www.cardiologyrounds.ca 2008 volume XIII, issue 4

CARDIOLOGY Rounds®

As presented in the Rounds of the Division of Cardiology, St. Michael's Hospital, University of Toronto

An Overview of Atrial Fibrillation After Cardiac Surgery

By AWAD A. ALQAHTANI, MD, FRCPC, and GORDON MOE, MD, FRCPC

Postoperative atrial fibrillation (POAF) is a common complication of cardiac surgery and is associated with an increased incidence of other complications (eg, postoperative stroke), increased hospital length of stay, and increased costs of hospitalization. Prevention of AF is a reasonable clinical goal and, consequently, many randomized trials have evaluated the effectiveness of pharmacological and nonpharmacological interventions.[1,2] POAF has also been demonstrated to independently predict postoperative delirium and neurocognitive decline.[3,4] The precise pathophysiology of POAF after heart surgery is unknown, although the mechanisms are thought to be multifactorial. Different risk factors have been reported, and many studies have evaluated the prophylactic effects of different pharmacological or physical interventions. This issue of *Cardiology Rounds* reviews the incidence, risk factors, pathogenesis, prevention, and treatment strategies of POAF.

What is the extent of the problem?

AF after coronary artery bypass grafting (CABG) is a common problem; however, the true incidence of POAF following cardiac surgery is unclear. Reported incidence ranges from 10%-65%. This range is wide because studies that examined AF following CABG differ in baseline patient characteristics, type of surgery, methods of detection, and definitions of AF.[5] It is estimated that POAF is approximately 30% after pure CABG surgery, 40% after valve replacements or repair, and increases to approximately 50% after combined procedures. Furthermore, these figures are expected to rise in the future, given that the population undergoing cardiac surgery is getting older and that the incidence of AF in the general population is strongly age-dependent. POAF tends to occur within 2-4 days after a procedure, with the peak incidence on postoperative Day 2. Of the patients who experienced an arrhythmia, 70% developed it before the end of postoperative Day 4 and 94% before the end of postoperative Day 6.[6] Furthermore, the impact of POAF on hospital resources is substantial and was estimated to lengthen hospital stay by 4.9 days, with an extra $10,000 to $11,500 in hospital-stay costs in the United States (US).[6]

What are the risk factors for POAF?

Several studies have identified risk factors for developing AF following open-heart surgery.[8] In addition to older age, many other risk factors for the development of POAF have been identified, such as: previous history of AF, male gender, decreased left-ventricular ejection fraction, left-atrial enlargement, valvular heart surgery, chronic obstructive pulmonary disease, chronic renal failure, diabetes mellitus, and rheumatic heart disease (Figure 1).[1,3,7-9]

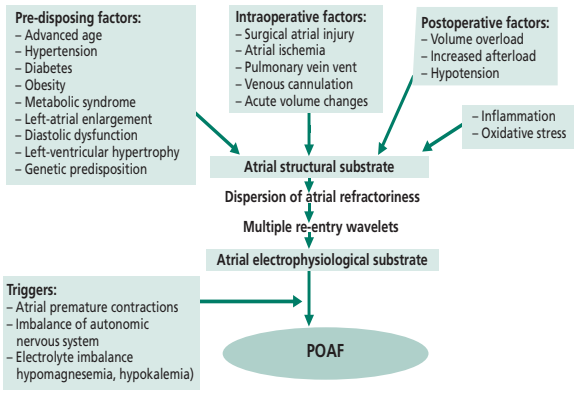
What are the mechanisms of POAF?

Classically, AF is attributed to enhanced automaticity in one or several rapidly depolarizing foci and re-entry involving one or more circuits.[10] Nevertheless, the underlying mechanisms involved in POAF development are likely to be multifactorial and have not been fully elucidated. However, some causative mechanisms have been proposed that include pericardial inflammation, excessive production of catecholamines, autonomic imbalance during the postoperative period, and interstitial mobilization of fluid with resultant changes in volume, pressure, and neurohumoral environment (Figure 1).[11-18]

