

Perioperative cardiac arrhythmias

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Cardiac arrhythmias are a significant cause of morbidity and mortality in the perioperative period. While literature on antiarrhythmic agent use in postoperative and non-surgical intensive care settings is expanding, randomized clinical trials examining the use of these agents in the perioperative period are scarce. Nonetheless, as our understanding of the relevant molecular targets for manipulating cardiac excitability grows, the range of options for treating arrhythmias during surgery expands. In the sections that follow, these molecular targets are used as a basis for clinical management strategies for arrhythmias in adults during surgery and anaesthesia. In addition, the controversy surrounding droperidol and its reported proarrhythmic effects will be addressed. Finally, since pacemakers and implantable cardioverter-defibrillators (ICD) have gained widespread use in the treatment of tachyarrhythmias and bradyarrhythmias, a basic understanding of their perioperative function and management is discussed.

Basic science

Ion channel mechanisms

Antiarrhythmic pharmacology is focused primarily on the cardiac ion channels and adrenergic receptors as drug targets. The number of drug targets for antiarrhythmic therapy is expanding exponentially, and detailed discussion is provided in recent reviews.⁴¹ Recognizing this complexity, it is still useful to consider the ion channel targets in three general classes (based on the cation they conduct): sodium (Na⁺), calcium (Ca²⁺) and potassium (K⁺) channels. Virtually all drugs that modulate the heart rhythm work through the adrenergic receptor/second-messenger systems, through one or more of the ion channel classes, or both. The classification scheme provided (Table 1) is not exhaustive, but lists the agents currently available for use in the US in

i.v. form.^{1 55} Although the molecular targets are distinctive, the drug receptor sites among the ion channel classes are highly homologous, causing some of the 'class overlap' (and clinical side-effects) associated with antiarrhythmic therapy.

Drug effects on the surface ECG can be predicted from their effects on the cardiac action potential, which in turn result from activity towards molecular targets (Fig. 1). The action potential represents the time-varying transmembrane potential of the myocardial cell during the cardiac cycle. As such, the ECG can be viewed as the ensemble average of the action potentials arising from all myocardial cells, and is biased toward the activity of the left ventricle because of its greater overall mass. The trajectory of the cardiac action potential is divided into five distinct phases, which reflect changes in the predominant ionic current flowing during the cardiac cycle (Fig. 2). The current responsible for 'phase 0', the initial period of the action potential, initiates impulse conduction through the cardiac tissue. A critical feature of arrhythmia management is the understanding that the current responsible for impulse initiation in the atria and ventricles differs from that of the sinoatrial (SA) and atrioventricular (AV) nodes. In the atria and ventricles, the impulse is initiated by Na⁺ current through Na⁺ channels. Hence, drugs that suppress Na⁺ current (class I agents, Fig. 1) slow myocardial conduction and prolong the QRS complex (ventricle) and the P wave (atrium). In AV and SA nodal cells, phase 0 is produced by Ca²⁺ current through L-type Ca²⁺ channels. Drugs that suppress Ca²⁺ current therefore slow the atrial rate (by acting on the SA node), and also slow conduction through the AV node. The latter effect prolongs the PR interval on the ECG, making the AV node a more efficient 'filter' for preventing rapid trains of atrial beats from passing into the ventricle (hence the rationale for AV nodal blockade during supraventricular tachyarrhythmias (SVT), see below). Because Ca²⁺ currents do not

Table 1 Antiarrhythmic agents principally used in anaesthesiology and critical care, listed by their molecular targets. Classification by functional effect according to the Vaughan Williams scheme 2 is also provided. *Available commercially in oral form only. (Modified Balser JR. Perioperative management of arrhythmias. In: Barash PG, Fleisher LA, Prough DS, eds. *Problems in Anaesthesia*. Lippincott-Raven, Philadelphia, 1998; Vol 10(2): 199)

| Receptor | Class ² | Drugs |
|---|--------------------|--|
| Na ⁺ , K ⁺ channels | IA | Procainamide, quinidine, amiodarone |
| Na ⁺ channels | IB | Lidocaine, phenytoin, *mexiletine, *tocainide |
| Beta adrenoceptors | II | Esmolol, amiodarone, propranolol, atenolol, *sotalol |
| K ⁺ channels | III | Bretium, ibutilide, *sotalol, *dofetilide |
| Ca ²⁺ channels | IV | Verapamil, diltiazem, amiodarone |

initiate impulse propagation in the atria and ventricles, these agents only slow the ventricular response to atrial tachycardia, and usually do not acutely terminate arrhythmias arising in either the atrium or the ventricle.

The later phases of the action potential (phases 1, 2 and 3; Fig. 1) inscribe repolarization. The long plateau (phase 2) is maintained by Ca²⁺ current and is terminated (phase 3) by K⁺ current. Hence, the QT interval on the ECG reflects the length of the action potential, and is determined by a delicate balance between these and many other smaller inward and outward currents. Drugs that reduce Ca²⁺ current, namely those with class II or class IV activity, abbreviate the action potential plateau, shorten the QT interval and reduce the inward movement of Ca²⁺ into the cardiac cell. Hence, all agents that reduce Ca²⁺ current have the clinical potential to act as negative inotropes. Conversely, agents with class IA or III activity block outward K⁺ current, prolonging the action potential and the QT interval on the ECG. The electrophysiological manifestations of QT prolongation may be either therapeutic or arrhythmogenic, as discussed below (Re-entry, automaticity and arrhythmias).

During phase 4 (Fig. 1) the properties in SA and AV nodal tissue are again distinctive from those in atrial and ventricular muscle. Nodal cells spontaneously depolarize ('pace'), and activation of the adenosine A₁ receptor triggers outward K⁺ currents⁵ that hyperpolarize the nodal cell and oppose pacing. Since atrial and ventricular tissues are normally hyperpolarized, adenosine has little or no effect in these tissues. However, in SA and AV nodal tissue, adenosine slows the SA node (reducing the sinus rate) and blocks conduction through the AV node, creating 'transient' third-degree AV block. Adenosine also slows nodal conduction by inhibiting Ca²⁺ current through reducing cyclic AMP (cAMP).

