

## Consensus Document for the Management of Patients with Atrial Fibrillation in Hospital Emergency Departments

Alfonso Martín,<sup>a</sup> José L. Merino,<sup>b</sup> Carmen del Arco,<sup>a</sup> Jesús Martínez Alday,<sup>b</sup> Pedro Laguna,<sup>a</sup> Fernando Arribas,<sup>b</sup> Pedro Gargantilla,<sup>a</sup> Luis Tercedor,<sup>b</sup> Juan Hinojosa,<sup>b</sup> and Lluís Mont<sup>b</sup>

<sup>a</sup>Consensus Panel of the Arrhythmia Group, Sociedad Española de Medicina de Urgencias y Emergencias (SEMES) (Spanish Society for Emergency Medicine), and the <sup>b</sup>Electrophysiology and Arrhythmia Section of the Sociedad Española de Cardiología (SEC) (Spanish Society of Cardiology).

Atrial fibrillation (AF) is the most prevalent arrhythmia in hospital emergency departments and is a serious disease associated with a twofold increase in morbidity and a high mortality rate. However, the management of AF in this scenario is variable and frequently inadequate. This is probably a consequence of the diverse clinical aspects and therapeutic options to consider in the management of patients with AF. Therefore, implementation of specific, coordinated management strategies by the different care providers involved is needed to improve the quality of care and optimize the use of human and material resources.

This document presents the guidelines recommended by the Spanish Society of Cardiology (SEC) and the Spanish Society of Emergency Medicine (SEMES) for the management of AF in hospital emergency departments. These guidelines are based on published scientific evidence and are applicable to most emergency departments in Spain. Specific management strategies are proposed for the conversion and maintenance of sinus rhythm, heart rate control during AF, prophylaxis for thrombi and emboli, and hospital admission and discharge protocols.

**Key words:** *Antiarrhythmic agents. Anticoagulants. Risk factors. Drugs. Atrial fibrillation. Heart rate. Guidelines. Emergency medicine.*

Full English text available at: [www.revespcardiol.org](http://www.revespcardiol.org)

### Documento de consenso sobre el tratamiento de la fibrilación auricular en los servicios de urgencias hospitalarios

La fibrilación auricular (FA) es la arritmia más prevalente en los servicios de urgencias hospitalarios (SUH) y es una enfermedad grave que duplica la mortalidad y que conlleva una elevada morbilidad. Sin embargo, a pesar de estas consideraciones, en nuestro medio se realiza un manejo heterogéneo y con frecuencia inadecuado de la FA en los SUH. Probablemente, esto es una consecuencia de la diversidad de aspectos clínicos que deben considerarse en los pacientes con FA, así como del elevado número de opciones terapéuticas posibles, lo que justifica la implementación de estrategias concretas y coordinadas de actuación entre los diversos profesionales implicados en el manejo de los pacientes con FA, con el fin de mejorar su tratamiento y optimizar los recursos humanos y materiales.

Este documento recoge las guías recomendadas por la Sociedad Española de Cardiología (SEC) y la Sociedad Española de Medicina de Urgencias y Emergencias (SEMES) para el manejo de la FA en los SUH, donde se proponen unas pautas generales basadas en la evidencia científica publicada hasta el momento y aplicables a la mayoría de los SUH de nuestro país. De esta forma, se proponen estrategias concretas de manejo de los pacientes con FA en los aspectos de recuperación y mantenimiento del ritmo sinusal, control de la frecuencia cardíaca durante FA, profilaxis tromboembólica e ingreso o alta hospitalaria, todo ello con el objetivo de promover una mejor atención a los pacientes con un uso más adecuado de los recursos disponibles en nuestro medio.

**Palabras clave:** *Agentes antiarrítmicos. Anticoagulantes. Factores de riesgo. Fármacos. Fibrilación auricular. Frecuencia cardíaca. Guías clínicas. Medicina de urgencia.*

Correspondence: Dr. J.L. Merino Llorens.  
Unidad de Arritmias y Electrofisiología. UMQ de Cardiología.  
Hospital General La Paz.  
P.º de la Castellana, 261. 28046 Madrid. España.  
E-mail: [jlmerino@secardiologia.es](mailto:jlmerino@secardiologia.es)

This article has also been submitted for publication in *Emergencias*, the official journal of the SEMES.

## ABBREVIATIONS

AF: atrial fibrillation.  
 CI: confidence interval.  
 INR: international normalized ratio.  
 RR: relative risk.  
 SEC: Sociedad Española de Cardiología (Spanish Society of Cardiology).  
 HF: heart rate.  
 SEMES: Sociedad Española de Medicina de Urgencias y Emergencias (Spanish Society for Emergency Medicine).  
 HEDs: hospital emergency departments.

## INTRODUCTION

Atrial fibrillation (AF) is the most common form of arrhythmia seen in hospital emergency departments (HEDs). It is responsible for over 3% of general emergencies<sup>1</sup> and for over 10% of admissions to internal medicine units.<sup>1-3</sup> It is a serious problem that can double mortality<sup>4-9</sup> and which has high associated morbidity, mainly related to heart failure and arterial thromboembolism. It increases the risk of ictus five-fold; the associated mortality, residual incapacity and recurrence being greater than that observed with ischemic accidents of other etiology.<sup>10-12</sup> The probability of terminating this kind of arrhythmia and of recovering normal sinus rhythm is greater the sooner therapeutic action is taken.<sup>13</sup> Given that most patients with symptoms of acute or flaring chronic disease either come directly to or are referred to HEDs,<sup>14</sup> the need for adequate and efficient management strategies in such departments is evident. Nevertheless, the management of AF in Spain is very heterogeneous, both in terms of its treatment and the prophylaxis of complications, but also with respect to logistics (the movement and destination of patients) and the coordination between HEDs and other levels of health care. This is probably due to the large number of clinical factors that must be taken into account in the management of AF, as well as with the range of treatment options. Unfortunately, inadequate management is a common result.<sup>15,16</sup> There is therefore a need to establish coordinated strategies of action for the different personnel involved in AF managements strategies that will improve treatment and optimize the use of human and material resources.

This situation has led the *Sociedad Española de Medicina de Urgencias y Emergencias* (SEMES) (Spanish Society for Emergency Medicine) and the *Sociedad Española de Cardiología* (SEC) (Spanish Society of Cardiology) (through the offices of their scientific sections specializing in cardiac arrhythmias) to define criteria for the management of AF in HEDs

that meet the above needs. Excellent reviews on the physiopathology, clinical presentation and management of AF are available, such as the guides recently published by the American Heart Association/American College of Cardiology/European Society of Cardiology. These are exhaustive reviews of the current scientific evidence related to practically every aspect of AF. They do not, however, recommend any particular approach to AF management since this largely depends on the organization of the receiving centers (recommendations appropriate for one may not be so for another). The present paper gathers together the strategies recommended by the SEMES and the SEC for the management of AF in HEDs in Spain. Some general criteria for the management of arrhythmias are offered, based on published scientific evidence.<sup>17,18</sup> These are appropriate for the majority of Spanish HEDs and should guarantee that patients receive the correct attention and that adequate use is made of available resources. The criteria proposed are not the only alternative; options found in other national and international clinical guides<sup>17,18</sup> are equally valid.

In the present paper, the levels of evidence available and the degree to which the proposed therapeutic strategies are recommended are classified following the suggestions of different international scientific societies<sup>17-21</sup> (Table 1).

**TABLE 1. Evidence levels and types of recommendation**

Evidence levels	
Grade A:	evidence based on large numbers of randomized, controlled studies and systematic reviews including meta-analyses
Grade B:	evidence based on high quality studies (not randomized), and on case control or case series studies
Grade C:	expert opinion not based on the above types of evidence
Types of therapeutic recommendation	
Class I:	evidence plus general agreement that a particular diagnostic procedure or treatment is useful and effective
Class II:	no clear evidence and differences in opinion on the validity and efficacy of a diagnostic procedure or treatment
	– Class IIa: most evidence and opinions in favor of validity and efficacy (probably useful)
	– Class IIb: efficacy and validation of treatment less well established but could be useful (possibly useful)
Class III:	evidence plus agreement that a treatment is neither valid nor effective, and that on occasion it may even harmful

## AIMS

The medical attention provided to all AF patients attending HEDs should have the following aims:<sup>22</sup>

1. The alleviation of the symptoms that caused the patient to seek help at the HED, via the control of heart rate (HR) and/or the restoration of sinus rhythm.

2. The prevention and avoidance of complications derived from the hemodynamic deterioration associated with AF itself, sustained high HRs, and thromboembolic phenomena.

These general aims transform into:

– The control of the ventricular response: achieving and maintaining a HR that ensures the control of arrhythmia-related symptoms, allows correct tolerance to exercise, and avoids the appearance of long term symptoms such as tachycardiomyopathy.

– The restoration of sinus rhythm in patients for whom this would be safe since the risk of thromboembolism is negligible if arrhythmia lasts less than 48 h. The management strategies required to meet these goals require admittance to hospital only in a small number of cases.

– The prophylaxis of arterial thromboembolic disease: this should be undertaken whenever there is a risk of this complication, independently of whether or not the patient presents at the HED because of AF. Given the catastrophic consequences of ictus and the high frequency with which AF patients present at HEDs, this objective is particularly important.

