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New-Onset Atrial Fibrillation in the Intensive Care Unit: An under-appreciated yet common phenomenon

BY SALMAAN KANJI, PHARM.D.

Atrial fibrillation (AF) is the most common dysrhythmia in adults. Prevalence increases with age from <1% in those <60-years-old to >8% in those >80-years-old.¹ Literature describing the epidemiology, outcomes, and treatment of AF in non-critically ill patients is extensive. For critically ill patients, studies of new-onset AF after cardiac surgery are abundant; however, similar studies in medical and non-cardiac surgery intensive care unit (ICU) patients are few. Published data on new-onset AF in medical and non-cardiac surgical ICU patients suggest that the prevalence is similar or greater than in the community and that the burden of illness may be greater in the ICU. The available literature describing the pathophysiology, epidemiology, and treatment of AF in the non-cardiac critically ill patient is reviewed in this issue of *Critical Care Rounds*.

Epidemiology

In the ICU, supraventricular tachyarrhythmias are common and usually transient, with AF being the most common dysrhythmia. Estimates of the incidence of new-onset AF in critically ill patients after non-cardiac surgery,²⁻¹³ in medical ICU patients,¹⁴⁻¹⁶ and in post-cardiac surgery patients¹⁷ are described in Table 1. The major limitation of these studies is that they are single centre trials that may not be extrapolated to other populations and are dependent on the relative case mix, techniques, and types of surgeries, etc. Nevertheless, it appears clear that AF is common among ICU patients and the incidence of new-onset AF approximates that described in post-cardiac surgery patients.

Several risk factors for AF have been identified in both surgical and medical ICU patients. In surgical patients, commonly identified risk factors include advanced age, blunt thoracic trauma, postoperative hypotension, postoperative septic shock and the systemic inflammatory response syndrome (SIRS), presence of a pulmonary artery catheter, calcium-channel blocker withdrawal in the perioperative period, postoperative pulmonary edema, and heart failure.^{2,4,13} The causes of new-onset AF in medical ICU patients are also multifactorial; the most common risk factors being underlying cardiac disease, high cardiac filling pressures, age, sepsis, cardiovascular failure, hypoxia, electrolyte abnormalities (especially those of magnesium and potassium), and multi-organ dysfunction.¹⁸

Course and outcomes of new-onset AF

While AF may occur at any time during the postoperative period, it tends to appear most frequently on postoperative days 2 and 3. In most cases, the arrhythmia has a reversible cause (eg, electrolyte abnormalities, septic shock, hypoxia, etc.) and rarely persists upon discharge from the ICU. However, AF and its management may complicate the treatment of underlying disease states, especially for patients who experience hemodynamic instability consequent to rapid AF. This may contribute to the consistent observation that ICU patients who develop AF have longer lengths of stay and higher mortality rates relative to similar patients who do not develop AF in the ICU. The risk of mortality associated with new-onset AF in the ICU differs among patient populations. Patients who develop AF after cardiac surgery have an approximate 2- to 2.5-fold increase in the risk of death compared to a 2- to 6-fold increase in the risk of death for



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Table 1: Incidence of atrial fibrillation (AF) among different critically ill populations

ICU Population	Subset	Incidence of new-onset AF
Surgical ICU	General non-cardiac ^{2,4}	5% - 9%
	Pulmonary surgery ^{5-8*}	8% - 22%
	Pneumonectomy ⁹⁻¹¹	10% - 23%
	Esophagectomy ¹³	22%
Medical ICU	Non-thoracic surgery ¹²	10%
	General medical ICU patients ^{14,15}	10% - 20%
Cardiac surgery ICU/CCU	Septic shock ¹⁶	17%
	Post-operative cardiac surgery ¹⁷	10% - 65%

* Refers to studies that included both lobectomies, pulmonary resections, and pneumonectomies, whereas pneumonectomy refers to studies that only looked at pneumonectomy.

those who develop AF after non-cardiac surgery.^{2,4,11-13,19} A single centre study involving 946 medical ICU patients reported a near 2-fold increase in mortality among patients developing new-onset AF.¹⁴ Although these studies describe an association between the development of AF and an increased risk of death, they were unable to establish causality. It has been suggested that the development of AF is a marker of severity of illness rather than an independent contributor to mortality.

