

Atrial fibrillation with high ventricular rate in emergency room: What's the best strategy for treatment?

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SUMMARY

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice and can lead to significant decline in functional status and quality of life among affected patients. The risk of developing AF increases with age and the presence of structural heart disease. Thus, the attendance of patients with high ventricular response to AF is common, which makes knowledge of its management mandatory. In this context, the choice of heart rate and/or rhythm control therapy is fundamental and complex, with multiple possibilities. Thus, this review aims to assist in the management of these patients, systematizing their care.

Keywords: atrial fibrillation, emergency, arrhythmia.

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice and is characterized by the absence of P waves and irregular interval between QRS complexes on the electrocardiogram (ECG).¹⁻³

AF can lead to a significant reduction in the functional status and quality of life of the affected patients. It increases mortality between 1.5 and 1.9 times on the account of hemodynamic deterioration caused by increased heart rate (HR), loss of atrioventricular (AV) synchrony and progressive dysfunction of the left atrium and ventricle, in addition to increasing the risk of stroke and other embolic events triggered by atrial thrombi.¹⁻⁵

The risk of developing AF increases with age and with the presence of structural heart disease. Prevalence increases from 0.1% in adults less than 55 years to 8% in those aged 80 years or older. It is higher among men compared with women (1.1% x 0.8%); and among white compared with black individuals (2.2% x 1.5%).^{2,4,5}

Arterial hypertension (SAH) and coronary artery disease (CAD) (post acute myocardial infarction or ischemic cardiomyopathy) are the most common comorbidities present in patients with AF in developed countries. Rheumatic heart disease, although currently uncommon in developed countries, has a much greater association with AF. AF is an infrequent form of manifestation of acute

myocardial infarction or ischemia in the absence of other signs and symptoms of CAD.¹⁻⁵

AF and heart failure (HF) often occur together, and a cause and effect relationship between the two is common. In addition, AF is associated with pulmonary disorders including chronic obstructive pulmonary disease (COPD) and pulmonary embolism. Similarly, both the clinical and subclinical forms of hyperthyroidism are associated with an increased risk of AF. Other risk factors related to AF include chronic renal failure, genetic factors, autonomic dysfunction, hypomagnesemia, alcohol consumption, and drugs such as theophylline, adenosine and digitalis.¹⁻⁵

The classification proposed by the ACC/AHA/ESC for AF divides it into five subtypes:¹⁻³

- First detected or diagnosed episode independent of its duration and presence of any symptoms.
- Paroxysmal: recurrent (more than two episodes) that terminate spontaneously lasting up to 7 days (usually ceases within 24 hours).
- Persistent: Episodes lasting longer than 7 days that require pharmacological or electrical cardioversion to return to sinus rhythm.
- Long-lasting persistent: the same as persistent AF, but lasting for one year or longer.

- Permanent: when it is not possible to maintain sinus rhythm after cardioversion, or when it has been decided not to attempt cardioversion for several factors (e.g. elderly, asymptomatic, AF with low or normal ventricular response and large left atrium).

Thus, the presence of a patient with high ventricular response AF is frequent, and makes the knowledge of its management compulsory. In this context, the choice of heart rate and/or rhythm control therapy is fundamental and complex, with multiple possibilities. This review therefore aims at assisting in the approach of these patients, systematizing their care.

CLINICAL PICTURE

Not all patients with AF are symptomatic and among those who are, there is a wide variety of symptoms. Information such as onset of symptoms, timing of diagnosis, frequency and duration of episodes and severity of symptoms is very important for the therapeutic decision. Episodes can be precipitated by exercise, emotions or acute intake of large amounts of alcohol. In other cases, they may be precipitated during sleep or after a meal.¹⁻⁵

The typical symptoms associated with AF are palpitations, tachycardia, fatigue, weakness, dizziness, reduced exercise capacity, increased urinary volume, dyspnea.¹⁻³ Follow-up studies of patients with AF have shown that approximately 90% of these individuals have recurrent episodes of AF, although more than 90% of the events are not recognized by them. Nevertheless, asymptomatic episodes lasting more than 48 hours are not uncommon, occurring in 17% of patients.^{4,5}