## DEFINITIONS AND GENERAL FEATURES

### Hemodynamic instability attributable to AF

#### Criteria

– A symptomatic decline of blood pressure of 30 mm Hg, or a fall to below 90/50 mm Hg. This is usually associated with organ dysfunction.

– Organ dysfunction: serious angina, serious heart failure, involvement of peripheral perfusion, decline in renal function and oligoanuria, diminished consciousness or lactic acidosis.

– Other immediately life-threatening situations.

This rarely occurs when the HR is below 100 beats/min, although with some heart problems, such as hypertrophic cardiomyopathy or mitral stenosis, the loss of atrial contraction *per se* can cause hemodynamic deterioration.

#### Where should patients be treated?

Patients should be kept in the emergency area of the

HED. This should be equipped with facilities for ECG, blood pressure and arterial oxygen saturation monitoring, as well as with a defibrillator and the necessary material for cardiopulmonary resuscitation.

#### General measures to be taken

ECG, blood pressure and oxygen saturation should be monitored constantly, high flow rate oxygen or assisted ventilation should be provided, a good caliber (16 G) peripheral vein should be accessed, and electric cardioversion be performed (synchronized to the QRS complex, 360 J).

#### Patient admittance

Patients should be admitted to critical or coronary care units.

## Electric cardioversion

#### Where should patients be treated?

Patients should be treated in the emergency area of the HED.

#### General measures

Cardiopulmonary resuscitation equipment should be available. The patient should be maintained lying flat on his/her back, ECG, blood pressure and oxygen saturation should be monitored, oxygenation should be maintained at 100%, and a good caliber (16 G) peripheral vein accessed.

#### Sedation

1-2.5 mg/kg i.v. propofol should be administered over 10 s, or, in patients with hemodynamic instability, 3-15 mg i.v. midazolam given.

#### Procedure for cardioversion

The paddles should be placed in the parasternal and apical positions using abundant conducting gel or swabs soaked in saline. A synchronized first shock with an output setting of 200-360 J is then administered. It is recommended that shocks begin at 360 J for maximum efficacy; sedation time is shorter and this practice causes no further damage to the myocardium.<sup>23</sup> Should the first shock fail, at least two further shocks at 360 J should be attempted, and at least one more with the paddles in a different position (e.g., right parasternal left posterior) or using a biphasic wave configuration. It is recommendable that an external, transcutaneous pacemaker be available, especially

if the patient has a history of atrioventricular conduction problems or sinus dysfunction. After cardioversion, the patient should be kept under observation for at least 2 h, preferably with ECG monitoring and pulse oximetry maintained until normal consciousness is restored.

Electrical cardioversion is safer and more efficient than pharmacological cardioversion, and can be performed by HED personnel.<sup>24</sup> According to the policy of each center, it can also be performed in coordination with cardiology or critical care units.

### Significant heart disease

All patients with structural heart disease, except for hypertensive cardiomyopathy with slight or moderate ventricular hypertrophy or mitral prolapse with valve failure, should be considered for anti-arrhythmia medication. In the absence of an echocardiogram, a patient can be considered very probably free of significant heart disease when the following parameters are normal:<sup>21</sup>

- Detailed anamnesis: absence of prior clinical heart problems or episodes of heart failure.
- Cardiological exploration.
- ECG: signs of necrosis, branch blocks, specific alterations in repolarization and an increase in chamber size should be given special consideration.
- Chest x-ray: normal from a cardiological point of view.

Should any of these parameters present an anomaly, the safety of the patient should be paramount and he/she be treated as though significant structural heart disease were present.

### AF with a wide QRS complex

When patients present with a wide QRS complex ( $\geq 0.12$  s), the possibility of AF with branch block, pre-excitation (Wolff-Parkinson-White syndrome) or ventricular tachycardia should be considered. When unequivocal information on the mechanism of the tachycardia is unavailable (e.g., when the QRS complex is similar to that seen in ECGs in the absence of tachycardia, or when there is atrioventricular dissociation, captures or fusions etc.), the AF should be managed as though it were of ventricular origin, and according to the recommendations of diagnostic and treatment guides for tachycardias with wide QRS complexes.<sup>18</sup> The following should also be performed:

— A 12-lead ECG (critically important for the later management of the patient), ECG monitoring, non-invasive blood pressure monitoring, and preparation of a defibrillator for immediate use should this be required. It is particularly important that, apart from obtain-

ing and keeping the 12-lead ECG results in the patient's medical record, a complete description of the tachycardia be included (frequency or length of the cycle, regularity or irregularity of frequency, patterns of right-left branch block, and vertical and right-left axes of the QRS complexes).

- Synchronized electrical cardioversion (360 J), whenever there is the minimum doubt about the diagnosis or hemodynamic stability.

### On discharge from the HED

All patients with AF require cardiological evaluation which completes the diagnosis, which monitors anti-arrhythmia and antithrombosis treatment, and which indicates whether electric cardioversion or alternative non-pharmacological therapies can be attempted. Therefore, on discharge from the HED, all patients should be referred to a cardiologist (unless their particular characteristics require some additional therapeutic intervention).

It is important that the discharge notes contain information on all the tests and periodic monitoring the patient should undergo, such as the evaluation of HR, anticoagulation levels, blood electrolyte levels and thyroid function, as well as the health care level at which such monitoring should be performed (with the general practitioner, at an anticoagulation unit, or at a geriatric or cardiology department, etc.).

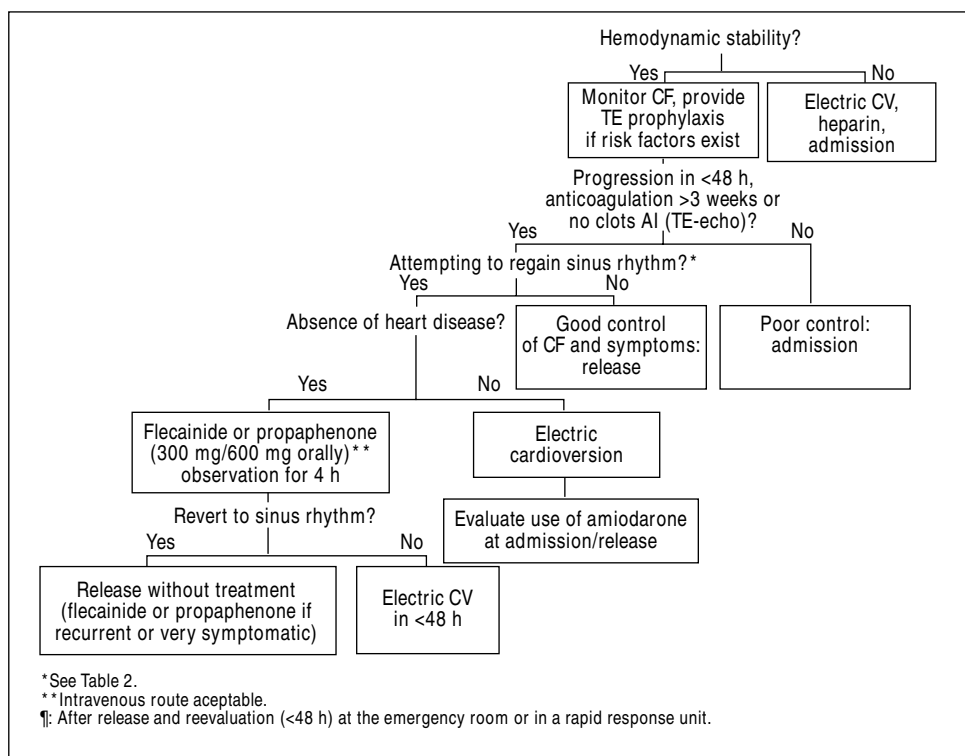
### Criteria for admittance to hospital

- Complications of AF, such as serious angina, heart failure or arterial thromboembolism.
- Inability to control the ventricular response, limiting or potentially serious symptoms despite treatment.
- Hemodynamic instability: immediate synchronized cardioversion in the HED followed by admittance to hospital.
- The initiation of therapies with a risk of pro-arrhythmia for any of the following reasons: specific drug, cardiac (heart failure, ischemic heart disease, short basal PR, history of ventricular arrhythmias) or extra-cardiac risk factors (kidney failure, hydroelectrolytic alterations, summation of arrhythmogenic drugs).
- Conversion of the AF to CI-type atrial flutter as a consequence of the drug used to restore sinus rhythm.

For the great majority of patients, hospitalization is not required for the proposed management strategies<sup>26</sup> (cardioversion, monitoring of ventricular response and thromboprophylaxis).

## GENERAL MANAGEMENT

Patients with AF presenting at an HED should be



**Fig. 1.** Overall management of patients with atrial fibrillation in hospital emergency rooms. CV indicates cardioversion; HR, heart rate; i.v., intravenous; TE, arterial thromboembolism; RF, risk factors; ECO-TE, transeosophageal echocardiogram.

treated—as should all patients—with two objectives in mind: the control of symptoms (quality of life) and the improvement of prognosis (length of life). AF mainly conditions two physiopathological problems: the loss of atrial systole (responsible for atrial blood stasis) and the loss of the contractile contribution of the atrium to the filling of the ventricle, plus the loss of control over HR (which becomes irregular, and, commonly, more rapid). These problems can cause the appearance of symptoms and affect prognosis.<sup>17</sup> The loss of atrial systole can cause weakness or asthenia to appear and, in extreme cases such as in mitral stenosis and hypertrophic cardiomyopathy, heart failure and shock. This reduces patient quality of life and could affect the prognosis. In addition, an irregular and elevated ventricular response can cause palpitations or hemodynamic deterioration which, if it persists over a long period (sometimes as short as two weeks), can lead to the development of tachycardiomyopathy – a ventricular dysfunction that occurs as a consequence of sustained and prolonged high HRs.<sup>28</sup> These factors should be borne in mind when AF patients present at the HED: they lie at the base of the proposed management scheme (Figure 1).