Pathophysiology

AF is characterized by rapid, ineffective, multifocal atrial contractions with the classic “irregularly - irregular” ventricular response. The multiple ectopic foci within the atria act as independent pacemakers that fire at such a rapid rate (ie, 350 to 600 beats per second) that impulses from the sinoatrial (SA) node are overridden. During AF, the atrial “kick” or systole that normally contributes 20% to 30% of the stroke volume is lost. If the atrial impulses cannot be sufficiently filtered by the AV node (due to the reduced refractory period of the AV node), patients may develop a rapid ventricular response characterized by ventricular rates that may exceed 200 beats per minute. The combination of the loss of atrial contraction, rapid ventricular rate, and reduced diastolic filling time can result in marked hemodynamic instability manifested by hypotension, syncope, myocardial ischemia, and pulmonary edema. Elderly patients and those with underlying cardiac disease are more likely to experience hemodynamic instability consequent to this reduction in cardiac output.

While the electrophysiological mechanisms of AF have been well described, the exact pathophysiology has not. Recent publications suggest that inflammation plays a significant role in the pathogenesis of AF. The initial hypothesis was generated from observations that activation of the complement system and release of proinflammatory cytokines occur after cardiac surgery. Furthermore, interleukin-6, C-reactive protein (CRP) levels, and complement-CRP complexes appear to peak during the first, second, and third postoperative days, coinciding with the peak incidence of

AF.²⁰ Subsequent studies describe not only associations between increased expression of CRP and AF, but also a predictive relationship.²¹⁻²⁴ One study of 77 patients with chronic AF suggested that interleukin-6 levels and CRP are independent predictors of stroke and death due to stroke.²⁵ Another study of 110 patients undergoing coronary artery bypass surgery suggested that genetic polymorphism of the promoter gene for interleukin-6 expression can predict the development of postoperative AF.²⁶ On the basis of these observations, trials designed to evaluate the role of anti-inflammatory therapies on the development of AF are emerging. In a canine pericarditis model, the HMG-CoA reductase inhibitor, atorvastatin, was shown to prevent the onset of AF when compared to placebo.²⁷ The authors hypothesized that the anti-inflammatory activity of atorvastatin, mediated by its ability to reduce CRP levels by up to 30%, was the mechanism behind the ability of atorvastatin to attenuate pericarditis-induced AF. Finally, a recent Canadian study randomized 68 patients undergoing cardiopulmonary bypass, in a 2x2 factorial design, to methylprednisolone and a biocompatible co-polymer circuit designed to reduce complement activation and inflammation associated with extracorporeal circulation.²⁸ In this study, methylprednisolone was found to significantly reduce interleukin (IL)-6, IL-8, and complement activation. A significant reduction in the incidence of post-operative AF was also observed in those treated with methylprednisolone (12%) when compared to those who were not (38%, p=0.02).

Although none of these studies describing the relationship between inflammation and AF were conducted in non-cardiac surgery or medical ICU patients, it would be reasonable to hypothesize that inflammation may play a role in the pathophysiology of AF in the ICU. Given the fact that several risk factors for AF involving inflammatory pathways have been identified including sepsis, shock, multiorgan failure, and trauma, it is apparent that clinical trials are necessary to address this hypothesis.

