

Acute Management of Atrial Fibrillation: Part II. Prevention of Thromboembolic Complications

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Family physicians should be familiar with the acute management of atrial fibrillation and the initiation of chronic therapy for this common arrhythmia. Initial management should include hemodynamic stabilization, rate control, restoration of sinus rhythm, and initiation of antithrombotic therapy. Part II of this two-part article focuses on the prevention of thromboembolic complications using anticoagulation. Heparin is routinely administered before medical or electrical cardioversion. Warfarin is used in patients with persistent atrial fibrillation who are at higher risk for thromboembolic complications because of advanced age, history of coronary artery disease or stroke, or presence of left-sided heart failure. Aspirin is preferred in patients at low risk for thromboembolic complications and patients with a high risk for falls, a history of non-compliance, active bleeding, or poorly controlled hypertension. The recommendations provided in this article are consistent with guidelines published by the American Heart Association and the Agency for Healthcare Research and Quality. (Am Fam Physician 2002;66:261-4,271-2. Copyright© 2002 American Academy of Family Physicians.)

 A patient information handout on atrial fibrillation, written by the authors of this article, is provided on page 271.

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This is part II of a two-part article on atrial fibrillation. Part I, "Rate and Rhythm Control," appears in this issue on pages 249-56.

Atrial fibrillation is the underlying cause of 30,000 to 40,000 embolic strokes per year in the United States.¹ The incidence of these strokes increases with age, rising from 1.5 percent in patients aged 50 to 59 years to 23.5 percent in patients aged 80 to 89 years.²

Although comorbid conditions such as hypertension and vascular disease are factors, the predominant cause of strokes in patients with atrial fibrillation is embolization of a clot from the left atrium. When evaluated using transesophageal echocardiography, up to 30 percent of patients with atrial fibrillation and embolic stroke are found to have atrial thrombi within 72 hours of the stroke.^{3,4} Risk factors for stroke in patients with atrial fibrillation include a history of transient ischemic attack or stroke, age greater than 65 years, a history of hypertension, the presence of a

prosthetic heart valve (mechanical or tissue), rheumatic heart disease, left ventricular systolic dysfunction, or diabetes.

Most atrial fibrillation–derived strokes occur within the first 72 hours after medical (pharmacologic) or electrical cardioversion. The risk of stroke is significant for both rhythm conversion methods and is presumed to be due to the presence of left atrial thrombi at the time of cardioversion, rather than to the method used.² These data offer compelling support for the use of antithrombotic therapy with heparin, warfarin (Coumadin), or aspirin in patients with atrial fibrillation, unless specific contraindications exist.

Anticoagulant Drugs

HEPARIN

Heparin is the preferred agent for initial anticoagulation because it provides almost immediate effects and can be discontinued rapidly if bleeding complications arise.⁵ The drug should be given as a continuous intravenous infusion, with the dose titrated to achieve an activated partial thromboplastin time of 1.5 to 2.5 times the baseline value.

Heparin should not be used in patients with signs of active bleeding. In addition, its use in patients with acute embolic stroke is contro-

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versial and should be guided by the results of transesophageal echocardiography to detect atrial thrombi.⁶

In patients with atrial fibrillation that has persisted for more than 48 hours, heparin can be used to reduce the risk of thrombus formation and embolization until the warfarin level is therapeutic or cardioversion is performed. Prevention of deep venous thrombosis and pulmonary embolism are potential added benefits of initial anticoagulation with heparin.

Low-molecular-weight heparins such as enoxaparin (Lovenox) and dalteparin (Fragmin) have not been studied extensively in patients with atrial fibrillation. However, low-molecular-weight heparin are easier to use than standard unfractionated heparin, and anticoagulation with these agents may facilitate early hospital discharge. Studies are currently being performed to evaluate anticoagulation with low-molecular-weight heparins before and after cardioversion in patients with atrial fibrillation.⁷

WARFARIN

Chronic warfarin therapy is commonly used to prevent thromboembolic complications in patients with atrial fibrillation. Warfarin acts by inhibiting the production of vitamin K–dependent clotting factors, thereby prolonging the prothrombin time.⁸

Warfarin therapy is monitored using the International Normalized Ratio (INR), which is derived from the prothrombin time. Treatment is challenging because of the narrow therapeutic window for efficacy and the risk of major bleeding (e.g., intracranial hemorrhage). Therefore, it is important to consider risk versus benefit before warfarin is prescribed. Risk factors for major bleeding include poorly controlled hypertension, propensity for falling, dietary factors, interactions with concomitant medications, and difficulty controlling the degree of anticoagulation because of patient noncompliance.^{9,10} To ensure efficacy and minimize harm, the INR should be kept between 2.0 and 3.0.

