Intentional asystole during endoluminal thoracic aortic surgery without cardiopulmonary bypass

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Summary
We describe in three patients the use of adenosine to arrest the heart without cardiopulmonary bypass during endoluminal repair of thoracic aortic aneurysms. The pharmacology of adenosine, a purine nucleoside present in all cells, is reviewed briefly, with special reference to its use in causing transient asystole, which is required for successful surgical expansion of the graft stent in the thoracic aorta. (Br. J. Anaesth. 1997; 78: 444–448).

Key words
Pharmacology, adenosine. Surgery, vascular.

The advent of endoluminal grafting of the aorta has required new approaches to the anaesthetic management of patients, particularly during balloon expansion of the aortic stent when arterial pressure must be reduced to prevent misplacement of the stent and damage to the proximal aorta or heart. We report three patients who received i.v. bolus doses of adenosine with the intention of causing asystole and hypotension at the time of expansion of the aortic stent of endoluminal grafts to the thoracic aorta.

Adenosine ("Adenocor" Sanofi Winthrop Pty Ltd), which is a relatively new antiarrhythmic agent for treating supraventricular tachycardia, is a naturally occurring purine nucleoside which transiently inhibits adenyl cyclase and 3, 5-cyclic adenosine monophosphate (cAMP) by binding to adenosine receptors, and has been shown to have major cardiovascular actions (depression of sinoatrial (SA) and atrioventricular (AV) nodes; reduction in atrial contractility; attenuation of catecholamine effects primarily on the ventricles; depression of ventricular automaticity; and attenuation, via a presynaptic action, of adrenaline-induced noradrenaline release). The short duration of action, short half-life and effects on heart conduction make adenosine a useful drug in the diagnosis and management of supraventricular tachycardias such as Wolff–Parkinson–White syndrome. Adenosine has also been useful in myocardial preservation during cardiac surgery because of cardiac arrest with a hyperpolarized myocardium rather than the more usual depolarized state, although this has been challenged.
operation she required a right brachial artery thrombectomy (10 cm thrombus) which was related most probably to the brachial artery sheath used for surgical access in that arm. She was discharged 10 days after her original aortic operation. Six month surgical follow-up showed that the aneurysmal sac had been isolated.

PATIENT NO. 2

A 66-yr-old male presented with a recurrent thoracic aortic aneurysm just distal to the site of a previous open repair under cardiopulmonary bypass performed 3 yr previously for a chronic dissection. This first repair was immediately distal to the left subclavian artery. At angiography the coronary arteries were normal and there was normal ventricular function. The patient also had non-insulin dependent diabetes mellitus and glaucoma, and was receiving atenolol 100 mg, ramipril 5 mg and aspirin 100 mg mane, loratidine 10 mg daily, mebeverine 135 mg as needed, 0.25% timolol eye drops twice daily and temazepam 10–20 mg at night. Preoperative creatinine was 121 μmol litre⁻¹ (increasing to 182 μmol litre⁻¹ after operation), haemoglobin 121 g litre⁻¹ (decreasing to 73 g litre⁻¹, 2 days after operation, and then increasing to 92 g litre⁻¹, 4 days after operation, all without blood transfusion) and platelets 113 × 10⁹ litre⁻¹ (decreasing to 64 × 10⁹ litre⁻¹, 2 days after operation, and then increasing to 102 × 10⁹ litre⁻¹, 4 days after operation). After premedication with papaveretum 15 mg and hyoscine 0.3 mg, anaesthesia consisted of tracheal intubation using thiopentone and tubocurarine/pancuronium block and low flow oxygen and nitrous oxide with isoflurane. Intra-arterial, pulmonary arterial, capillary wedge and central venous pressures were measured.

Surgical access was via the right common femoral artery. Adenosine was used at the time of balloon inflation to expand the stents in the descending thoracic aorta. Two grafts were used, one inside the distal part of the other (White-Yu GAD 30 mm and 24 mm 7 mm).8 With the patient heparinized, receiving 100% oxygen, and after trial doses of 9, 15, 24, 36 and 45 mg administered peripherally via an arm vein to determine the correct dose to stop the heart for the required time of 20–30 s, a dose of adenosine 45 mg was used on each occasion at the time of balloon inflation to expand the stent grafts. The patient’s oxygen saturation was never less than 100% at this time and his temperature was 35.5°C, again solely from environmental conditions. There were no adverse complications of the procedure. The patient was nursed initially in the ICU with IPPV overnight. The tracheal tube was removed on the first postoperative day and the patient transferred to the ward on the second day and discharged from hospital on the fifth postoperative day. Six month surgical follow-up showed that the aneurysmal sac had been isolated.