More severe symptoms include restless dyspnea, angina, pre-syncope, syncope (infrequent). Some patients may also have thromboembolic events and/or stroke as their first presentation.^{4,5}

FIVE STEPS FOR THE SYSTEMATIC APPROACH OF AF IN THE EMERGENCY ROOM

1) Recognize/ward off clinical instability related to AF

It is not always easy to recognize whether AF is the main cause of clinical instability presented by the patient. Anamnesis and physical examination should be performed in all patients with AF, seeking signs of hemodynamic instability (hypotension, significant pulmonary congestion, history of syncope, mental confusion, angina/chest pain), adequate use of medications, signs/symptoms of infection, time of onset of symptoms, presence of structural heart changes (systolic HF and/or left ventricular hypertrophy) and coronary artery disease.¹⁻³

Those presenting signs of hemodynamic instability at baseline (hypotension, significant pulmonary congestion, history of syncope, mental confusion, angina/chest pain – these being attributable to arrhythmia [usually in HR greater than 150 to 160 beats per minute]) should be taken to the emergency room for peripheral venous access, continuous monitoring and oxygen therapy, and promptly submitted to synchronized electrical cardioversion with 100 to 200 J, regardless of the time of onset. A bolus dose of 10,000 units of unfractionated heparin is recommended prior to this emergency cardioversion. In such cases, after the reversal, associated diseases such as CAD, valvopathy and ventricular dysfunction should always be investigated. The same is true for patients with AF and pre-excitation with elevated HR or hemodynamic instability.¹⁻³

2) Remove secondary causes that induce high ventricular response

The main cause for high ventricular response AF should always be evaluated, especially in those patients with refractory HR control or who already have permanent/persistent AF and presented recent lack of HR control even while correctly using the medications. When drug adherence is appropriate, drug or alcohol use, hyperthyroidism, anemia, hydroelectrolytic disorders (especially hypo or hyperkalemia and hypomagnesemia), infections and pulmonary thromboembolism should always be considered. In these cases, all patients should perform a chest x-ray and, in women, even if asymptomatic, the collection of type I urine and uroculture must be performed.¹⁻³

A recently published retrospective study evaluated the management of patients with high ventricular response AF in the ER, either according to the rhythm control or reversal strategy or not, when the patient arrives at the site. In about 30% of patients, the cause of high ventricular response AF was sepsis. The rate of adverse events among patients undergoing control/reversal strategies *versus* uncontrolled strategy was 40.7% x 7.1%, and only about 20% of patients achieved adequate control with therapy when a secondary cause was present. This reinforces the idea of investigating the secondary cause before adopting complementary measures in the initial approach, unless the patient presents with hemodynamic instability.⁶

3) Obtain proper control of HR

There are two main strategies for managing the symptoms of patients with AF: control of HR using AV node blockers, or rhythm control (reversion to sinus rhythm followed by maintenance), either with antiarrhythmic drugs or by catheter ablation.¹⁻³

The results of two large multicentric studies, AFFIRM and RACE, demonstrated that both rhythm control and ventricular rate control strategies are associated with similar rates of mortality and severe comorbidities. Generally, the choice of one or another strategy takes into account factors such as the age of the patient and the presence of symptoms associated with AF with an impact on the quality of life, and reduction of the left ventricular systolic function attributed to the presence of the arrhythmia.^{7,8}

Thus, theoretically, the initial and main objective adopted in the care of patients in the emergency room who do not present clinical instability related to AF is HR control, especially in those with more than 48 hours of symptoms, multiple comorbidities or heart disease (left ventricular dysfunction, left ventricular hypertrophy and left atrium > 50 mm).¹⁻³ When controlling HR, unrestricted control maintenance (HR < 110 bpm) proved to be similar to the restricted control (HR < 80 bpm), and the most flexible measure was also adopted in the emergency sector approach.⁷ Exception is made for patients with left ventricular dysfunction, symptomatic mitral stenosis or coronary stenosis, in whom HR control should be more rigorous due to underlying heart disease.¹⁻³