The first evaluation of the patient should be directed towards establishing whether or not he/she is stable from both clinical and hemodynamic points of view. If the patient presents with hemodynamic instability, and it is suspected that AF might have a role in this, attempts should be made to terminate the latter imme-

diately via electric cardioversion (class I recommendation, evidence level A),<sup>17,18</sup> as described above. If there is a precocious return of AF, or it is believed that there is practically no chance of restoring sinus rhythm, it is acceptable to try to control the HR alone.

If the patient presents with no hemodynamic instability, attempts should be made to control the HR and antithrombotic prophylaxis started if there are risk factors (see recommendations below). This might be sufficient if the duration of the AF is unknown at presentation, or if it is greater than 48 h. Unless the presence of intra-atrial clots can be ruled out by transeosophageal echocardiography, or the patient has been on anticoagulants for the previous three weeks, the possibility of clots forming and causing an embolism when sinus rhythm is restored cannot be ignored.<sup>17</sup> If these patients experience a spontaneous reversion to sinus rhythm, they should be released from the HED with treatment to control the HR (see below), and should receive oral anticoagulants for at least three weeks to avoid the risk of later embolism (see later). Chronic treatment with oral anticoagulants should be evaluated later on visiting a cardiologist.

If the patient, however, has spent less than 48 h in AF, has received adequate anticoagulant treatment over the prior three weeks, or the presence of atrial clots can be ruled out, the recovery of sustained sinus rhythm should be considered. This is controversial owing to the results of recent multicenter studies in which no differences were found between approaches

**TABLE 2. Factors to remember when deciding on whether to attempt the cardioversion of recent-onset atrial fibrillation**

1. Factors in favor of attempting the restoration of sinus rhythm
First episode of atrial fibrillation
History of paroxysmic but not persistent or permanent atrial fibrillation
Atrial fibrillation secondary to a transitory or correctable condition (fibrillation caused by hyperthyroidism, surgery, drugs, substance abuse, febrile syndrome etc.)
Atrial fibrillation causing serious or limiting symptoms (angina, heart failure, syncope, poor subjective tolerance)
Patient election
2. Factors against trying to recover sinus rhythm
High probability or precocious or late recurrence: When the duration of the arrhythmia has been >1 year
History of at least two previous electric cardioversions or the failure of at least two anti-arrhythmia drugs to maintain sinus rhythm
Early recurrence of arrhythmia (<1 month) after cardioversion
Mitral valve disease
Seriously dilated left atrium (>55 mm)
Patient rejection

to control HR and to re-establish sinus rhythm.<sup>29-34</sup> The mid term results obtained with both approaches were similar, not so much because of any similarity in the course of AF and sinus rhythm (for both strategies the majority of adverse events were related to episodes of AF) but because of the difficulty of maintaining sinus rhythm with repeated cardioversions associated with anti-arrhythmic drugs. Nonetheless, the majority of experts concur that, when a patient presents with a first episode of persistent AF, it is worth trying to restore sinus rhythm.

Certain factors are known to increase the probability of maintaining sinus rhythm in the mid term (Table 2). Patients should be considered individually when deciding about whether to attempt a conversion to sinus rhythm. Should it be decided to try, the possibility of any significant structural heart problem should be taken into account. This is particularly important since such problems limit the use of certain anti-arrhythmia drugs—and because in the absence of any such pro-

**TABLA 4. Evidence levels and type of recommendation for pharmacological cardioversion of recent-onset atrial fibrillation**

Drug	Route	Type of recommendation	Evidence level
Demonstrated efficacy			
Flecainide	Oral or intravenous	I	A
Propafenone	Oral or intravenous	I	A
Amiodarone	Oral or intravenous	IIa	B
Quinidine	Oral	IIb	B
Less effective or studies less complete			
Procainamide	Intravenous	IIb	C
Sotalol	Oral or intravenous	III	A
Digoxin	Oral or intravenous	III	A

blem the chances of a spontaneous return to sinus rhythm are much greater (Tables 3 and 4). If the patient is free of structural heart problems, a CI group anti-arrhythmia agents such as flecainide or propafenone can be tried. Given the rapid action of these substances it is recommended, for the sake of patient safety, that they be orally administered. Patients receiving an anti-arrhythmia agent on an out-patient basis should not be started on a new one. If they are receiving CI drugs, a loading dose of the same agent should be administered or electric cardioversion attempted. Following administration of this loading dose, the patient should be monitored for four hours, after which he/she can be discharged whether sinus rhythm has been restored or not. Ninety percent of patients recover sinus rhythm within 24 h of the start of treatment,<sup>35</sup> anti-arrhythmics intervening almost solely by accelerating conversion. Nevertheless, AF persists in approximately 10% of patients after 24 h. All patients in whom the recovery of sinus rhythm is not demonstrated should be seen in a rapid response consultation setting or again at the HED, depending upon the possibilities and the structure of each center. The aim is to evaluate whether to attempt electric cardioversion before 48 h have passed since the onset of AF. Following this procedure, the patient should be admitted to hospital (as above), and a decision taken (using the criteria below) on whether treatment is required to maintain sinus rhythm.

**TABLE 3. Recommended doses and side effects of the drugs most commonly used for cardioversion of atrial fibrillation**

Drug	Initial dose	Side effects
Flecainide	200-300 mg (oral) 1.5-2 mg/kg i.v. over 20 min	↓ BP, flutter A 1:1
Propafenone	450-600 mg (oral) 1.5-2 mg/kg i.v. over 20 min	↓ BP, flutter A 1:1
Amiodarone	5-7 mg/kg i.v. over 30 min followed by 1200 mg/day (continuous infusion) or 400 mg/8 h (oral)	↓ BP, TdP, GI, hyper/hypothyroidism

Flutter A 1:1 indicates atrial flutter with atrioventricular conduction 1:1; GI, gastrointestinal; i.v., intravenous; VR, ventricular response; BP, blood pressure; TdP, ventricular tachycardia due to *torsade de pointes*.

In patients with structural heart disease and AF of less than 48 h duration, and for whom it is considered that conversion to sinus rhythm is worth attempting, CI drugs should not be used because of their strong depressant effect on contractility. Further, the efficacy of amiodarone in converting AF to sinus rhythm is low.<sup>36-39</sup> The opinion of the present authors is that elective electric cardioversion be performed without delay. However, given the efficacy of amiodarone in preventing precocious recurrences of AF after electric cardioversion,<sup>40</sup> the use of this agent beforehand can be justified. Before its use, however, the benefits and the probability of being able to maintain sinus rhythm should be carefully weighed against the risk of side effects for each patient. It is important to remember that patients with structural heart problems are at high risk of suffering arterial thromboembolism. Therefore, following the recovery of sinus rhythm, anticoagulation treatment should be considered (using the criteria below).

Finally, a decision should be made on whether to admit the patient to hospital or to proceed to his/her discharge—whether an attempt to recover sinus rhythm has been made or simply HR controlled.

## CONTROL OF VENTRICULAR RESPONSE

The control of the HR should always be a therapeutic objective in patients with AF.<sup>17,18,22</sup> As mentioned above, such control has the aim of alleviating symptoms, improving the patient's hemodynamics and, in some cases, of avoiding the appearance of tachycardia and heart failure.<sup>28,41</sup> The control of HR should be guided by the disappearance of the secondary signs and symptoms of high HR and by ventricular frequency per se. A HR of under 100 beats/min at rest has been accepted as the aim, but this limit is usually hard to control during physical activity. Currently, a resting HR of 60-80 beats/min and values of 90-115 beats/min during activity are preferred.<sup>17</sup>

The present paper offers some general recommendations for the control of HR, but not all situations have been contemplated. It is also proposed that treatment be individualized in accordance with the expectations of being able to maintain an adequate long term ventricular response, and in consonance with the strategies recommended at different centers.<sup>17,18</sup> In the absence of any ventricular pre-excitation syndrome, the control of ventricular frequency can be undertaken with five groups of drugs that decelerate nodal conduction: digitalic agents, beta-blockers, non-dihydropyridine calcium antagonists, amiodarone and propafenone. Agents with rapid but short-lasting effects, such as ATP or adenosine, have no therapeutic value in AF. As a general recommendation, drugs for the control of AF should be orally administered, although when a more rapid effect is required the intravenous

