Update on cardiac arrhythmias in the ICU

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Purpose of review

To explore recent findings on the treatment and outcome of cardiac arrhythmias and how they affect ICU activities.

Recent findings

The rate vs. rhythm control debate for the treatment of chronic atrial fibrillation continues. It is still unclear whether the postcardiac surgery inflammatory response contributes to the development of atrial fibrillation. In noncardiothoracic surgery/trauma patients hospitalized in an ICU, new-onset supraventricular arrhythmias are associated with markedly elevated mortality when compared with patients with a prior history of such arrhythmias and patients who do not develop arrhythmias. The onset of new supraventricular arrhythmias in such patients appears to be a manifestation of multiple system organ failure as it is closely associated with sepsis. Cardioversion of supraventricular arrhythmias with biphasic waveforms is being studied to determine whether it is more effective than cardioversion with monophasic waveforms.

Summary

Supraventricular arrhythmias, especially atrial fibrillation, occur frequently in ICU patients. Intensivists not only treat atrial fibrillation itself but also its complications and the complications of the therapies used to prevent these complications. In ICU patients, ventricular arrhythmias have ominous implications because they usually portend either a major cardiac or a systemic dysfunction or both.

Keywords

atrial fibrillation, cardiac arrhythmias, ventricular tachycardia

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Introduction

Cardiac arrhythmias occur frequently in ICU patients. The most common arrhythmia is sinus tachycardia caused by the increased catecholamine secretions that occur as part of the response to stress and as a reaction to shock states. Atrial arrhythmias also occur with some frequency, whereas ventricular arrhythmias are less common but usually more ominous. Not all arrhythmias seen in the ICU are of new onset as some patients have preexisting arrhythmias that can be exacerbated by their critical illness. Such arrhythmias often need continued or additional treatment while the patient is in the ICU.

Atrial fibrillation

Atrial fibrillation occurs at epidemic levels worldwide, affecting 1–1.5% of the population in the developed world. It presents an economic burden to healthcare systems as it leads to more hospitalizations than any other arrhythmia. It is estimated that 1% of French and British healthcare outlays are due to atrial fibrillation and its complications [1••,2•]. Atrial fibrillation is also associated with longer ICU stays and higher inpatient mortality when accompanied by myocardial infarction (MI) (25 vs. 16%) [3•]. The complications of atrial fibrillation include stroke and congestive heart failure. To prevent the former, patients with atrial fibrillation are generally anticoagulated with warfarin that has a narrow therapeutic window. Although the risk of intracranial hemorrhage is low with controlled anticoagulation (0.3–0.5% per 100 patient-years), it rises exponentially as the international normalized ratio (INR) increases above therapeutic levels [1••]. Alternately, lack of anticoagulation or insufficient anticoagulation increases a patient's vulnerability to embolic strokes. These strokes are typically more severe and result in greater disability than strokes from other causes. They are often amenable to aggressive treatment with thrombolytic agents and invasive interventions. Therefore, intensivists may not only be called upon to treat atrial fibrillation but also its complications and the complications of the therapies used to prevent the complications.

The pharmacological treatment of chronic atrial fibrillation has been the subject of some controversy over the past few years, with some advocating rhythm control and

others rate control. Recent literature has focused more on rate, than rhythm, control because of poorer outcomes when pharmacologic rhythm-control modalities are used [4••]. These poorer outcomes with rhythm control are likely due to the proarrhythmic and even mortal effects of therapy with drugs such as quinidine, disopyramide, flecainide and propafenone. As a result, an increasing number of atrial fibrillation patients are receiving rate-control therapy with beta-blockers [5•]. The combination of beta-blockers with digoxin appeared more effective than either drug alone [6]. Rate-control patients must be anticoagulated to prevent strokes and other embolic diseases. Patients who remain symptomatic from their arrhythmias despite aggressive medical treatment and who have adverse reactions to antiarrhythmic medications or complications from anticoagulation are candidates for catheter ablation therapy in the electrophysiology laboratory or surgical ablation (Maze procedure). The reported success rates range from 37–95% [7••]. Intensivists should be aware that catheter ablation therapy is associated with risks of stroke (~1%), pericardial tamponade (1.2%), phrenic nerve injury (0.2%) and rarely, atrioesophageal fistulae.