These transient and specific effects make adenosine a choice agent for terminating SVT that involves SA or AV node re-entrant pathways, and it is therefore possible to classify supraventricular arrhythmias according to their response to adenosine (Table 2).¹⁶ SVT due to re-entry in atrial tissue, such as atrial flutter or fibrillation, responds to adenosine with transient slowing of the ventricular response

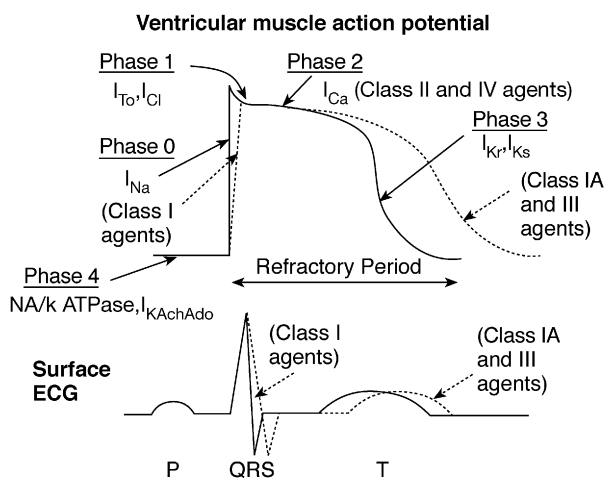


Fig 1 The action potential in ventricular muscle and its temporal relationship with the surface ECG. The QRS interval is related to the rate of upstroke of the action potential, which partly determines the rate of impulse conduction through the ventricular myocardium. The QT interval is related to the length of the action potential (the absolute refractory period). The phases of the action potential are indicated, as are the major ionic currents (I) that flow during each phase. The dotted lines indicate anticipated effects on the action potential and ECG when drugs suppress either the sodium (Na⁺) current (class IA or IB) or potassium (K⁺) current (class IA or III). ACh, acetylcholine; Ado, adenosine; Cl, chloride; To, transient outward K⁺ current; Ks, slow component of rectifier K⁺ current; Kr, rapid component of rectifier K⁺ current. (Adapted from Balser JR. Perioperative management of arrhythmias. In: Barash PG, Fleisher LA, Prough DS, eds. *Problems in Anaesthesia*. Lippincott-Raven, Philadelphia, 1998; Vol 10(2): 199.)

rate, but does not terminate. Similarly, atrial tachycardias that result from enhanced phase 4 depolarization will transiently slow, but rarely cease. Atrial tachycardia due to cAMP-mediated triggered activity in the SA node is a rare exception, where adenosine-mediated inhibition of adenylate cyclase sometimes terminates the arrhythmia.¹⁶

Conversely, SVTs that utilize the AV nodal tissue as a substrate for re-entry are terminated by bolus adenosine administration (Table 2). Junctional tachycardias, common during the surgical period, also sometimes convert to sinus rhythm in response to adenosine. Ventricular arrhythmias exhibit no response to adenosine since these rhythms originate in tissues distal to the AV conduction pathway. The vasodilatory properties of adenosine, and all other AV nodal blocking agents used for rate control in SVT, may be harmful in patients with 'stable' ventricular tachycardias (VT) because of their marginal haemodynamic stability. Hence, i.v. adenosine is no longer recommended as a means to distinguish wide-complex SVT from VT.²

Re-entry, automaticity and arrhythmias

Re-entry

Re-entry is a mechanism that may precipitate a wide variety of supraventricular and ventricular arrhythmias, and implies

Table 2 The response of common supraventricular tachyarrhythmias (SVT) to i.v. adenosine. AV, atrioventricular; WPW, Wolff–Parkinson–White. (Adapted from Balser JR. Perioperative management of arrhythmias. In: Barash PG, Fleisher LA, Prough DS, eds. *Problems in Anaesthesia*. Lippincott-Raven, Philadelphia, 1998; Vol 10(2): 201)

| SVT | Mechanism | Adenosine response |
|--|---|---|
| AV nodal re-entry | Re-entry within AV node | Termination |
| AV reciprocating tachycardias (orthodromic and antidromic) | Re-entry involving AV node and accessory pathway (WPW) | Termination |
| Intra-atrial re-entry | Re-entry in the atrium | Transiently slows ventricular response |
| Atrial flutter/fibrillation | Re-entry in the atrium | Transiently slows ventricular response |
| Other atrial tachycardias | 1 Abnormal automaticity 2 cAMP-mediated triggered activity | 1 Transient suppression of the tachycardia 2 Termination |
| AV junctional rhythms | Variable | Variable |

the existence of a pathological circus movement of electrical impulses around either an anatomic (i.e. Wolff–Parkinson–White syndrome) or functional (i.e. myocardial ischaemia) loop. Fibrillation, in either the atrium or ventricle, is believed to involve multiple coexistent re-entrant circuits of the functional type. These re-entrant loops may result from disparities in either the repolarization rates or conduction rates between normal and ischaemic myocardium, or even from refractory period differences between epicardial and endocardial layers.³² Unfortunately, our understanding of re-entry and its pharmacological termination by ion channel current suppression is incomplete. Drugs can terminate re-entry through at least two mechanisms. Agents that suppress currents responsible for phase 0 of the action potential (I_{Na} in atrium and ventricle, I_{Ca} in the SA and AV node, Table 1) may slow or block conduction in a re-entrant pathway, and thus terminate an arrhythmia. Alternatively, by prolonging the action potential, drugs with K^+ channel blocking activity (Table 1) prolong the refractory period of cells in a re-entrant circuit, and thus ‘block’ impulse propagation through the circuit. In clinical trials, agents operating through this latter mechanism have proven to be more successful in suppressing fibrillation.³⁴

Automaticity

This refers to abnormal depolarization of atrial or ventricular muscle cells during periods of the action potential normally characterized by repolarization (phases 2 or 3) or rest (phase 4). Studies over the last decade have identified some of the key molecular substrates that underlie triggered automaticity. Although K^+ channel blockade is highly effective for treating certain arrhythmias in the atrium and ventricle, delaying repolarization (manifest as prolongation of the QT interval) may at the same time provoke ventricular arrhythmias in 2–10% of patients. Low serum potassium concentrations slow the heart rate, and K^+ -channel blocking drugs (class IA or III) synergistically induce a polymorphic VT known as ‘torsades de pointes’.⁴⁵ Similarly, mutations in ion channels critical to repolarization have also been identified in the genes of patients with inherited forms of the long-QT syndrome.⁴¹ Hence, the proarrhythmic features of drug therapy with repolarization-

prolonging agents appear to be acquired manifestations of the same molecular mechanisms involved in forms of the congenital long-QT syndrome.⁴⁷ To extend this connection further, ‘silent’ mutations have been identified in the protein substituents of K^+ channels that do not cause excessive QT prolongation unless patients are also exposed to K^+ -channel blocking drugs.³ These mutations sensitize the cardiac cell to K^+ -channel blockade, and provide a pharmacogenetic rationale for the ‘idiosyncratic’ incidence of torsade upon exposure to QT-prolonging drugs.⁴⁴ (See also Ventricular arrhythmias below and Table 4.)