A heart rate control strategy generally requires drugs that reduce AV node conduction, such as B-blockers, non-dihydropyridine calcium channel blockers or digoxin, either alone or in combination (Table 1).¹⁻³

B-blockers and/or calcium channel blockers (diltiazem and verapamil) are generally the drugs of choice for initiation of therapy. It has been proven that drugs such as diltiazem, esmolol, metoprolol and verapamil are superior in the control of HR compared to digitalis and amiodarone.⁹⁻¹³ In patients without ventricular dysfunction we may use intravenous metoprolol (maximum dose of 15 mg), diltiazem 0.25 mg intravenously (repeat 0.35 mg/kg if necessary), or verapamil 5 to 10 mg intravenously.⁹⁻¹³

Digoxin may also be used, but it is not as effective in controlling HR during physical activity.^{1-3,14} In patients with ventricular dysfunction, the use of C-lanatoside, 0.4

mg intravenously (maximum dose of 0.8 mg), or amiodarone, 150 mg intravenously in 10 minutes, is considered as the first option.¹⁻³ The fact that amiodarone can lead to the reversal of the rhythm in up to 28% of the patients, predisposing them to the occurrence of embolic events, is highlighted.¹⁵

In patients with hemodynamic shock and AF, heart rate control should be done only when HR exceeds 130 to 150 beats per minute and preferably amiodarone via continuous infusion pump (450 to 1,200 mg daily) depending on the chronotropic response of the patient. In these cases, the HR target is usually around 120 beats per minute, without damaging the compensatory response to shock, and its indication should be reviewed daily and individually.¹⁻³

4) Consider heart rate control/AF reversal

Although HR control is the main target in the treatment of high ventricular response AF in the emergency room, there are some situations in which the rhythm control strategy should be considered: if the symptoms have clearly started less than 48 hours; persistent symptoms despite adequate HR control; inability to achieve adequate HR control (ruling out secondary causes); young patients with a first episode of AF diagnosed or those in whom arrhythmia had a recent onset and the risk of recurrence appears to be lower; and, in the latter case, according to the patient's preference.¹⁻³

If cardioversion is chosen, it may be chemical (using antiarrhythmic drugs) or electric (Figure 1). In such cases, the patient's HR should be kept preferably high, since after the reversal the risk of sinus bradycardia associated with clinical instability becomes lower.¹⁻³

For chemical reversal, the recommended medications are: flecainide, dofetilide, ibutilide, propafenone and amiodarone. The first three are not available in Brazil. Before administering antiarrhythmic medication for cardioversion, a B-blocker or a calcium channel blocker should be given to prevent rapid AV conduction.¹⁻³

TABLE 1 Main drugs used to control HR in patients with high ventricular response AF.

Medication	Dose	Contraindication
Metoprolol	5 mg IV in 5 min. (max. 15 mg)	BCS, low blood pressure, heart failure
Diltiazem	0.25 mg/kg IV / Can be repeated at a dose of 0.35 mg/kg	Heart failure, low blood pressure
Verapamil	5 to 10 mg IV	Heart failure, low blood pressure
C-lanatoside	0.4 mg IV (max. 0.8 mg)	
Amiodarone	150 mg IV in 10 min. (max. 2.2 g in 24 h)	

IV: intravenous; BCS: bronchospasm.

