Atrial fibrillation following cardiac surgery

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LB Mitchell, E Crystal, B Heilbron, P Pagé. Atrial fibrillation following cardiac surgery. Can J Cardiol 2005;21(Suppl B): 45B-50B.

Atrial tachyarrhythmias, usually atrial fibrillation or atrial flutter, are the most common complications of cardiac surgery. Atrial tachyarrhythmias are associated with patient discomfort/anxiety, hemodynamic deterioration, cognitive impairment, thromboembolic events (including stroke), exposure to the risks of antiarrhythmic treatments, longer hospital stays and increased costs. Many approaches to the prevention of postoperative atrial tachyarrhythmias have been studied. Of these, studies using perioperative beta-blocking agents or amiodarone provide level A evidence of efficacy and, in properly selected patients, have shown a high degree of safety. Less convincing, level B evidence exists for the use of postoperative temporary atrial pacing and for perioperative intravenous magnesium treatment. The treatment of postoperative atrial tachyarrhythmias is similar to those occurring in other settings and includes excluding other potential causes of atrial tachyarrhythmias, antithrombotic or anticoagulation therapy, control of the ventricular response rate and consideration of restoring/maintaining sinus rhythm. The selection of therapies to achieve these goals should consider the sympathetic nervous system discharge state of the postoperative environment and the natural history of postoperative atrial fibrillation, which includes spontaneous resolution of the arrhythmogenic tendency after approximately six weeks. The Canadian Cardiovascular Society Consensus Conference recommendations for the prevention of atrial tachyarrhythmias after cardiac surgery and for the treatment of atrial tachyarrhythmias that occur after cardiac surgery are presented along with evidence that supports these recommendations.

Key Words: *Atrial fibrillation; Cardiac surgery; Consensus guidelines; Postoperative*

La fibrillation auriculaire après une intervention chirurgicale cardiaque

Les tachyarythmies auriculaires (TA), habituellement la fibrillation auriculaire ou le flutter auriculaire, sont les complications les plus fréquentes de la chirurgie cardiaque. Ces troubles du rythme sont associés à divers inconvénients : malaises et anxiété, détérioration hémodynamique, déficience cognitive, accidents thrombo-emboliques (y compris l'accident vasculaire cérébral), exposition aux risques des traitements antiarythmiques, prolongement du séjour à l'hôpital et augmentation des coûts. De nombreuses interventions visant à prévenir les TA postopératoires ont fait l'objet d'étude. Parmi celles-ci, l'administration de bêta-bloquants ou d'amiodarone en phase périopératoire a été associée à des données d'efficacité de niveau A et, chez les patients bien sélectionnés, à un degré élevé d'innocuité. La stimulation auriculaire temporaire postopératoire et l'administration intraveineuse de magnésium en phase périopératoire donnent des résultats moins probants (niveau B). Le traitement des TA postopératoires est le même que celui qui est appliqué dans d'autres contextes et il consiste en l'exclusion d'autres causes possibles de TA, en l'administration d'un traitement anticoagulant ou antithrombotique, en la maîtrise de la fréquence ventriculaire et dans le rétablissement et le maintien possibles du rythme sinusal. Le choix des traitements pour atteindre les objectifs visés devrait tenir compte de l'état de décharge du système nerveux sympathique après une opération et de l'évolution naturelle de la fibrillation auriculaire postopératoire, notamment de sa tendance à disparaître spontanément au bout de six semaines environ. Sont présentées dans l'article les recommandations consensuelles de la Société canadienne de cardiologie concernant la prévention et le traitement des TA après une intervention chirurgicale cardiaque, ainsi que les données à l'appui de ces recommandations.

RECOMMENDATIONS FOR THE PREVENTION AND TREATMENT OF ATRIAL FIBRILLATION FOLLOWING CARDIAC SURGERY

Class I

1) Patients who have been receiving a beta-blocker before cardiac surgery should have that therapy continued through the operative period in the absence of the development of a new contraindication (level of evidence A).
2) Temporary ventricular epicardial pacing electrode wires should be placed at the time of cardiac surgery to allow for backup pacing as necessary (level of evidence C).
3) Postoperative atrial fibrillation (AF) with a rapid ventricular response rate should be treated with a beta-blocker, a nondihydropyridine calcium antagonist or amiodarone to establish ventricular rate control. In the absence of a specific contraindication, the order of choice is as listed (level of evidence B).

Class IIa

1) Patients who have not been receiving a beta-blocker before cardiac surgery should be considered for prophylactic therapy to prevent postoperative AF with a beta-blocker or amiodarone (level of evidence A) or with atrial pacing or magnesium (level of evidence B).
2) Postoperative AF may be appropriately treated with either a ventricular response rate-control strategy or a rhythm-control strategy (level of evidence A).
3) Consideration should be given to anticoagulation therapy if postoperative AF persists for more than 48 h (level of evidence C).