Recent studies suggest that patients with postoperative AF may have pre-existing electrophysiologic abnormalities.[19,20] Mariscalco et al[21] found an association between preprocedural atrial histopathology and postoperative AF. The histological abnormalities found were interstitial fibrosis, cytoplasmatic vacuolisation, and nuclear derangement of myocytes. This supported the hypothesis that, in patients with postoperative AF, vulnerability to AF (triggers) and the ability to maintain AF (substrate) are associated with pre-existing degenerative changes. Moreover, multiple re-entry wavelets resulting from the dispersion of atrial refractoriness seem to be the electrophysiological mechanism of POAF. Neurohormonal activation is

St. Michael's Hospital
30 Bond St.,
Suite 7049, Queen Wing
Toronto, Ont. M5B 1W8
Fax: (416) 864-5941

Figure 1: Pathogenesis of POAF[18]



POAF = postoperative atrial fibrillation

another mechanism that increases susceptibility to POAF.[4] Increased sympathetic and parasympathetic activation alter atrial refractoriness (eg, shortening of the atrial effective refractory period), possibly contributing to the arrhythmia substrate.[16]

Reports also suggest that patients developing POAF have either higher or lower RR interval variability, indicating that increased sympathetic or vagal tone occurs before arrhythmia onset. These findings imply that interventions to modulate both the sympathetic and parasympathetic nervous systems may be beneficial in suppressing this postoperative arrhythmia. Further, an increasing body of evidence is revealing that inflammation plays an important role in the pathogenesis of POAF. Two recent studies demonstrated that inflammation can alter atrial conduction, facilitating re-entry, and predisposing to the development of POAF (Figure 1).[11,12] It is well known that extracorporeal circulation contains systemic inflammatory mediators that may be, in part, responsible for the occurrence of POAF. Interestingly, recent reports also suggest that increased leukocytosis, which is usually encountered in the days after cardiopulmonary bypass, is an independent predictor for the occurrence of POAF.[13,14]

Other studies have demonstrated that early POAF correlates with an increased inflammatory response after cardiac surgery.[22-24] In an animal study,[11] atrial conduction properties were found to be altered by postoperative atrial inflammation, and the degree of inflammation was proportional to the inhomogeneity of atrial conduction. This resulted in an increased incidence and duration of POAF. Inflammation, inhomogeneity of atrial conduction, and incidence of POAF were significantly decreased by anti-inflammatory treatment with prednisone.[11] Moreover, with increasing surgical trauma to the atria, there is also an increased incidence of POAF that explains why patients undergoing valvular surgery have the highest risk of developing POAF.[1,8] A further study demonstrated that less manipulation of the atria decreases atrial inflammation and, subsequently, AF.[25]

Why do we need to treat?

POAF is associated with a higher incidence of heart failure, stroke, prolonged hospital stay, and increased costs. In a retrospective study, the Texas Heart Institute Cardiovascular Research database was used to identify patients developing POAF. AF was diagnosed in 16% (n=994) of the population (n=6475) and was associated with greater in-hospital mortality, more strokes, and prolonged hospital stays. A case-matched substudy revealed that 5-year survival was worse in patients with POAF, and POAF was an independent predictor of long-term mortality.[13] Furthermore, the impact of POAF on hospital resources is substantial, with an estimated increased hospital stay of 4.9 days in the US.[6] According to the American Heart Association (AHA) statistics in 2004,[26] there are at least 640,000 open-heart surgeries performed every year in the US; assuming a 30% incidence of POAF, the incremental cost related to this postoperative complication could be conservatively estimated at approximately $2 billion per year.

Prevention of POAF

Many studies have evaluated the effectiveness of pharmacologic and nonpharmacologic interventions to prevent or decrease the high incidence of POAF. In 2006, guidelines for the prevention and management of POAF were published jointly by the American College of Cardiology, the AHA, and the European Society of Cardiology (Table 1).[27]

Beta-blockers

Sympathetic activation may facilitate POAF in susceptible patients and, given the increased sympathetic tone in patients undergoing cardiac surgery, beta-blockers have been the most-studied drugs to date for the prevention of POAF. These drugs are primary in AF prevention and should be used routinely in every patient.[28,29] Several clinical trials have evaluated the effect of various beta-blockers on the incidence of POAF,[30-32] indicating an overall reduction of this complication. However, it should be realized that even in recent large trials where this strategy was widely applied, the incidence of POAF remains nearly 60% in selected patients.[7] This clearly emphasizes the need for further preventive strategies in addition to beta-blockade.