PATIENT NO. 3

A 51-yr-old male with Marfan’s syndrome who had previously undergone two aortic valve replacements 17 and 12 yr earlier, and an abdominal aortic repair 10 yr previously, presented with acute dissection of his thoracic aorta which required a Bentall’s procedure (replacement of the aortic valve and ascending aorta in continuity); 22 days later, while still in hospital, a further deterioration with interscapular back pain and angiographic and ultrasound evidence of a rapidly expanding thoracic aortic aneurysm required endoluminal repair. This endoluminal repair was immediately distal to the left subclavian artery. At angiography the coronary arteries were normal with moderately impaired left ventricular function. The patient was receiving i.v. heparin, and captopril 50 mg three times daily, sotalol 80 mg twice daily, diltiazem 240 mg mane, amiloride 5 mg mane, frusemide 40 mg twice daily, minoxidil 10 mg twice daily, atenolol 100 mg mane, digoxin 25 μg mane and allopurinol 300 mg mane. Preoperative creatinine was 67 μmol litre⁻¹ (increasing to 182 μmol litre⁻¹ after operation), haemoglobin 89 g litre⁻¹ (decreasing to 73 g litre⁻¹, 2 days after operation, and then increasing to 92 g litre⁻¹, 4 days after operation, all without blood transfusion) and platelets 365 × 10⁹ litre⁻¹ (decreasing to 64 × 10⁹ litre⁻¹, 2 days after operation, and then increasing to 102 × 10⁹ litre⁻¹, 4 days after operation). After premedication with papaveretum 15 mg and hyoscine 0.3 mg, anaesthesia consisted of tracheal intubation using thiopentone and tubocurarine/pancuronium block and low flow oxygen and nitrous oxide with isoflurane. Intra-arterial, pulmonary arterial, capillary wedge and central venous pressures were measured.

Surgical access was via the left common femoral artery and right brachial artery. Adenosine was used at the time of balloon inflation to expand the stents in the descending thoracic aorta. Two grafts were used, one inside the distal part of the other (White-Yu GAD 24 mm × 15 mm and 24 mm × 7 mm).8 With the patient heparinized, receiving 100% oxygen, and after trial doses of 9 and 15 mg administered centrally via the pulmonary artery catheter to determine the correct dose to stop the heart for the required time of 20–30 s, a dose of adenosine 21 mg was used on the first occasion and 27 mg on the second occasion at the time of balloon inflation to expand the stent grafts. The patient’s oxygen saturation was never less than 100% at this time and his temperature was 35.5°C, again solely from environmental conditions. There were no adverse complications of the procedure. The patient was nursed initially in the ICU but his trachea was not intubated or his lungs ventilated. The patient was transferred to the ward the next day and discharged from hospital on the fifth postoperative day.

Discussion

Parodi, Palmaz and Barone9 introduced endoluminal grafting of the aorta after animal experimentation by several groups,10–14 and surgeons at our hospital have performed more than 150 abdominal aortic grafts.15 Recently, repair of the thoracic aorta has also been performed by the endoluminal
technique, and this operation has required further evaluation of the place of hypotension at the time of expansion of the aortic stent to prevent both displacement of the stent and major damage to the aorta or undue strain on the myocardium leading to ischaemia or infarction. If the stent is moved by the pressure of blood in the aorta forcing the inflating balloon distally at the time of expansion of the graft stent, there may be major problems in placement of the graft which is measured precisely before insertion. There may also be major problems, with aortic rupture or dissection, because of increased pressure in the aorta caused by balloon obstruction. The heart may also be stressed because of the increased demands on contractility and myocardial oxygen at the time of aortic obstruction by the balloon. For endoluminal grafting of the abdominal aorta various anaesthetic hypotensive techniques, such as the use of sodium nitroprusside, glyceryl trinitrate, heavy volatile anaesthetic dose, and both lumbar and thoracic extradural block, have been used to reduce arterial pressure at the time of balloon inflation to expand the graft stent.

The work of Dorros and Cohn during endoluminal grafting of the thoracic aorta suggested that adenosine would be an ideal agent to use to reduce arterial pressure by stopping the heart during surgical expansion of the proximal stent of the graft, which in these cases was to be by balloon inflation totally obstructing the thoracic aortic outflow. Adenosine occurs naturally in all cells, has no negative inotropic effects, has transient actions and decreases arterial pressure dramatically by causing asystole when given in high doses. The pharmacology of adenosine is species specific but there appear to be two main adenosine receptors—the A1 receptor leading to inhibition of adenylate cyclase and thus decreased production of cAMP which is the dominant effect on cardiac electrophysiology and the A2 receptor leading to stimulation of adenylate cyclase and increased cAMP which is the dominant effect on vasodilatation. Recently in the rat there was a suggestion that there is a separate A3 receptor effect on vasodilatation. Recently in the rat there was a suggestion that there is a separate A3 receptor effect on vasodilatation.