Supraventricular arrhythmias

Acute management of perioperative supraventricular arrhythmias

A cascade of adverse physiological phenomena can precipitate SVT in critically ill or anaesthetized patients. The management of the surgical patient who suddenly develops SVT requires a thorough but rapid consideration of potential aetiologies. Aetiology should be considered before therapy is instituted, except in cases of extreme haemodynamic instability. SVT is among the clinician’s most valuable warning signs, often foreshadowing life-threatening conditions that may be easily corrected (Table 3). Antiarrhythmic therapy should only be considered after these aetiologies have been excluded. Patients with narrow complex tachycardias who are dangerously hypotensive (e.g. loss of consciousness, cardiac ischaemia, or a systolic pressure below 80 mm Hg) require immediate synchronous DC cardioversion in order to prevent the life-threatening complications of hypoperfusion, such as central nervous system or cardiac ischaemia. While some patients may only respond transiently to cardioversion in this setting (or not at all), a brief period of sinus rhythm may provide valuable time for correcting the reversible causes of SVT (discussed above), instituting pharmacological therapies, or both. In less urgent cases, adenosine may be administered as a 6 mg i.v. bolus (repeated with 12 mg if no response). In practice, the SVTs most commonly seen in the perioperative period (such as atrial fibrillation, Table 2) do not involve the AV

Table 3 Reversible causes of supraventricular tachycardias and non-sustained ventricular tachycardia. Listed are some of the most common conditions in the operating room environment that predispose patients to arrhythmias. These conditions are usually reversible, and should be treated before considering use of pharmacological antiarrhythmic therapies

| |
|--|
| Hypoxaemia |
| Hypercarbia |
| Acidosis |
| Hypotension |
| Electrolyte imbalances |
| Mechanical irritation |
| Pulmonary artery catheter |
| Chest tube |
| Hypothermia |
| Adrenergic stimulation (light anaesthesia) |
| Proarrhythmic drugs |
| Micro/macro shock |
| Cardiac ischaemia |

node in a re-entrant pathway, and AV nodal block by adenosine will therefore produce only transient slowing of the ventricular rate. According to the 2000 American Heart Association guidelines, adenosine is no longer recommended to differentiate wide-complex SVT from ventricular tachycardias because of its vasodilatory properties.²

Patients with underlying structural heart disease are at greatest risk for developing either supraventricular or ventricular arrhythmias during the induction of anaesthesia secondary to hypotension, autonomic imbalance or airway manipulation.⁵⁶ In addition, during cardiac or major vascular surgery, patients may experience SVT during dissection of the pericardium, placement of atrial sutures or insertion of the venous canulae required for cardiopulmonary bypass. If haemodynamically unstable SVT occurs during cardiac surgery, the surgeon will usually attempt open synchronous DC cardioversion. However, in patients with critical coronary lesions or severe aortic stenosis, SVT may be refractory to cardioversion and provoke a malignant cascade of ischaemia and worsening arrhythmias that requires the institution of cardiopulmonary bypass. Hence, early preparation for cardiopulmonary bypass is recommended before inducing anaesthesia in cardiac surgery patients who are at exceptionally high risk for SVT and consequent haemodynamic deterioration.

The majority of patients who develop intraoperative SVT remain haemodynamically stable and do not require cardioversion. Ventricular rate control is the mainstay of therapy for SVT that does not require immediate DC cardioversion. The advantages of slowing the ventricular rate during SVT are twofold. First, lengthening diastole serves to enhance left ventricular filling, thus enhancing stroke volume and improving haemodynamic stability. Second, slowing the ventricular rate reduces myocardial oxygen consumption and lowers the risk of cardiac ischaemia. Intraoperatively, rate control is readily achieved with one of a variety of AV nodal blockers (agents with class II or IV activity, Table 1). Among the i.v. beta blockers, esmolol has ultra-rapid elimination properties that

render it titratable on a minute-by-minute basis,⁹ allowing meaningful dose adjustments during periods of surgery that provoke changes in haemodynamic status (i.e. bleeding, abdominal traction). While esmolol is largely β_1 -receptor selective and is generally well tolerated by patients with chronic obstructive lung disease, the drug has obligatory negative inotropic effects that may not be well tolerated in patients with severe left ventricular dysfunction. Both i.v. verapamil and i.v. diltiazem are calcium channel blockers that are less easily titrated than esmolol but nonetheless provide rapid slowing of the ventricular rate in SVT within minutes. The agents are therapeutically equivalent for purposes of AV nodal blockade,⁴⁶ but i.v. diltiazem has less negative inotropic action and is preferable in patients with heart failure.^{7,57} Thus, for patients with congestive heart failure, digitalis, diltiazem and amiodarone are all recommended for rate control management of SVT.² In a prospective randomized study of 60 patients in a cardiology intensive care unit who had atrial arrhythmias and heart rates over 120 beats min⁻¹, diltiazem was found to have better heart rate control than amiodarone (load and load plus infusion); however, diltiazem was more frequently discontinued because of hypotension.¹⁰ I.V. digoxin slows the ventricular response during SVT through its vagotonic effects, but should be either substituted or temporarily supplemented with other agents because of its slow onset (about 6 h).⁵³