Sotalol is a beta-blocker that has important class III antiarrhythmic effects and has also been effective for the prevention of POAF, both compared with placebo[33] and with other beta-blockers to elucidate the specific class III action.[34,35] However, side effects of sotalol (hypotension, bradycardia) and, in particular, its proarrhythmic effects may limit its use in perioperative management.

Amiodarone

Amiodarone is a Vaughan-Williams class III drug that also has alpha- and beta-adrenergic-blocking properties, which may attenuate the sympathetic overstimulation found in patients undergoing cardiac surgery. A short perioperative course of oral amiodarone in addition to routine beta-blockade has been demonstrated as the most promising approach. This therapy was associated with a 50% reduction of postoperative atrial tachyarrhythmias in patients undergoing CABG and/or valve replacement/repair. The number needed to treat in the largest prospective trial, the Prophylactic Oral Amiodarone for the Prevention of Arrhythmias that Begin Early After Revascularization, Valve Replacement, or Repair (PAPABEAR) trial, was only 7.5, to prevent one patient from developing POAF.[36] A meta-analysis, which included 19 trials comparing amiodarone with placebo for the prevention of POAF, revealed that the results of the large PAPABEAR trial were consistent with the pooled results of these trials.[37] In these 19 trials, amiodarone reduced AF by 50% (95% confidence interval [CI], 0.43 to 0.59; $P<0.0001$); amiodarone also significantly reduced ventricular tachyarrhythmias, strokes, and hospital stay. Furthermore, amiodarone-treated patients had significantly lower heart rates during the AF episodes, one of the main determinants of AF-related morbidity. The authors concluded that prophylactic amiodarone should be implemented

Table 1: Indications for intervention in AF after cardiac surgery based on the ACC/AHA/ESC Guidelines[10]

Indication Class I	Unless contraindicated, treatment with an oral beta-blocker drug to prevent POAF is recommended for patients undergoing cardiac surgery.	Level of Evidence: A
	Administration of AV nodal blocking agents is recommended to achieve rate control in patients who develop POAF.	Level of Evidence: B
Indication Class IIa	Preoperative administration of amiodarone reduces the incidence of AF in patients undergoing cardiac surgery and represents appropriate prophylactic therapy for patients at high risk for POAF.	Level of Evidence: A
	It is reasonable to restore sinus rhythm by pharmacologic cardioversion with ibutilide or direct-current cardioversion in patients who develop POAF, as advised for nonsurgical patients.	Level of Evidence: B
	It is reasonable to administer antiarrhythmic medications in an attempt to maintain sinus rhythm in patients with recurrent or refractory POAF, as recommended for other patients who develop AF.	Level of Evidence: B
	It is reasonable to administer antithrombotic medication in patients who develop POAF, as recommended for nonsurgical patients.	Level of Evidence: B
Indication Class IIb	Prophylactic administration of sotalol may be considered for patients at risk of developing AF after cardiac surgery.	Level of Evidence: B

ACC = American College of Cardiology; AHA = American Heart Association; ESC = European Society of Cardiology; AV = atrioventricular.

as routine therapy for high-risk patients undergoing cardiac surgery.[37]

Atrial pacing

There are several mechanisms through which atrial pacing may prevent AF, including:

- reduction of the bradycardia-induced dispersion of atrial repolarization that contributes to the electrophysiological substrate for AF
- suppression of atrial premature beats and runs of supraventricular premature beats, thus avoiding the trigger for AF
- dual-site atrial pacing, which may change atrial activation patterns, thus preventing the development of intra-atrial re-entry.

The effect of prophylactic pacing has been investigated in a number of trials. Meta-analyses of these clinical trials[38-40] have consistently demonstrated that single- or dual-site atrial pacing significantly reduces the risk of new-onset POAF. However, the number of enrolled patients was small, and the pacing sites and protocols varied widely among the studies.

Other Medications

Calcium-channel blockers

Numerous studies have evaluated nondihydropyridine calcium-channel blocker medications. A recent meta-analysis of these trials revealed that calcium-channel blockers reduce the risk of supraventricular tachyarrhythmia. However, in some studies, the perioperative use of these drugs was associated with an increased incidence of atrioventricular (AV) block and low-output syndrome, which might be related to the negative chronotropic and inotropic effects of this class of drugs. As a result, the use of these agents should be considered with caution until more data on their safety profile become available.