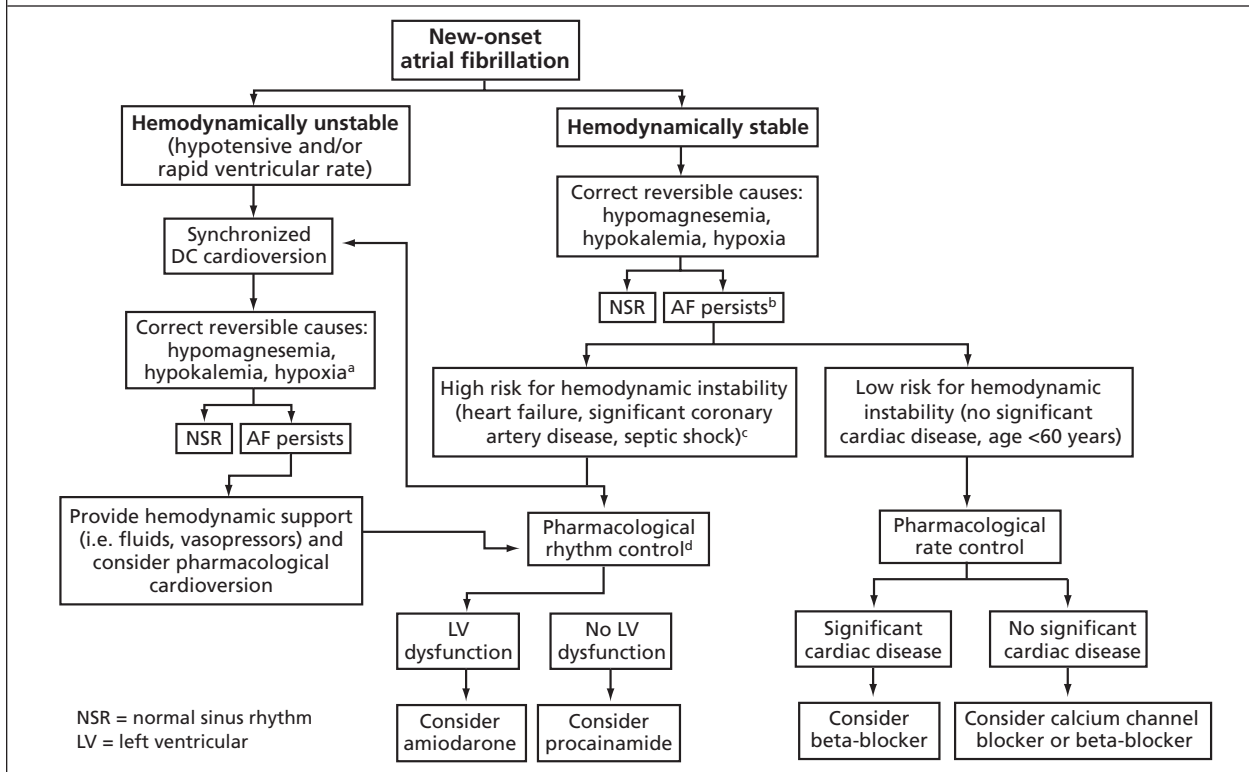
Treatment

The three cornerstones of treatment for AF include rhythm control, rate control, and thromboembolism prophylaxis. The approach to treatment depends on the hemodynamic stability of the patient. ICU patients with hypotension, pulmonary edema, or myocardial ischemia related to acute AF require immediate intervention, whereas the approach to the hemodynamically stable ICU patient with AF is somewhat more controversial. There are many trials of prophylactic and treatment strategies in cardiac surgery patients, but few in other critically ill populations. A proposed algorithm for the management of AF in the critically ill patient is presented in Figure 1.

New-onset AF in the hemodynamically unstable patient

Although a rapid ventricular rate is often associated with hypotension, pharmacological intervention targeting rate control (eg, with beta-adrenergic or calcium channel blockade) can often worsen hypotension before controlling the heart rate. This effect is compounded by the fact that it may take hours to reach a target-controlled heart rate. Even pharmacologic approaches to rhythm control (eg, antiarrhythmic drugs) may not work immediately, thereby placing the patient at risk for myocardial ischemia and prolonged

Figure 1: Suggested algorithm for the management of new-onset atrial fibrillation (AF) in critically ill patients



a The likelihood of successful electrical cardioversion may be improved by correcting reversible precipitating factors prior to or simultaneously with electrical cardioversion, if possible.

b Patients who develop hemodynamic instability at any time should be considered for electrical cardioversion.

c Hemodynamically stable patients who are at high risk may be considered for either pharmacological or electrical cardioversion.

d Patients who fail attempted cardioversion should be considered for rate control.

multiorgan hypoperfusion. Precipitating factors (eg, electrolyte abnormalities, hypoxia, etc.) can often be identified, but may not be immediately or easily reversible (eg, septic shock, underlying cardiac disease, postoperative pulmonary edema, etc.).