Paroxysmal SVT (PSVT) due to re-entrant circuits that involve accessory pathways (congenital electrical connections between the atrium and ventricle that bypass the AV node, such as Wolff-Parkinson-White Syndrome) pose caveats in the management of SVT. A detailed discussion of this interesting subgroup is beyond the scope of this review. However, it should be noted that patients with accessory pathways, in addition to PSVT, may also develop atrial fibrillation, and in the latter situation are at increased risk for developing ventricular fibrillation (VF) upon exposure to classic AV-nodal blocking agents (digoxin, calcium channel blockers, beta blockers, adenosine) because these agents reduce the accessory bundle refractory period. In such cases, i.v. procainamide, which slows conduction over the accessory bundle, is an acceptable option. Flecainide and amiodarone should also be considered, and cardiology consultation may be helpful.²

Chemical cardioversion of SVT

Efforts to chemically convert SVT to sinus rhythm using antiarrhythmic agents in the operating room should be aimed at those patients who cannot tolerate (or do not respond to) rate control therapy, or who fail DC cardioversion and remain haemodynamically unstable. For intraoperative patients who are stable and rate controlled in SVT, the wisdom of chemical cardioversion is questionable. First, the 24 h rate of spontaneous conversion to sinus rhythm for recent-onset perioperative SVT exceeds 50%,

and many patients who develop SVT under anaesthesia will remit spontaneously before or during emergence. Moreover, most of the antiarrhythmic agents with long-term activity against atrial arrhythmias have limited efficacy when utilized for rapid chemical cardioversion. While 50–80% efficacy rates are cited for many i.v. antiarrhythmics in uncontrolled studies, these findings are largely an artifact of high placebo rates of conversion. For example, the efficacy of i.v. procainamide for conversion of SVT has not been established in placebo-controlled trials.⁴³ Moreover, a placebo-controlled trial of patients with atrial fibrillation recently found a 60% 24 h conversion rate for patients in the placebo arm, statistically indistinguishable from that of patients treated with i.v. amiodarone (68%).¹⁸ Although improved rates of chemical cardioversion are seen with high doses of i.v. amiodarone (approximately 2 g per day),²⁷ the potential for undesirable side-effects in the operating room requires further study.

While the most effective agents for converting atrial fibrillation are K⁺ channel blockers that prolong atrial repolarization, the use of these agents is hampered by the proarrhythmic risk inherent in coexistent prolongation of ventricular repolarization (manifest as QT prolongation and torsades de pointes). Ibutilide, a rapid-acting antiarrhythmic, produced a 31% rate of conversion in non-surgical patients with atrial fibrillation, with a mean time from treatment to conversion of only 27 min.⁵¹ Unfortunately, rates of torsades de pointes as high as 8% have been reported, and the risk/benefit ratio for i.v. ibutilide use in perioperative SVT remains questionable. Intraoperative elective DC cardioversion in an otherwise stable patient with SVT also carries risks (VF, asystole, stroke). Moreover, the underlying factors provoking SVT during or shortly after surgery are likely to persist beyond the time of cardioversion, inviting recurrence.⁵⁶ A recent trial of patients with SVT (mainly atrial fibrillation) who had undergone coronary artery bypass grafting (CABG) did find that low-energy DC cardioversion (utilizing indwelling atrial pacing leads) was 80% effective and minimized sedation requirements, but the rate of recurrence within 1 min was nearly 50%.³¹ Hence, when elective DC cardioversion is considered, it may be prudent to first establish a therapeutic level of an antiarrhythmic agent that maintains sinus rhythm (i.e. procainamide, amiodarone) in order to minimize the risk of SVT recurrence following electrical cardioversion.

Ventricular arrhythmias

Non-sustained ventricular arrhythmias

Ventricular arrhythmias can be subdivided according to their morphology (monomorphic vs polymorphic) and their duration (sustained vs non-sustained). Non-sustained ventricular tachycardia (NSVT) is defined as three or more premature ventricular contractions that occur at a rate

exceeding 100 beats min⁻¹ and last 30 s or less without haemodynamic compromise. These arrhythmias are routinely seen in the absence of cardiac disease, and may not require drug therapy in the perioperative period. Conversely, in patients with structural heart disease, these non-sustained rhythms do predict subsequent life-threatening ventricular arrhythmias.²⁹ However, particular antiarrhythmic drug therapies in patients with structural heart disease and NSVT may either worsen (encainide, flecainide)¹³ or improve (amiodarone)⁴⁹ survival.

NSVT occurs in nearly 50% of patients during and after cardiac and major vascular surgery, but does not influence early or late mortality in patients with preserved left ventricular function.^{4 39 50} These patients usually do not require antiarrhythmic drug therapy; however, their arrhythmias, like SVT, may signal reversible aetiologies that should be treated (Table 3). Conversely, nearly 2% of patients experience sustained VT or VF after cardiac surgery,^{4 28 54} and low cardiac output following CABG (requiring pressor support) has been identified as an independent predictor of life-threatening VT/VF within 72 h of surgery.¹⁴ In most cases, symptoms of postoperative ischaemia are not apparent, although one trial did identify saphenous vein graft failure at angiography in three out of seven patients experiencing unanticipated VT/VF, suggesting that subclinical graft occlusion is a frequent aetiology of postoperative VT/VF.⁵⁴ After aortic valve replacement, a retrospective analysis found that patients who died unexpectedly had an elevated incidence of NSVT on their postoperative ECG (44%) compared with survivors (10%, $P < 0.05$).⁴⁸ Nonetheless, the incidence of NSVT after aortic valve replacement approaches 50%,³⁶ and the role for electrophysiological diagnostic evaluation in this population has not been clarified.

There are few studies available to guide therapeutic decision-making for patients with ventricular arrhythmias in the early postoperative period. While NSVT has not been linked to increased morbidity or mortality after cardiopulmonary bypass, unstable patients with marginal perfusion may deteriorate with recurrent episodes of NSVT (problematic ventricular pacing or intra-aortic balloon counterpulsation) and may benefit from suppression with lidocaine²⁶ or beta blockade.^{4 50} In addition, repletion of post-bypass hypomagnesaemia (MgCl₂ 2 g i.v.) reduces the incidence of NSVT after cardiac surgery,¹⁷ and is now standard at most centres. A retrospective evaluation has suggested a survival benefit with electrophysiological-guided prophylaxis in post-CABG patients with low ejection fraction who survive an episode of sudden cardiac death,²⁵ although a definitive role for prophylactic antiarrhythmic drug therapy in this setting has not been evaluated prospectively. A multicentre trial (CABG Patch) found no survival advantage with implantation of a cardiac defibrillator in high-risk patients (those with low ejection fractions) at the time of elective cardiac surgery.⁶ Hence, identification of effective strategies for preventing ventri-

cular arrhythmias after thoracic surgery is an ongoing challenge.