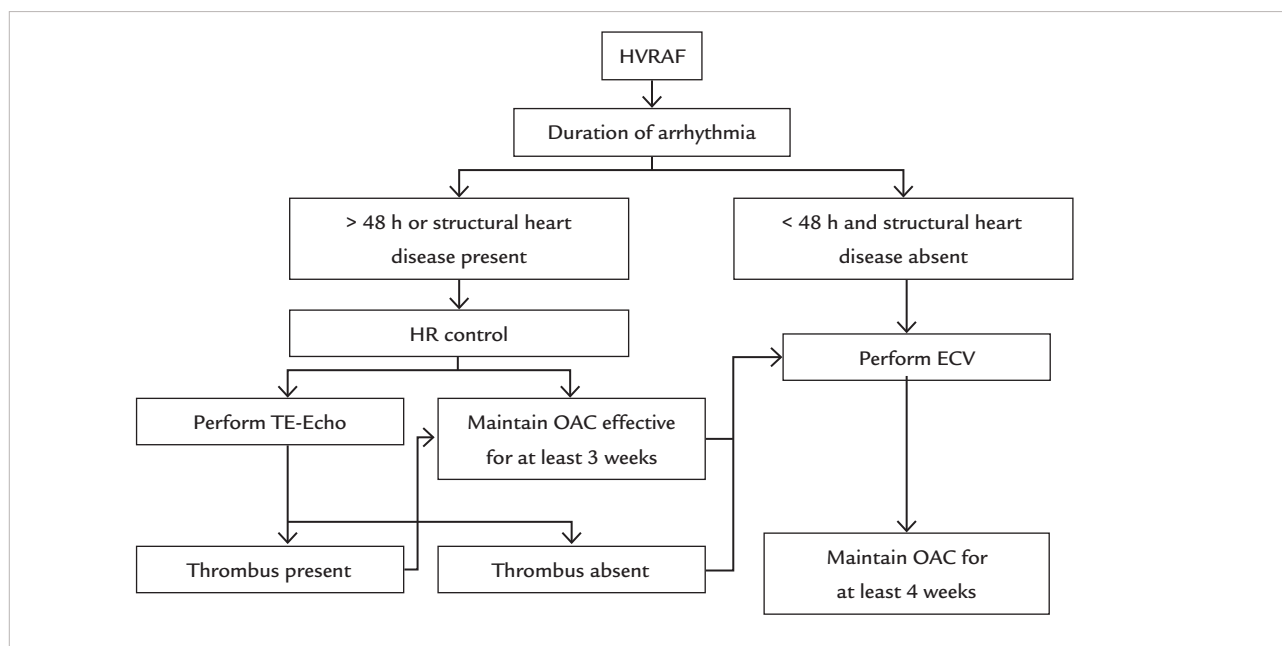


FIGURE 1 Algorithm for evaluation of patients with high ventricular AF for ECV. HVRAF: high ventricular response AF; HR: heart rate; TE-Echo: transesophageal echocardiography; OAC: oral anticoagulation; ECV: synchronized electrical cardioversion.

In patients without structural heart disease, the option of choice is propafenone. In the first event, it should be administered in hospital orally at a dose of 450 mg (if the patient's weight is less than 70 kg) or 600 mg (weight 70 kg or more). If the treatment is well tolerated and effective, the patient can be discharged with the guidance of home use at the same dose, if there is recurrence, in a strategy called *pill in the pocket*. In these cases, the probability of AF reversion in up to 6 hours is around 94% of cases. This strategy should be done only in cases of AF with few recurrences (up to 2 every 6 months).¹⁻³

In patients with structural heart disease [left ventricular hypertrophy (septum and posterior wall thickness > 1.2 cm), ischemia, valvular disease and/or ventricular dysfunction], amiodarone is the best option for chemical cardioversion. Amiodarone should be given at a dose of 150 mg intravenously in 10 minutes, or 5-7 mg/kg in 1 hour (up to a maximum dose of 2.2 g in 24 hours). Amiodarone is associated with higher rates of maintenance of sinus rhythm, but is also associated with a greater number of adverse effects in the long term.¹⁻³

Sotalol may be beneficial in patients with paroxysmal AF also in sinus rhythm, provided that the patient has minimal structural disease or normal heart, and QTc < 460 ms. It is the antiarrhythmic drug of choice in patients with AF and CAD who do not have left ventricular systolic dysfunction. In this situation, propafenone is contraindicated.¹⁻³

If electric cardioversion is chosen, it should be done with the administration of shock initially synchronized at 100 to 200 J in a single-phase defibrillator or 100 J in a biphasic defibrillator, after explaining the procedure and adequate sedation to the patient. Administration of amiodarone prior to electrical cardioversion increases the chance of success and may prevent immediate recurrence of AF.¹⁻³

Finally, radiofrequency ablation (RFA) is also useful in maintaining sinus rhythm mainly in symptomatic patients with paroxysmal AF who have failed an antiarrhythmic, have normal or slightly increased left atrium, and normal or discreetly decreased function of the left ventricle. However, its use should be considered an exception when it comes to patients seen in emergency units.¹⁻³