Statins

Observational studies have previously suggested that patients under statin therapy have a lower incidence of POAF after CABG[41] and that statins have been shown to reduce inflammation in patients with coronary artery disease. Recently, the prospective, randomized study, Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery (ARMYDA-3)[42] demonstrated that treatment with atorvastatin (40 mg/day), started 7 days before elective cardiac surgery under cardiopulmonary bypass and continued in the postoperative period, reduces the occurrence of POAF by 61%.

N-3 polyunsaturated fatty acids (PUFAs)

Recent experimental studies in rats and dogs have revealed that PUFAs have significant antiarrhythmic effects on the atrial muscle.[43,44] Furthermore, in a 12-year follow-up study from the general population, consumption of fish that induces high-plasma concentrations of PUFA has been associated with a lower incidence of AF.[45] Calo et al,[46] in a randomized, controlled trial of 160 patients undergoing elective CABG, found that PUFA supplementation significantly reduced the incidence of POAF, with an effect similar to those obtained with beta-blockers, sotalol, or amiodarone.

Anti-inflammatory agents

In a recent multicentre trial,[47] 241 consecutive patients undergoing cardiac surgery were randomized to receive either 100 mg hydrocortisone or placebo. The incidence of POAF during the first 84 hours was significantly lower in the hydrocortisone group (36 of 120; 30%) than in the placebo group (58 of 121; 48%), and the adjusted hazard ratio (HR) was 0.54 (95% CI, 0.35 to 0.83; P=0.004).

Magnesium

A meta-analysis by Miller et al[48] concluded that magnesium administration was effective for reducing POAF with a similar efficacy to common antiarrhythmic drugs. However, the studies included in this analysis involved small numbers of patients and the designs varied among the different studies, limiting the interpretation of the results.

N-acetylcysteine

N-acetylcysteine (NAC) is a free-radical scavenger antioxidant agent that reduces cellular oxidative damage.[49,50] It has

Table 2: Dosage, advantages, and side effects of drugs used for rhythm control in POAF

Drugs	Adult dosage	Advantages	Side effects
Amiodarone	2.5-5 mg/kg IV over 20 min then 15 mg/kg or 1.2 g over 24 h	Can be used in patients with severe LV dysfunction	Thyroid and hepatic dysfunction, torsades de pointes, pulmonary fibrosis, photosensitivity, bradycardia
Procainamide	10-15 mg/kg IV up to 50 mg/min	Therapeutic levels quickly achieved	Hypotension, fever, accumulates in renal failure, can worsen heart failure, requires drug-level monitoring
Ibutilide	1 mg IV over 10 min, can repeat after 10 min if no effect	Easy to use	Torsades de pointes more frequent than with amiodarone and procainamide

IV = intravenous; LV = left ventricular.

been demonstrated that NAC may reduce ischemia/reperfusion injury,[51] reperfusion arrhythmias, and/or extension of infarction. The combination of NAC and reperfusion therapy for acute myocardial infarction in patients has also been associated with less oxidative stress and better preservation of left ventricular function.[52] NAC has also demonstrated beneficial effects in chronic pulmonary disease,[49] which is a risk factor for POAF. A recent small study published in the *European Heart Journal*[50] revealed the potential benefits of using NAC perioperatively and continuing for 48 h postoperatively to reduce the incidence of POAF.

Treatment of POAF

Although POAF can be transient and generally self-limiting, treatment is indicated for patients who remain symptomatic, are hemodynamically unstable, and who develop cardiac ischemia or heart failure. Conventional treatment strategies include prevention of thromboembolic events, control of the ventricular rate response, and restoring/maintaining sinus rhythm.

Rhythm control

Currently, the evidence suggests a trend towards a strategy of rhythm control over rate control. The advantages of rhythm control are a decreased time to cardioversion, prolonged maintenance of sinus rhythm, and decreased length of overall hospital stay.[53] Different agents may be effective in converting AF to sinus rhythm (Table 2), including amiodarone,[54] procainamide,[55] ibutilide,[56] and sotalol.[57]

In one study,[56] ibutilide was more effective than placebo for the treatment of POAF, but polymorphic ventricular tachycardia was reported and attributed to electrolyte imbalance. In the postoperative period, the beta-blocking action of sotalol is particularly effective at reducing the ventricular rate and its proarrhythmic toxicity is relatively infrequent, but this agent seems less effective than others for inducing cardioversion of AF.

