

Management of atrial fibrillation in the emergency department and following acute myocardial infarction

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Atrial fibrillation (AF) is the most common arrhythmia managed by emergency physicians and there is increasing evidence that selected patients with acute AF can be safely managed in the emergency department without the need for hospital admission. The principles of management are identification and treatment of precipitating or underlying causes, hemodynamic stabilization/rate control, reduction of thromboembolism risk and the conversion/maintenance of sinus rhythm.

A strategy of rate or rhythm control should be chosen based on the patient's clinical status, the duration of AF, the experience of the treating physician and the status of anticoagulation.

Before either electric or pharmacological cardioversion, anticoagulation should be considered. Most patients should be given heparin or low molecular weight heparin while preparing for cardioversion. All patients should be considered for long-term anticoagulation based on their thromboembolic risk and bleeding risk from antithrombotic therapy. Following restoration of sinus rhythm, a decision regarding the use of antiarrhythmic drugs should be made based on the estimated frequency of recurrence and degree of symptoms.

In the setting of acute myocardial infarction, beta-blockers should be administered whenever possible. If beta-blockers are contraindicated, the rate can be slowed with digoxin or amiodarone. Cardioversion should be performed if the patient is hemodynamically unstable. Class IC antiarrhythmic drugs should not be administered in this setting.

Key Words: Anticoagulation; Atrial fibrillation; Electrical cardioversion; Emergency department; Myocardial infarction

RECOMMENDATIONS FOR THE MANAGEMENT OF ATRIAL FIBRILLATION IN THE EMERGENCY DEPARTMENT

Class I

- 1) In stable patients with a duration of atrial fibrillation (AF) greater than 48 h or of uncertain duration in whom a decision has been made to attempt cardioversion, optimize rate control and anticoagulate to an international normalized ratio (INR) of 2.0 to 3.0 for three weeks before cardioversion (level of evidence C).
- 2) In patients with a duration of AF greater than 48 h or of uncertain duration who are highly symptomatic after efforts to achieve adequate rate control, transesophageal echocardiography (TEE) to exclude atrial thrombus can be considered before cardioversion (level of evidence B).

Le traitement de la fibrillation auriculaire au service d'urgence et après un infarctus aigu du myocarde

La fibrillation auriculaire (FA) est le trouble du rythme le plus fréquent, traité par les urgentologues, et, selon des données de plus en plus nombreuses, il est possible de traiter en toute sécurité des épisodes aigus de FA au service d'urgence, sans recourir à l'hospitalisation, chez certains patients. Le traitement repose sur quatre grands principes : la recherche et le traitement des causes déclenchantes ou des causes sous-jacentes, la stabilisation hémodynamique et la maîtrise de la fréquence cardiaque, la diminution du risque de thrombo-embolie, ainsi que le rétablissement et le maintien du rythme sinusal.

Il faudrait choisir une stratégie de traitement entre la maîtrise de la fréquence cardiaque et la maîtrise du rythme cardiaque selon l'état clinique du patient, la durée de la FA, l'expérience du médecin traitant et le degré d'anticoagulation.

Il faudrait envisager un traitement anticoagulant avant de procéder à la cardioversion électrique ou médicamenteuse. On devrait administrer à la plupart des patients soit de l'héparine ordinaire, soit de l'héparine de faible masse moléculaire pendant la préparation à la cardioversion. L'anticoagulation devrait être envisagée à long terme chez tous les patients, compte tenu du risque de thrombo-embolie et du risque de saignement associé au traitement antithrombotique. Une fois que le rythme sinusal a été rétabli, il faudrait prendre une décision quant à l'emploi d'antiarythmiques, selon la fréquence prévue des récidives et l'intensité des symptômes.

Dans les cas d'infarctus aigu du myocarde, il faudrait administrer des bêta-bloquants chaque fois que c'est possible. Si les bêta-bloquants sont contre-indiqués, on peut ralentir la fréquence cardiaque par la digoxine ou l'amiodarone. La cardioversion est souhaitable chez les patients se trouvant dans un état instable sur le plan hémodynamique. Enfin, les antiarythmiques de classe IC ne devraient pas être prescrits dans le présent contexte.