If there is structural heart disease, after the reversal, the patient should be discharged with amiodarone prescribed at a dose of 200 mg orally, three times a day for 2 weeks, followed by 200 mg twice daily for another 2 weeks. Thereafter, amiodarone at 200 mg daily. In the absence of evidence of structural heart disease, amiodarone should preferably be replaced with propafenone, 150 to 300 mg every 12 hours.¹⁻³

In all cases with more than 48 hours of AF or in those with structural heart disease, if reversion is chosen, it is mandatory that the patient be anti-coagulated for at least 3 weeks.¹⁻³ In the case of warfarin, the weekly INR control should show values between 2.0 and 3.0. Currently one

option is to use one of the new anticoagulants. In a prospective study, rivaroxaban was validated and showed the same level of safety of warfarin related to electrical cardioversion (ECV).¹⁶ Apixaban and dabigatran, on the other hand, also showed the same safety profile of warfarin in subanalyses.^{17,18} Thus, the guidelines release their use when choosing to reverse the patient's rhythm. After reversion, any of the anticoagulants used should be maintained for a minimum period of 4 weeks, and may be extended indefinitely if the patient presents risk factors for AF recurrence (ventricular dysfunction and/or structural heart disease, atrial dilatation, previous episodes, etc).¹⁻³

In those without oral anticoagulant use for at least three continuous weeks, transesophageal echocardiography must be performed. In the absence of thrombi, the patient may be cardioverted with synchronized electrical therapy or chemical therapy.¹⁻³

If a thrombus is seen, only HR control should be performed and the patient is discharged with oral anticoagulation prescription to schedule the procedure after at least 3 weeks at an outpatient clinic.¹⁻³

5) Define the indication for oral anticoagulation

All patients with AF should be evaluated for the need for anticoagulation and this is done by applying the CHADS2 and/or CHA2DS2VASC scores. The latter is a refinement of the former and has been the most used in recent years because it identifies patients with actual "low risk" more accurately. For the evaluation of bleeding risk, the most commonly used criterion is HAS-BLED, which serves as a guideline for the rational and cautious choice of anticoagulation. However, it should not contraindicate it.^{1-3,19}

There are two indications of anticoagulation in AF. In the short term, in patients with low thromboembolic risk in which the strategy of rhythm control is chosen and cardioversion is performed to the sinus rhythm, and in the long term, patients that meet criteria for chronic anticoagulation.¹⁻³

Antithrombotic therapy to prevent thromboembolism should be indicated for all patients with AF, except for those with isolated AF without other risk factors, and those with a contraindication to it. Anticoagulation is recommended for patients at high risk of thromboembolic event (two or more risk factors considering the CHA2DS2VASC score). If the CHA2DS2VASC criterion only scores for the female sex, chronic oral anticoagulation is not mandatory.¹⁻³

The selection of the anticoagulant agent should be based on the absolute risk of stroke and bleeding and the risk/benefit ratio to the patient. In patients with significant

heart valve disease, mechanical valvular prostheses and/or chronic renal insufficiency (CrCl < 30 mL/min), the option is warfarin. The target INR is 2.0 to 3.0, except for mitral and aortic mechanical prostheses, in which case the target varies between 2.5 and 3.5.¹⁻³

In the remaining patients, warfarin or any of the new anticoagulants (apixaban, rivaroxaban or dabigatran) may be used.^{1-3,20-22}

The association of ASA and clopidogrel to reduce the risk of thromboembolic events may be considered for patients with AF in case of possible inadequate anticoagulation with warfarin, either at the choice of the patient or when the attending physician is not sure of the safety for the patient. In this case, the level of evidence is lower and comes from simple non-multicentre studies.²

When the patient with AF remains hospitalized for another reason, the use of warfarin should be routinely withdrawn at least in the initial phase. Although there is limited evidence in hospitalized patients, when INR is below 2.0, anticoagulation should be initiated with subcutaneous enoxaparin, 1 mg/kg every 12 hours, or unfractionated heparin via continuous infusion.²

CONCLUSION

Management of patients with high ventricular response AF in the emergency room is complex. Identifying factors that cause AF is critical to correct treatment. When possible, heart rate control is the priority. At the time of hospital discharge, the patient should be evaluated for indication and possibility of oral anticoagulation. In a simplified manner, the algorithm for conduct is shown in Figure 2.