The acute treatment of rapid new-onset atrial fibrillation in hemodynamically stable patients involves attempts at rate control with intravenous beta-blockers (e.g. esmolol, propranolol), calcium channel blockers (e.g. diltiazem) or amiodarone. The latter controls the ventricular rate as effectively as diltiazem, but with less hypotension [8•]. Amiodarone also converts new-onset atrial fibrillation to normal sinus rhythm with an efficacy superior to placebo as shown by most, but not all, trials [8•]. However, amiodarone is neither superior in conversion capability nor does it act faster than drugs such as ibutilide, dofetilide, flecainide and propafenone [8•]. Despite these observations, the American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) guidelines support the use of amiodarone for converting atrial fibrillation to sinus rhythm (class IIa recommendation, evidence level A). Cardioversion of new-onset atrial fibrillation should not be attempted 48 h after onset without anticoagulation.

Postoperative atrial arrhythmias

Atrial fibrillation occurs frequently after surgery. It is a particular problem following cardiac and thoracic surgery.

Cardiac surgery

Atrial fibrillation is the most common complication of postcardiac surgery and has significant economic and clinical implications. It results in prolonged postoperative ICU and hospital lengths of stay [9•]. Atrial fibrillation occurs with an incidence of 25–40% after coronary artery bypass graft (CABG) surgery and up to 60% after CABG and valve surgery, with the peak incidence on postoperative days 2 and 3. Even after off-pump CABG, the incidence of postoperative atrial fibrillation is 20–25%, indicating that not only the cardiopulmonary bypass but also the surgery itself contributes to the arrhythmia's development. Therefore, there has been much research performed on its prevention and treatment. A retrospective study of the risk factors for the development of atrial fibrillation among patients undergoing cardiac surgery [CABG, $n = 7056$; aortic valve replacements (AVR), $n = 690$; and combinations, $n = 688$] revealed that age, type of surgery (AVR and combined AVR/CABG > CABG), temporary pacing, inotropic support, increasing New York Heart Association classification and complicated weaning from cardiopulmonary bypass were major predictors for the development of postoperative atrial fibrillation [9•]. Obesity in patients more than 50 years of age was also identified as a risk factor for the development of atrial fibrillation, as was the metabolic syndrome [10]. Among AVR patients, aortic regurgitation was more of a risk for the development of atrial fibrillation than aortic stenosis. Cardiac cachexia and poor left ventricular function were also independent risk factors for post-AVR atrial fibrillation [11]. Among off-pump CABG surgery patients, advanced age, a positive intraoperative fluid balance and low postoperative cardiac indices were predictive of atrial fibrillation [12]. Genetic factors, such as the Met439Thr substitution in the heat shock protein 70 gene, also increased the propensity for developing post-CABG atrial fibrillation [13,14•].

The mechanism responsible for postcardiac surgery atrial fibrillation development has not been definitely elucidated. One of the prominent proposed mechanisms is catecholamine stimulation of irritated atria. Therefore, it is not surprising that prophylaxis with beta-blockers reduces the postoperative incidence of atrial fibrillation after both on and off-pump CABG [15]. The atrial irritation may be due to direct manipulation and surgical injury causing inflammation. Evidence for the latter comes from the observation that patients receiving routine preoperative treatment with statins were noted to have less atrial fibrillation (29.5 vs. 40.9% for patients not taking statins, $P = 0.02$) after CABG surgery [16]. Treatment with statins thus reduced the risk of atrial fibrillation by 42% possibly due to their anti-inflammatory effects [16]. A recent study failed to link inflammation, as evidenced by postoperative elevated serum C-reactive protein (CRP) concentrations, with the development of postoperative atrial fibrillation [17]. Alternately, another study showed that elevated serum interleukin-6 (IL-6) and CRP concentrations on postoperative day 1 were associated with the development of atrial fibrillation [18]. This is in distinction to a study, in which IL-6 was measured immediately after bypass and protamine administration, which failed to find similar associations