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4) When anticoagulation therapy, rate-control therapy, and/or rhythm control therapy has been prescribed for postoperative AF, formal reconsideration of the ongoing need for such therapy should be undertaken six to eight weeks later (level of evidence B).

POSTOPERATIVE ATRIAL TACHYARRHYTHMIAS

Incidence of postoperative atrial tachyarrhythmias

Given that AF and atrial flutter are facilitated by atrial trauma, atrial stretch, atrial ischemia, epicardial inflammation, hypoxia, acidosis, electrolyte disturbances and the refractoriness changes that accompany sympathetic nervous system discharge, and given that all of these factors are often present immediately after cardiac surgical procedures, it is not surprising that AF and atrial flutter are frequent complications of these procedures. Indeed, atrial tachyarrhythmias are the most common postoperative complication of cardiac surgery that requires intervention or prolongs intensive care unit and total hospital stay (1-10). The incidence of AF and atrial flutter after cardiac surgery ranges from approximately 30% for patients undergoing isolated coronary artery bypass graft (CABG) surgery to approximately 40% for patients undergoing valve replacement or repair, and this incidence increases to approximately 50% for patients undergoing both procedures (11). Furthermore, there is evidence that the incidence of postoperative AF and atrial flutter is increasing because older individuals with a higher prevalence of atrial tachyarrhythmia risk factors are more commonly having these surgeries (2,8).

The peak incidence of these atrial tachyarrhythmias is between postoperative days 2 and 4. Of the patients who develop an atrial tachyarrhythmia, 70% do so before the end of postoperative day 4, and 94% do so before the end of posthospital day 6 (8).

Risk factors for postoperative atrial tachyarrhythmias

Independent patient characteristics that predict the occurrence of atrial tachyarrhythmias after cardiac surgery include older age, being male, history of hypertension, requirement for an intraoperative balloon pump, requirement for prolonged ventilation (greater than 24 h), and withdrawal of beta-blocker therapy (2-8,12,13). As in the general population (14), age has the greatest predictive value. Operative variables reported to be atrial tachyarrhythmia risk factors include the procedure performed (isolated CABG, valve repair/replacement or both), the number of bypass grafts, the duration of the surgery and the aortic cross-clamp time (2,15-17).

Consequences of postoperative atrial tachyarrhythmias

Postcardiac surgery atrial tachyarrhythmias may be transient and cause little morbidity. However, for some patients these tachyarrhythmias have important consequences including patient discomfort/anxiety, hemodynamic deterioration, cognitive impairment, thromboembolic events including stroke, exposure to the risks of arrhythmia treatments, longer hospital stay and increased health care costs (2,4,8,9,18-23). Linear regression models indicate that postoperative atrial tachyarrhythmias are independently associated with an increase in health care costs and the duration of hospital stay (8,24).

Prophylaxis against postoperative atrial tachyarrhythmias

Many therapies have been evaluated for the prevention of postoperative AF and atrial flutter after cardiac surgery (17,25-74). In the section that follows, published meta-analysis data are provided and referenced when current. When published meta-analysis data are either unavailable or are not current, individual study data were meta-analyzed using a random-effects model and are provided without a reference.

Seven randomized trials (17,25-30) have evaluated digoxin therapy in 709 patients. One trial showed a significant advantage for digoxin (26), one showed a significant disadvantage (28), and the other five showed no difference between treatment and control group outcomes (17,25,27,29,30). The OR for the postoperative incidence of atrial tachyarrhythmia in our weighted meta-analysis of prophylactic digoxin therapy studies is 0.91 (95% CI 0.59 to 1.40, P = not significant [NS]).

Three randomized trials (31-33) have evaluated verapamil in 432 patients. No trial showed a significant advantage or disadvantage to having therapy. The OR in our weighted meta-analysis of prophylactic verapamil therapy studies is 0.94 (95% CI 0.56 to 1.58, P=NS).

Twenty-seven randomized trials (34) evaluated beta-blocker prophylaxis in 3840 patients. Sixteen of the 27 trials showed a significant advantage for beta-blocker therapy. No beta-blocker trial showed a significant disadvantage to having therapy. The OR in this meta-analysis (34) of prophylactic beta-blocker therapy studies was 0.39 (95% CI 0.28 to 0.52, P<0.0001). Sotalol is a beta-blocker that also has important class III antiarrhythmic drug effects. Eight randomized trials (34) evaluated sotalol prophylaxis in 1294 patients. One of these trials produced a neutral result and the other seven trials reported a statistically significant benefit from sotalol therapy. The OR in that meta-analysis (34) of prophylactic sotalol drug therapy studies was 0.35 (95% CI 0.26 to 0.49, P<0.0001). Four trials (34) compared sotalol prophylaxis with that of other beta-blockers in 900 patients. One of these trials produced a neutral result and the other three trials reported a statistically significant benefit from sotalol therapy. Compared with other beta-blocker drugs, the OR in that meta-analysis (34) of prophylactic sotalol drug therapy studies was 0.50 (95% CI 0.34 to 0.74, P<0.0001). However, one trial comparing sotalol with metoprolol in doses considered to provide equivalent beta-blockade reported a higher prevalence of postoperative bradyarrhythmias with sotalol prophylaxis (35).