Adenosine should be used with caution in patients with bronchial asthma because inhaled adenosine has precipitated asthma, and in patients with sick sinus syndrome or second- or third-degree heart block unless there is a pacemaker inserted. Patients receiving methyIxanthines are resistant to adenosine because of competitive inhibition of A1 and A2 adenosine receptors, and patients receiving dipyridamole may have prolonged asystole with adenosine because of inhibition of the transport system into cells, with subsequent increases in adenosine concentrations. Slow channel calcium blocking agents such as verapamil and nifedipine also inhibit the transport of adenosine into cells. Benzodiazepines enhance the effects of adenosine and carbamazepine is reported in the company's product information leaflet also to increase the degree of heart block.

Potentially, patients who have endoluminal repair of the thoracic aortic may need to have this procedure converted to open surgical repair if there is sudden rupture of the diseased aorta by intra-aortic surgical manipulations or if there are other surgical problems with placement of the endoluminal graft. Thus anaesthesia techniques need to take such possibilities into account when preparing the patient for surgery. This was the main reason why our second patient had a thoracic extradural inserted, although extradural block of the cardiac sympathetics was also planned to assist with myocardial function, lower contractility and myocardial oxygen demand, and improve myocardial blood flow. In addition, there may be synergistic reduction in arterial pressure with administration of adenosine, which may prevent hypertension overcompensation on recovery from adenosine asystole.

The normal dose of adenosine for termination of supraventricular tachycardias is 3–6 mg and in some patients this dose has caused transient asystole. Larger doses cause some hypotension because of decreased peripheral vascular resistance even when asystole is not produced. The dose of adenosine to be used during expansion of the stent must be determined before the surgical manoeuvre, otherwise the duration of asystole and hence surgical time are unpredictable. Because the dose of adenosine required to produce asystole and the duration of asystole are unpredictable it is preferable to start with a dose of 9 mg, increasing in steps until asystole of the desired duration of approximately 20–30 s is produced. Our second patient proved relatively resistant requiring larger doses of adenosine than previously recommended, but this may have been caused by administration of adenosine via a peripheral vein in this patient. Rankin and colleagues showed that lower doses were needed (by a factor of one-third—3 mg vs 10 mg) when adenosine was administered centrally rather than peripherally, and we intend to give adenosine via a central vein in future. This patient was not receiving any drug therapy, such as methylxanthine, which has been reported to antagonize adenosine.
possible cause for the increased dose of adenosine in our second patient was the use of a thoracic extradural with full sympathetic block of the heart, as adenosine effects are reported to be more prominent when there is increased sympathetic tone.

There were no apparent cardiac, vascular or neurological sequelae to cessation of cardiac output for periods up to 45 s in our patients who were not specifically protected by hypothermic techniques throughout surgery, although mild hypothermia occurred in both patients, which may have had some protective effect on cerebral metabolism. Life-threatening events after adenosine would appear to be rare and although minor side effects are common in awake patients, most of these symptoms and signs are masked during anaesthesia. The major complications which are possible after this technique using adenosine would be fatal arrhythmias, thromboembolism, cerebral ischaemia or infarction, coronary ischaemia or infarction, stroke or paraplegia. All of these complications are possible with any surgical repair of thoracic aortic aneurysms, and we believe that in the endoluminal surgical repair they may be less likely or at least no more likely to occur than in standard open repair of the thoracic aorta with or without cardiopulmonary bypass. Caution in the use of adenosine in this way to cause asystole intentionally should be exercised in patients with cerebrovascular or cardiac ischaemia which could potentially be exacerbated by the period of hypotension and circulatory arrest, although adenosine has been used for both cerebral and coronary protection against ischaemic damage. These contraindications should be borne in mind when surgeons are contemplating the use of adenosine in endoluminal thoracic aortic repair, as Dorros and Cohn have recommended that adenosine should be used in all aortic repairs by the endoluminal technique, including abdominal. White, in a commentary on their article, cautioned that such sweeping recommendations may be “detrimental to the wider application and appeal of the endoluminal technique”. In any case it would appear to be unnecessary in endoluminal repair of the abdominal aorta.

We believe that the use of adenosine in considered cases of endoluminal repair of the thoracic aorta enhances the management of balloon inflation of the graft stent to allow better expansion to match the aortic diameter. This technique has the advantages of controlled transient hypotension with potential protection of the heart and brain.

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References