- 3) Select a strategy of rate control or rhythm control based on symptoms and clinical variables (see text; level of evidence B).
- 4) When a decision is made to cardiovert patients with an AF duration of less than 48 h, synchronized electrical cardioversion or pharmacological cardioversion may be used. See Talajic and Roy, pages 19B-25B (level of evidence C).
- 5) When electrical cardioversion is chosen, use biphasic waveform when available to increase success and reduce cardioversion energy (level of evidence B).
- 6) After acute conversion of an episode of AF or atrial flutter, long-term antithrombotic therapy should be prescribed based on thromboembolic risk and bleeding risk from antithrombotic therapy. See Connolly and Gillis, pages 71B-73B (level of evidence A).

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- 7) In patients with AF and pre-excitation, perform urgent cardioversion if the patient is hemodynamically unstable. If stable, consider using class I (eg, procainamide) or class III (eg, ibutilide) antiarrhythmic agents (level of evidence C).
- 8) Hospital admission can be limited to highly symptomatic patients, those with structural heart disease, those who have had an embolic event or those at high risk for thromboembolism, and those with failure of rate control in the emergency department (ED) (level of evidence C).

Class IIa

- 1) Anticoagulation therapy with either unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) should be considered for most patients presenting to the ED with AF. Exceptions include those already on warfarin with an INR greater than 2.0, or those in whom the short-term risk of bleeding on anticoagulation therapy is thought to exceed the risk of thromboembolism (level of evidence C).
- 2) After conversion to sinus rhythm has been achieved, decide whether antiarrhythmic drug therapy is indicated based on the estimated probability of recurrence and the symptoms during AF (level of evidence C).

Class III

- 1) Do not administer digoxin, calcium channel blocking agents or beta-blocking agents alone to patients with pre-excitation during AF (level of evidence B).
- 2) Do not administer adenosine to attempt rate control or cardioversion during AF (level of evidence B).

RECOMMENDATIONS FOR THE MANAGEMENT OF PATIENTS WITH AF AND ACUTE MYOCARDIAL INFARCTION

Class I

- 1) Use electrical cardioversion for patients requiring urgent restoration of sinus rhythm for hemodynamic reasons (level of evidence C).
- 2) Administer beta-blockers to slow a rapid ventricular response in patients without contraindication to beta-blockers. Diltiazem may be used as an alternative. These agents may be given orally or intravenously, depending on the urgency (level of evidence C).
- 3) Administer intravenous digitalis or amiodarone to slow a rapid ventricular response in patients with impaired left ventricular (LV) function (level of evidence C).
- 4) Administer heparin for patients with AF and acute myocardial infarction (MI), unless contraindicated (level of evidence C).

Class III

- 1) Do not administer class IC antiarrhythmic drugs in patients with AF in the setting of acute MI (level of evidence C).

INTRODUCTION

AF accounts for approximately one-third of hospital admissions for cardiac arrhythmias, and is the most common arrhythmia managed by emergency physicians (1). The incidence of AF is steadily increasing, likely owing mainly to the increasing age of the population (2). There is increasing evidence that selected patients with acute AF can be safely managed in the ED without the need for hospital admission (3,4).

There exists a wide range of management practices regarding patients with AF, which highlights the need for evidence-based consensus guidelines for the management of these patients (5).

CLASSIFICATION OF AF

There is no universal consensus on the classification of AF, but a clinically useful and widely used classification exists in the American College of Cardiology/American Heart Association/European Society of Cardiology practice guidelines for the management of AF (6). In this classification, paroxysmal AF is self-terminating, and persistent AF requires treatment for termination. In permanent AF, sinus rhythm cannot be maintained after cardioversion of AF or a decision has been made to leave the patient in AF.

The term 'lone AF' refers to AF in the absence of demonstrable underlying cardiovascular disease (eg, coronary artery disease, valvular disease, heart failure and cardiomyopathy) or a history of hypertension. Physicians frequently overlook hypertension as a cause of AF, and patients should not be labelled as having 'lone AF' in the presence of a history of hypertension. 'Lone AF' occurs in 3% to 35% of AF cases, depending on the population studied (7).