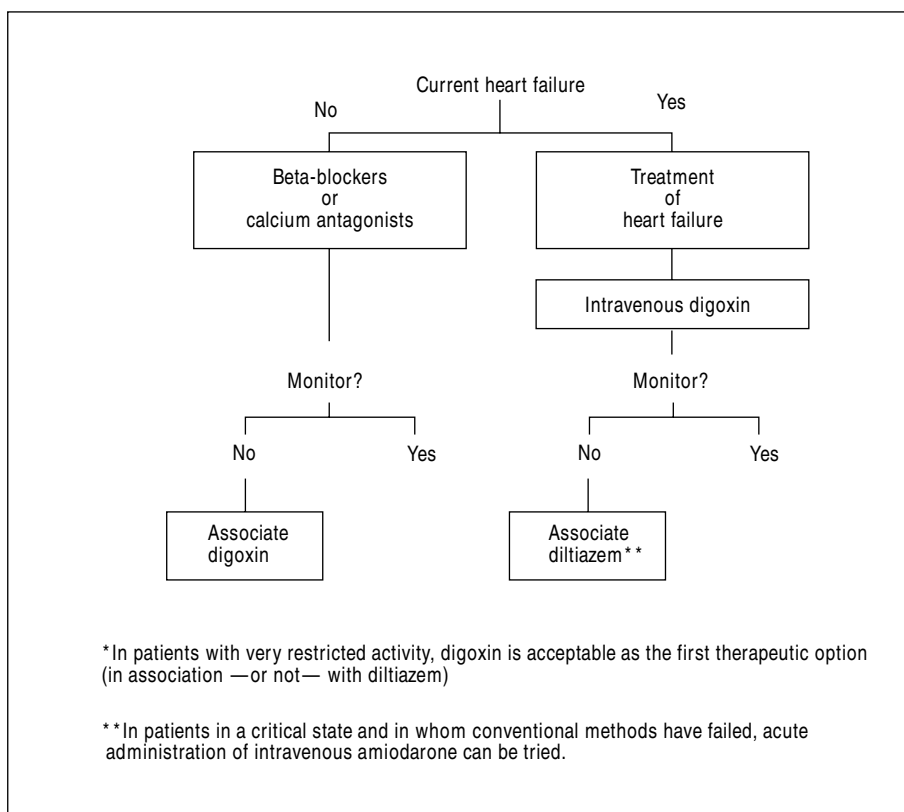
route can be used.

To control HR during AF (Figure 2), it should first be determined whether the patient has any problem associated with high HR, for example an infection. If this is the case, treatment should focus mainly on this rather than on the HR itself. It should also be established whether the patient is suffering heart failure, since this limits the use of drugs with negative inotropic effect. Such patients should first receive treatment for this condition: there should be no hurry to begin specific treatment to control HR since a high HR is often an adaptive response to this problem and will require no further treatment. However, if it is considered necessary to reduce the ventricular response in this situation, intravenous digoxin should be administered simultaneously with the treatment for heart failure.<sup>42-44</sup> If, despite these measures, adequate control over HR is not achieved, intravenous diltiazem can be used for acute control, or, in extreme cases if there is a risk of conversion to sinus rhythm and the patient is not adequately protected against coagulation, intravenous amiodarone can be used.

There are few pharmacological restrictions for patients who are not suffering heart failure. The most effective or rapid can therefore be chosen, such as beta-blockers or the non-hydropyridine calcium antagonists diltiazem and verapamil. These drugs have been shown effective in the control of the ventricular response, both at rest and during exercise.<sup>45,46</sup> Any of these can be the first choice, but this should be made considering the possible side effects in relation to each patient's clinical profile and concomitant disease.<sup>41,47-50</sup> In HEDs, calcium channel antagonists are preferable if the patient is diabetic, has bronchial hyper-reactivity or symptomatic peripheral vascular disease. Patients with ischemic heart disease should receive beta-blockers. Intravenous administration of diltiazem has several advantages: the dose can be widely adjusted during continuous infusion, it does not increase plasma digoxin levels, and it has a lesser negative inotropic effect.<sup>50</sup> It is therefore recommended as the first choice.<sup>51</sup> If the control achieved by monotherapy with one of these agents is insufficient, digoxin can be added. This is slow to begin its action and is of limited efficacy, especially in the presence of adrenergic stimuli owing to its mainly vagotonic action.<sup>43</sup> It should therefore only be used in monotherapy for the control of HR in patients with very restricted physical activity.

When contemplating the association of drugs for controlling the ventricular response, the following should be borne in mind:<sup>47-49</sup>

- The association of digoxin may require a dose reduction, especially in elderly patients.
- Diltiazem and beta-blockers do not significantly increase plasma digoxin levels, something which can occur with verapamil.
- The association of beta-blockers and digoxin



**Fig. 2.** Strategies for controlling the ventricular response during atrial fibrillation. HF indicates heart failure; i.v., intravenous.

usually causes more bradycardia than does digoxin and diltiazem.

–Associations of the calcium antagonists mentioned and beta-blockers should not be used.

The evidence levels, treatment recommendations and normal dosages of the drugs employed in acute and chronic control of the ventricular response are shown in Tables 5 and 6. The main side effects are shown in Table 7.

## POST-CARDIOVERSION MAINTENANCE OF SINUS RHYTHM

### General features

Approximately 50% of patients in whom AF reverts to sinus rhythm experience a recurrence during the first year of anti-arrhythmia treatment, usually during the first month. This rises to some 80% if no anti-arrhythmia treatment is provided. The treatment of AF is therefore frequently unsatisfactory, and this has a great effect on the quality of life.<sup>52</sup>

Currently, the main aim of treatment with anti-arrhythmia agents is to improve patient quality of life since, as already mentioned, no effect on prognosis has been demonstrated. Pharmacological anti-arrhythmia treatment for the maintenance of sinus rhythm does not appear justifiable in two circumstances: for

the first episode of AF and for well-tolerated, infrequent paroxysmic AF. Further, there is no defined pharmacological treatment for patients with short-lived multiple crises; these would probably benefit more from alternatives to drugs such as catheter ablation. Maintenance anti-arrhythmia treatment should be limited to patients with frequent and clinically or hemodynamically poorly-tolerated episodes of AF.

Finally, once the decision to start pharmacological anti-arrhythmia treatment has been taken, it is important that the recurrence of AF should not be seen as a failure if the episodes are less frequent and better tolerated than before, always given that patient quality of life is acceptable.

### Choice of drug

All anti-arrhythmia drugs can become pro-arrhythmogenic, especially under certain circumstances (Table 8).<sup>53</sup> Along with that mentioned above, this means that the safety of the drug should be the main characteristic considered during the making of treatment decisions, with efficacy being considered in second place. Generally, the safest drug for the patient should be chosen, even though it may be less effective.

The concept of pro-arrhythmia<sup>54</sup> refers to the appearance of an arrhythmia or the worsening of an existing arrhythmia as a consequence of treatment with a drug at a non-toxic dose or plasma concentration. This in-



TABLE 5. Drug doses most commonly used in acute control of the ventricular response (intravenous route)

Drug	Loading dose	Onset of effect	Maintenance dose	Type of recommendation
Diltiazem	0.25 mg/kg over 2 min	2-7 min	5-15 mg/h	I
Verapamil	0.075-0.15mg/kg over 2 min	3-5 min	—	I
Esmolol	0.5 mg/kg over 1 min	5 min	0.05-0.2 mg/kg/min	I
Metoprolol	2.5-5 mg/kg over 2 min Up to a max. of 3 doses	5 min	—	I
Propranolol	0.15 mg/kg	5 min	—	I
Amiodarone	5-7 mg/kg over 30 min followed by 1200 mg/day (continuous infusion) or 400 mg/8 h (oral)		200 mg/day	IIb
Digoxin	0.25 mg /2 h to a max. of 15 mg	2 h	0.125-0.25 mg/day	II

TABLE 6. Drug doses most commonly used in the chronic control of the ventricular response (oral route)

Drug	Loading dose	Onset	Maintenance dose	Type of recommendation
Digoxin	0.25 mg/2 h (max. 1.5 mg)	2 h	0.125-0.325 mg/day	I
Diltiazem	—	2-4 h	120-360 mg/day	I
Metoprolol	—	4-6 h	25- 100 mg/12 h	I
Propranolol	—	60-90 min	80-240 mg/day	I
Verapamil	—	1-2 h	120-360 mg/day	I

TABLE 7. Most important side effects, apart from bradycardia, of the drugs recommended for control of the ventricular response

Drug	Secondary effects
Digoxin	Digitalic intoxication (digestive, ocular, neurological, pro-arrhythmic)
Beta-blockers	Hypotension, heart failure, bronchospasm
Calcium antagonists (diltiazem and verapamil)	Hypotension, heart failure, interaction with digoxin (verapamil)
Amiodarone	Hypo/hyperthyroidism, pulmonary toxicity, liver toxicity, photosensitivity, corneal deposits, skin discoloration, polyneuropathy, optical neuropathy, interaction with acenocoumarol.

cludes the appearance of sustained ventricular arrhythmias, the conversion of a non-sustained into a sustained arrhythmia, the acceleration of tachycardia, the appearance of bradycardia or a conduction problem (e.g., SA node dysfunction), atrioventricular block or the widening of the QRS complex. It is important to avoid anti-arrhythmic polytherapy if possible since this might potentiate individual pro-arrhythmic effects. An exception to this recommendation is the addition of beta-blockers or calcium antagonists to HR treatment regimens. These do not potentiate pro-arrhythmic effects directly, although they can potentiate the development of bradycardias and blockage of conduction.

Many anti-arrhythmics can be used for the maintenance of sinus rhythm in patients with AF,<sup>17</sup> though in practice they are reduced to four in Spain: flecainide, propafenone, sotalol and amiodarone (Table 9 and Figure 3). In these guidelines, no mention is made of procainamide since there is no adequate oral dose known, disopiramide is not mentioned because it has

been withdrawn from the market, dofetilide is not considered since it is still to be marketed in Spain, and quinidine is not considered since it has a risk profile that advises administration be initiated with the patient hospitalized for at least 48 h (its use should be decided upon by cardiologists for use in special situations).