The treatment of choice in the unstable patient is synchronized electrical cardioversion, since this is the fastest way to restore normal sinus rhythm. When electrical cardioversion is ineffective, further efforts to correct the rate and rhythm may have to be performed simultaneously with efforts to provide supportive care (eg, fluids, vasopressor support) as appropriate. While studies of electrical cardioversion report conversion rates of 67% to 94% in non-ICU patients, the only study involving critically ill patients reported a successful conversion rate of only 35% in 37 postoperative general surgery patients.²⁹ This study highlights the need for alternative courses of action in unstable patients with AF.

Rhythm control for new-onset AF in the stable patient

Direct current cardioversion may also be considered for the hemodynamically stable patient in order to avoid the transformation to unstable AF with its attendant morbidity and mortality. Pharmacological conversion with antiarrhythmic drugs has been extensively studied in ambulatory and hospitalized patients, but very few trials involve critically ill patients. Since the etiology and definition of “new-onset” AF in the ICU is different from that in the community, extrapolation from these studies is difficult. The likelihood

of successful conversion electrically, pharmacologically, or spontaneously is inversely proportional to the duration of AF. This is due to the electrical and structural remodeling of the atria associated with AF. Shortening of the atrial refractory period has been described even weeks after conversion to sinus rhythm, increasing the risk of reversion to AF. Structural remodeling includes atrial atrophy, fibrosis, and progressive dilatation that can perpetuate AF.³⁰ Unfortunately, the definitions of both “new-onset” AF and successful conversion have not been standardized in clinical trials. In trials of new-onset AF, the duration of AF can range from 6 hours to 90 days and the definition of successful cardioversion may be defined as sinus rhythm for as short a duration as 1 minute to as long as 24 hours. Spontaneous conversion to sinus rhythm is as common as reversion to AF after conversion. One study of new-onset (<72 hours) AF suggests that the likelihood of spontaneous conversion (for any length of time) occurred in 68% of patients, most frequently within the first 24 hours.³¹ Attention to these definitions is critical when evaluating and comparing clinical trials of rhythm control.

When choosing an antiarrhythmic drug in the ICU, expected efficacy rates, side effects, and the availability of different dosage forms must be considered. If AF is considered as a marker of illness severity, the patients who develop AF are more likely to have multiple acute medical problems (eg, septic shock, recent major surgery, etc). Consequently, the approach to AF treatment may differ for the critically ill patient than the ambulatory or hospitalized patient. The

choice of rhythm vs rate control and even the choice of drug within each category depends on the underlying disease and severity of the illness. Indeed, during the acute stage of critical illness, drug absorption via enteral administration is unpredictable and often significantly reduced. Hence, drug selection may be limited to those available in intravenous forms.

Currently, only amiodarone, procainamide, and ibutilide are available in intravenous forms in Canada. Their side effects warrant special consideration, since all can cause hypotension, exacerbate heart failure, and be proarrhythmic. Procainamide has been reported to cause significant hypotension and exacerbate heart failure. Although amiodarone is likely the most frequently used drug in the critical care setting, it can cause significant hypotension, bradycardia, and rarely, acute pulmonary toxicity. Ibutilide, while considered to be one of the more effective new agents for atrial rhythm control, has a disconcerting potential for proarrhythmia. Clinical trials with ibutilide report a relatively high incidence of sustained polymorphic ventricular tachycardia (VT) (1.7%), nonsustained polymorphic VT (2.6%), and nonsustained monomorphic VT (4.9%).³² The risk of *torsades des pointes* has been reported to be as high as 8% in patients with significant underlying cardiac disease.

More recently, magnesium has been recognized for its antiarrhythmic properties.³³ It is an essential cofactor in the maintenance of myocardial membrane potential and is relatively safe in patients with adequate renal function. Its role as a preventive strategy in the perioperative setting and as a treatment alternative (alone and in combinations with other strategies for rhythm control) is being studied.

Only 2 trials have compared available antiarrhythmic drugs for the conversion of new-onset AF in non-cardiac surgery critically ill patients.