AF occurring in the setting of Wolff-Parkinson-White (WPW) syndrome deserves special mention because rapid atrioventricular conduction through the accessory pathway may precipitate ventricular fibrillation (VF). In these patients, drugs that block atrioventricular conduction (digoxin, beta-blockers and nondihydropyridine calcium channel blockers) are relatively contraindicated because they do not slow conduction through the accessory pathway and, therefore, may precipitate VF.

MANAGEMENT PRINCIPLES IN PATIENTS WHO PRESENT TO THE ED WITH AF

The principles of management are identification and treatment of precipitating or underlying causes, hemodynamic stabilization/rate control, reduction of thromboembolism risk, and conversion/maintenance of sinus rhythm.

In all patients presenting to the ED with acute AF, consideration should be given to the establishment of an intravenous line, continuous electrocardiographic monitoring and supplemental oxygen if needed. Most patients should have their hemoglobin, electrolytes and creatinine checked, with additional tests as indicated by special circumstances.

Identification and treatment of precipitating or underlying causes

AF may be related to acute temporary causes such as alcohol use ('holiday heart syndrome'), surgery, electrocution, MI, myocarditis, pericarditis, pulmonary embolism or other pulmonary diseases, and hyperthyroidism and other metabolic disorders (1). Successful treatment of these underlying conditions may result in the resolution of the AF.

Other supraventricular tachycardias or WPW syndrome may be associated with AF, and treatment of these dysrhythmias

may reduce the frequency of AF recurrence. AF is a common postoperative complication of both cardiac and noncardiac surgery.

The initial evaluation of AF should include characterization of the arrhythmia as paroxysmal or persistent if possible, determining the cause and defining associated cardiac and extracardiac factors.

Hemodynamic stabilization/rate control

The heart rate is generally considered controlled when it is between 60 beats/min and 80 beats/min at rest (6), but rates of up to 100 beats/min are usually well tolerated. Overly aggressive rate control can risk causing symptomatic bradycardia. Adenosine is only briefly effective for rate control in AF, owing to its very short duration of action of only a few seconds. It does not cardiovert the patient and is associated with a significant risk of causing serious ventricular arrhythmias in WPW syndrome patients with AF.

Drugs used for rate control include beta-blockers (eg, metoprolol, esmolol), calcium channel blockers (eg, diltiazem, verapamil), digoxin and amiodarone. The selection of a beta-blocker or calcium channel blocker should be based on the patient's clinical condition and the physician's experience. Beta-blockers are preferable for acute MI, ischemic heart disease and 'holiday heart syndrome', but contraindicated for asthma. Beta-blockers and calcium channel blockers are both relatively contraindicated for WPW syndrome and decompensated heart failure. Beta-blockers may be very effective for rate control in compensated heart failure, although clinical trials verifying this have not been performed.

Digoxin is often inappropriately used as a first-line agent for rate control despite the fact that it has some important limitations (8). These limitations include the fact that it has little or no effect in terminating AF, and that it may promote AF by shortening the atrial refractory period (9). Peak systemic levels are not achieved for up to 6 h, and there is a delay of the effect on heart rate reduction of at least 1 h in most patients (10-14). Because the effect of digoxin is predominantly mediated by enhanced vagal tone, it is less effective for rate control in patients with high sympathetic tone. However, digoxin may be a useful adjunctive agent when used in conjunction with beta-blockers or nondihydropyridine calcium channel blockers, allowing lower doses of these drugs to be used (eg, in patients with LV systolic dysfunction).

Reduction of thromboembolism risk

Most patients presenting to the ED with AF should be considered for anticoagulation therapy with either UFH or LMWH. Exceptions include those patients already on warfarin with a therapeutic INR greater than 2.0, or those in whom the short-term bleeding risk from anticoagulation is believed to exceed the risk of thromboembolism. Anticoagulation therapy should be used regardless of the method (chemical or electrical) used to restore sinus rhythm (6).

An AF duration of 48 h is considered the point beyond which the thromboembolic risk of acute conversion is considered significant. These patients require a minimum of three weeks of anticoagulation therapy with warfarin to an INR of greater than 2.0 before attempted cardioversion; for three weeks before anticoagulation therapy, antiarrhythmic drugs (eg, amiodarone, sotalol and propafenone) should be avoided. An alternative strategy is the use of TEE to guide

cardioversion (15-20). The absence of atrial thrombus at the time of TEE does not remove the need for subsequent anticoagulation.