Sustained VT generally falls into one of two categories: monomorphic and polymorphic. In monomorphic VT, the amplitude of the QRS complex remains constant, while in polymorphic ventricular tachycardia the QRS morphology continually changes. The best understood mechanism for monomorphic VT is formation of a re-entrant pathway around scar tissue from a healed myocardial infarction.³³ Although lidocaine has traditionally been the primary drug therapy for all sustained ventricular arrhythmias, a recent study of 29 patients with haemodynamically stable monomorphic VT found termination within 24 h was more common with i.v. procainamide therapy (12 out of 15 patients) than with i.v. lidocaine (3 out of 14; $P < 0.01$).¹⁹ I.V. amiodarone is also recommended for management of monomorphic VT.²

In contrast, the therapeutic approach for polymorphic VT depends critically on whether the QT interval during a prior interval of sinus rhythm was prolonged. Polymorphic VT in the setting of a normal QT interval usually occurs in a setting of ischaemia or structural heart disease, although idiopathic cases are seen.¹⁵ The rhythm degenerates into VF; pharmacological management is discussed in the section below. Conversely, polymorphic VT in the setting of a prolonged QT interval (torsades de pointes) is focused at reversal of the QT prolongation. As discussed above, a predisposition to torsades may be inherited and usually manifests as an acquired complication of therapy with drugs that prolong the QT interval. In addition to QT-prolonging antiarrhythmic drugs (class IA or III), a number of other medications used in the perioperative period may evoke QT prolongation and torsades de pointes (see, for example, www.Torsades.org/druglist.cfm for a current on-line summary).

The management of torsades de pointes differs markedly from other forms of VT, and includes i.v. magnesium sulfate (2–4 g), repleting potassium, and manoeuvres aimed at increasing the heart rate (atropine, isoprenolol or temporary atrial or ventricular pacing). Haemodynamic collapse with torsades requires asynchronous DC countershocks. When antiarrhythmic therapy is deemed necessary, agents devoid of K^+ -channel blocking properties such as lidocaine or phenytoin (Table 1) are usually chosen to avoid further prolongation of the QT interval.⁴² In practice, it may be relatively unclear whether an observed episode of polymorphic VT is related to QT-interval prolongation. In such cases, magnesium and Na^+ -channel blocking agents may be administered empirically. Among the antiarrhythmic agents that prolong the QT interval, the incidence of torsades de pointes is lowest with amiodarone;³⁵ hence, i.v. amiodarone may be a rational alternative therapy for refractory polymorphic VT of unclear aetiology. The risk of proarrhythmic events may be increased by the simultaneous use of more than one antiarrhythmic agent, and should be avoided if possible.

Drug selection for acute management of unstable VT and VF

The necessity to treat life-threatening arrhythmias in the operating room is self-evident, and in this setting the risks of drug therapy would appear to be small. However, objective evidence to support the notion that i.v. antiarrhythmic therapy improves survival during cardiac arrest has developed only recently. The most important first manoeuvres in patients who experience VF intraoperatively are non-pharmacological and are nearly the same as those utilized in haemodynamically destabilizing SVT: rapid defibrillation (as opposed to synchronous cardioversion in SVT), and correction of reversible aetiologies (Table 3).

In the realm of pharmacological intervention, there are no human clinical studies available to suggest that i.v. lidocaine, the putative Na^+ -channel blocker most often used during intraoperative cardiac arrest, promotes the conversion of sustained VT or VF to sinus rhythm in any setting. Recent evidence-based recommendations by the American Heart Association have therefore changed the recommendation for lidocaine to 'indeterminate', below amiodarone and procainamide. In support of this change, a recent prospective trial in Seattle, WA, USA (ARREST) examined the efficacy of i.v. amiodarone compared with placebo (the amiodarone carrier) in patients experiencing out-of-hospital cardiac arrest due to pulseless VT or VF refractory to DC cardioversion.³⁰ Of the 504 patients enrolled, those who received amiodarone had a higher survival to hospital admission (44% vs 34%, $P = 0.03$). These were the first randomized prospective data to show a short-term survival advantage to the use of an antiarrhythmic agent during cardiac arrest. A more recent comparable study in Toronto (ALIVE) compared amiodarone with lidocaine.¹¹ Enrollment required VF resistant to three shocks, epinephrine and a fourth shock, or alternatively recurrent VF after initially successful defibrillation. The lidocaine group was treated with lidocaine 1.5 mg kg^{-1} and placebo amiodarone, followed by a second dose of lidocaine 1.5 mg kg^{-1} if defibrillation was not successful. The amiodarone group received amiodarone 5 mg kg^{-1} and placebo lidocaine, followed by amiodarone 3.5 mg kg^{-1} if the defibrillation was not successful. Of the 347 patients enrolled, 22.8% in the amiodarone-treated group survived to hospital admission, compared with 12% of the lidocaine group ($P = 0.0083$).

There was no significant advantage to amiodarone therapy in survival to hospital discharge in either ARREST or ALIVE. At the same time, neither study controlled the elements of patient management after emergency room admission, and both trials were underpowered for detecting longer-term survival differences. In ALIVE, the time between cardiac arrest and administration of drug also influenced survival to hospital admission. In the amiodarone group, short-term survival for those treated within 24 min was 28%, vs only 18% for those receiving

Table 4 Droperidol black box warning, issued by the US Food and Drug Administration in December 2001. <http://www.fda.gov/medwatch/safety/2001/safety01.htm#inapsi>**WARNING**

Cases of QT prolongation and/or torsade de pointes have been reported in patients receiving INAPSINE at doses at or below recommended doses. Some cases have occurred in patients with no known risk factors for QT prolongation and some cases have been fatal.

Due to its potential for serious proarrhythmic effects and death, INAPSINE should be reserved for use in the treatment of patients who fail to show an acceptable response to other adequate treatments, either because of insufficient effectiveness or the inability to achieve an effective dose due to intolerable adverse effects from those drugs (see WARNINGS, ADVERSE REACTIONS, CONTRAINDICATIONS, AND PRECAUTIONS).