between IL-6 and atrial fibrillation [19]. These different results may be due to the timing of the IL-6 determination, as IL-6 concentrations peak 4–6 h after surgery. Another study showed significant correlations between postoperative troponin I concentrations and clinical markers of inflammation, such as postoperative fever, but found no correlation with the development of atrial fibrillation [20]. Alternately, plasminogen activator inhibitor-1 (an acute phase reactant and the primary inhibitor of tissue-type plasminogen activator) concentrations measured preoperatively or immediately after bypass and protamine administration were an independent predictor for the appearance of atrial fibrillation after CABG [19]. An attempt at reducing the incidence of atrial fibrillation after combined CABG and valve surgery by reducing inflammation with a single dose of dexamethasone (0.6 mg/kg) administered after anesthesia induction decreased the release of inflammatory mediators (IL-6, IL-8, IL-10, CRP and exhaled nitric oxide) but failed to reduce the incidence of atrial fibrillation [21]. These often conflicting studies point to the uncertainty of the role inflammation plays in the development of postoperative atrial fibrillation.

Because of the high incidence of postcardiac surgery atrial fibrillation, there has been much interest in prophylactic therapy. Amiodarone (10 mg/kg) begun 6 days prior and continued for 6 days after cardiac surgery significantly reduced postcardiac surgery atrial tachyarrhythmias compared with placebo. No toxicity was observed with this short use of amiodarone, and it is recommended to administer amiodarone for not more that 6–12 weeks postoperatively so as to limit its adverse effects [8•]. Two meta-analyses using studies that included cardiac surgery patients hinted that treatment with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers reduces the risk of developing postoperative atrial fibrillation. Patients taking these drugs chronically before their cardiac surgery had a tendency (not statistically significant) to reduced odds of developing postoperative atrial fibrillation [22]. A large statistically valid prospective study is thus needed to determine whether these two classes of drugs have a place in the prophylaxis of postcardiac surgery atrial fibrillation.

Thoracic surgery

Atrial fibrillation is one of the most common complications after thoracic surgery, with the reported prevalence ranging from 2.9% after video-assisted thoracic surgery (VATS), 10–20% after lobectomy to 46% after extrapleural pneumonectomy [1••,2•,3•,14•]. The clinical relevance of postoperative atrial fibrillation is still controversial [23]. In some studies, it was found to be benign and transient, although hospitalization was prolonged and costs were increased [23], whereas in others, it has been related to a significantly increased morbidity and mortality [23]. The peak time for onset of postoperative dysrhythmias is during the first and second postoperative days [24].

Proposed precipitating factors for postoperative supraventricular arrhythmias in patients recovering from thoracic surgery are pulmonary gas exchange disturbances [25], systemic inflammation [25] and autonomic denervation inflicted by anatomic pulmonary resection [26]. In support of a multifactorial mechanism is a recent study, which demonstrated that atrial fibrillation occurred in 12% of patients undergoing VATS and 16% of patients undergoing thoracotomy, a nonsignificant difference [26]. However, a large single institution series of 1100 VATS lobectomies reported a postoperative atrial fibrillation rate of 2.9% [27], implying that minimally invasive VATS technique, perhaps by reducing the stress induced by a rib-spreading thoracotomy, may decrease the incidence of atrial fibrillation.

Prospective studies designed to identify factors predisposing for postthoracotomy atrial fibrillation produced contradictory results [28–31]. The most robust risk factors for increased incidence of postoperative atrial fibrillation that were most consistently reported were advanced age and extent of pulmonary resection (with decreasing incidence: pneumonectomy vs. lobectomy vs. VATS) [24,32]. Other factors included male gender, preoperative arrhythmias, peripheral vascular disease, mediastinal lymph node dissection, need for repeated thoracotomy or right sided procedure, history of diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), preoperative pulmonary functional status, postoperative respiratory complication, chylothorax, history of congestive heart failure, coronary artery disease, beta-blocker ingestion, previous cardiopulmonary disease and anesthetic technique [24,25,28–31,33]. Hence, the ability to accurately identify patients at high risk for atrial fibrillation is limited. Consequently, a targeted prophylactic treatment cannot easily be designed [24,31].