Following cardioversion, most patients should be considered for warfarin anticoagulation therapy (to a goal INR of 2.0 to 3.0) for a minimum of one month, and possibly indefinitely. The decision regarding the duration of anticoagulation should take into account patient preference, the risk of AF recurrence, the risk of thromboembolism and the risk of bleeding from anticoagulation therapy.

Following acute cardioversion, the decision to anticoagulate with UFH or LMWH before attainment of a therapeutic INR with warfarin is controversial. Warfarin, when used alone, may theoretically increase the risk of thromboembolism in the first few days following initiation because it antagonizes protein C. In most patients, however, the risks and inconvenience of UFH or LMWH therapy for an average of two to seven days (the general time needed to attain a therapeutic INR) outweigh their benefits, except in patients with a very high risk of thromboembolism.

Conversion/maintenance of sinus rhythm

In hemodynamically unstable patients (eg, acute coronary syndromes, hypotension or pulmonary edema), consideration should be given to acute electrical cardioversion; however, AF seldom causes significant hemodynamic compromise in the absence of significant underlying cardiac disease, and electrical cardioversion in these patients will usually only be of modest benefit unless the ventricular rate is particularly fast (greater than 140 beats/min) (6). Additionally, cardioversion may be unsuccessful (or only briefly successful) unless the underlying cardiovascular problem is successfully treated. Patients with severe underlying cardiovascular disease often have permanent AF, with rapid rates during acute decompensation.

Although the results of two recent large clinical trials (21,22) suggest that many patients with persistent AF are best treated with a strategy of rate control rather than rhythm control, the optimal initial strategy for patients presenting to the ED with acute-onset or recent-onset AF is controversial and has not been subjected to rigorous clinical trials.

Spontaneous conversion of AF to sinus rhythm within 24 h is common, occurring in up to two-thirds of patients (23-25). The decision regarding the timing and method (chemical or electrical) of cardioversion depends on a number of factors, including patient and physician preference, expertise and available facilities.

Chemical cardioversion is simpler but less efficacious than electrical cardioversion, being successful in approximately 50% to 80% of patients presenting to the ED with recent-onset AF. Electrical cardioversion is effective in approximately 80% to 90% of similar patients (26-28), but requires intravenous sedation. Patients in whom chemical cardioversion is unsuccessful can be considered for electrical cardioversion.

Options for oral chemical cardioversion include propafenone, flecainide and amiodarone. Oral amiodarone is less effective for early cardioversion, but may result in cardioversion at a later time. Sotalol has not been shown to be more effective than placebo in effecting cardioversion, but has been shown to maintain sinus rhythm (2). Intravenous options include procainamide, ibutilide and amiodarone.

All patients undergoing electrical or chemical cardioversion require continuous electrocardiographic monitoring

and temporary pacing capability. Standard drugs used for cardiac resuscitation need to be readily available.

The decision to initiate maintenance antiarrhythmic therapy following conversion to sinus rhythm should involve consideration of the likelihood of recurrence of AF and the risks of antiarrhythmic drug therapy. Outpatient (rather than inpatient) initiation of antiarrhythmic drug therapy is controversial but may be considered for patients who are asymptomatic, have a normal QT interval and have no significant underlying structural or ischemic cardiovascular diseases (3,4,29-31). Amiodarone, however, appears to be safer than other antiarrhythmic agents and may be considered for outpatient initiation in patients with structural heart disease, including LV dysfunction (see Talajic and Roy, pages 19B-25B, Drugs for Termination and Maintenance of Sinus Rhythm). Hemodynamically stable patients with WPW syndrome and AF of a duration less than 48 h are best managed with class I (eg, procainamide) or class III (eg, ibutilide) agents.

ELECTRICAL CARIOVERSION

The efficacy of cardioversion depends on the nature of the underlying heart disease and the current density delivered to the atria. Large paddles result in lower impedance than smaller ones, but when the paddles are too large, the current density through the cardiac tissue is insufficient to cause cardioversion, whereas smaller paddles may produce too much current density and cause injury. A paddle or gel-electrode diameter of 8 cm to 12 cm is generally recommended (6). If paddles are used, then firm-chest-wall pressure will maximize the delivered current and minimize the potential for a cutaneous electrical burn.

