, transient ischemic attack, or thromboembolism	0	+2
V	History of vascular disease	0	+1
A	Age 65 to 74 years	0	+1
Sc	Sex categories	Male 0	Female +1

TABLE 4. HAS-BLED score[13,14]

Patients with a score of 3 or greater are considered high-risk and may require stricter INR monitoring or adjustment in anticoagulation dosing. Calculations must be rechecked and should not be used alone to guide patient care, nor should they substitute for clinical judgment.

Criteria		Description	No	Yes
H	Hypertension	Uncontrolled or greater than 160 mm Hg systolic	0	+1
A	Abnormal renal function	Dialysis, transplant, creatinine greater than 2.26 mg/dL	0	+1
	Abnormal liver function	Cirrhosis; aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, or bilirubin greater than 2x normal	0	+1
S	Stroke history		0	+1
B	Bleeding history	Predisposition to bleeding or previous major bleeding	0	+1
L	Labile INR	Unstable or high INR; less than 60% of the time in therapeutic range	0	+1
E	Elderly	Age over 65 years	0	+1
D	Drugs	Aspirin, clopidogrel, NSAID, or alcohol use	0	+1

for men with a CHA_2DS_2-VASc score of 2 or greater and for women with a score of 3 or greater.[13,14] DOACs, such as direct factor Xa and direct thrombin inhibitors, have overtaken warfarin as the mainstay for stroke prevention.[13,14] Although DOACs are powerful tools in stroke prevention, they carry a risk for bleeding, particularly gastrointestinal bleeding, in older adults, and are contraindicated in patients with mechanical heart valves and moderate-to-severe mitral stenosis.[14,33-35]

Patients with a HAS-BLED score of 3 or greater are considered high-risk and may require stricter international normalized ratio monitoring or anticoagulant dosing adjustment.[13,14,30] Other methods of long-term stroke prevention, such as left atrial appendage occlusion devices, may be indicated as alternatives for patients who cannot tolerate long-term anticoagulation.[14,36]

CONCLUSION

Rate and rhythm control strategies are powerful tools for stabilizing and managing patients with AF in the ED. Rate control still serves as the primary means of acute management of AF in the ED, particularly in patients with established AF, because it is associated with fewer hospitalizations than rhythm control strategies.[11-13] In patients with established AF, rhythm control strategies showed no significant difference in cardiovascular outcomes or mortality.[12,13] Rhythm control is useful in patients with AF refractory to rate control, patients who are hemodynamically unstable because of AF, and patients with reversible new-onset AF.[11-13] In patients with AF diagnosed within the past year, recent data have shown that rhythm control strategies reduced stroke risk, cardiovascular deaths, and AF progression.[11-13] In the recent multicenter Hospital EmeRgency department Management Strategies of Atrial Fibrillation (HERMES-AF) study carried out in 124 EDs, rhythm control strategies in patients with recent-onset AF (less than 48 hours) resulted in a higher rate of symptom alleviation and reduced rate of hospital admissions than rate control strategies.[27] These results highlight the value of further randomized studies evaluating rate and rhythm control strategies to reduce hospitalization and adverse clinical events and improve patient outcomes.

A multidisciplinary team is essential to quality patient care, particularly in complex cases. ED clinicians should consider involving their cardiology team for recommendations for inpatients whose AF is refractory to rate and rhythm control or to ensure continuity of care in the outpatient setting.[11] Patients who received follow-up within 7 days had a 0.5% reduction in all-cause mortality by 1 year and 0.8% lower risk of cardiovascular hospitalization within 1 year compared with patients who had follow-up in 8 to 30 days.[37] Additional guidance in AF management as well as other strategies, such as catheter ablation, may be required based on the patient's response to initial therapies. Such a decision would be made between the patient and a multidisciplinary team to reduce the burden of AF.[11]

Optimal patient care must be patient-focused. Consider the patient's wishes when deciding whether to start rate or rhythm control strategies, and individualize care based on the patient's duration of symptoms, comorbidities, plan for outpatient follow-up, and clinical circumstances. An integrated, patient-focused, team-based approach to AF management has been associated with reductions in adverse clinical outcomes, hospitalization, and mortality and with improved quality of life and treatment adherence.[12]

The chief predictor of treatment adherence in patients with cardiovascular disease is the patient-clinician relationship.[38] Many patients are diagnosed with AF in the ED. This offers a vital opportunity to not only address the patient's acute concerns but prepare them for the next steps in the management of their chronic condition. Clinicians must make every effort to involve patients in their care by communicating the treatment options, risks, and benefits; encouraging engagement; and promoting disease awareness to improve adherence to long-term therapy and reduce repeated ED visits.[12,37] **JAAPA**

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