ASPIRIN

If bleeding risk prohibits the use of warfarin, aspirin is an appropriate alternative. Aspirin acts to inhibit platelet aggregation and thrombus formation by irreversibly inhibiting the production of cyclooxygenase and thromboxane.¹¹ Compared with warfarin, aspirin is slightly less effective in preventing stroke in patients with atrial fibrillation, but it is safer in patients at high risk for bleeding.¹²

TABLE 1

Recommendations for Antithrombotic Therapy in Cardioversion for Atrial Fibrillation

<i>Timing of cardioversion</i>	<i>Anticoagulation</i>
Early cardioversion* in patients with atrial fibrillation for less than 48 hours	Heparin during cardioversion period to achieve PTT of 1.5 to 2.5 times the baseline value
Early cardioversion* in patients with atrial fibrillation for more than 48 hours or an unknown duration, but without documented atrial thrombi	Heparin during cardioversion period to achieve PTT of 1.5 to 2.5 times the baseline value Warfarin (Coumadin) for 4 weeks after cardioversion to achieve target INR of 2.5 (range: 2.0 to 3.0)
Elective cardioversion in patients with atrial fibrillation for more than 48 hours or an unknown duration	Warfarin for 3 weeks before and 4 weeks after cardioversion to achieve target INR of 2.5 (range: 2.0 to 3.0)

PTT = partial thromboplastin time; INR = International Normalized Ratio.

**—Electrical or medical (pharmacologic) cardioversion.*

Information from references 2, 9, and 10.

OTHER ANTIPLATELET AGENTS

Other antiplatelet agents, such as ticlopidine (Ticlid), clopidogrel (Plavix), and the combination of aspirin and extended-release dipyridamole (Aggrenox), have not been studied in the prevention of embolic strokes in patients with atrial fibrillation. Hence, they are not recommended for use in these patients.

Anticoagulation During Cardioversion

EARLY CARDIOVERSION

Early medical or electrical cardioversion may be instituted without prior anticoagulation therapy when atrial fibrillation has been present for less than 48 hours. No specific data suggest significant benefit for heparin therapy in the first 48 hours of atrial fibrillation; however, heparin is routinely used.⁶

If the duration of atrial fibrillation exceeds 48 hours or is unknown, transesophageal echocardiography (to rule

out atrial thrombi) followed by early cardioversion is a clinically effective strategy.^{6,9,13} Heparin therapy should be instituted during transesophageal echocardiography. If no atrial thrombi are observed, cardioversion can be performed. If atrial thrombi are detected, cardioversion should be delayed and anticoagulation continued. To decrease the risk of thrombus extension, heparin should be continued, and warfarin therapy should be initiated. Once the INR is above 2.0, heparin can be discontinued, but warfarin should be continued for four weeks (Table 1).^{2,9,10}

If cardioversion is unsuccessful and patients remain in atrial fibrillation, warfarin or aspirin may be considered for long-term prevention of stroke.

ELECTIVE CARIOVERSION

Warfarin should be given for three weeks before elective electrical cardioversion is performed. After successful cardioversion, warfarin should be continued for four weeks to decrease the risk of new thrombus formation.^{2,9} Alternative approaches using low-molecular-weight heparins are under investigation.^{7,9}

If atrial fibrillation recurs or patients are at high risk for recurrent atrial fibrillation, warfarin may be continued indefinitely, or aspirin therapy may be considered. Factors that increase the risk of recurrent atrial fibrillation include an enlarged left atrium and left ventricular dysfunction.

Long-Term Anticoagulation

Long-term anticoagulation therapy should be considered in patients with persistent atrial fibrillation who have failed cardioversion and in patients who are not candidates for medical or electrical cardioversion. Patients with a significant risk of falling, a history of noncompliance, active bleeding, or poorly controlled hypertension should not receive long-term anticoagulation therapy because of the high risk of bleeding complications.