Fourteen randomized trials (36-49) evaluated amiodarone prophylaxis in 2823 patients. Eight (37,38,40,43,45,47-49) of the 14 trials showed a significant advantage for amiodarone therapy. No amiodarone trial showed a significant disadvantage to having therapy. The OR in our meta-analysis of prophylactic amiodarone therapy studies is 0.59 (95% CI 0.50 to 0.69, P<0.001). In a recent study involving 600 patients (49), the prophylactic effect of amiodarone was consistent in subgroup analyses of young and older patients, patients undergoing isolated CABG, undergoing valve repair/replacement with or without concomitant CABG, and patients also receiving or not receiving beta-blocker therapy.

Thirteen randomized trials (30,42,50-60) evaluated intravenous magnesium prophylaxis in 2009 patients. Two of the 13 trials showed a significant advantage for magnesium therapy (53,54). No magnesium trial showed a significant disadvantage to having therapy. The OR in our meta-analysis of prophylactic magnesium therapy studies is 0.83 (95% CI 0.65 to 1.06, P=NS).

Two randomized trials (61,62) evaluated procainamide prophylaxis in 146 patients. Neither showed a significant

TABLE 1
Prophylactic therapies for the prevention of postoperative atrial tachyarrhythmias

Therapy	Dose*	OR†	Cautions	Adverse effects
Preoperative beta-blocker	Any usual therapeutic dose (ie, metoprolol 50 mg po q12h or q8h for at least 2 preoperative days, day of surgery, and at least 6 postoperative days)	0.39 (0.28 to 0.52)	Reactive airways disease, decompensated CHF	Sinus bradycardia, AV block, hypotension, bronchospasm
Preoperative amiodarone	10 mg/kg/day (rounded to nearest 100 mg) divided into two daily po dosages for 6 preoperative days, day of surgery, and 6 postoperative days‡	0.61 (0.50 to 0.74)	30% to 50% reduction in the doses of other drugs with antiarrhythmic or sinus/AV nodal effects and warfarin will be required	Sinus bradycardia, AV block hypotension, torsade de pointes VT (rare), pulmonary toxicity (rare)
Postoperative amiodarone	900 mg to 1200 mg IV over 24 h beginning within 6 h of surgery, then 400 mg po three times daily each of the next 4 days§	0.53 (0.39 to 0.71)	30% to 50% reduction in the doses of other drugs with antiarrhythmic or sinus/AV nodal effects and warfarin will be required	Sinus bradycardia, AV block hypotension, torsade de pointes VT (rare), pulmonary toxicity (rare)
Magnesium sulfate	1.5 g IV over 4 h first preoperative day, immediately postoperatively and next 4 postoperative days¶. Other trials have omitted the preoperative dosage	0.83 (0.65 to 1.06)	Renal failure	Hypotension (rare), sedation (very rare), respiratory depression (very rare)
Atrial pacing	Right, left or biatrial pacing for 3 to 4 days postoperatively**. Rate set to overdrive sinus rate either manually or using sensing algorithms	0.67 (0.54 to 0.84)	May increase atrial tachyarrhythmias if pacing continues in setting of sensing malfunction	Diaphragmatic stimulation, increased myocardial oxygen requirements, possible increased infection rate

Doses used in the randomized studies vary widely and the optimal doses for this indication have not been established. The doses provided are those used in the largest positive trial of that therapy and are referenced to that study; †The ORs provided are from meta-analyses of the studies of each prophylactic approach (not for the single study referenced for dose). For further information on doses, see references 49‡, 40§, 57¶ and 72. Comparisons of the efficacies of various prophylactic approaches require randomized trials, which, for the most part, have not been performed. Accordingly, comparisons among the ORs provided in the Table should be avoided. AV Atrioventricular; CHF Congestive heart failure; IV Intravenous; po By mouth; q Every; VT Ventricular tachycardia*

advantage for procainamide therapy. The OR in our meta-analysis of these underpowered prophylactic procainamide therapy studies is 0.47 (95% CI 0.22 to 0.99, P=0.05). The well-documented hazards of class I antiarrhythmic drug therapies in patients with structural heart disease have precluded acceptance of this form of postoperative atrial tachyarrhythmia prophylaxis.