Cases of QT prolongation and serious arrhythmias (e.g., torsade de pointes) have been reported in patients treated with INAPSINE. Based on these reports, all patients should undergo a 12-lead ECG prior to administration of INAPSINE to determine if a prolonged QT interval (i.e., QTc greater than 440 msec for males or 450 msec for females) is present. If there is a prolonged QT interval, INAPSINE should NOT be administered. For patients in whom the potential benefit of INAPSINE treatment is felt to outweigh the risks of potentially serious arrhythmias, ECG monitoring should be performed prior to treatment and continued for 2–3 hours after completing treatment to monitor for arrhythmias.

INAPSINE is contraindicated in patients with known or suspected QT prolongation, including patients with congenital long QT syndrome. INAPSINE should be administered with extreme caution to patients who may be at risk for development of prolonged QT syndrome (e.g., congestive heart failure, bradycardia, use of a diuretic, cardiac hypertrophy, hypokalemia, hypomagnesemia, or administration of other drugs known to increase the QT interval). Other risk factors may include age over 65 years, alcohol abuse, and use of agents such as benzodiazepines, volatile anaesthetics, and i.v. opiates. Droperidol should be initiated at a low dose and adjusted upward, with caution, as needed to achieve the desired effect.

later therapy ($P=0.001$). In the surgical venue, successful use of i.v. amiodarone in ventricular arrhythmia management has been reported,^{23,40} although placebo-controlled trials are not yet available (for any antiarrhythmic agent). It should be recognized that amiodarone has non-competitive alpha- and beta-blocking effects, so that rapid i.v. loading may exacerbate haemodynamic instability during the initial (rapid) loading phase in patients with severe left ventricular dysfunction. In these cases, systemic perfusion may be maintained during the initial bolus with additional pressors, and occasionally intra-aortic balloon counterpulsation.²³ If time permits, the negative inotropic effects of i.v. amiodarone are also mitigated by slowing the loading infusion.

Droperidol and ventricular arrhythmias

A recent controversy surrounds the association between ventricular arrhythmias and droperidol, and has caused a 'black box' warning to be issued by the US Food and Drug Administration (FDA) (Table 4). Droperidol, a butyrophenone, is a dopamine subtype-2 receptor antagonist which exhibits mild alpha-adrenergic receptor blockade and peripheral vasodilation. Since its approval by the FDA in 1970, droperidol has been used as a first-line agent in the prevention and treatment of postoperative nausea and vomiting. Its properties as a cost-effective antiemetic have been well established in large-scale randomized trials.^{21,22,52} Droperidol was widely used for three decades in the fields of psychiatry, emergency medicine and anaesthesia; therefore, many physicians were surprised when the FDA issued a 'black box' warning for droperidol in December 2001.

The decision to recommend caution with droperidol administration was based on several reports of adverse cardiac events associated with less-than-maximal doses of droperidol. The cases reported to the FDA suggest an

association between droperidol, QT prolongation and malignant arrhythmias such as torsades de pointes.²⁴ While the relative risk of arrhythmia from droperidol, compared with other antiemetics or placebo, has not been clearly established, the labelling for droperidol now recommends a 12-lead ECG before administration, with continuous ECG monitoring for 2–3 h after administration. If the corrected QT interval is prolonged on the baseline ECG, droperidol administration is not recommended. Additionally, extreme caution is recommended when droperidol is used in patients with risk factors for developing a prolonged QT interval, such as congestive heart failure, bradycardia, diuretic use, ventricular hypertrophy, hypokalaemia, hypomagnesaemia, or use of drugs known to increase the QT interval (Table 4).

I.V. pacemakers and implantable cardioverter defibrillators

Pacemaker and ICD placement has risen tremendously over the past few years, partly because of the expanded indications for insertion of these devices. Worldwide, the number of pacemakers implanted has risen from 780 000 in 2000 to more than 900 000 in 2003. The increase in defibrillator implantation is even more impressive, rising from 80 000 in 2000 to more than 160 000 in 2003. The ACC/AHA/NASPE Guidelines for implantation of pacemakers and ICDs have been updated recently, with some important additions to the indications for placement, particularly regarding ICD insertion. According to the updated guidelines, ICD insertion is a class IIa indication (weight of evidence/opinion in favour of usefulness/efficacy) for patients with an ejection fraction of 30% or lower for whom it is at least 1 month since myocardial infarction and 3 months since coronary artery revascularization surgery.²⁰ This recommendation was based on a published study where 1232 patients with a prior myocardial

infarction and reduced left ventricular ejection fraction ($\leq 30\%$) were randomized to receive an implantable defibrillator or conventional medical therapy. No electrophysiological testing was required before randomization. There was a 31% reduction in the risk of death in patients receiving defibrillators compared with those receiving conventional medical therapy.³⁷ This study is significant because in the US alone, 3–4 million patients have coronary artery disease and advanced left ventricular dysfunction, with 400 000 new cases annually.^{8,38} With the increase in patients who may benefit from defibrillator placement, the likelihood that these patients will present for non-cardiac surgery also increases. Therefore, anaesthetists will require a basic understanding of these devices in order to safely, effectively and expeditiously manage patients with pacemakers and defibrillators.

The major perioperative issue regarding pacemakers and ICDs is the risk of electromagnetic interference (EMI) from electrocautery or cardioversion. EMI can result in inhibition of pacemaker output, activation of rate-responsive sensor resulting in increased pacing rate, ICD firing and myocardial injury at the lead tip resulting in failure to sense or capture, or both.¹² Improved pacemaker and ICD design, including the nearly universal use of bipolar leads and better shielding from EMI, has greatly reduced the probability of the aforementioned adverse interactions. Except in urgent or emergent situations, management of pacemakers and ICDs in the perioperative setting begins with the preoperative visit, which should include documentation of the patient's cardiac history, including the type of device, indication and date of device implantation. Since pacemakers and ICDs are programmable, obtaining the most recent interrogation report can be helpful in determining magnet response, and while definitive guidelines have yet to be established, it is recommended that, to prevent unintended therapy due to EMI, ICDs be reprogrammed to suspend arrhythmia detection in cases where electrocautery is used. Magnet suspension of arrhythmia detection can also be used with most ICDs if the feature is programmed into the device, leaving the pacemaker function of some ICDs unaffected. All of the three major manufacturers of arrhythmia devices (Guidant/CPI, Medtronic, Ventritex/St Jude) recommend interrogation of ICDs after surgical procedures to ensure EMI or magnet use has not altered the device. All three manufacturers have technical support available to assist with device issues, and cardiology consultation may be helpful.