The lack of reliable clinical markers led to an attempt to identify laboratory predictive markers such as correlation of simple indicators such as P-wave duration and dispersion from standard 12-lead ECG with the risk of developing atrial fibrillation after thoracic surgery [32]. Atrial fibrillation occurred in 12 out of 105 patients (11%) within 96 h of surgery. The only parameter significantly more common in the group with postoperative atrial fibrillation was P-wave dispersion [32]. P-wave dispersion is an ECG parameter associated with the inhomogeneous and discontinuous propagation of sinus impulses. It was shown to predict atrial fibrillation in other clinical settings such as idiopathic paroxysmal atrial fibrillation and aortic stenosis [34,35]. The amount of P-wave dispersion tends to be higher in atrial fibrillation patients [32].

Others are looking for biomarkers as possible predictors of atrial fibrillation. A recent study found that elevated plasma N-terminal pro-B-type natriuretic peptide before or soon after thoracic surgery for lung cancer was a strong independent predictor of atrial fibrillation occurrence [23].

Identifying reliable markers for the development of atrial fibrillation might allow clinicians to accurately risk stratify patients and might have important clinical implications [23,32]. On the basis of this information, targeted prophylactic therapy started either before or immediately after surgery might be planned only in selected high-risk patients to prevent the occurrence of atrial fibrillation. Additionally, low-risk patients, who represent the majority of this population, may be safely excluded from a prophylactic strategy, thus minimizing costs and drug-related adverse effects to those patients who are unlikely to derive benefit from such interventions.

Noncardiothoracic patients

In noncardiothoracic surgery/trauma patients, atrial arrhythmias, especially atrial fibrillation, are frequently observed. A recent review of the literature revealed that the overall incidence of new-onset arrhythmias (all except 0.45% were atrial in origin) in noncardiothoracic surgery patients is about 7–8% [36••]. Most of these arrhythmias occurred within 4 days of surgery. In over 80% of patients, new-onset arrhythmias converted to sinus rhythm prior to discharge, with all except 20–30% requiring therapeutic interventions. Many such patients are admitted to the ICU either with active atrial fibrillation or a history of paroxysmal atrial fibrillation. In a recent study, 12% of patients admitted to a general ICU had a prior history of atrial arrhythmias, and another 9% developed new-onset atrial arrhythmias while in the ICU [37]. This high incidence of preexisting atrial fibrillation is secondary to the increasing incidence and prevalence of atrial fibrillation with age. A prevalence of 10% is observed in those who are more than 80 years of age. The Framingham Heart Study data suggest that the lifetime risk of developing atrial fibrillation in persons older than 40 years is about one in four. The ICU patients with preexisting atrial arrhythmias were older, had more underlying heart disease and higher mortality rates than patients without any atrial arrhythmias [37]. Many of these patients received medications for rate or rhythm control, which needed to be continued during the critical illness. However, many of these medications are taken orally and, thus, may need to be administered parenterally during the acute illness.

New-onset atrial arrhythmias arising in ICU patients are extremely problematic. In a study of noncardiothoracic surgery/trauma patients, new-onset atrial fibrillation occurred in 29.5% of patients older than 50 years (4.02 episodes/100 patient-days). These patients had a higher mortality rate than those without any arrhythmias. Independent predictors for developing such arrhythmias include an age of more than 75 years, Acute Physiology and Chronic Health Evaluation II (APACHE II) score of more than 20 and sepsis upon ICU admission [38]. Another study found a 9% rate of new-onset atrial arrhythmias in the entire ICU population. This group of patients had a high mortality rate. Eighteen percent of those without atrial arrhythmias died while hospitalized, whereas 29 (56%) and 23 (31%) of those with new onset and prior history of atrial arrhythmias, respectively, died while hospitalized. Within a year of hospital admission, almost 70% of patients with new onset, about 50% with prior history and 20% without such arrhythmias died. ICU mortality in all groups was associated with sepsis, acute renal failure, myocardial ischemia and high APACHE II scores. Unlike the association of pre-ICU admission cardiac disease with prior atrial arrhythmias, new-onset atrial arrhythmias were associated with a history of chronic pulmonary disease and hypothyroidism. In both studies [37,38], the new-onset atrial arrhythmias were not the cause of death but were thought to be markers of increased mortality and possibly a manifestation of multiple system organ failure. Although most of the surviving patients rapidly reverted to normal sinus rhythm either spontaneously or with treatment, those who did not revert to sinus rhythm presented a challenge as after 48 h of atrial fibrillation it is recommended that patients be anticoagulated. However, many of these patients were postoperative or had other contraindications to anticoagulation.