Finally, 12 randomized trials (40,63-73) evaluated atrial pacing prophylaxis in 1708 patients. Three of the 12 trials showed a significant advantage for atrial pacing therapy (64,72,73). No atrial pacing trial showed a significant disadvantage to having therapy. The OR in our meta-analysis of prophylactic atrial pacing therapy studies is 0.67 (95% CI 0.54 to 0.84, P<0.0001).

In summary, published clinical trial evidence supports the contention that beta-blockers, amiodarone, atrial pacing and (perhaps) magnesium therapy prevent postoperative AF and atrial flutter after cardiac surgery (Table 1). To determine if such prophylactic therapy was associated with a reduction in any of the presumed adverse consequences of postoperative atrial tachyarrhythmias, a meta-analysis (74) of 13 of the trials summarized above that also reported on length of hospital stay was performed. That analysis suggested that prophylactic therapy is associated with a significant reduction of 1.0±0.2 days (P<0.001) in the length of hospital stay, and with a nearly significant reduction of US$1287±673 (P=0.056) in hospital costs. Although there was a directional trend in the reduction of the incidence of postoperative cerebrovascular accidents with an OR of 0.50 (95% CI 0.22 to 1.17), this trend was not statistically significant. Of note, two completed trials (49,75) were powered to specifically detect a reduction in the length of hospital stay in patients receiving prophylactic therapy for prevention of atrial tachyarrhythmias. A large beta-blocker trial (75) did not identify a reduction in hospital stay. A large amiodarone trial (49) demonstrated a trend toward a reduction in total hospital stay duration. Furthermore, a previous meta-analysis limited to amiodarone trials (34) found a significant reduction in the length of hospital stay in amiodarone-treated patients.

Treatment of postoperative atrial tachyarrhythmias

The treatment options for AF and atrial flutter that occur after cardiac surgery are similar to those of AF and atrial flutter that occur in other settings. The therapeutic goals that are considered include prevention of thromboembolic events, slowing the ventricular response rate, conversion to sinus rhythm and maintenance of sinus rhythm. Nevertheless, the postoperative setting does have features that may favour some strategies over others. First, the natural history of postoperative AF and flutter after cardiac surgery is dominated by self-terminating, but frequently recurrent, tachyarrhythmia episodes and resolution of the tachyarrhythmia propensity in six to eight weeks, regardless of the treatment approach used (76-78). Second, the adrenergic discharge in the postoperative state lessens the effectiveness of therapies that do not include beta-blockade.

Several studies have demonstrated associations between AF after cardiac surgery and cerebrovascular events (2,3,8,20,21) and cognitive impairment (19). Accordingly, in the absence of a specific contraindication, anticoagulation therapy is recommended for patients with prolonged (greater than 48 h) AF. Once initiated, anticoagulation therapy is usually continued for at least six weeks.

In the postoperative setting, therapy for ventricular rate control for atrial tachyarrhythmias is usually required. Because the postsurgical state includes adrenergic discharge, beta-blocker

therapy is often very effective. When beta-blocker therapy is ineffective, poorly tolerated or contraindicated, the other therapeutic options for ventricular response rate control include a nondihydropyridine calcium antagonist (eg, diltiazem or verapamil) or amiodarone. In the postoperative state, therapy with digoxin is usually insufficient for adequate control of the ventricular response rate. Specific information regarding the doses, efficacies and adverse effects of these rate-control therapies are provided in Dorian and Connors, pages 26B-30B.

The general considerations for the advisability of conversion of a sustained atrial tachyarrhythmia in the postoperative setting are similar to those in other settings. However, because early recurrence of the atrial tachyarrhythmia is the rule rather than the exception, pharmacological cardioversion or direct current cardioversion after the initiation of pharmacological therapy to prevent atrial tachyarrhythmia recurrences are preferred over isolated direct current cardioversion provided that time is not of the essence. Intravenous ibutilide has been studied as a rapidly acting approach for pharmacological cardioversion of atrial tachyarrhythmias after cardiac surgery (79). In that study, ibutilide infusion was associated with conversion to sinus rhythm in 48% of patients. Success rates were higher in patients with atrial flutter than in patients with AF. The major adverse effect of ibutilide administration was the precipitation of torsade de pointes ventricular tachycardia in approximately 2% to 5% of those who receive it in this setting (79). Specific information regarding the doses, efficacies and adverse effects of rhythm-control therapies are provided in Talajic and Roy, pages 19B-25B.