- Chapman et al randomized 26 critically ill ICU patients with new-onset tachyarrhythmias (16 of whom had AF) to 24-hour infusions of either amiodarone or procainamide.³⁴ Conversion was defined as normal sinus rhythm within 12 hours with no requirement for maintenance of sinus rhythm. At 12 hours, tachyarrhythmias were converted to normal sinus rhythm in 70% of patients receiving amiodarone and 71% receiving procainamide. The authors concluded that procainamide and amiodarone are equally efficacious.
- In the second study, Moran et al randomized 42 non-cardiac surgery ICU patients with supraventricular tachyarrhythmias to 24-hour infusions of amiodarone and magnesium.³⁵ Unfortunately, only 34 had new-onset (not defined) supraventricular tachyarrhythmias, 26 of whom had AF. Conversion was defined as normal sinus rhythm within 24 hours with no requirement for maintenance of conversion. Among those with new-onset supraventricular tachyarrhythmias, the conversion rates were 78% and 50% for magnesium and amiodarone, respectively. The authors concluded that the probability of conversion is significantly greater at 24 hours with magnesium when compared to amiodarone. No patient with chronic AF converted with either drug. At this time, ibutilide has not been studied in critically ill patients.

Clearly, there is a paucity of clinical trials investigating the role of antiarrhythmic drugs for the critically ill patient with new-onset AF. The heterogeneity of these trials and the lack of standardized definitions of “new-onset” AF and successful conversion make interpretation and comparison difficult. Furthermore, very few of these trials evaluate maintenance of conversion, a more meaningful and relevant clinical outcome. When interpreting these clinical trials it is impossible to separate spontaneous conversion from pharmacological conversion, especially when other studies suggest that spontaneous conversion rates within 24 hours are at least as high, if not higher, than reported conversion rates of drugs in these trials. In fact, a recent systematic review of pharmacological conversion of AF concluded that in new-onset AF (defined as <7 days duration), conventional doses of amiodarone are no better than placebo.³⁰ The authors recommend procainamide as the agent with the best evidence of efficacy for new-onset AF of <7 days duration. For patients with significant left ventricular dysfunction, electrical cardioversion may be a more reasonable option with amiodarone as an alternative treatment for rhythm control, since procainamide may exacerbate heart failure and ibutilide may put patients at risk of life-threatening arrhythmias.

Rate control for new-onset AF in the stable patient

Given that both electrical and pharmacological strategies for rhythm control appear only marginally effective with arguably similar conversion rates to that of spontaneous conversion, ventricular rate control with AV nodal blocking agents (eg, beta blockers, calcium-channel blockers, digoxin, and amiodarone) is an attractive alternative to rhythm control in the hemodynamically stable ICU patient. The question of rhythm versus rate control for AF is an ongoing debate. There are 2 published trials that have enrolled >500 patients comparing pharmacological rhythm and rate control strategies. Although neither of these trials included critically ill patients, the results may still have implications for the management of AF in the ICU patient.

- The AFFIRM trial randomized 4060 patients with persistent AF to rhythm control or rate control; the primary outcome was mortality at 5 years.³⁶ Drug selection was at the discretion of the physician. Amiodarone and sotalol were the most commonly prescribed agents for rhythm control, while digoxin, beta-blockers, and diltiazem were the most prescribed drugs for rate control. After 5 years, the mortality rates were 23.8% in the rhythm control group and 21.3% in the rate control group (p=0.008). The authors concluded that rhythm control offers no mortality advantage over rate control.
- In the RACE study, 522 patients with recurrent or persistent AF after attempted electrical cardioversion were randomized to pharmacological rhythm or rate control.³⁷ The primary outcome of this study was a composite endpoint of death from cardiovascular causes, heart failure, thromboembolic complications, implantation of a pacemaker, and serious drug-related adverse events. Patients randomized to rhythm control were initially treated with sotalol and then flecainide, propafenone, and amiodarone sequentially, if sinus

rhythm was not achieved at 6-month intervals. Patients in the rate control group were treated with digoxin, calcium channel blockers, or beta-blockers, alone or in combination. After a mean of 2.3 years, the composite primary endpoint occurred in 22.6% of patients in the rhythm control group and in 17.2% of patients in the rate control group (hazard ratio=0.73, p=0.11). The results of this study demonstrate that rhythm control is not superior to rate control for the prevention of mortality or morbidity from cardiovascular causes in patients who fail an attempt at electrical cardioversion.