Electrical cardioversion

Electrical cardioversion should be urgently performed when POAF results in hemodynamic instability, acute heart failure, or myocardial ischemia; it should be used, electively,

Table 3: Dosage, advantages, and side effects of drugs used for rate control in POAF

Drugs	Adult dosage	Advantages	Side effects
Digoxin	0.25-1.0 mg IV then 0.125-0.5 mg/day IV or PO	Can be used in heart failure	Nausea, AV block moderate effect in POAF
Beta-blockers			
Esmolol	500 µg/kg over 5 min, then 0.05-0.2 mg/kg/min	Short-acting effect and short duration	Might worsen congestive heart failure; can cause bronchospasm, hypotension; AV block
Atenolol	1-5 mg IV over 5 min, repeat after 10 min then 50-100 mg bid PO	Rapid onset of rate control (IV)	
Metoprolol	1-5 mg IV over 2 min, then 50-100 mg bid PO	Rapid onset of rate control (IV)	
Calcium-channel blockers			
Verapamil	2.5-10 mg IV over 2 min, then 80-120 mg/day bid PO	Short-acting effect	Might worsen congestive heart failure, AV block
Diltiazem	0.25 mg/kg IV over 2 min, then 5-15 mg/h IV		

bid = twice daily; PO = by mouth.

to restore sinus rhythm after the first onset of AF when a pharmacologic attempt has failed to resume a sinus rhythm.

Rate control

The postoperative period is characterized by increased adrenergic stress, thus, it may be difficult to control ventricular rate in patients with POAF. Short-acting beta-blockers are the therapy of choice, particularly in ischemic heart disease, but they may be poorly tolerated or relatively contraindicated in patients with known asthma or bronchospastic disease, congestive heart failure, or atrioventricular (AV) conduction block. Alternatively, other AV nodal blocking agents, their dosages and side effects are shown in Table 3.

Thromboembolism prevention

POAF is associated with an increased risk of perioperative strokes[58,59] that may be reduced by therapeutic anticoagulation. In contrast, anticoagulation in the postoperative period may increase the risk of bleeding or cardiac tamponade;[60] nevertheless, no controlled trials have specifically evaluated the efficacy and safety of anticoagulation therapy for new-onset POAF, which often resolves spontaneously after 4-6 weeks. Generally, anticoagulation is instituted for prolonged (>48 h) and/or frequent POAF episodes. The American College of Chest Physicians recommends the use of anticoagulation therapy, particularly for high-risk patients, such as those with a history of stroke or transient ischemic attack in whom AF develops after surgery. In these patients, it is also recommended to continue anticoagulation therapy for another 30 days after the return of a normal sinus rhythm.[61]

Conclusion

POAF is the most frequent arrhythmia after cardiac surgery, with an incidence of 30%. The frequency of this arrhythmia is increasing, most likely due to rising proportions of elderly patients undergoing cardiac surgery. Currently, there are significant variations in the prevention strategy for POAF. However, current evidence suggests that beta-blockers are effective, safe, and can be used in most patients. Therefore, unless contraindicated, beta-blockers should be continued perioperatively or initiated in all patients. In addition, amiodarone, biatrial pacing, statins, N-3 PUFAs, or NAC, could be used with beta-blocker-based therapy and may be beneficial in further reducing this postoperative arrhythmia.