Synchronization of the electrical discharge with the intrinsic cardiac rhythm is necessary to ensure that the vulnerable phase of the cardiac cycle (80 ms before to 30 ms after the apex of the T wave) is avoided, thus reducing the risk of precipitating ventricular tachycardia or VF. Because all currently available external cardioverter/defibrillators revert to the unsynchronized mode after each shock, they need to be changed back to synchronized mode before delivery of the next shock.

The optimum electrode positioning is controversial, but the evidence suggests that the anterior-posterior position is more effective for cardioversion, despite the fact that the impedance is greater with this approach because of the greater distance between the electrodes (6,32-34).

When the resting heart rate is relatively slow (less than 60 beats/min), atropine can be given before cardioversion to reduce the risk of postprocedural bradycardia; however, there are no published data to support this practice.

In patients scheduled for elective outpatient electrical cardioversion, frequent INR monitoring to ensure that the INR is consistently in the therapeutic range (2.0 to 3.0) will reduce the risk of thromboembolism.

Biphasic cardioverters/defibrillators have been shown to be more efficacious than monophasic devices (35-37). Because biphasic devices require delivery of a much lower energy for cardioversion, the potential for cutaneous and cardiac injury is reduced with these devices. As a general rule, biphasic devices require delivery of approximately one-half the energy of monophasic devices to effect cardioversion.

There is a general tendency for physicians to underdose the delivered energy when attempting to cardiovert patients. This can result in higher cumulative doses (if multiple attempts are

required), longer sedation times and more 'unsuccessful' cardioversions. The literature suggests that the most appropriate initial dose is 100 joules biphasic (or 200 joules monophasic). Higher initial doses should be considered if a higher dose was required on a previous successful attempt. Lower initial doses should be considered for frail, low body weight, elderly and postoperative patients.

CRITERIA FOR HOSPITAL ADMISSION

Hospital admission can be limited to highly symptomatic patients, those with structural heart disease, those who have had an embolic event or are at high risk for thromboembolism, and those with failure of rate control in the ED (3,4,30,31).

Inpatient electrocardiographic monitoring may also be required for high-risk patients (eg, advanced age and renal failure) who, following cardioversion, are started on oral antiarrhythmic therapy with high proarrhythmia potential (eg, sotalol).

Patients with noncardiac causes of AF (eg, pneumonia) may require admission for investigation and treatment of the underlying condition.

PATIENTS WITH AF AND ACUTE MI

The incidence of AF with acute MI in the modern era has been reported to be between 10.4% and 22% (38-40). Older age, higher Killip class, ventricular dysfunction and extent of ischemic burden are generally acknowledged as the major risk factors for AF (39,41-46). AF is associated with increased mortality (39) and a higher stroke rate (40).

Measures directed at reducing infarct size, ischemia and preserving LV function according to current standards would be expected to reduce the incidence of AF, as was demonstrated by angiotensin-converting enzyme inhibition (38). With a paucity of controlled trials evaluating therapy for AF in the setting of acute MI, current therapy is largely guided by consensus and therapeutic strategies recommended for AF in the general context (41).

There is no proven benefit of a rhythm-control strategy over a rate-control strategy; such decisions must be individualized. Rate control with beta-blockers is preferable when feasible because of the general benefits of beta-blockers in ischemic syndromes, but calcium channel blockers and digitalis are also acceptable. Intravenous and oral amiodarone are useful for rate control, especially when other rate control agents are relatively or absolutely contraindicated, such as with bronchospasm or heart failure. Intravenous and oral amiodarone are also useful for rhythm control (46,47).

Electrical cardioversion is the treatment of choice when acute restoration of sinus rhythm is desirable for hemodynamic improvement. Ibutilide has shown efficacy in acute restoration of sinus rhythm with atrial flutter and, to a lesser extent, with AF (48-50). Its use in acute MI has not been specifically and extensively evaluated but it is safe and effective in AF of relatively recent onset in critical care settings and after cardiac surgery. Serious adverse effects have been reported in patients with congestive heart failure (51). In the future, it is possible that ibutilide will have a greater role in the conversion of AF in the setting of acute MI.