Because the vast majority of patients who experience a postoperative atrial tachyarrhythmia in the absence of a history of preoperative atrial tachyarrhythmias will lose their propensity to atrial tachyarrhythmia recurrences within six weeks, a rate-control strategy without resort to a rhythm-control strategy has appeal because it does not expose the patient (who by definition has structural heart disease) to the risks of class I or class III antiarrhythmic drugs. To date, no large randomized clinical trial has specifically evaluated the advantages and disadvantages of the rate-control strategy versus the rhythm-control strategy for AF or atrial flutter that occurs early after cardiac surgery. One small randomized pilot study (77) addressing this question found a statistically significant reduction in the duration of the postsurgical hospital stay in patients developing postoperative AF who were assigned to a rhythm-control approach versus a rate-control approach to treatment. On the other hand, a retrospective evaluation (80) of the question has suggested a statistically significant reduction in the duration of postsurgical hospital stay in patients discharged in AF (after ventricular response rate control and anticoagulation therapy) compared with patients discharged in sinus rhythm. Accordingly, the relative advantages, disadvantages and risk of a rate-control versus a rhythm-control approach to the treatment of atrial tachyarrhythmia that occurs after cardiac surgery have not been determined. Nevertheless, all agree that therapy provided for postoperative AF and atrial flutter can usually be withdrawn after six to eight weeks.

REFERENCES

1. Andrews TC, Reimold SC, Berlin JA, Antman EM. Prevention of supraventricular arrhythmias after coronary artery bypass surgery: A meta-analysis of randomized control trials. Circulation 1991;84(Suppl 5):III236-44.
2. Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of postoperative atrial arrhythmias. Ann Thorac Surg 1993;56:539-49.
3. Fuller JA, Adams GG, Buxton B. Atrial fibrillation after coronary artery bypass grafting. Is it a disorder of the elderly? J Thorac Cardiovasc Surg 1989;97:821-5.
4. Leitch JW, Thomson D, Baird DK, Harris PJ. The importance of age as a predictor of atrial fibrillation and flutter after coronary artery bypass grafting. J Thorac Cardiovasc Surg 1990;100:338-42.
5. Crosby LH, Pifalo WB, Woll KR, Burkholder JA. Risk factors for atrial fibrillation after coronary artery bypass grafting. Am J Cardiol 1990;66:1520-2.
6. Hashimoto K, Ilstrup DM, Schaff HV. Influence of clinical and hemodynamic variables on risk of supraventricular tachycardia after coronary artery bypass. J Thorac Cardiovasc Surg 1991;101:56-65.
7. Frost L, Mølgaard H, Christiansen EH, Hjortholm K, Paulsen PK, Thomsen PE. Atrial fibrillation and flutter after coronary artery bypass surgery: Epidemiology, risk factors and preventative trials. Int J Cardiol 1992;36:253-61.
8. Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery: Current trends and impact of hospital resources. Circulation 1996;94:390-7.
9. Khaja F, Parker JO. Hemodynamic effects of cardioversion in chronic atrial fibrillation. Special reference to coronary artery disease. Arch Intern Med 1972;129:433-40.
10. Wong DT, Cheng DC, Kustra R, et al. Risk factors of delayed extubation, prolonged length of stay in the intensive care unit, and mortality in patients undergoing CABG with fast track cardiac anesthesia: A new cardiac risk score. Anesthesiology 1999;91:936-44.
11. Mitchell LB. Incidence, timing and outcome of atrial tachyarrhythmias after cardiac surgery, In: Steinberg JS, ed. Atrial Fibrillation After Cardiac Surgery. Norwell, Massachusetts: Kluwer Academic Publishers, 2000:37-50.
12. Abel RM, van Gelder HM, Pores IH, Liguori J, Gielchinsky I, Parsonnet V. Continued propranolol administration following coronary bypass surgery: Antiarrhythmic effects. Arch Surg 1983;118:727-31.
13. Silverman NA, Wright R, Levitsky S. Efficacy of low-dose propranolol in preventing postoperative supraventricular tachyarrhythmias. Ann Surg 1982;196:194-7.
14. Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: The Framingham Study. N Engl J Med 1982;306:1018-22.
15. Caretta Q, Mercanti CA, De Nardo D, et al. Ventricular conduction defects after coronary artery bypass grafting: Multivariate analysis of preoperative, intra-operative and postoperative variables. Eur Heart J 1991;12:1107-11.
16. Roffman JA, Fieldman A. Digoxin and propranolol in the prophylaxis of supraventricular tachydysrhythmias after coronary artery bypass surgery. Ann Thorac Surg 1981;31:496-501.
17. Ormerod OJ, McGregor CG, Stone DL, Wisbey C, Petch MC. Arrhythmias after coronary bypass surgery. Br Heart J 1984;51:618-21.
18. Orlando JR, van Herick R, Aronow WS, Olson HG. Hemodynamics and echocardiograms before and after cardioversion of atrial fibrillation to normal sinus rhythm. Chest 1979;76:521-6.
19. Stanley TO, Mackensen GB, Grocott HP, et al; Neurological Outcome Research Group; CARE Investigators of the Duke Heart Center. The impact of post-operative atrial fibrillation on neurocognitive outcome after coronary artery bypass graft surgery. Anesth Analg 2002;94:290-5.
20. Taylor GJ, Malik SA, Colliver JA, et al. Usefulness of atrial fibrillation as a predictor of stoke after isolated coronary artery bypass grafting. Am J Cardiol 1987;60:905-7.
21. Lynn GM, Stefanko K, Reed JF III, Gee W, Nicholas G. Risk factors for stoke after coronary artery bypass. J Thorac Cardiovasc Surg 1992;104:1518-23.
22. 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 control trials. Circulation 1990;82:1106-16. (Erratum in 1991;83:714).
23. Flaker GC, Blackshear JL, McBride R, et al. Antiarrhythmic drug therapy and cardiac mortality in atrial fibrillation. The Stroke