Dr. Alqahtani *is a cardiology resident at St. Michael's Hospital.*

References

1. Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of postoperative atrial arrhythmias. *Ann Thorac Surg*. 1993;56:539-549.
2. 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(5 Suppl): III236-244.
3. Mathew JP, Fontes ML, Tudor IC, et al. A multicenter risk index for atrial fibrillation after cardiac surgery. *JAMA*. 2004;291:1720-1729.
4. Allessie MA, Boyden PA, Camm AJ, et al. Pathophysiology and prevention of atrial fibrillation. *Circulation*. 2001;103:769-777.
5. Maisel WH, Rawn J, Stevenson WG. Atrial fibrillation after cardiac surgery. *Ann Intern Med*. 2001;135:1061-1073.
6. Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. *Circulation*. 1996;94:390-397.
7. Mathew JP, Parks R, Savino JS, et al. Atrial fibrillation following coronary artery bypass graft surgery: predictors, outcomes, and resource utilization. MultiCenter Study of Perioperative Ischemia Research Group. *JAMA*. 1996;276:300-306.
8. Almassi GH, Schowalter T, Nicolosi AC, et al. Atrial fibrillation after cardiac surgery: a major morbid event? *Ann Surg*. 1997;226:501-511.
9. Banach M, Rysz J, Drozdz JA, et al. Risk factors of atrial fibrillation following coronary artery bypass grafting: a preliminary report. *Circ J* 2006;70:438-441.
10. Fuster V, Rydén LE, Asinger RW, 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 (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the North American Society of Pacing and Electrophysiology. *J Am Coll Cardiol*. 2001;38:1231-1266.
11. Levy MN. Sympathetic-parasympathetic interactions in the heart. *Circ Res*.1971;29:437-445.
12. Ishii Y, Schuessler RB, Gaynor SL, et al. Inflammation of atrium after cardiac surgery is associated with inhomogeneity of atrial conduction and atrial fibrillation. *Circulation*. 2005;111:2881-2888.
13. Tselentakis EV, Woodford E, Chandy J, Gaudette GR, Saltman AE.Inflammation effects on the electrical properties of atrial tissue and inducibility of postoperative atrial fibrillation. *J Surg Res*. 2006;135: 68-75.
14. Abdelhadi RH, Gurm HS, Van Wagoner DR, Chung MK. Relation of an exaggerated rise in white blood cells after coronary bypass or cardiac valve surgery to development of atrial fibrillation postoperatively. *Am J Cardiol* 2004;93:1176-1178.
15. Lamm G, Auer J, Weber T, Berent R, Ng C, Eber B. Post-operative white blood cell count predicts atrial fibrillation after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2006;20:51-56.
16. Spach MS, Dolber PC, Heidlage JF. Influence of the passive anisotropic properties on directional differences in propagation following modification of the sodium conductance in human atrial muscle. A model of reentry based on anisotropic discontinuous propagation. *Circ Res*. 1988; 62:811-832.
17. Wang TJ, Parise H, Levy D, et al. Obesity and the risk of new-onset atrial fibrillation. *JAMA*. 2004;292:2471-2477.
18. Echahidi N, Pibarot P, O'Hara G, Mathieu P. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery. *J Am Coll Cardiol*. 2008;51:793-801.
19. Ad N, Snir E, Vidne BA, Golomb E. Potential preoperative markers for the risk of developing atrial fibrillation after cardiac surgery. *Semin Thorac Cardiovasc Surg*. 1999;11:308-313.
20. Ak K, Akgun S, Tecimer T, et al. Determination of histopathologic risk factors for postoperative atrial fibrillation in cardiac surgery. *Ann Thorac Surg*. 2005;79:1970-1975.
21. Mariscalco G, Engstrom KG, Ferrarese S, et al. Relationship between atrial histopathology and atrial fibrillation after coronary bypass surgery. *J Thorac Cardiovasc Surg*. 2006;131:1364-1372.
22. Bruins P, te Velthuis H, Yazdanbakhsh AP, et al. Activation of the complement system during and after cardiopulmonary bypass surgery: postsurgery activation involves C-reactive protein and is associated with postoperative arrhythmia. *Circulation*. 1997;96:3542-3548.
23. Chung MK, Martin DO, Sprecher D, et al. C-reactive protein elevation in patients with atrial arrhythmias: inflammatory mechanisms and persistence of atrial fibrillation. *Circulation*. 2001;104:2886-2891.
24. Aviles RJ, Martin DO, Apperson-Hansen C, et al. Inflammation as a risk factor for atrial fibrillation. *Circulation*. 2003;108:3006-3010.
25. Stamou SC, Dangas G, Hill PC, et al. Atrial fibrillation after beating heart surgery. *Am J Cardiol*. 2000;86:64-67.
26. American Heart Association. Heart Disease and Stroke Statistics—An Update 2007. Dallas, TX: American Heart Association, 2007.
27. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 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 (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). *J Am CollCardiol*. 2006;48:854-906.
28. Lamb RK, Prabhakar G, Thorpe JA, Smith S, Norton R, Dyde JA. The use of atenolol in the prevention of supraventricular arrhythmias following coronary artery surgery. *Eur Heart J*. 1988;9:32-36.
29. Matangi MF, Strickland J, Garbe GJ, et al. Atenolol for the prevention of arrhythmias following coronary artery bypass grafting. *Can J Cardiol*. 1989;5:229-234.