The use of class I antiarrhythmics and sotalol were associated with lower unadjusted one year mortality in patients with AF in the global use of strategies to open occluded coronary arteries (GUSTO)-III trial (46). Class IC drugs are

not generally recommended in ischemic syndromes (52). Sotalol and amiodarone are efficacious for rhythm control, with amiodarone associated with a low proarrhythmia risk and no significant negative inotropic effect. Dofetilide (53,54) is not currently approved in Canada, but has shown safety and efficacy in rhythm control in patients with ventricular dysfunction after MI. Heparin is generally used in AF with acute MI, and long-term anticoagulation with persistent or permanent AF is dictated by the presence of established risk factors (55).

The recommendations are generally based on consensus and do not differ appreciably from those recommended by the American College of Cardiology/American Heart Association/European Society of Cardiology (41). The recommendations in the present article are directed at management issues in AF that are unique to a context of acute MI, with general recommendations otherwise applicable.

REFERENCES

- Bialy D, Lehmann MH, Schumacher DN, Steinman RT, Meissner MD. Hospitalization for arrhythmias in the United States: Importance of atrial fibrillation. *J Am Coll Cardiol* 1992;19:41A. (Abst)
- Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). *Am J Cardiol* 1994;74:236-41.
- Maisel WH, Kuntz KM, Reimold SC, et al. Risk of initiating antiarrhythmic drug therapy for atrial fibrillation in patients admitted to a university hospital. *Ann Intern Med* 1997;127:281-4.
- Prystowsky EN. Inpatient versus outpatient initiation of antiarrhythmic drug therapy for patients with supraventricular tachycardia. *Clin Cardiol* 1994;17(Suppl 2):II7-10.
- Wakai A, O'Neill JO. Emergency management of atrial fibrillation. *Postgrad Med J* 2003;79:313-9.
- Fuster V, Ryden LE, Asinger RW, et al; American College of Cardiology; American Heart Association; European Society of Cardiology; North American Society of Pacing and Electrophysiology. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation. 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 (Committee to develop guidelines for the management of patients with atrial fibrillation) developed in collaboration with the North American Society of Pacing and Electrophysiology. *Eur Heart J* 2001;22:1852-923.
- Brand FN, Abbott RD, Kannel WB, Wolf PA. Characteristics and prognosis of lone atrial fibrillation. 30-year follow-up in the Framingham Study. *JAMA* 1985;254:3449-53.
- Fang MC, Stafford RS, Ruskin JN, Singer DE. National trends in antiarrhythmic and antithrombotic medication use in atrial fibrillation. *Arch Intern Med* 2004;164:55-60.
- Falk RH, Knowlton AA, Bernard SA, Gotlieb NE, Battinelli NJ. Digoxin for converting recent-onset atrial fibrillation to sinus rhythm. A randomized, double-blinded trial. *Ann Intern Med* 1987;106:503-6.
- Lewis RV, Laing E, Moreland TA, Service E, McDevitt DG. A comparison of digoxin, diltiazem and their combination in the treatment of atrial fibrillation. *Eur Heart J* 1988;9:279-83.
- Jordaens L, Trouerbach J, Calle P, et al. Conversion of atrial fibrillation to sinus rhythm and rate control by digoxin in comparison to placebo. *Eur Heart J* 1997;18:643-8.
- Intravenous digoxin in acute atrial fibrillation. Results of a randomized, placebo-controlled multicentre trial in 239 patients. The Digitalis in Acute Atrial Fibrillation (DAAF) Trial Group. *Eur Heart J* 1997;18:649-54.
- Koh KK, Kwon KS, Park HB, et al. Efficacy and safety of digoxin alone and in combination with low-dose diltiazem or betaxolol to control ventricular rate in chronic atrial fibrillation. *Am J Cardiol* 1995;75:88-90.
- Ang EL, Chan WL, Cleland JG, et al. Placebo controlled trial of xamoterol versus digoxin in chronic atrial fibrillation. *Br Heart J* 1990;64:256-60.