The treatment of new-onset atrial fibrillation in ICU patients is dependent on whether the patient is hemodynamically stable. In cases of hemodynamic instability, synchronized cardioversion is indicated although it may not always be successful. A retrospective study of 2522 attempts at cardioversion in 1896 patients showed that with shocks of less than 200 J, ventricular fibrillation occurred more often than when higher energy levels were used. Conversion of atrial flutter or atrial tachycardia to atrial fibrillation was also more common when cardioversion with less than 200 J was used [39]. After cardioversion, bradyarrhythmias were rare and not clinically significant. Initial shocks of more than 200 J reduced the number of shocks required to effect cardioversion and also reduced the total energy delivered. Failure of proper synchronization can also result in atrial fibrillation leading to the recommendation that the synchronization be checked prior to the shock. The authors also recommended that initial shocks of 200–360 J be used for monophasic cardioversion instead of the traditional 50–100 J. When biphasic cardioversion is used, the initial energy should be 200 J [39]. The pharmacological treatment of acute-onset atrial fibrillation and flutter in the

ICU is reserved for patients who are hemodynamically stable. Intravenous amiodarone is commonly used as a first-line drug. However, a recent article showed that magnesium infusion often converts patients. Intravenous procainamide has also been used in the emergency department (1 gm over 60 min) to successfully convert new-onset atrial fibrillation and flutter in 52 and 28% of patients, respectively [40]. Hypotension occurred in 8.5% of patients and bradycardia and atrioventricular block each in another 0.6% [40]. Therefore, this approach might not be ideal for ICU patients.

Ventricular arrhythmias

Significant ventricular arrhythmias (ventricular tachycardia, ventricular fibrillation, torsade de point) occur less frequently than atrial arrhythmias in most adult ICU patients [41]. However, their appearance has ominous connotations. During in-hospital cardiac arrests, asystole or pulseless electrical activity more often was the first documented cardiac rhythm among children than among adults. However, among adults, the first documented cardiac rhythm more often was a ventricular arrhythmia [42]. In both adults and children, survival was better with asystole or pulseless electrical activity than with ventricular arrhythmias. Therefore, survival among children was higher than among adults. In adult ICU patients, ventricular tachycardia/fibrillation was more common than pulseless electrical activity [43]. Survival was highest (39%) with pulseless electrical activity and lower with ventricular arrhythmias (33%) and asystole (24%). Overall, 47% of patients who sustained a cardiac arrest during their ICU stays were ultimately discharged from the hospital. In another study of in-hospital cardiac arrests, the hospitalization of a patient in a critical care unit was among the independent variables associated with survival till hospital discharge [44]. The 47% survival rate in ICU patients till discharge is higher than the 39% reported overall among in-hospital cardiac arrests in patients who received defibrillation for ventricular arrhythmias within 2 min of arrest. Patients who were defibrillated after more than 2 min had only a 22% survival rate [45•]. Survival rates from in-hospital cardiac arrest are lower on nights and weekends than during days and evenings [46•]. The greater survival of ICU patients is at least partially attributable to the quick discovery of the arrest along with the swift response of highly trained personnel. The not unexpected high incidence of cardiac arrests in ICUs mandates that intensivists be well versed in the latest cardiopulmonary resuscitation procedures [47••].

There has been much interest in using biphasic instead of monophasic waveforms for defibrillation. The use of biphasic defibrillation, when compared with monophasic waveforms, increases the first shock success rate but does not result in a higher return of spontaneous circulation or survival [47••]. A recent study of out-of-hospital arrests showed that escalating higher energy (200–300–360 J) biphasic automatic defibrillation had a greater success rate than a fixed lower energy regimen (150–150–150 J) [48•]. The actual energy delivered by defibrillators is proportional to the patient's transthoracic impedance so methods that provide the same energy equivalents independent of the impedance need to be developed [49].