### Vaughan & Williams CI drugs

Given their safety profile, these are the drugs of choice for patients with no structural heart disease, although they are probably less effective than amiodarone.<sup>40,55</sup> If the patient has significant structural heart disease they should be avoided because of their depression of contractibility and their favoring ventricular arrhythmia in this clinical context. These drugs can also transform episodes of AF into episodes of atrial flutter (known as type CI, although they can also be caused by IA and III drugs). The depressant action

**TABLE 8. Risk factors for developing pro-arrhythmia during pharmacological treatment of atrial fibrillation**

Drug interactions: macrolides, antihistamines or other anti-arrhythmia drugs
Electrolytic changes: hypopotasemia and hypomagnesemia
Kidney failure
Presence of structural heart disease
Long QT interval before or after treatment
Female sex (QT interval is physiologically longer)
Short PR, result of accelerated nodal conduction
Bradycardia or tachycardia
History of tachycardia or ventricular fibrillation
Previous pro-arrhythmia

on conduction velocity also means this flutter is slower than a common atrial flutter, with frequencies of around 200 beats/min.

Commonly—especially if the patient suffers intrinsic or sympaticomimetic treatment-related acceleration of nodal conduction—the atrioventricular conduction system can cause these frequencies in a proportion of 1:1. Paradoxically, this can lead to an increased HR associated with poor hemodynamic tolerance. High HR and the sensitivity of the His-Purkinje system to these drugs frequently causes branch block that simulates ventricular tachycardia. Currently, the best treatment for this is thought to be catheter ablation of the CI-type atrial flutter (as long as the patient has suffered little recurrence of AF under treatment with the drug responsible for the flutter and when, after ablation, is to continue with the same drug in combination with another to control the ventricular response in any recurrence).

CI drugs have a good safety profile in patients with no structural heart disease, are reasonably well tolerated,<sup>56</sup> and their use can be started outside hospital as long as there is no SA node dysfunction, atrioventricular conduction problem or branch block. The effects of flecainide and propafenone are similar. Although the latter may be less effective and less well tolerated,<sup>57</sup> it controls the ventricular response

better because of its slight beta-blocking effect. Both drugs can be used as *pill in the pocket* treatments, (i.e., at a single dose when an AF crisis strikes in place of chronic treatment of patients who only experience infrequent episodes). However, the recommendation of this type of treatment should only be made after its safety has been demonstrated by clinical trial.

**Vaughan & Williams CIII drugs**

Amiodarone and sotalol belong to this group. Amiodarone is the most effective drug for maintaining sinus rhythm after AF conversion,<sup>40,58</sup> but its frequent and serious side effects in prolonged, chronic treatment make it a second choice in patients with no structural heart disease. However, there are few anti-arrhythmic drugs that do not increase mortality,<sup>40,55,58</sup> so it is particularly indicated for patients with poor ventricular function. Pro-arrhythmic phenomena are rare with amiodarone, so it can be started outside the hospital, although careful monitoring is required during the administration of the loading dose, especially in patients with heart failure.

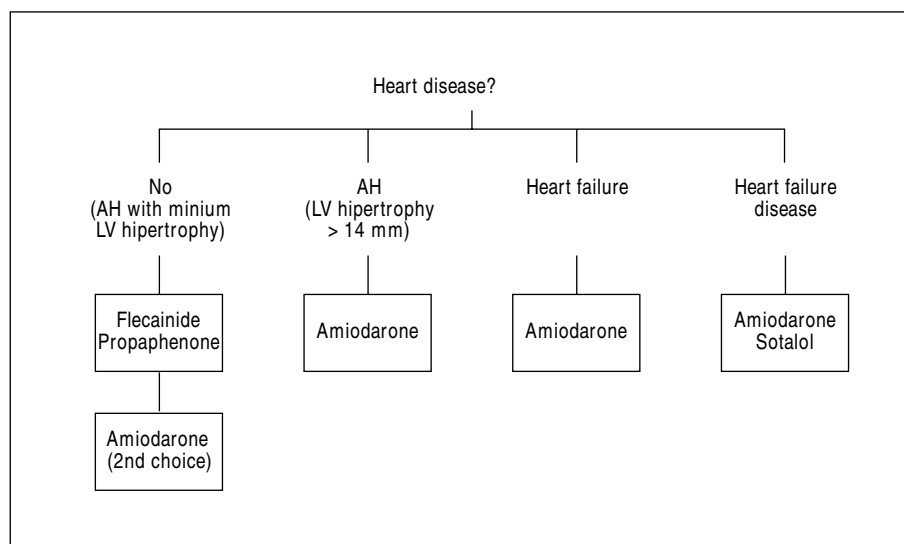
Sotalol is of similar efficacy to propafenone but less effective than amiodarone, and, because of its beta-blocking effect, is especially indicated for patients with AF and ischemic heart disease. In these patients it should be the first choice, along with amiodarone.<sup>40,59</sup> Sotalol can be started outside the hospital when there are no risk factors for the development of ventricular tachycardias due to *torsade de pointes*, such as a prolonged QT interval, hydroelectrolytic alterations, heart failure or female sex.<sup>59</sup> Treatment is safer when started after the patient has achieved sinus rhythm.

Finally, the risk of ventricular tachycardias due to *torsade de pointes* is greater when there is ventricular hypertrophy. In hypertensive patients with left ventricles thicker than 14 mm, the drug of choice should be amiodarone.

**TABLE 9. Doses and side effects of anti-arrhythmia drugs most commonly used for the maintenance of post-cardioversion sinus rhythm**

Drug	Dose	Side effects
Flecainide	100-150 mg/12 h	Conversion to atrial flutter, HF, VT
Propafenone	150-300 mg/8 h	Conversion to atrial flutter, HF, VT
Sotalol	80-160 mg/12 h	Bradycardia and atrioventricular block, VT TdP
Amiodarone	200 mg	Hypo/hyperthyroidism, pulmonary toxicity, liver toxicity, photosensitivity, corneal deposits, skin discoloration, polyneuropathy, optical neuropathy, interaction with acenocoumarol

HF indicates heart failure; TdP, *torsade de pointes*; VT, ventricular tachycardia.



**Fig. 3.** Pharmacological maintenance of sinus rhythm following cardioversion of atrial fibrillation. AH indicates arterial hypertension; LV, left ventricle.

### Other drugs

Given their lower efficacy, greater long term toxicity, and their association with high mortality in AF patients, group IA drugs should be exclusively reserved for the treatment of refractory cases.<sup>60</sup> Quinidine can be of some use in vagal-type AF because of its low vagolytic effect. Given that the risk of tachycardias through *torsade de pointes* occurs in the first days of quinidine treatment, even with subtherapeutic doses, the use of this drug should always begin with the patient hospitalized.<sup>60</sup>

Dofetilide is a group III drug but it is still unavailable in Spain. Its efficacy in AF is moderate, though it would seem not to increase mortality in patients with serious ventricular dysfunction. It might therefore be considered an alternative to amiodarone in these patients.<sup>61</sup> As with sotalol, treatment should normally begin in hospital because of the risk of ventricular tachycardia owed to *torsade de pointes*.

### PROPHYLAXIS OF ARTERIAL THROMBOEMBOLIC DISEASE

Paroxistic, persistent or permanent AF is a risk factor for arterial thromboembolism. In 70%-90% of cases, embolism occurs in the cerebral circulation and is manifested as ischemic ictus, increasing mortality and the chances of permanent neurological sequelae.<sup>3,8,10,11</sup> Embolic phenomena can occur in three different clinical situations: *a*) after elective cardioversion of AF (incidence 5.3%);<sup>17</sup> *b*) in patients with AF associated with mitral valve disease (annual incidence 22%-32%),<sup>10,11,17</sup> and *c*) and in AF patients without mitral valve disease (annual incidence 5%).<sup>3,11,17</sup> In these situations, prophylactic antithrombotic treatment can significantly reduce the risk of embolism.<sup>62</sup>

### Prophylaxis in cardioversion

Several echocardiographic studies have shown that the conversion of AF to sinus rhythm is followed by a period of mechanical dysfunction or «atrial stunning» which can last several weeks. Therefore, even patients with no clots in the left ventricle can suffer an embolism after cardioversion.<sup>63</sup>

Cardioversion is usually elective and can follow two approaches: pharmacological and electrical. There is no evidence that the risk of embolism is greater with one or the other. Therefore, the same recommendations referring to anticoagulation should be followed for both.<sup>17,64</sup> A risk of embolism has been shown in atrial flutter; the same therapeutic approach as in AF is therefore recommended.<sup>17,65,66</sup>

The risk of embolism in cardioversion of AF is reported to be 1%-5% in case control studies.<sup>67,68</sup> This is reduced to about 1% when anticoagulation treatment has been provided over the three previous weeks.<sup>65</sup> If the AF has lasted less than 48 h and the patient has no mitral valve disease or history of embolisms, the risk of embolism can be considered low, and electric or pharmacological cardioversion can be attempted in this time interval.<sup>17,65</sup> However, when AF has lasted more than 48 h, when the time of onset is unknown, or when the patient has mitral valve disease or a history of arterial embolisms, anticoagulation therapy should be started with an international normalized ratio (INR) of 2-3 maintained for the three weeks prior to any attempt at cardioversion. Such treatment should also continue for the three following weeks.<sup>65</sup> An alternative strategy is to perform transesophageal echocardiography before attempting cardioversion, and, if no intracardial clots are detected, anticoagulation treatment should be started with heparin. Anticoagulation with coumarinic drugs should then continue for four weeks.<sup>69</sup> Both stra-

regies are equally effective, though echocardiography has a better safety profile. The majority of patients who undergo cardioversion have some risk factor making it advisable to maintain anticoagulation indefinitely: the need for chronic therapy should be evaluated when pre-cardioversion treatment is begun.