Although neither of these trials involved critically ill patients nor those with new-onset AF, they emphasized that a therapeutic goal of rate control may be acceptable for many hemodynamically stable patients, particularly when considering that AF in the critical care setting is often transient and many patients spontaneously convert to normal sinus rhythm as they respond to treatment of their underlying disease. One study of 55 general surgery patients who developed supraventricular tachyarrhythmias (44 patients had AF) as a postoperative complication, compared rate control strategies with continuous infusions of esmolol versus diltiazem.³⁸ Patients were treated within 15 minutes of arrhythmia recognition and conversion was assessed at 12 hours. Eighty-five percent of patients randomized to esmolol were in sinus rhythm at 12 hours compared to 62% in the diltiazem group (p=0.116). The authors hypothesized that in the immediate postoperative period, beta-blocking agents were associated with high conversion rates due to their ability to attenuate arrhythmogenesis caused by catecholamine-stimulated atrial cells. Regardless of the choice of rate-controlling drugs, the contribution of spontaneous conversion to normal sinus rhythm is difficult to assess in these trials.

In the ICU, acceptable agents for rate control include beta-blocking agents (eg, metoprolol, esmolol) and calcium-channel blocking agents (eg, diltiazem, verapamil). All are available in intravenous forms and can be titrated via continuous infusion or bolus dosing, except for esmolol, which should only be administered via continuous infusion because it has such a short half-life. Beta-blocking agents may be more appropriate for patients with underlying cardiovascular disease including heart failure, since they are less likely to cause significant hypotension or reduce cardiac output. Diltiazem or verapamil are preferred for patients with severe reactive airway disease. Digoxin is commonly used to control rate in ambulatory patients, but its role in critical illness is limited. Since the ventricular rate-lowering effects of digoxin are partially mediated by vagal stimulation, its efficacy may be limited during critical illness or in the immediate postoperative period when patients are in a hyperadrenergic state and have high levels of catecholamines.

Anticoagulation for stroke prevention

In chronic AF, anticoagulation with warfarin is an essential element of AF management to prevent thromboembolic complications.¹ Pooled analyses of stroke

prevention trials suggest that anticoagulation with warfarin in patients with persistent AF reduces the relative risk of stroke by 62%. The most commonly identified risk factors for stroke among patients with AF include age, hypertension, thyrotoxicosis, diabetes, cardiovascular disease, congestive heart failure, and a history of stroke/transient ischemic attack or thromboembolism.³⁹ Although the benefits of warfarin have been well documented in this setting, it is difficult to extrapolate these data to critically ill patients since it is clear that the etiology and consequences of AF in the ICU are different from that in the community. As in all patients with persistent or paroxysmal AF, the benefits of stroke prevention must be weighed against the risk of bleeding. In the ICU, continuous infusion of unfractionated heparin is the preferred method of anticoagulation simply because, in the event of a bleeding complication or the need for invasive intervention (eg, catheter insertion, chest tube placement, etc.), it has a shorter duration of action and can be more predictably reversed than low molecular weight heparin or warfarin. In non-critically ill patients, AF that persists >48 hours is associated with an increased risk of stroke. In the absence of large epidemiological and treatment trials in critically ill patients, it would be prudent to consider anticoagulation for patients in whom AF persists >48 hours.⁴⁰

Conclusion

Considering the prevalence and associated morbidity and mortality of AF in the critically ill patient, there is a considerable lack of available literature to guide clinicians in the management of these patients. Extrapolation of clinical trial results from other populations with AF must be done cautiously since the etiology, course, and outcomes of AF in the ICU differ considerably. Appropriate treatment of AF in the ICU patient is based on an appreciation of potential underlying triggers, recognizing that some may be immediately reversible and others will resolve as the clinical condition of the patient improves. An aggressive approach to rhythm control with electrical cardioversion is warranted in hemodynamically unstable patients. In the hemodynamically stable patient, the benefit of rhythm versus rate control is debatable. Therapeutic anticoagulation with unfractionated heparin should be considered for all patients in whom AF persists beyond 48 hours. Further research should be directed towards addressing the roles of rhythm and rate control, drug selection for pharmacological cardioversion, the epidemiology of thromboembolic complications, and the role of stroke prevention in noncardiac surgery critically ill patients.