Prevention in Atrial Fibrillation Investigators. J Am Coll Cardiol 1992;20:527-32.
24. Kowey PR, Stanowski A, Schnoor E. Impact of atrial fibrillation on duration of hospital stay and cost of coronary artery bypass surgery. Clin Res 1992;40:A365. (Abst)
25. Rubin DA, Nieminski KE, Reed GE, Herman MV. Predictors, prevention, and long-term prognosis of atrial fibrillation after coronary bypass graft operations. J Thorac Cardiovasc Surg 1987;94:331-5.
26. Johnson LW, Dickstein RA, Fruehan CT, et al. Prophylactic digitalization for coronary artery bypass surgery. Circulation 1976;53:819-22.
27. Weiner B, Rheinlander HF, Decker EL, Cleveland RJ. Digoxin prophylaxis following coronary artery bypass surgery. Clin Pharm 1986;5:55-8.
28. Tyras DH, Stothert JC Jr, Kaiser GC, Barner HB, Codd JE, Willman VL. Supraventricular tachyarrhythmias after myocardial revascularization: A randomized trial of prophylactic digitalization. J Thorac Cardiovasc Surg 1979;77:310-4.
29. Yazicioglu L, Eryilmaz S, Sirlak M, et al. The effect of preoperative digitalis and atenolol combination on postoperative atrial fibrillation incidence. Eur J Cardiothorac Surg 2002;22:397-401.
30. Bert AA, Reinert SE, Singh AK. A beta-blocker, not magnesium, is effective prophylaxis for atrial tachyarrhythmias after coronary artery bypass graft surgery. J Cardiothorac Vasc Anesth 2001;15:204-9.
31. Davison R, Hartz R, Kaplan K, Parker M, Feiereisel P, Michaelis L. Prophylaxis of supraventricular tachyarrhythmia after coronary bypass surgery with oral verapamil: A randomized, double-blind trial. Ann Thorac Surg 1985;39:336-9.
32. Williams DB, Misbach GA, Kruse AP, Ivey TD. Oral verapamil for prophylaxis of supraventricular tachycardia after myocardial revascularization. A randomized trial. J Thorac Cardiovasc Surg 1885;90:592-6.
33. Smith EE, Shore DF, Monro JL, Ross JK. Oral verapamil fails to prevent supraventicular tachycardia following coronary artery surgery. Int J Cardiol 1985;9:37-44.
34. Crystal E, Connolly SJ, Sleik K, Ginger TJ, Yusuf S. Interventions on prevention of postoperative atrial fibrillation in patients undergoing heart surgery: A meta-analysis. Circulation 2002;106:75-80.
35. Nystrom U, Edvardsson N, Berggren H, Pizzarelli GP, Radegran K. Oral sotalol reduces the incidence of atrial fibrillation after coronary artery bypass surgery. Thorac Cardiovasc Surg 1993;41:34-7.
36. Butler J, Harriss DR, Sinclair M, Westaby S. Amiodarone prophylaxis for tachycardias after coronary artery surgery: A randomized, double-blind, placebo controlled trial. Br Heart J 1993;70:56-60.
37. Lee SH, Chang CM, Lu MJ, et al. Intravenous amiodarone for prevention of atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg 2000;70:157-61.
38. Guarnieri T, Nolan S, Gottlieb SO, Dudek A, Lowry DR. Intravenous amiodarone for the prevention of atrial fibrillation after open heart surgery: the Amiodarone Reduction in Coronary Heart (ARCH) trial. J Am Coll Cardiol 1999;34:343-7.
39. Dörge H, Schoendube FA, Schoberer M, et al. Intraoperative amiodarone as prophylaxis against atrial fibrillation after coronary operations. Ann Thorac Surg 2000:69:1358-62.
40. White CM, Caron MF, Kalus JS, et al; Atrial Fibrillation Suppression Trial II. Intravenous plus oral amiodarone, atrial septal pacing, or both strategies to prevent post-cardiothoracic surgery atrial fibrillation: The Atrial Fibrillation Suppression Trial II (AFIST II). Circulation 2003;108(Suppl 1):II200-6.
41. Hohnloser SH, Meinertz T, Dammbacher T, et al. Electrocardiographic and antiarrhythmic effects of intravenous amiodarone: Results of a prospective, placebo-controlled study. Am Heart J 1991;121:89-95.
42. Treggiari-Venzi MM, Waeber JL, Perneger TV, et al. Intravenous amiodarone or magnesium sulphate is not cost-beneficial prophylaxis for atrial fibrillation after coronary artery bypass surgery. Br J Anaesth 2000;85:690-5.
43. Giri S, White CM, Dunn AB, et al. Oral amiodarone for prevention of atrial fibrillation after open heart surgery, the Atrial Fibrillation Suppression Trial (AFIST): A randomised placebo-controlled trial. Lancet 2001;357:830-6.
44. Redle JD, Khurana S, Marzan R, et al. Prophylactic oral amiodarone compared with placebo for prevention of atrial fibrillation after coronary artery bypass surgery. Am Heart J 1999;138:144-50.