Some authors suggest that cardioversion be attempted urgently since arrhythmia leads to hemodynamic deterioration. In such cases, the status of the patient does not allow a conventional approach and cardioversion should be attempted immediately and heparin treatment begun. Compared to conventional sodium heparinate, the ease of administration and the similar efficacy afforded by low molecular weight heparin preparations make the latter the better choice.<sup>70</sup>

### *General rules for anticoagulation in cardioversion*

- Maintain INR between 2 and 3 for three weeks before and at least three weeks after cardioversion if AF has lasted longer than 48 h or the time of its onset is unknown.

- Make no distinction between anticoagulation treatment for flutter and AF.

- Make no distinction between electric and pharmacological cardioversion.

- An alternative, transesophageal echocardiographic approach can be taken, but anticoagulation must be maintained for at least three weeks following cardioversion.

- Cardioversion without anticoagulation can be attempted if AF has lasted no more than 48 h in patients without mitral valve disease and with no history of embolisms.

- When urgent cardioversion must be performed, treatment with heparin is advisable.

- Patients who present with spontaneous cardioversion to sinus rhythm should be managed following the same criteria as for electric or pharmacological cardioversion.

### **Prophylaxis in atrial fibrillation associated with mitral valve disease**

All patients presenting with AF and mitral valve disease (stenosis or rheumatic mitral failure, degenerative mitral failure, mitral valve prolapse, or calcification of the mitral valve annulus) should receive anticoagulant therapy.<sup>17,62,65</sup>

### **Prophylaxis in non-valvular atrial fibrillation**

The annual incidence of embolism in non-valvular AF patients is greater than 5% (and greater than 12% when prior episodes have occurred).<sup>10,65</sup> It has been shown that oral anticoagulation therapy reduces the risk of embolism by 62% (95% confidence interval

[CI]=48%-72%), while platelet antiaggregants only reduce it by 24% (95% CI=7%-39%).<sup>65</sup>

The main risk associated with anticoagulation therapy is hemorrhage, especially intracranial hemorrhage. The latter is feared because it is frequently fatal or leaves important neurological sequelae comparable to those of ictus—the problem such therapy was designed to avoid. In general, no greater incidence of major hemorrhages (including intracranial hemorrhages) has been detected in patients treated with antiaggregants than in control/placebo subjects.

The risk of hemorrhage due to the use of anticoagulants is strongly related to the intensity of anticoagulation and to its variability, a good indirect marker of the quality control of treatment.<sup>71,72</sup> It is therefore necessary to evaluate the risk-benefit ratio of prophylactic antithrombosis treatment in each patient. The analysis of five prospective studies designed to determine the effect of anticoagulation on the prevention of arterial thromboembolic disease associated with AF<sup>73</sup> identified the following risk factors in the control/placebo groups: a history of embolisms (relative risk [RR]=2.5), age (RR=1.4/decade), high blood pressure (RR=1.6), diabetes mellitus (RR=1.7), ischemic heart disease (RR=1.5) or heart failure (RR=1.4), and a moderately or seriously reduced ejection fraction (RR=2.5). The analysis of the three SPAF (Stroke Prevention in Atrial Fibrillation) studies showed the following risk factors for patients treated with acetylsalicylic acid±low dose anticoagulation (INR<1.4): a history of embolisms (RR=2.9), age (RR=1.8/decade), a history of high blood pressure (RR=2), diabetes mellitus (RR=1.7), high systolic pressure >160 mm Hg (RR=2.3), female sex (RR=1.6) and hormone replacement therapy with estrogens (RR=3.2).

With respect to the degree of anticoagulation, the aim is to prevent embolisms without increasing the risk of bleeding. So far, this has been achieved with INR values of 2-3. INR values <1.6 are ineffective.<sup>17,65</sup>

Patients with a valve prosthesis who are subjected to procedures involving a risk of bleeding, such as surgery or endoscopy with biopsy, in whom oral anticoagulation must be stopped, require no other therapy if the interruption of prophylaxis lasts less than one week. In patients with a very high risk of embolism, or in those for whom a suspension of treatment of longer than one week is foreseen, low molecular weight heparin treatment is recommended.<sup>17</sup>

There is no consensus on the absolute and relative contraindications of anticoagulation therapy, but these include a history of hemorrhagic ictus, serious hemorrhage in the previous six months, alterations in homeostasis, complications with prior anticoagulation therapies, alcoholism, poorly controlled convulsive crises, internal secondary hemorrhage or recent trauma, surgery in the preceding month, chronic liver disease, poorly controlled hypertension, pregnancy, lactation, life

**TABLA 10. Risk factors and recommendations for the prevention of arterial thromboembolism in atrial fibrillation (paroxistic and chronic)**

High risk factors	
TIA/ischemic stroke or peripheral arterial embolism	
High blood pressure	
Mitral valve disease	
Systolic HF or EF<40%	
Age>75 years	
Moderate risk factors	
Diabetes mellitus	
Ischemic heart disease	
Age>65 years	
Therapeutic recommendations	
Anticoagulation:	≥1 high RF or ≥2 moderate RFs
Anticoagulation or antiaggregation:	1 moderate RF*
Antiaggregation:	<65 years and without RFs

\*Individualized and according to the risk of bleeding, the possibility of adequate monitoring and patient choice.  
TIA indicates transient ischemic accident; EF, left ventricle ejection fraction; HF, heart failure; RF, risk factor

expectancy of less than six months, dementia, frequent falls, and when patient compliance to therapy or monitoring are likely to be deficient.<sup>74</sup>

**Doses for antithrombosis treatment**

Acenocoumarol doses should be adjusted to achieve an INR of 2-3.<sup>64,75</sup> Acetylsalicylic acid (300 mg/day) should be used as a platelet antiaggregant. If this is contraindicated, clopidogrel (75 mg/day) can be used. The recommendations for antithrombosis prophylaxis

are summarized in Table 10. The types of recommendation and the evidence levels supporting them are shown in Table 11.<sup>7,65</sup>

**ANNEX 1. PANEL MEMBERS FOR CONSENSUS ON THE MANAGEMENT OF ATRIAL FIBRILLATION IN HOSPITAL EMERGENCY ROOMS**

Grupo de Arritmias de la Sociedad Española de Medicina de Urgencias y Emergencias (SEMES)<sup>a</sup> and the Sección de Electrofisiología y Arritmias de la Sociedad Española de Cardiología (SEC)<sup>b</sup>.

*Coordinators*

Alfonso Martín Martínez:<sup>a</sup> coordinator of the Grupo de Arritmias de la SEMES, Servicio de Urgencias, Hospital de Móstoles, Madrid, Spain.

José Luis Merino Llorens:<sup>b</sup> Secretary of the Sección de Electrofisiología y Arritmias de la SEC, Unidad de Arritmias y Electrofisiología, UMQ Cardiología, Hospital Universitario La Paz, Madrid, Spain.

*Members of the panel of experts*

Carmen del Arco Galán:<sup>a</sup> Servicio de Urgencias, Hospital Universitario de la Princesa, Madrid, Spain.

Jesús Martínez Alday:<sup>b</sup> Laboratorio de Electrofisiología, Servicio de Cardiología, Clínica San Sebastián, Bilbao, Spain.

Pedro Laguna del Estal:<sup>a</sup> Servicio de Urgencias, Hospital Universitario Clínica Puerta de Hierro,

**TABLA 11. Evidence levels and types of recommendation for prophylaxis of arterial thromboembolism associated with atrial fibrillation**

Risk factors	Prophylaxis	Evidence level	Type of recommendation
≥1 high RF OAC	A	I	
≥2 moderate RFs	OAC	C	IIa
1 moderate RF	OAC or PLA	A	I
No RF	PLA	C	IIb
Patients with AF (non-solitary)	OAC or PLA (according to RF)	A	I
High RF	OAC (INR=2-3)	A	I
Periodic re-evaluation of the need for OAC	OAC	A	I
High RF and contraindication of OAC	PLA	A	I
<75 years plus risk of hemorrhage	OAC (INR=1.6-2.5)	C	IIa
Paroxistic or chronic AF	Same management	B	IIa
Procedures with risk of hemorrhage	Interrupt prophylaxis (<1 week)	C	IIb
Procedures with no risk of hemorrhage	LMW heparin (>1 week)	C	IIb
Electric or pharmacological CV	Same management B	I	
CV of AF of >48 h duration or onset unknown	OAC 3 weeks before or ECO-TE	B	I B I
Urgent CV	LMW heparin	C	I
CV of AF of <48 h duration	No OAC nor ECO-TE	C	IIb
CV of atrial flutter	Manage as for AF	C	IIb

RF indicates risk factors; OAC, oral anticoagulants; PLA, platelet antiaggregants; AF, atrial fibrillation; RH, risk of hemorrhage; LMW, low molecular weight; CV, cardioversion; ECO-TE, transesophageal echocardiography negative for atrial clots; AF, atrial fibrillation.