- Leung DY, Davidson PM, Cranney GB, Walsh WF. Thromboembolic risks of left atrial thrombus detected by transesophageal echocardiogram. *Am J Cardiol* 1997;79:626-9.
- Stollberger C, Chnupa P, Kronik G, et al; ELAT Study Group. Transesophageal echocardiography to assess embolic risk in patients with atrial fibrillation. *Ann Intern Med* 1998;128:630-8.
- The Stroke Prevention in Atrial Fibrillation Investigators Committee on Echocardiography. Transesophageal echocardiographic correlates of thromboembolism in high-risk patients with nonvalvular atrial fibrillation. *Ann Intern Med* 1998;128:639-47.
- Zabalgaitia M, Halperin JL, Pearce LA, Blackshear JL, Asinger RW, Hart RG. Transesophageal echocardiographic correlates of clinical risk of thromboembolism in nonvalvular atrial fibrillation. Stroke Prevention in Atrial Fibrillation III Investigators. *J Am Coll Cardiol* 1998;31:1622-6.
- Jones EF, Calafiore P, McNeil JJ, Tonkin AM, Donnan GA. Atrial fibrillation with left atrial spontaneous echo contrast detected by transesophageal echocardiography is a potent risk factor for stroke. *Am J Cardiol* 1996;78:425-9.
- Leung DY, Black IW, Cranney GB, Hopkins AP, Walsh WF. Prognostic implications of left atrial spontaneous echo contrast in nonvalvular atrial fibrillation. *J Am Coll Cardiol* 1994;24:755-62.
- Wyse DG, Waldo AL, DiMarco JP, et al; Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002;347:1825-33.
- Van Gelder IC, Hagens VE, Bosker HA, et al; Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation Study Group. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med* 2002;347:1834-40.
- 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.
- Segal JB, McNamara RL, Miller MR, et al. Anticoagulants or antiplatelet therapy for non-rheumatic atrial fibrillation and flutter. *Cochrane Database Syst Rev* 2001:CD001938.
- Roden DM. Risks and benefits of antiarrhythmic therapy. *N Engl J Med* 1994;331:785-91.
- Kim MH, Conlon B, Ebinger M, et al. Clinical outcomes and costs associated with a first episode of uncomplicated atrial fibrillation presenting to the emergency room. *Am J Cardiol* 2001;88:A7,74-6.
- Michael JA, Stiell IG, Agarwal S, Mandavia DP. Cardioversion of paroxysmal atrial fibrillation in the emergency department. *Ann Emerg Med* 1999;33:379-87.
- Koenig BO, Ross MA, Jackson RE. An emergency department observation unit protocol for acute-onset atrial fibrillation is feasible. *Ann Emerg Med* 2002;39:374-81.
- Crozier I, Melton I, Pearson S. Management of atrial fibrillation in the emergency department. *Intern Med J* 2003;33:182-5.
- Zimetbaum PJ, Schreckengost VE, Cohen DJ, et al. Evaluation of outpatient initiation of antiarrhythmic drug therapy in patients reverting to sinus rhythm after an episode of atrial fibrillation. *Am J Cardiol* 1999;83:450-2, A9.
- Mulcahy B, Coates WC, Henneman PL, Lewis RJ. New-onset atrial fibrillation: When is admission medically justified? *Acad Emerg Med* 1996;3:114-9.
- Lown B, Perlroth MG, Kaidbey S, Abe T, Harken DE. "Cardioversion" of atrial fibrillation. A report on the treatment of 65 episodes in 50 patients. *N Engl J Med* 1963;269:325-31.
- Levy S, Lauribe P, Dolla E, et al. A randomized comparison of external and internal cardioversion of chronic atrial fibrillation. *Circulation* 1992;86:1415-20.
- Alt E, Ammer R, Schmitt C, et al. A comparison of treatment of atrial fibrillation with low-energy intracardiac cardioversion and conventional external cardioversion. *Eur Heart J* 1997;18:1796-804.
- Page RL, Kerber RE, Russell JK, et al; BiCard Investigators. Biphasic versus monophasic shock waveform for conversion of atrial fibrillation: The results of an international randomized, double-blind multicenter trial. *J Am Coll Cardiol* 2002;39:1956-63.
- Mittal S, Ayati S, Stein KM, et al. Transthoracic cardioversion of atrial fibrillation: Comparison of rectilinear biphasic versus damped sine wave monophasic shocks. *Circulation* 2000;101:1282-7.