45. Daoud EG, Strickberger SA, Man KC, et al. Preoperative amiodarone as prophylaxis against atrial fibrillation after heart surgery. N Engl J Med 1997;337:1785-91.
46. Maras D, Boskovic SD, Popovic Z, et al. Single-day loading dose of amiodarone for the prevention of new-onset atrial fibrillation after coronary artery bypass surgery. Am Heart J 2001;141:E8
47. Tokmakoglu H, Kandemir O, Gunaydin S, Catav Z, Yorgancioglu C, Zorlutuna Y. Amiodarone versus digoxin and metoprolol combination for the prevention of postcoronary bypass atrial fibrillation. Eur J Cardiothorac Surg 2002;21:401-5.
48. Yazigi A, Rahbani P, Zeid HA, Madi-Jebara S, Haddad F, Hayek G. Postoperative oral amiodarone as prophylaxis against atrial fibrillation after coronary artery surgery. J Cardiothorac Vasc Anesth 2002;16:603-6.
49. Mitchell LB, Exner DV, Wyse DG, et al. Prophylactic amiodarone for the prevention of arrhythmias that begin early after revascularization, valve repair, or replacement (PAPABEAR): Preliminary results. Circulation 2003;108:2723. (Abst)
50. Fanning WJ, Thomas CS Jr, Roach A, Tomichek R, Alford WC, Stoney WS Jr. Prophylaxis of atrial fibrillation with magnesium sulfate after coronary artery bypass grafting. Ann Thorac Surg 1991;52:529-33.
51. England MR, Gordon G, Salem M, Chernow B. Magnesium administration and dysrhythmias after cardiac surgery. A placebo-controlled, double-blind, randomised trial. JAMA 1992;268:2395-402.
52. Parikka H, Toivonen L, Pellinen T, Verkkala K, Järvinen A, Nieminen MS. The influence of intravenous magnesium sulphate on the occurrence of atrial fibrillation after coronary artery by-pass operation. Eur Heart J 1993;14:251-8.
53. Colquhoun IW, Berg GA, el-Fiky M, Hurle A, Fell GS, Wheatley DJ. Arrhythmia prophylaxis after coronary artery surgery. A randomised controlled trial of intravenous magnesium chloride. Eur J Cardiothorac Surg 1993;7:520-3.
54. Karmy-Jones R, Hamilton A, Dzavik V, Allegreto M, Finegan BA, Koshal A. Magnesium sulphate prophylaxis after cardiac operations. Ann Thorac Surg 1995;59:502-7.
55. Nurozler F, Tokgozoglu L, Pasaoglu I, Boke E, Ersoy U, Bozer AY. Atrial fibrillation after coronary artery bypass surgery: Predictors and the role of $MgSO_4$ replacement. J Card Surg 1996;11:421-7.
56. Solomon AJ, Berger AK, Trivedi KK, Hannan RL, Katz NM. The combination of propranolol and magnesium does not prevent postoperative atrial fibrillation. Ann Thorac Surg 2000;69:126-9.
57. Toraman F, Karabulut EH, Alhan HC, Dagdelen S, Tarcan S. Magnesium infusion dramatically decreases the incidence of atrial fibrillation after coronary artery bypass surgery. Ann Thorac Surg 2001;72:1256-62.
58. Yeatman M, Caputo M, Narayan P, et al. Magnesium-supplemented warm blood cardioplegia in patients undergoing coronary artery revascularization. Ann Thorac Surg 2002;73:112-08.
59. Kaplan M, Kut MS, Icer UA, Demirtas MM. Intravenous magnesium sulphate prophylaxis for atrial fibrillation after coronary artery bypass surgery. J Thorac Cardiovasc Surg 2003;125:344-52.
60. Hazelrigg SR, Boley TM, Cetindag IB, et al. The efficacy of supplemental magnesium in reducing atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg 2004;77:824-830.
61. Laub GW, Janeira L, Muralidharan S, et al. Prophylactic procainamide for prevention of atrial fibrillation after coronary bypass grafting: A prospective, double-blind, randomized, placebo-controlled pilot study. Crit Care Med 1993;21:1474-8.
62. Gold MR, O'Gara PT, Buckley MJ, DeSanctis RW. Efficacy and safety of procainamide in preventing arrhythmias after coronary artery bypass surgery. Am J Cardiol 1996;78:975-9.
63. Schweikert RA, Grady TA, Gupta N, et al. Atrial pacing in the prevention of atrial fibrillation after cardiac surgery: results of the second postoperative pacing study (POPS-2). J Am Coll Cardiol 1998;31:117A. (Abst)
64. Orr W, Tsui S, Stafford P, et al. Synchronized bi-atrial pacing after coronary artery by-pass surgery. Pacing Clin Electrophysiol 1999;22:755. (Abst)
65. Goette A, Mittag J, Friedl A, et al. Pacing of Bachmann's bundle after coronary artery bypass grafting. Pacing Clin Electrophysiol 2002;25:1072-8.