RESUMO

Fibrilação atrial de alta resposta ventricular na sala de emergência: qual é a melhor estratégia de tratamento?

A fibrilação atrial (AF) é a arritmia mais comum da prática clínica e pode levar à redução significativa do estado funcional e da qualidade de vida dos pacientes acometidos. O risco de desenvolvimento de AF aumenta com a idade e com a presença de doença cardíaca estrutural. Dessa forma, o comparecimento de paciente com AF de alta resposta ventricular é frequente, o que torna o conhecimento de seu manejo obrigatório. Nesse âmbito, a escolha da terapia de controle de frequência cardíaca e/ou ritmo é fundamental e complexa, com múltiplas possibilidades. Esta revisão tem o objetivo de auxiliar a abordagem desses pacientes, sistematizando o atendimento.

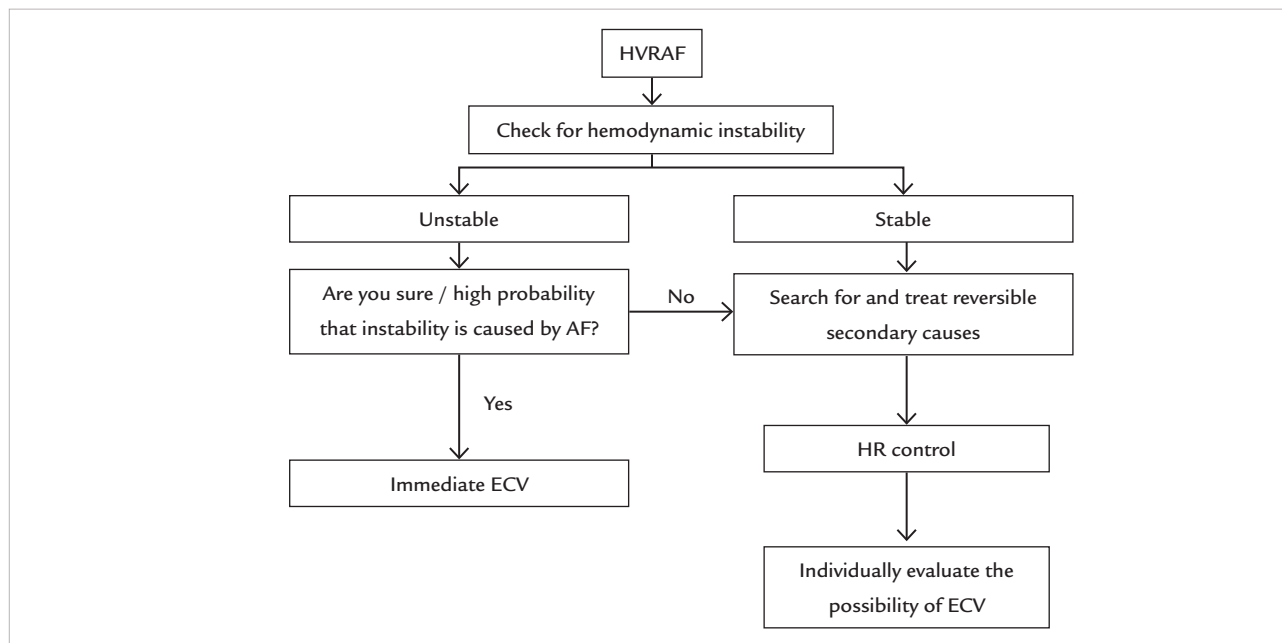


FIGURE 2 General algorithm for approaching patients with high ventricular response AF in the emergency unit. HVRAF: high ventricular response atrial fibrillation; ECV: synchronized electrical cardioversion; HR: heart rate.

Palavras-chave: fibrilação atrial, emergência, arritmia.

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