References

- 1 Task Force of the Working Group on Arrhythmias of the European Society of Cardiology. The Sicilian gambit. A new approach to the classification of antiarrhythmic drugs based on their actions on arrhythmogenic mechanisms. *Circulation* 1991; **84**: 1831–51
- 2 The American Heart Association, in collaboration with the International Liaison Committee on Resuscitation. Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 6: advanced cardiovascular life support: 7D: the tachycardia algorithms. *Circulation* 2000; **102**: 1158–65
- 3 Abbott GW, Sesti F, Splawski I, et al. MiRP1 forms IKr potassium channels with HERG and is associated with cardiac arrhythmia. *Cell* 1999; **97**: 175–87
- 4 Abedin Z, Soares J, Phillips DF, Sheldon WC. Ventricular tachyarrhythmias following surgery for myocardial revascularization. *Chest* 1977; **72**: 426–8
- 5 Belardinelli L, Isenberg G. Isolated atrial myocytes: adenosine and acetylcholine increase potassium conductance. *Am J Physiol* 1983; **244**: H737–47
- 6 Bigger JT, Jr. Prophylactic use of implanted cardiac defibrillators in patients at high risk for ventricular arrhythmias after coronary-artery bypass graft surgery. Coronary Artery Bypass Graft (CABG) Patch Trial Investigators [see comments]. *N Engl J Med* 1997; **337**: 1569–75
- 7 Chew C, Hecht H, Colett J, McCallister R, Singh B. Influence of severity of ventricular dysfunction on hemodynamic responses to intravenously administered verapamil in ischemic heart disease. *Am J Cardiol* 1981; **47**: 927–32
- 8 Cohn JN, Bristow MR, Chien KR, et al. Report of the National Heart, Lung, and Blood Institute Special Emphasis Panel on Heart Failure Research. *Circulation* 1997; **95**: 766–70
- 9 Das G, Ferris J. Esmolol in the treatment of supraventricular tachyarrhythmias. *Can J Cardiol* 1988; **4**: 177–80
- 10 DelleKarth G, Geppert A, Neunteufl T, et al. Amiodarone versus diltiazem for rate control in critically ill patients with atrial tachyarrhythmias. *Crit Care Med* 2001; **29**: 1149–53
- 11 Dorian P, Cass D, Schwartz B, Cooper R, Gelaznikas R, Barr A. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. *N Engl J Med* 2002; **346**: 884–90
- 12 Eagle KA, Berger PB, Calkins H, et al. ACC/AHA Guideline Update for Perioperative Cardiovascular Evaluation for Noncardiac Surgery – Executive Summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *Anesth Analg* 2002; **94**: 1052–64
- 13 Echt DS, Liebson PR, Mitchell LB, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. *N Engl J Med* 1991; **324**: 781–8
- 14 Elami A, Merin G, Flugelman MY, et al. Usefulness of late potentials on the immediate postoperative signal-averaged electrocardiogram in predicting ventricular tachyarrhythmias early after isolated coronary artery bypass grafting. *Am J Cardiol* 1994; **74**: 33–7
- 15 El-Sherif N. Polymorphic ventricular tachycardia. In: Podrid PJ, Kowey PR, eds. *Cardiac Arrhythmia: Mechanisms, Diagnosis, and Management*. Baltimore: Williams and Wilkins, 1995; 936–50
- 16 Engelstein ED, Lippman N, Stein KM, Lerman BB. Mechanism-specific effects of adenosine on atrial tachycardia. *Circulation* 1994; **89**: 2645–54
- 17 England MR, Gordon G, Salem M, Chernow B. Magnesium administration and dysrhythmias after cardiac surgery. *JAMA* 1992; **268**: 2395–402
- 18 Galve E, Rius T, Ballester R, et al. Intravenous amiodarone in treatment of recent-onset atrial fibrillation: results of a randomized, controlled study. *J Am Coll Cardiol* 1996; **27**: 1079–82
- 19 Gorgels APM, van den Dool A, Hofs A, et al. Comparison of procainamide and lidocaine in terminating sustained monomorphic ventricular tachycardia. *Am J Cardiol* 1996; **78**: 43–6
- 20 Gregoratos G, Abrams J, Epstein AE, Freedman RA, Hayes DL,