30. Connolly SJ, Cybulsky I, Lamy A, et al. 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;145:226-232.
31. Coleman CI, Perkerson KA, Gillespie EL, et al. Impact of prophylactic post-operative beta-blockade on post-cardiothoracic surgery length of stay and atrial fibrillation. *Ann Pharmacother*. 2004;38:2012-2016.
32. Ferguson TB Jr., Coombs LP, Peterson ED. Preoperative betablocker use and mortality and morbidity following CABG surgery in North America. *JAMA*. 2002;287:2221-2227.
33. Pfisterer ME, Kloter-Weber UC, Huber M, et al. Prevention of supraventricular tachyarrhythmias after open heart operation by low-dose sotalol: a prospective, double-blind, randomized, placebo-controlled study. *Ann Thorac Surg*. 1997; 64:1113-1119.
34. Sanjuan R, Blasco M, Carbonell N, et al. Preoperative use of sotalol *vs* atenolol for atrial fibrillation after cardiac surgery. *Ann Thorac Surg*. 2004;77:838-843.
35. Parikka H, Toivonen L, Heikkila L, Virtanen K, Jarvinen A. Comparison of sotalol and metoprolol in the prevention of atrial fibrillation after coronary artery bypass surgery. *J Cardiovasc Pharmacol.* 1998;31:67–73.
36. Mitchell LB, Exner DV, Wyse DG, et al. Prophylactic oral amiodarone for the prevention of arrhythmias that begin early after revascularization, valve replacement, or repair (PAPABEAR): a randomized controlled trial. *JAMA*. 2005;294:3093-3100.
37. Bagshaw SM, Galbraith PD, Mitchell LB, Sauve R, Exner DV, Ghali WA. Prophylactic amiodarone for prevention of atrial fibrillation after cardiac surgery: a meta-analysis. *Ann Thorac Surg*. 2006;82:1927-1937.
38. Burgess DC, Kilborn MJ, Keech AC. Interventions for prevention of post-operative atrial fibrillation and its complications after cardiac surgery: a meta-analysis. *Eur Heart J*. 2006;27:2846-2857.
39. 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.
40. Daoud EG, Snow R, Hummel JD, Kalbfleisch SJ, Weiss R, Augostini R. Temporary atrialepicardial pacing as prophylaxis against atrial fibrillation after heart surgery: a meta-analysis. *J Cardiovasc Electrophysiol*. 2003;14:127-132.
41. Marin F, Pascual DA, Roldan V, et al. Statins and postoperative risk of atrial fibrillation following coronary artery bypass grafting. *Am J Cardiol*. 2006;97: 55-60.
42. Patti G, Chello M, Candura D, et al. Randomized trial of atorvastatin for reduction of post-operative atrial fibrillation in patients undergoing cardiac surgery: results of the ARMYDA-3 (Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery) study. *Circulation*. 2006;114:1455-1461.
43. Jahangiri A, Leifert WR, Patten GS, McMurchie EJ. Termination of asynchronous contractile activity in rat atrialmyocytes by N-3 polyunsaturated fatty acids. *Mol Cell Biochem*. 2000;206:33-41.
44. Sarrazin JF, Comeau G, Daleau P, et al. Reduced incidence of vagally-induced atrial fibrillation and expression levels of connexins by N-3 polyunsaturated fatty acids in dogs. *J Am CollCardiol*. 2007;50:1505-1512.
45. Mozaffarian D, Psaty BM, Rimm EB, et al. Fish intake and risk of incident atrial fibrillation. *Circulation*. 2004;110:368-373.
46. Calo L, Bianconi L, Colivicchi F, et al. N-3 Fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial. *J Am Coll Cardiol.* 2005;45:1723-1728.
47. Halonen J, Halonen P, Järvinen O, et al. Corticosteroids for the prevention of atrial fibrillation after cardiac surgery: a randomized controlled trial. *JAMA*. 2007;297:1562-1567.