Madrid, Spain.

Fernando Arribas Ynsaurriaga:<sup>b</sup> Unidad de Arritmias, Servicio de Cardiología, Hospital Universitario 12 de Octubre, Madrid, Spain:

Pedro Gargantilla Madera:<sup>a</sup> Servicio de Urgencias, Hospital Universitario San Carlos, Madrid, Spain.

Luis Tercedor Sánchez:<sup>b</sup> Unidad de Arritmias, Servicio de Cardiología, Hospital Universitario Virgen de las Nieves, Granada, Spain.

Juan Hinojosa Mena-Bernal:<sup>a</sup> Servicio de Urgencias, Hospital Universitario San Carlos, Madrid, Spain.

Lluís Mont i Girbau:<sup>a</sup> Unidad de Arritmias, Institut de Malalties Cardiovasculars, Hospital Clínic, Barcelona, Spain.

## REFERENCES

- Martín A, Laguna P, Del Arco C, Gargantilla P, on behalf of the GEFAUR-1 investigators. A prospective multicenter study on atrial fibrillation in the emergency department. The Spanish Atrial Fibrillation in Emergency Medicine Study Group (GEFAUR-1): Epidemiological data and risk factors [abstract]. *Eur Heart J* 2001;22(Suppl):190.
- Feinberg WM, Blackshear JL, Lapaucis A, Kronmal R, Hart J. Prevalence, age distribution and gender of patients with atrial fibrillation: analysis and implications. *Arch Intern Med* 1995; 155:469-73.
- Lip GYH, Beevers DG. History, epidemiology and importance of atrial fibrillation. *BMJ* 1995;311:1361-3.
- The National Heart, Lung and Blood Institute working group on atrial fibrillation. Atrial fibrillation: current understandings and research imperatives. *J Am Coll Cardiol* 1993;22:1830-4.
- Ryder KM, Benjamin EJ. Epidemiology and significance of atrial fibrillation. *Am J Cardiol* 1993;84:R131-8.
- Wolf PA, Benjamin EJ, Belanger AJ, Kannel WB, Levy D, D'Agostino RB. Secular trends in the prevalence of atrial fibrillation: The Framingham Heart Study. *Am Heart J* 1996;131:790-5.
- Cameron A, Schwartz MJ, Kronmal RA, Kosinski AS. Prevalence and significance of atrial fibrillation in coronary artery disease (CASS registry). *Am J Cardiol* 1998;61:714-7.
- Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: The Framingham Heart Study. *Circulation* 1995;92:835-41.
- Krahn AD, Manfreda J, Tate RB, Mathewson FA, Cuddy TE. The natural history of atrial fibrillation: incidence, risk factors and prognosis in the Manitoba Follow-up Study. *Am J Med* 1995;98:476-84.
- Secondary prevention in non-rheumatic atrial fibrillation transient ischemic attack or minor stroke: EAFAT (European Atrial Fibrillation Trial) Study Group. *Lancet* 1993;342:1255-62.
- Wolf PA, Abbot RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The Framingham Heart Study. *Stroke* 1991;22:983-8.
- Lin HJ, Wolf PA, Kelly-Hayes M, Beiser AS, Kase CS, Benjamin EJ, et al. Stroke severity in atrial fibrillation: The Framingham Heart Study. *Stroke* 1996;27:1760-4.
- Danias PG, Caulfield TA, Weigner MJ, Silverman DI, Manning WJ. Likelihood of spontaneous conversion of atrial fibrillation to sinus rhythm. *J Am Coll Cardiol* 1998;31:588-92.
- Balanzó X, Pujol R. Estudio multicéntrico de las urgencias en hospitales generales básicos de Catalunya. *Med Clin (Barc)* 1989;92:86-90.
- Laguna P, Martín A, Gargantilla P, Del Arco C, on behalf of the GEFAUR-1 investigators. The Spanish atrial fibrillation in emergency medicine study group (GEFAUR-1). A prospective multicenter study of atrial fibrillation in the emergency department: VII - Accuracy of thromboprophylaxis [abstract]. *Stressa: Book of abstracts of The First Mediterranean Emergency Medicine Congress*, 2001; p. 93.
- Martín A, Gargantilla P, Laguna P, Del Arco C, on behalf of the GEFAUR-1 investigators. A prospective multicenter study on atrial fibrillation in the emergency department. The Spanish Atrial Fibrillation in Emergency Medicine Study Group (GEFAUR-1): rate control issues [abstract]. *Eur Heart J* 2001; 22(Suppl):552.
- Fuster V, Ryden LE, Asinger RW, Cannom DS, Crijs HJ, Frye RL, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences. *Circulation* 2001;104:2118-50.
- Almendral J, Martín E, Medina O, Peinado R, Pérez L, Ruiz R, et al. Guías de práctica clínica de la Sociedad Española de Cardiología en arritmias cardíacas. *Rev Esp Cardiol* 2001;54:307-67.
- Grading of recommendations and levels of evidence used in evidence based cardiology. En: Yusuf S, Cairns JA, Cernin AJ, Fallen EL, Gersch BJ, editors. *Evidence based cardiology*. London: BMJ Books, 1998; p. 525-75.
- Ryan TJ, Anderso JL, Antman EM, Braniff BA, Brooks NH, Califf RM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 1996;28:1328-428.
- Cook DJ, Guyatt GH, Lapaucis A, Sackett DL. Rules of evidence and clinical recommendations on the use of antithrombotic agents. *Chest* 1992;102(Suppl 4):305-11.
- Martín A, Laguna P, Del Arco C, Gargantilla P, en nombre de los investigadores del GEFAUR. El Grupo para el Estudio de la Fibrilación Auricular en Urgencias (GEFAUR): fundamentos, objetivos y diseño de un estudio prospectivo de la fibrilación auricular en los servicios de urgencias hospitalarios. *Emergencias* 2001; 13:235-40.
- Metcalf MJ, Smith F, Jennings K, Patterson N. Does cardioversion of atrial fibrillation result in myocardial damage? *BMJ* 1988;290:1364.
- Michael JA, Stiell IG, Agarwall S, Mandavia DP. Cardioversion of paroxysmal atrial fibrillation in the emergency department. *Am J Emerg Med* 1999;33:379-87.
- Desbiens NA. Should all patients with atrial fibrillation be screened with echocardiography? *J Gen Intern Med* 1992;7:131-9.
- Martín A, Gargantilla P, Laguna P, Del Arco C, on behalf of the GEFAUR-1 investigators. The Spanish atrial fibrillation in emergency medicine study group (GEFAUR-1). A prospective multicenter study of atrial fibrillation in the emergency department: IX-Assessment of the impact of the management strategies on outcome and final destination from the emergency department [abstract]. *Stressa: Book of abstracts of The First Mediterranean Emergency Medicine Congress*, 2001; p. 98.
- Jung W, Lüderitz B. Quality of life in patients with atrial fibrillation. *J Cardiovasc Electrophysiol* 1998;9(Suppl):S177-86.
- Shinbane JS, Wood MA, Jensen DN, Ellenbogen KA, Fitzpatrick AP, Scheinman MM. Tachycardia-induced cardiomyopathy: a review of animal models and clinical studies. *J Am Coll Cardiol* 1997;29:709-15.
- Hohnloser SH, Kuck KH, Lillenthal J. Rhythm or rate control in atrial fibrillation - Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomised trial. *Lancet* 2000;356:1789-94.
- Wyse G. Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial. Atlanta. American College of