66. Kurz DJ, Naegeli B, Kunz M, et al. Epicardial, biatrial synchronous pacing for prevention of atrial fibrillation after cardiac surgery. Pacing Clin Electrophysiol 1999;22:721-6.
67. Gerstenfeld EP, Hill MR, French SN, et al. Evaluation of right atrial and biatrial temporary pacing for the prevention of atrial fibrillation after coronary artery bypass surgery. J Am Coll Cardiol 1999;33:1981-8.
68. Blommaert D, Gonzalez M, Mucumbitsi J, et al. Effective prevention of atrial fibrillation by continuous atrial overdrive pacing after coronary artery surgery. J Am Coll Cardiol 2000;35:1411-5.
69. Chung MK, Augostini RS, Asher CR, et al. Ineffectiveness and potential proarrhythmia of atrial pacing for atrial fibrillation prevention after coronary artery bypass grafting. Ann Thorac Surg 2000;69:1057-63.
70. Daoud EG, Dabir R, Archambeau M, et al. Randomized, double-blind trial of simultaneous right and left atrial epicardial pacing for prevention of post-open heart surgery atrial fibrillation. Circulation 2000;102:761-5.
71. Fan K, Lee KL, Chiu CS, et al. Effects of biatrial pacing in prevention of postoperative atrial fibrillation after coronary artery bypass surgery. Circulation 2000;102:755-60.
72. Greenberg MD, Katz NM, Iuliano S, Tempesta BJ, Solomon AJ. Atrial pacing for the prevention of atrial fibrillation after cardiovascular surgery. J Am Coll Cardiol 2000;35:1416-22.
73. Levy T, Fotopoulos G, Walker S, et al. Randomized controlled study investigating the effect of biatrial pacing in prevention of atrial fibrillation after coronary artery bypass grafting. Circulation 2000;102:1382-7.
74. Zimmer J, Pezzullo J, Choucair W, et al. Meta-analysis of antiarrhythmic therapy in the prevention of postoperative atrial fibrillation and the effect on hospital length of stay, costs, cerebrovascular accidents, and mortality in patients undergoing cardiac surgery. Am J Cardiol 2003;91:1137-40.
75. Connolly SJ, Cybulsky I, Lamy A, et al; Beta-Blocker Length Of Stay (BLOS) study. Double-blind, placebo-controlled, randomized trial of prophylactic metoprolol for reduction of hospital length of stay after heart surgery: The beta-Blocker Length Of Stay (BLOS) study. Am Heart J 2003;145:226-32.
76. Kowey PR, Stebbins D, Igidbashian, et al. Clinical outcome of patients who develop PAF after CABG surgery. Pacing Clin Electrophysiol 2001;24:191-3.
77. Lee JK, Klein GJ, Krahn AD, et al. Rate-control versus conversion strategy in postoperative atrial fibrillation: A prospective, randomized pilot study. Am Heart J 2000;140:871-7.
78. Danias PG, Caulfield TA, Weigner MJ, et al. Likelihood of spontaneous conversion of atrial fibrillation to sinus rhythm. J Am Coll Cardiol 1998;31:588-92.
79. VanderLugt JT, Mattioni T, Denker S, et al. Efficacy and safety of ibutilide fumarate for the conversion of atrial arrhythmias after cardiac surgery. Circulation 1999;100:369-75.
80. Solomon AJ, Kouretas PC, Hopkins RA, Katz NM, Wallace RB, Hannan RL. Early discharge of patients with new-onset atrial fibrillation after cardiovascular surgery. Am Heart J 1998;135:557-63.