48. Miller S, Crystal E, Garfinkle M, Lau C, Lashevsky I, Connolly SJ. Effects of magnesium on atrial fibrillation after cardiac surgery: a meta-analysis. *Heart* 2005;91:618-623.
49. Arfsten D, Johnson E, Thitoff A, et al. Impact of 30-day oral dosing with N-acetyl-L-cysteine on Sprague-Dawley rat physiology. *Int J Toxicol*. 2004;23:239-247.
50. Ozaydin M, Peker O, Dogan E, et al. N-acetylcysteine for the prevention of postoperative atrial fibrillation: a prospective,randomized, placebo-controlled pilot study, *Eur Heart J*. 2008;29:625-631.
51. Orhan G, Yapici N, Yuksel M, et al. Effects of N-acetylcysteine on myocardial ischemia–reperfusion injury in bypass surgery. *Heart Vessels*. 2006;21:42-47.
52. Sajkowska A, Wykretowicz A, Szczepanik A, Kempa M, Minczykowski A, Wysocki H. Fibrinolytic therapy and N-acetylocysteine in the treatment of patients with acute myocardial infarction: its influence on authentic plasma hydroperoxide levels and polymorphonuclear neutrophil oxygen metabolism. *Cardiology*. 1999;91:60-65.
53. Lee JK, Klein GJ, Krahn AD, et al. Rate-control versus conversion strategy in post-operative atrial fibrillation: trial design and pilot study results. *Card Electrophysiol Rev*. 2003;7:178-184.
54. Daoud EG, Strickberger SA, Man KC, et al. Preoperative amiodarone as prophylaxis against atrial fibrillation after heart surgery. *N Engl J Med.* 1997;337: 1785-1791.
55. Kowey PR, Taylor JE, Rials SJ, Marinchak RA. Meta-analysis of the effectiveness of prophylactic drug therapy in preventing supraventricular arrhythmia early after coronary artery bypass grafting. *Am J Cardiol.* 1992;69:963-965.
56. 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;100:369-375.
57. Gomes JA, Ip J, Santoni-Rugiu F, et al. Oral d,l sotalol reduces the incidence of post-operative atrial fibrillation in coronary artery bypass surgery patients: a randomized, double-blind, placebo-controlled study. *J Am Coll Cardiol.* 1999; 34:334-339.
58. Bucerius J, Gummert JF, Borger MA, et al. Stroke after cardiac surgery: a risk factor analysis of 16,184 consecutive adult patients. *Ann Thorac Surg*. 2003; 75:472-478.
59. Hogue CW Jr, Murphy SF, Schechtman KB, Davila-Roman VG. Risk factors for early or delayed stroke after cardiac surgery. *Circulation*. 1999;100:642-647.
60. Meurin P, Weber H, Renaud N, et al. Evolution of the post-operative pericardial effusion after day 15. *Chest* 2004;125:2182–2187.
61. Epstein AE, Alexander JC, Gutterman DD, Maisel W, Wharton JM. Anticoagulation: American College of Chest Physicians guidelines for the prevention and management of post-operative atrial fibrillation after cardiac surgery. *Chest*. 2005;128:24S–27S.

Upcoming Meetings

27 July – 8 August 2008
34th Ten-Day Seminar on the Epidemiology and Prevention of Cardiovascular Disease
Tahoe City, CA
Contact: Web site: www.heart.org/presenter.jhtml?identifier=3051442
Telephone: (888) 242-2453

30 August – 3 September 2008
ESC Congress 2008
Munich, Germany
Contact: Web site: www.escardio.org/

Disclosure Statement: *Drs. Alqahtani and Moe have no disclosures to announce in association with the contents of this issue.*

Change of address notices and requests for subscriptions to *Cardiology Rounds* are to be sent by mail to P.O. Box 310, Station H, Montreal, Quebec H3G 2K8 or by fax to (514) 932-5114 or by e-mail to info@snellmedical.com. Please reference *Cardiology Rounds* in your correspondence. Undeliverable copies are to be sent to the address above. Publications Post #40032303

This publication is made possible by an educational grant from
Merck Frosst Canada Ltd.