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References

1. McNamara RL, Tamariz LJ, Segal JB, Bass EB. Management of atrial fibrillation: review of the evidence for the role of pharmacologic therapy, electrical cardioversion, and echocardiography. *Ann Intern Med* 2003;139(12):1018-1033.
2. Seguin P, Signouret T, Laviolle B, Branger B, Malledant Y. Incidence and risk factors of atrial fibrillation in a surgical intensive care unit. *Crit Care Med* 2004;32:722-726.
3. Bender JS. Supraventricular tachyarrhythmias in the surgical intensive care unit: an under-recognized event. *Am Surg* 1996;62(1):73-75.
4. Knotzer H, Mayr A, Ulmer H, et al. Tachyarrhythmias in a surgical intensive care unit: a case-controlled epidemiologic study. *Intensive Care Med* 2000;26(7):908-914.
5. Dyszkiewicz W, Skrzypczak M. Atrial fibrillation after surgery of the lung: clinical analysis of risk factors. *Eur J Cardiothorac Surg* 1998;13(6):625-628.
6. Curtis JJ, Parker BM, McKenney CA, et al. Incidence and predictors of supraventricular dysrhythmias after pulmonary resection. *Ann Thorac Surg* 1998;66(5):1766-1771.
7. Rena O, Papalia E, Oliaro A, et al. Supraventricular arrhythmias after resection surgery of the lung. *Eur J Cardiothorac Surg* 2001;20(4):688-693.
8. von Knorring J, Lepantalo M, Lindgren L, Lindfors O. Cardiac arrhythmias and myocardial ischemia after thoracotomy for lung cancer. *Ann Thorac Surg* 1992;53(4):642-647.
9. Krowka MJ, Pairolero PC, Trastek VF, Payne WS, Bernatz PE. Cardiac dysrhythmia following pneumonectomy. Clinical correlates and prognostic significance. *Chest* 1987;91(4):490-495.
10. Wahi R, McMurtrey MJ, DeCaro LF, et al. Determinants of perioperative morbidity and mortality after pneumonectomy. *Ann Thorac Surg* 1989;48(1):33-37.
11. Foroulis CN, Kotoulas C, Lachanas H, Lazopoulos G, Konstantinou M, Lioulis AG. Factors associated with cardiac rhythm disturbances in the early post-pneumonectomy period: a study on 259 pneumonectomies. *Eur J Cardiothorac Surg* 2003;23(3):384-389.
12. Brathwaite D, Weissman C. The new onset of atrial arrhythmias following major noncardiothoracic surgery is associated with increased mortality. *Chest* 1998;114(2):462-468.
13. Murthy SC, Law S, Whooley BP, Alexandrou A, Chu KM, Wong J. Atrial fibrillation after esophagectomy is a marker for postoperative morbidity and mortality. *J Thorac Cardiovasc Surg* 2003;126(4):1162-1167.
14. Artucio H, Pereira M. Cardiac arrhythmias in critically ill patients: epidemiologic study. *Crit Care Med* 1990;18(12):1383-1388.
15. Reinelt P, Karth GD, Geppert A, Heinz G. Incidence and type of cardiac arrhythmias in critically ill patients: a single center experience in a medical-cardiological ICU. *Intensive Care Med* 2001;27(9):1466-1473.
16. Ledingham IM, McArdle CS. Prospective study of the treatment of septic shock. *Lancet* 1978;1(8075):1194-1197.
17. Maisel WH, Rawn JD, Stevenson WG. Atrial fibrillation after cardiac surgery. *Ann Intern Med* 2001;135(12):1061-1073.
18. Trappe HJ, Brandts B, Weismueller P. Arrhythmias in the intensive care patient. *Curr Opin Crit Care* 2003;9(5):345-355.
19. Almassi GH, Schowalter T, Nicolosi AC, et al. Atrial fibrillation after cardiac surgery: a major morbid event? *Ann Surg* 1997;226(4):501-511.
20. Bruins P, de 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(10):3542-3548.
21. Anderson JL, Allen Maycock CA, Lappe DL, et al. Frequency of elevation of C-reactive protein in atrial fibrillation. *Am J Cardiol* 2004;94(10):1255-1259.