Conclusion

Arrhythmias affect the care of ICU patients in many ways. The arrhythmias themselves, the systemic problems they cause and the complications of antiarrhythmic therapy are often reasons for ICU admission. In addition, many such patients have comorbidities such as heart and renal disease that are associated with increased incidences of atrial arrhythmias [50•,51•]. Furthermore, the sudden onset of arrhythmias can be a sign of systemic problems brought about by hypoxemia, electrolyte disturbances, acid-base abnormalities and, as recently observed, multiple system organ failure. Advances in cardiac electrophysiology occur continually, as do advances in antiarrhythmic pharmacology. The present review pointed out that many of these advances have a bearing on the practice of critical care. Therefore, intensivists need to be well versed in the causes, prevention and treatment of cardiac rhythm disturbances and their consequences.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 613).

1 Savelieva I, Camm J. Update on atrial fibrillation: part 1. Clin Cardiol 2008; •• 31:55–62.
A review of the latest pathophysiology of atrial fibrillation.

2 Blaauw Y, Crijns HJGM. Atrial fibrillation: insights from clinical trials and novel • treatment options. J Int Med 2007; 262:593–614.
Review of recent experimental studies, latest clinical trials and novel treatments of atrial fibrillation.

3 Crawford TC, Oral H. Cardiac arrhythmias: management of atrial fibrillation in • the critically ill patient. Crit Care Clin 2007; 23:855–872.
Review of the management of acute and chronic atrial fibrillation in the acute care setting.

4 Lafuente-Lafuente C, Mouly S, Longas-Tejero MA, Bergmann JF. Antiarrhyth-•• mics for maintaining sinus rhythm after cardioversion of atrial fibrillation. Cochrane Database Syst Rev 2007; 4:CD005049.
A systematic review of the antiarrhythmic drugs used to maintain sinus rhythm following cardioversion of atrial fibrillation.

5 Hansen ML, Gadsbell N, Gislason GH, *et al.* Atrial fibrillation pharmacotherapy • after hospital discharge between 1995 and 2004: a shift towards beta-blockers. Europace 2008; 10:395–402.
The therapeutic approach to atrial fibrillation appears to have switched to rate control rather than rhythm control according to this study of 108 791 Danish patients.

6 Rienstra M, Van Gelder IC. Who, when and how to rate control for atrial fibrillation. Curr Opin Cardiol 2007; 23:23–27.

7 Marine JE. Catheter ablation therapy for supraventricular arrhythmias. JAMA •• 2007; 298:2768–2778.
A good review of the uses and limitations of ablation therapy for atrial arrhythmias.

8 Vassallo P, Trohman RG. Prescribing amiodarone. JAMA 2007; 298:1312–1322.
This article reviews the advantages and disadvantages of using amiodarone.

9 Mariscalco G, Engstrom KG. Atrial fibrillation after cardiac surgery: risk factors and their temporal relationship in prophylactic drug strategy decision. Int J Cardiol 2008 [Epub ahead of print].
A large retrospective study of 10 years of data identifying risk factors and the consequences of postcardiac surgery atrial fibrillation. Only among CABG patients, and not among valve replacement patients, was atrial fibrillation associated with increased 1-year mortality.

10 Echahidi N, Mohty D, Pibarot P, *et al.* Obesity and metabolic syndrome are independent risk factors for atrial fibrillation after coronary artery bypass graft surgery. Circulation 2007; 116 (Suppl I):I-213–I-219.

11 Banach M, Goch A, Misztal M, *et al.* Predictors of paroxysmal atrial fibrillation in patients undergoing aortic valve replacement. J Thorac Cardiovasc Surg 2007; 134:1569–1576.

12 Hosokawa K, Nakalima Y, Umenai T, *et al.* Predictors of atrial fibrillation after off-pump coronary artery bypass graft surgery. Br J Anaesth 2007; 98:575–580.

13 Afzl AR, Mandal K, Nyamweya SM, *et al.* Association of Met439THr substitution in heat shock protein 70 gene with postoperative atrial fibrillation and serum HSP70 protein levels. Cardiology 2008; 110:45–52.

14 Andalib A, Brugada R, Nattel S. Atrial fibrillation: evidence for genetically determined disease. Curr Opin Cardiol 2008; 23:176–183.
A review of the evidence that there may be genetic–environmental factors in the pathogenesis of atrial fibrillation.

15 Imren Y, Benson AA, Zor H, *et al.* Preoperative beta-blocker use reduces atrial fibrillation in off-pump coronary bypass surgery. ANZ J Surg 2007; 77:429–432.