37. Niebauer MJ, Chung MK, Wilkoff BL, et al. Success rate of the rectilinear biphasic waveform in atrial cardioversion in a large cohort of patients. *Circulation* 2000;102:574F. (Abst)
 38. Pedersen OD, Bagger H, Kober L, Torp-Pedersen C. Trandolapril reduces the incidence of atrial fibrillation after acute myocardial infarction in patients with left ventricular dysfunction. *Circulation* 1999;100:376-80.
 39. Rathore SS, Berger AK, Weinfurt KP, et al. Acute myocardial infarction complicated by atrial fibrillation in the elderly: Prevalence and outcomes. *Circulation* 2000;101:969-74.
 40. Crenshaw BS, Ward SR, Granger CB, Stebbins AL, Topol EJ, Califf RM. Atrial fibrillation in the setting of acute myocardial infarction: The GUSTO-I experience. *Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries. J Am Coll Cardiol* 1997;30:406-13.
 41. Fuster V, Ryden LE, Asinger RW, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation); North American Society of Pacing and Electrophysiology. 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 (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation) Developed in Collaboration With the North American Society of Pacing and Electrophysiology. *Circulation* 2001;104:2118-50.
 42. Goldberg RJ, Yarzebski J, Lessard D, Wu J, Gore JM. Recent trends in the incidence rates of and death rates from atrial fibrillation complicating initial acute myocardial infarction: A community-wide perspective. *Am Heart J* 2002;143:519-27.
 43. Pizzetti F, Turazza FM, Franzosi MG, et al. Incidence and prognostic significance of atrial fibrillation in acute myocardial infarction: The GISSI-3 data. *Heart* 2001;86:527-32.
 44. Waldecker B. Atrial fibrillation in myocardial infarction complicated by heart failure: Cause or consequence? *Eur Heart J* 1999;20:710-2.
 45. Wong CK, White HD, Wilcox RG, et al. New atrial fibrillation after acute myocardial infarction independently predicts death: The GUSTO-III experience. *Am Heart J* 2000;140:878-85.
 46. Wong CK, White HD, Wilcox RG, et al; GUSTO-III Investigators. Management and outcome of patients with atrial fibrillation during acute myocardial infarction: The GUSTO-III experience. Global use of strategies to open occluded coronary arteries. *Heart* 2002;88:357-62.
 47. Kontoyannis DA, Anastasiou-Nana MI, Kontoyannis SA, Zaga AK, Nanas JN. Intravenous amiodarone decreases the duration of atrial fibrillation associated with acute myocardial infarction. *Cardiovasc Drugs Ther* 2001;15:155-60.
 48. Zaqa M, Afshar H, Rasekh A, Khoshnevis R, Vaughn WK, Massumi A. Predictors of conversion to sinus rhythm using ibutilide for atrial fibrillation or flutter. *Am J Cardiol* 2000;85:112-4, A9.
 49. Varriale P, Sedighi A. Acute management of atrial fibrillation and atrial flutter in the critical care unit: Should it be ibutilide? *Clin Cardiol* 2000;23:265-8.
 50. Hennesdorf MG, Perings SM, Zuhlke C, et al. Conversion of recent-onset atrial fibrillation or flutter with ibutilide after amiodarone has failed. *Intensive Care Med* 2002;28:925-9.
 51. Harg P, Madsen S, Amlie JP. [Severe ibutilide-induced arrhythmia in patients with heart failure.] *Tidsskr Nor Laegeforen* 2001;121:2834-5.
 52. Preliminary report: Effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. The Cardiac Arrhythmia Suppression Trial (CAST) Investigators. *N Engl J Med* 1989;321:406-12.
 53. Al-Dashti R, Sami M. Dofetilide: A new class III antiarrhythmic agent. *Can J Cardiol* 2001;17:63-7.
 54. Pedersen OD, Bagger H, Keller N, Marchant B, Kober L, Torp-Pedersen C. Efficacy of dofetilide in the treatment of atrial fibrillation-flutter in patients with reduced left ventricular function: A Danish investigations of arrhythmia and mortality on dofetilide (diamond) substudy. *Circulation* 2001;104:292-6.
 55. Hart RG, Benavente O, McBride R, Pearce LA. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: A meta-analysis. *Ann Intern Med* 1999;131:492-501.
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