22. Asselbergs FW, van den Berg MP, Diercks GF, van Gilst WH, van Veldhuisen DJ. C-reactive protein and microalbuminuria are associated with atrial fibrillation. *Int J Cardiol* 2005;98(1):73-77.
23. Aviles RJ, Martin DO, Apperson-Hansen C, et al. Inflammation as a risk factor for atrial fibrillation. *Circulation* 2003;108(24):3006-3010.
24. 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(24):2886-2891.
25. Conway DS, Buggins P, Hughes E, Lip GY. Prognostic significance of raised plasma levels of interleukin-6 and C-reactive protein in atrial fibrillation. *Am Heart J* 2004;148(3):462-466.
26. Gaudino M, Andreotti F, Zamparelli R, et al. The -174G/C interleukin-6 polymorphism influences postoperative interleukin-6 levels and postoperative atrial fibrillation. Is atrial fibrillation an inflammatory complication? *Circulation* 2003;108 Suppl 1:II195-II199.
27. Kumagai K, Nakashima H, Saku K. The HMG-CoA reductase inhibitor atorvastatin prevents atrial fibrillation by inhibiting inflammation in a canine sterile pericarditis model. *Cardiovasc Res* 2004;62(1):105-111.
28. Rubens FD, Nathan H, Labow R, et al. Effects of methylprednisolone and a biocompatible copolymer circuit on blood activation during cardiopulmonary bypass. *Ann Thorac Surg* 2005;79(2):655-665.
29. Mayr A, Ritsch N, Knotzer H, et al. Effectiveness of direct-current cardioversion for treatment of supraventricular tachyarrhythmias, in particular atrial fibrillation, in surgical intensive care patients. *Crit Care Med* 2003;31(2):401-405.
30. Slavik RS, Tisdale JE, Borzak S. Pharmacologic conversion of atrial fibrillation: a systematic review of available evidence. *Prog Cardiovasc Dis* 2001;44(2):121-152.
31. Danias PG, Caulfield TA, Weigner MJ, Silverman DI, Manning WJ. Likelihood of spontaneous conversion of atrial fibrillation to sinus rhythm. *J Am Coll Cardiol* 1998;31(3):588-592.
32. Kowey PR, VanderLugt JT, Luderer JR. Safety and risk/benefit analysis of ibutilide for acute conversion of atrial fibrillation/flutter. *Am J Cardiol* 1996;78(8A):46-52.
33. Piotrowski AA, Kalus JS. Magnesium for the treatment and prevention of atrial tachyarrhythmias. *Pharmacotherapy* 2004;24(7):879-895.
34. Chapman MJ, Moran JL, O'Fathartaigh MS, Peisach AR, Cunningham DN. Management of atrial tachyarrhythmias in the critically ill: a comparison of intravenous procainamide and amiodarone. *Intensive Care Med* 1993;19(1):48-52.
35. Moran JL, Gallagher J, Peake SL, Cunningham DN, Salagaras M, Leppard P. Parenteral magnesium sulfate versus amiodarone in the therapy of atrial tachyarrhythmias: a prospective, randomized study. *Crit Care Med* 1995;23(11):1816-1824.
36. Wyse DG, Waldo AL, DiMarco JP, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002;347(23):1825-1833.
37. Van Gelder IC, Hagens VE, Bosker HA, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med* 2002;347(23):1834-1840.
38. Balser JR, Martinez EA, Winters BD, et al. Beta-adrenergic blockade accelerates conversion of postoperative supraventricular tachyarrhythmias. *Anesthesiology* 1998;89(5):1052-1059.
39. Rockson SG, Albers GW. Comparing the guidelines: anticoagulation therapy to optimize stroke prevention in patients with atrial fibrillation. *J Am Coll Cardiol* 2004;43(6):929-935.
40. Weigner MJ, Caulfield TA, Danias PG, Silverman DI, Manning WJ. Risk for clinical thromboembolism associated with conversion to sinus rhythm in patients with atrial fibrillation lasting less than 48 hours. *Ann Intern Med* 1997;126(8):615-620.

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