16 Mariscalco G, Lorusso R, Klersy C, *et al.* Observational study on the beneficial effect of preoperative statins in reducing atrial fibrillation after coronary surgery. Ann Thorac Surg 2007; 84:1158–1165.

17 Ahlsson AJ, Bodin L, Lundblad OH, Englund AG. Postoperative atrial fibrillation is not correlated to C-reactive protein. Ann Thorac Surg 2007; 83:1332–1337.

18 Ucar HI, Tok M, Atalar E, *et al.* Predictive significance of plasma levels of interleukin-6 and high sensitivity C-reactive protein in atrial fibrillation after coronary artery bypass surgery. Heart Surg Forum 2007; 10:E131–E135.

19 Pretorius M, Donahue BS, Yu C, *et al.* Plasminogen activator inhibitor-1 as a predictor of postoperative atrial fibrillation after cardiopulmonary bypass. Circulation 2007; 116:I-1–I-7.

20 Knayzer B, Abramov D, Natalia B, *et al.* Atrial fibrillation and plasma troponin I elevation after cardiac surgery: relation to inflammation-associated parameters. J Card Surg 2006; 22:117–123.

21 Yared JP, Bakri MH, Erzurum SC, *et al.* Effect of dexamethasone on atrial fibrillation after cardiac surgery: prospective, randomized double-blind, placebo-controlled trial. J Cardiothorac Vasc Anesth 2007; 21:68–75.

22 White CM, Kluger JM, Lertsburapa K, *et al.* Effect of preoperative angiotensin converting enzyme inhibitor or angiotensin receptor blocker use on the frequency of atrial fibrillation after cardiac surgery: a cohort study for the atrial fibrillation suppression trials II and III. Euro J Cardiothorac Surg 2007; 31:817–820.

23 Cardinale D, Colombo A, Sandri MT, *et al.* Increased perioperative N-terminal pro-B-type natriuretic peptide levels predict atrial fibrillation after thoracic surgery for lung cancer. Circulation 2007; 115:1339–1344.

24 Barbetakis N, Vassiliadis M. Is amiodarone a safe antiarrhythmic to use in supraventricular tachyarrhythmias after lung cancer surgery? BMC Surg 2004; 11:4–7.

25 Bobbio A, Caporale D, Internullo E, *et al.* Postoperative outcome of patients undergoing lung resection presenting with new-onset atrial fibrillation managed by amiodarone or diltiazem. Eur J Cardiothorac Surg 2007; 31:70–74.

26 Park BJ, Zhang H, Rusch VW, Amar D. Video-assisted thoracic surgery does not reduce the incidence of postoperative atrial fibrillation after pulmonary lobectomy. J Thorac Cardiovasc Surg 2007; 133:775–779.

27 McKenna RJ Jr, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1,100 cases. Ann Thorac Surg 2006; 81:421–426.

28 Amar D, Roistacher N, Burt M, *et al.* Clinical and echocardiographic correlates of symptomatic tachydysrhythmias after noncardiac thoracic surgery. Chest 1995; 108:349–354.

29 Curtis JJ, Parker BM, McKenney CA, *et al.* Incidence and predictors of supraventricular dysrhythmias after pulmonary resection. Ann Thorac Surg 1998; 66:1766–1771.

30 Vaporciyan AA, Correa AM, Rice DC, *et al.* Risk factors associated with atrial fibrillation after noncardiac thoracic surgery: analysis of 2588 patients. J Thorac Cardiovasc Surg 2004; 127:779–786.

31 Cardinale D, Martinoni A, Cipolla CM, *et al.* Atrial fibrillation after operation for lung cancer: clinical and prognostic significance. Ann Thorac Surg 1999; 68:1827–1831.

32 Materazzo C, Piotti P, Mantovani C, *et al.* Atrial fibrillation after noncardiac surgery: P-wave characteristics and Holter monitoring in risk assessment. Eur J Cardiothorac Surg 2007; 31:812–816.

33 Schussler O, Alifano M, Dermine H, *et al.* Postoperative pneumonia after major lung resection. Am J Respir Crit Care Med 2006; 173:1161–1169.