- Hlatky MA, et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee to Update the 1998 Pacemaker Guidelines). *Circulation* 2002; **106**: 2145–61
- 21 Henzi I, Sonderegger J, Tramer MR. Efficacy, dose-response, and adverse effects of droperidol for prevention of postoperative nausea and vomiting. *Can J Anaesth* 2000; **47**: 537–51
 - 22 Hill RP, Lubarsky DA, Phillips-Bute B, et al. Cost-effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol, or placebo. *Anesthesiology* 2000; **92**: 958–67
 - 23 Installe E, Schoevaerdts JC, Gadisseux P, Charles S, Tremouroux J. Intravenous amiodarone in the treatment of various arrhythmias following cardiac operations. *J Thorac Cardiovasc Surg* 1981; **81**: 302–8
 - 24 Kao LW, Kirk MA, Evers SJ, Rosenfeld SH. Droperidol, QT prolongation, and sudden death: what is the evidence? *Ann Emerg Med* 2003; **41**: 546–58
 - 25 Kaul TK, Fields BL, Riggins LS, Wyatt DA, Jones CR. Ventricular arrhythmia following successful myocardial revascularization: incidence, predictors and prevention. *Eur J Cardiothorac Surg* 1998; **13**: 629–36
 - 26 King FG, Addetia AM, Peters SD, Peachey GO. Prophylactic lidocaine for postoperative coronary artery bypass patients, a double-blind, randomized trial. *Can J Anaesth* 1990; **37**: 363–8
 - 27 Kochiadakis GE, Igoumenidis NE, Solomou MC, Kaleboubas MD, Chlouverakis GI, Vardas PE. Efficacy of amiodarone for the termination of persistent atrial fibrillation. *Am J Cardiol* 1999; **83**: 58–61
 - 28 Kron I, DiMarco J, Harman P, et al. Unanticipated postoperative ventricular arrhythmias. *Ann Thorac Surg* 1984; **38**: 317–22
 - 29 Kuchar DL, Thorburn CW, Sammel NL. Prediction of serious arrhythmic events after myocardial infarction: signal-averaged electrocardiogram, Holter monitoring, and radionuclide ventriculography. *J Am Coll Cardiol* 1987; **9**: 531–8
 - 30 Kudenchuk PJ, Cobb LA, Copass MK, et al. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *N Engl J Med* 1999; **341**: 871–8
 - 31 Liebold A, Wahba A, Birnbaum DE. Low-energy cardioversion with epicardial wire electrodes: new treatment of atrial fibrillation after open heart surgery. *Circulation* 1998; **98**: 883–6
 - 32 Lukas A, Antzelevitch C. Differences in the electrophysiological response of canine ventricular epicardium and endocardium to ischemia: role of the transient outward current. *Circulation* 1993; **88**: 2903–15
 - 33 Mandel WJ. Sustained monomorphic ventricular tachycardia. In: Podrid PJ, Kowey PR, eds. *Cardiac Arrhythmia: Mechanisms, Diagnosis, and Management*. Baltimore: Williams and Wilkins, 1995; 919–35
 - 34 Mason JW, Investigators ftE. A comparison of seven antiarrhythmic drugs in patients with ventricular tachyarrhythmias. *N Engl J Med* 1993; **329**: 452–8
 - 35 Mattioni TA, Zheutlin TA, Dunnington C, Kehoe RF. The proarrhythmic effects of amiodarone. *Prog Cardiovasc Dis* 1989; **31**: 439–46
 - 36 Michel PL, Mandagout O, Vahanian A, et al. Ventricular arrhythmias in aortic valve disease before and after aortic valve replacement. *Acta Cardiol* 1992; **47**: 145–56
 - 37 Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med* 1996; **335**: 1933–40
 - 38 Myerburg RJ. Sudden cardiac death: exploring the limits of our knowledge. *J Cardiovasc Electrophysiol* 2001; **12**: 369–81
 - 39 O'Kelly B, Browner WS, Massie B, Tubau J, Ngo L, Mangano DT. Ventricular arrhythmias in patients undergoing noncardiac surgery. *JAMA* 1992; **268**: 217–21
 - 40 Perry JC, Knilans TK, Marlow D, Denfield SW, Fenrich AL, Friedman RA. Intravenous amiodarone for life-threatening tachyarrhythmias in children and young adults. *J Am Coll Cardiol* 1993; **22**: 95–8
 - 41 Priori SG, Barhanin J, Hauer RN, et al. Genetic and molecular basis of cardiac arrhythmias: impact on clinical management parts I and II. *Circulation* 1999; **99**: 518–28
 - 42 Priori SG, Diehl L, Schwartz PJ. Torsade de Pointes. In: Podrid PJ, Kowey PR, eds. *Cardiac Arrhythmia: Mechanisms, Diagnosis, and Management*. Baltimore: Williams and Wilkins, 1995; 951–63
 - 43 Roden DM. Antiarrhythmic drugs. In: JG Hardman LL, ed. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 9th Edn. New York: McGraw-Hill, 1996; 839–74
 - 44 Roden DM. Taking the 'idio' out of 'idiosyncratic': predicting torsades de pointes [editorial]. *Pacing Clin Electrophysiol* 1998; **21**: 1029–34
 - 45 Roden DM, Woosley RL, Primm K. Incidence of clinical features of the quinidine associated long QT syndrome. Implications for patient care. *Am Heart J* 1986; **111**: 1088–93
 - 46 Rowland E, McKenna WJ, Gulker H, Krikler DM. The comparative effects of diltiazem and verapamil on atrioventricular conduction and atrioventricular reentry tachycardia. *Circ Res* 1983; **52**: 163–8
 - 47 Sanguinetti MC, Jiang C, Curran ME, Keating MT. A mechanistic link between an inherited and an acquired cardiac arrhythmia: HERG encodes the I_{Kr} potassium channel. *Cell* 1995; **81**: 299–307
 - 48 Santinga JT, Kirsh MM, Flora JD, Brymer JF. Factors relating to late sudden death in patients having aortic valve replacement. *Ann Thorac Surg* 1980; **29**: 249–53
 - 49 Singh SN, Fletcher RD, Fisher SG, et al. Amiodarone in patients with congestive heart failure and asymptomatic ventricular arrhythmia. *N Engl J Med* 1995; **333**: 77–82
 - 50 Smith RC, Leung JM, Keith FM, Merrick S, Mangano DT. Ventricular dysrhythmias in patients undergoing coronary artery bypass graft surgery: incidence, characteristics, and prognostic importance. *Am Heart J* 1992; **123**: 73–81
 - 51 Stambler BS, Wood MA, Ellenbogen KA, et al. Efficacy and safety of repeated intravenous doses of ibutilide for rapid conversion of atrial flutter or fibrillation. *Circulation* 1996; **94**: 1613–21
 - 52 Tang J, Watcha MF, White PF. A comparison of costs and efficacy of ondansetron and droperidol as prophylactic antiemetic therapy for elective outpatient gynecologic procedures. *Anesth Analg* 1996; **83**: 304–13
 - 53 Tisdale JE, Padhi ID, Goldberg AD, et al. A randomized, double-blind comparison of intravenous diltiazem and digoxin for atrial fibrillation after coronary artery bypass surgery. *Am Heart J* 1998; **135**: 739–47
 - 54 Topol EJ, Lerman BB, Baughman KL, Platia EV, Griffith LSC. De novo refractory ventricular tachyarrhythmias after coronary revascularization. *Am J Cardiol* 1986; **57**: 57–9
 - 55 Vaughan Williams EM. A classification of antiarrhythmic actions reassessed after a decade of new drugs. *J Clin Pharmacol* 1984; **24**: 129–47
 - 56 Waldo AL, Henthorn RW, Epstein AE, Plumb VJ. Diagnosis and treatment of arrhythmias during and following open heart surgery. *Med Clin North Am* 1984; **68**: 1153–70
 - 57 Walsh RW, Porter CB, Starling MR, O'Rourke RA. Beneficial hemodynamic effects of intravenous and oral diltiazem in severe congestive heart failure. *J Am Coll Cardiol* 1984; **3**: 1044–50