Several studies^{2,14,15} have evaluated the effects of aspirin, warfarin, and the combination of aspirin and warfarin for stroke prevention in patients with atrial fibrillation. Current recommendations for anticoagulant drug selection are based on the risk factors for stroke. Guidelines from the American College of Chest Physicians, the American Heart Association, and the Agency for Healthcare Research and Quality suggest that patients at highest risk for future stroke should receive warfarin and that patients at lowest risk should receive aspirin (Table 2).^{2,9,10}

Factors that significantly increase the risk for stroke

Warfarin should be given for three weeks before elective electrical cardioversion and continued for four weeks after successful cardioversion.

include previous stroke, previous transient ischemic attack or systemic embolus, hypertension, poor left ventricular systolic function, age greater than 75 years, prosthetic heart valve, and history of rheumatic mitral valve disease. With persistent atrial fibrillation, patients older than 65 years and those with diabetes are also at increased risk. The lowest risk for stroke is in patients with atrial fibrillation who are less than 65 years of age and have no history of cardiovascular disease, diabetes, or hypertension.

Overall, warfarin therapy has been shown to reduce the absolute risk of stroke by 0.8 percent per year, compared with aspirin.¹⁴ In patients with a history of stroke, warfarin

TABLE 2
Recommendations for Antithrombotic Therapy in Chronic Atrial Fibrillation

Stroke risk	Anticoagulation
High risk Previous stroke, transient ischemic attack, or systemic embolus History of hypertension Poor left ventricular systolic function Patient age > 75 years Rheumatic mitral valve disease Prosthetic heart valve	Warfarin (Coumadin) to achieve target INR of 2.5 (range: 2.0 to 3.0)
Moderate risk Patient age 65 to 75 years Diabetes mellitus Coronary artery disease with preserved left ventricular systolic function	One risk factor: warfarin to achieve target INR of 2.5 (range: 2.0 to 3.0), or aspirin (325 mg per day) More than one risk factor: warfarin
Low risk Patient age < 65 years Absence of cardiovascular disease	Aspirin (325 mg per day)

INR = International Normalized Ratio.

Information from references 2, 9, and 10.

TABLE 3

General Recommendations for Anticoagulation in Atrial Fibrillation

Heparin therapy should be considered in hospitalized patients with atrial fibrillation persisting beyond 48 hours and in patients undergoing medical (pharmacologic) or electrical cardioversion.

Antithrombotic therapy using warfarin (Coumadin) should be given for 3 weeks before cardioversion and 4 weeks after successful cardioversion.

Patients with persistent or recurrent atrial fibrillation after attempted cardioversion should be given chronic warfarin or aspirin therapy for stroke prevention.

Warfarin is the preferred agent in patients at high risk for stroke because of previous stroke, age over 75 years, and/or poor left ventricular function.

Aspirin is the preferred agent in patients at low risk for stroke and in patients with a risk of falling, history of noncompliance, active bleeding, and/or poorly controlled hypertension.

Information from references 2, 9, and 10.

reduces the absolute risk of stroke by 7 percent per year.¹⁴ In recent meta-analyses,^{14,15} all-cause mortality was similar in patients receiving warfarin and aspirin. A meta-analysis¹⁰ of studies involving patients with atrial fibrillation but no history of stroke found that warfarin would prevent 30 strokes at the expense of six additional major bleeding episodes. Aspirin would prevent 17 strokes without increasing the incidence of major hemorrhage. No difference in mortality was found for anticoagulation with aspirin or warfarin.¹⁰

Evidence on stroke prevention using combined low-dose warfarin and aspirin or using low-molecular-weight heparin has been inconclusive. Combination therapy is not currently recommended.¹⁰

The price of stroke prevention is an added risk of major bleeding and intracranial hemorrhage. Compared with aspirin, warfarin is associated with a 0.3 percent increase in the risk of major bleeding and a 0.9 percent increase in the risk of intracranial hemorrhage.¹⁴ The risk of major bleeding increases dramatically with age over 75 years and when

the INR is above 4.0. Blood pressure control (i.e., maintaining systolic pressure below 160 mm Hg) is imperative to reducing the risk of intracranial hemorrhage in patients taking warfarin.⁹

General recommendations for anticoagulation in patients with atrial fibrillation are summarized in *Table 3*.^{2,9,10}

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