- Cardiology 51st Annual Scientific Session, 2002.
31. Mortality and stroke rate in a trial of rhythm control versus rate control in atrial fibrillation: results from the strategies of treatment of atrial fibrillation (STAF) Pilot Phase. Atlanta: American College of Cardiology 50th Scientific Sessions, 2001.
  32. Crijns H, Van Gelder IC. Rate Control vs Electrical Cardioversion for Persistent Atrial Fibrillation (RACE) study. Atlanta: American College of Cardiology 51st Annual Scientific Session, 2002.
  33. Deedwania PC, Singh BN, Ellenbogen K, Fisher S, Fletcher R, Singh SN. Spontaneous conversion and maintenance of sinus rhythm by amiodarone in patients with heart failure and atrial fibrillation. Observations from the Veterans Affairs Congestive Heart Failure Survival Trial of Antiarrhythmic Therapy (CHF-STAT). *Circulation* 1998;98:2574-9.
  34. Pedersen OD. Restoration and maintenance of sinus rhythm in patients with left ventricular dysfunction and atrial fibrillation/flutter is associated with improved survival. A DIAMOND substudy. *J Am Coll Cardiol* 2001;37(Suppl A):A1-64.
  35. Capucci A, Lenzi T, Boriani GM, Trisolino G, Binetti N, Cavazza L, et al. Effectiveness of loading oral flecainide for converting recent onset atrial fibrillation to sinus rhythm in patients without organic heart disease or only systemic hypertension. *Am J Cardiol* 1992;70:69-72.
  36. Vardas PE, Kochiadakis GE, Igoumenidis NE, Tsatsakis AM, Simantirakis EN, Chlouverakis GI. Amiodarone as a first-choice drug for restoring sinus rhythm in patients with atrial fibrillation: a randomized, controlled study. *Chest* 2000;117:1538-45.
  37. Kochiadakis GE, Igoumenidis NE, Simantirakis EN, Marketou ME, Parthenakis FI, Mezilis NE, et al. Intravenous propafenone versus intravenous amiodarone in the management of atrial fibrillation of recent onset: a placebo-controlled study. *Pacing Clin Electrophysiol* 1998;21:2475-9.
  38. Donovan KD, Power BM, Hockings BE, Dobb GJ, Lee KY. Intravenous flecainide versus amiodarone for recent-onset atrial fibrillation. *Am J Cardiol* 1995;75:693-7.
  39. Kerin NZ, Faitel K, Naini M. The efficacy of intravenous amiodarone for the conversion of chronic atrial fibrillation. Amiodarone vs quinidine for conversion of atrial fibrillation. *Arch Intern Med* 1996;156:49-53.
  40. Galve E, Rius T, Ballester R, Artaza MA, Arnau JM, Garcia-Dorado D, et al. Intravenous amiodarone in treatment of recent-onset atrial fibrillation: results of a randomized, controlled study. *J Am Coll Cardiol* 1996;27:1079-82.
  41. Roy D, Talajic M, Dorian P, Connolly S, Eisenberg MJ, Green M, et al. Amiodarone to prevent recurrence of atrial fibrillation. *N Engl J Med* 2000;342:913-20.
  42. Schumacher B, Lüderitz B. Rate issues in atrial fibrillation: consequences of tachycardia and therapy for rate control. *Am J Cardiol* 1998;82:N29-36.
  43. Roberts SA, Díaz C, Nolan PE, Salerno DM, Stapczynski JS, Zbrozek AS, et al. Effectiveness and costs of digoxin treatment for atrial fibrillation and flutter. *Am J Cardiol* 1993;72:567-73.
  44. Falk RH, Leavitt JJ. Digoxin for atrial fibrillation: a drug whose time has gone? *Ann Intern Med* 1991;114:573-5.
  45. Roth A, Harrison E, Mitani G, Cohen J, Rahimtoota SH, Elkayam U. Efficacy and safety of medium and high-dose diltiazem alone and in combination with digoxin for control of heart rate at rest and during exercise in patients with chronic atrial fibrillation. *Circulation* 1986;73:316-24.
  46. Atwood JE, Myers JN, Sullivan MJ, Forbes SM, Pewen WF, Froelicher VF. Diltiazem and exercise performance in patients with chronic atrial fibrillation. *Chest* 1988;93:20-5.
  47. Dibianco R, Morganroth J, Freitag JA, Ronan JA Jr, Lindgren KM, Donohue DJ, et al. Effects of nadolol on the spontaneous and exercise-provoked heart rate of patients with chronic atrial fibrillation receiving stable dosages of digoxin. *Am Heart J* 1984;108:1121-7.
  48. Segal JB, McNamara RL, Miller MR, Kim N, Goodman SN, Powe NR, et al. The evidence regarding the drugs used for ventricular rate control. *J Fam Pract* 2000;49:47-59.
  49. Lewis RV, McMurray J, McDevitt DG. Effects of atenolol, verapamil, and xamoterol on heart rate and exercise tolerance in digitalised patients with chronic atrial fibrillation. *J Cardiovasc Pharmacol* 1989;13:1-6.
  50. Blumgart H. The reaction to exercise of the heart affected by auricular fibrillation. *Heart* 1984;11:49-56.
  51. Schreck DM, Rivera AR, Tricarico VJ. Emergency management of atrial fibrillation and flutter: intravenous diltiazem versus intravenous digoxin. *Ann Emerg Med* 1997;29:135-40.
  52. Dorian P, Jung W, Newman D, Paquette M, Wood K, Ayers GM, et al. The impairment of health-related quality of life in patients with intermittent atrial fibrillation: implications for the assessment of investigational therapy. *J Am Coll Cardiol* 2000;36:1303-9.
  53. Falk RH. Proarrhythmia in patients treated for atrial fibrillation and flutter. *Ann Intern Med* 1992;117:141-50.
  54. Friedman PL, Stevenson WG. Proarrhythmia. *Am J Cardiol* 1998;82:N50-8.
  55. Waldo A. AFFIRM First Antiarrhythmic Drug Study. 23rd Annual Scientific Sessions of the North American Society of Pacing and Electrophysiology, San Diego, 2002.
  56. Anderson JL, Gilbert EM, Alpert BL, Paquette M, Wood K, Ayers GM, et al. Prevention of symptomatic recurrences of paroxysmal atrial fibrillation in patients initially tolerating antiarrhythmic therapy: a multicenter, double blind, crossover study of flecainide and placebo with transtelephonic monitoring. *Circulation* 1989;80:1557-70.
  57. Alliot E, Denjoy I and the Flecainide AF French Study Group. Comparison on the safety and efficacy of flecainide versus propafenone in hospital out-patients with symptomatic paroxysmal atrial fibrillation/flutter. *Am J Cardiol* 1996;77:66-71.
  58. Conolly SJ. Evidence-based analysis of amiodarone efficacy and safety. *Circulation* 1999;100:2025-34.
  59. Waldo AL, Camm AJ, DeRuyter H, Friedman PL, McNeil DJ, Paulus JF, et al for the SWORD Investigators. Effect of d-Sotalol on mortality in patients with left ventricular dysfunction after myocardial infarction. *Lancet* 1996;348:7-12.
  60. Coplen SE, Antman EM, Berlin JA, Hewitt P, Chalmers TC. Efficacy and safety of quinidine therapy for maintenance of sinus rhythm after cardioversion: a meta-analysis of randomized controlled trials. *Circulation* 1990;82:1106-16.
  61. Singh S, Zoble RG, Yellen L, Brodsky MA, Feld GK, Berk M, et al. Efficacy and safety of oral dofetilide in converting to and maintaining sinus rhythm in patients with chronic atrial fibrillation or atrial flutter: the symptomatic atrial fibrillation investigative research on dofetilide (SAFIRE-D) study. *Circulation* 2000;102:2385-90.
  62. Hart RG, Benavente O, McBride R, Pierce LA. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. *Ann Intern Med* 1999;131:492-501.
  63. Fatkin D, Kuchar DL, Thoburn CW, Feneley MP. Transesophageal echocardiography before and during direct current cardioversion of atrial fibrillation: evidence for «atrial stunning» as a mechanism of thromboembolic complications. *J Am Coll Cardiol* 1994;23:307-16.
  64. Hart RG, Pearce LA, Rothbart RM, McAnulty JH, Asinger RW, Halperin JL, for the Stroke Prevention in Atrial Fibrillation. Stroke with intermittent atrial fibrillation: incidence and predictors during aspirin therapy. *Stroke Prevention in Atrial Fibrillation Investigators. J Am Coll Cardiol* 2000;35:183-7.
  65. Albers GW, Dalen JE, Laupacis A, Manning WJ, Petersen P, Singer DE. Antithrombotic therapy in atrial fibrillation. *Chest* 2001;119:S194-206.
  66. Biblo LA, Yuan Z, Quan KJ, Mackall JA, Rimm AA. Risk of stroke in patients with atrial flutter. *Am J Cardiol* 2001;87:346-9.
  67. Arnold AZ, Mick MJ, Mazurek MP, Loop FD, Trohman RG. Role of prophylactic anticoagulation for direct current cardioversion in patients with atrial fibrillation and flutter. *J Am Coll Cardiol* 1992;19:851-5.

68. Naccarelli GV, Dell'Orfano JT, Wolbrete DL, Patel HM, Luck JC. Cost-effective management of acute atrial fibrillation: role of rate control, spontaneous cardioversion, medical, and direct current cardioversion, transesophageal ecocardiography, and antiembolic therapy. *Am J Cardiol* 2000;85:D36-45.
69. Klein EA. Assessment of cardioversion using transesophageal ecocardiography (TEE) multicenter study (ACUTE I): Clinical outcomes at eight weeks. *J Am Coll Cardiol* 2000;36:324.
70. Murray RD, Deitcher SR, Shah A, Jasper SE, Bashir M, Grimm RA, et al. Potential clinical efficacy and cost benefit of a transe-sophageal echocardiography-guided low-molecular-weight hepa-tin (enoxaparin) approach to antithrombotic therapy in patients undergoing immediate cardioversion from atrial fibrillation. *J Am Soc Ecocardiography* 2001;14:200-8.
71. Adjusted-dose warfarin versus low-intensity, fixed-dose warfarin plus aspirin for high-risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial. *Lancet* 1996;342:633-8.
72. Hylek EM, Singer DE. Risk factors for intracranial hemorrhage in outpatients taking warfarin. *Ann Intern Med* 1994;120:897-902.
73. Atrial Fibrillation Investigators. Risk factors for stroke and effi-cacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. *Arch Intern Med* 1994;154:1449-57.
74. Sudlow M, Thomson R, Thwaites B, Rodgers H, Kenny RA. Prevalence of atrial fibrillation and elegibility for anticoagulants in the community. *Lancet* 1998;352:1167-71.
75. Hart RG, Pearce LA, McBride R, Rothbart RM, Asinger RW, on behalf of the Stroke Prevention in Atrial Fibrillation (SPAF) Investigators. Factors associated with ischemic stroke during as-pirin therapy in atrial fibrillation. Analysis of 2012 participants in the SPAF I-III clinical trials. *Stroke* 1999;30:1223-9.