34 Andrikopoulos GK, Dilaveris PE, Richter DJ, *et al.* Increased variance of P wave duration on the electrocardiogram distinguishes patients with idiopathic paroxysmal atrial fibrillation. Pacing Clin Electrophysiol 2000; 23:1127–1132.

35 Turhan H, Yetkin E, Atak R, *et al.* Increased P-wave duration and P-wave dispersion in patients with aortic stenosis. Ann Noninvasive Electrocardiol 2003; 8:18–21.

36 Walsh SR, Tang T, Wijerardena C, *et al.* Postoperative arrhythmias in general surgical patients. Am R Coll Surg Engl 2007; 89:91–95.
A review article that examines the incidence and significance of new-onset arrhythmias following major noncardiothoracic surgery.

37 Goodman S, Shirov T, Weissman C. Supraventricular arrhythmias in intensive care unit patients: short and long-term consequences. Anesth Analg 2007; 104:880–886.

38 Arora S, Lang I, Nayyar V, *et al.* Atrial fibrillation in a tertiary multidisciplinary intensive care unit: incidence and risk factors. Anaesth Intensive Care 2007; 35:707–713.

39 Gallagher MM, Yap YG, Padula M, *et al.* Arrhythmic complications of electrical cardioversion: relationship in shock energy. Int J Cardiol 2008; 123:307–312.

40 Stiell IG, Clement CM, Symington C, *et al.* Emergency department use of intravenous procainamide for patients with acute atrial fibrillation or flutter. Acad Emerg Med 2007; 14:1158–1164.

41 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; 27:1466–1473.

42 Nadkarni VM, Larkin GL, Peberdy MA, *et al.,* National Registry of Cardiopulmonary Resuscitation Investigators. First documented rhythm and clinical outcome from in-hospital cardiac arrest among children and adults. JAMA 2006; 295:50–57.

43 Enohumah KO, Moerer O, Kirmse C, *et al.* Outcome of cardiopulmonary resuscitation in intensive care units in a university hospital. Resuscitation 2006; 71:161–170.

44 Peters R, Boyde M. Improving survival after in-hospital cardiac arrest: the Australian experience. Am J Crit Care 2007; 16:240–246.

45 Chan PS, Krumholz HM, Nichol G, Nallamothu BK, American Heart Association Cardiopulmonary Resuscitation Investigators. Delayed time to defibrillation after in-hospital cardiac arrest. N Engl J Med 2008; 358:77–79.
Important article reporting on 6789 patients in 369 hospitals who had cardiac arrest due to ventricular fibrillation or pulseless ventricular tachycardia. The article shows that delayed defibrillation is common and is associated with lower rates of survival.

46 Peberdy MA, Ornato JP, Larkin GL, *et al.* Survival from in-hospital cardiac arrest during nights and weekends. JAMA 2008; 299:785–792.
A report including 86 748 consecutive adult in-hospital cardiac arrest events in the National Registry of Cardiopulmonary Resuscitation obtained from 507 medical/surgical participating hospitals from 1 January 2000 through 1 February 2007. The study shows reduced survival in patients sustaining cardiac arrest at night and on weekends.

47 Bakhtiar A, Zafari AM. Narrative review: cardiopulmonary resuscitation and emergency cardiovascular care – review of the current guidelines. Ann Intern Med 2007; 147:171–179.
A comprehensive review of Advanced Cardiac Life Support guidelines.

48 Steill JG, Walker RG, Nesbitt LP, *et al.* BIPHASIC Trial: a randomized comparison of fixed lower versus escalating higher energy levels for defibrillation in out-of-hospital cardiac arrest. Circulation 2007; 115:1511–1517.
A randomized trial of various patterns of biphasic waveform defibrillation.

49 Zelinka M, Buic D, Zelinka I. Comparison of five different defibrillators using recommended energy protocols. Resuscitation 2007; 74:500–507.

50 Efremidis M, Pappas L, Sideris A, Filippatos G. Management of atrial fibrillation in patients with heart failure. J Card Fail 2008; 14:232–237.
An excellent review of the management of atrial fibrillation in patients with heart failure.

51 Lainscak M, Dagres N, Filippatos GS, *et al.* Atrial fibrillation in chronic non-cardiac disease: where do we stand? Int J Cardiol 2008 [Epub ahead of print].
A review of atrial fibrillation in cancer, COPD and renal failure.