Brief Review

Anaesthesia for non-cardiac surgery in heart-transplanted patients

D.C.H. Cheng MD MSc FRCPC, D.D. Ong MD

This review documents the anaesthetic management, haemodynamic function and outcome in 18 of 86 heart-transplanted recipients, who returned for 32 non-cardiac surgical procedures at the Toronto Hospital from 1985 to 1990. General anaesthesia was administered in eight of the 27 elective operations and four of the five emergency operations. Induction medications included thiopentone (2–4 mg · kg^{-1}), fentanyl (1–7 μg · kg^{-1}) and succinylcholine (1–1.5 mg · kg^{-1}). Anaesthesia was maintained with a combination of oxygen/nitrous oxide and isoflurane or enflurane. Muscle relaxation was maintained with vecuronium or pancuronium. No delayed awakening or unplanned postoperative ventilation was observed. Neuroleptanaesthesia was administered to 63.0% and 20.0% of the elective and emergency operations, respectively. The anaesthetics included fentanyl (25–100 μg) and midazolam (0.5–1.5 mg) or diazemuls (2.5–5.0 mg). Spinal anaesthesia (75 mg lidocaine) was administered to only two of the 27 elective operations. No important haemodynamic changes were observed in any anaesthetic group, but lower systolic BP was found after induction and during maintenance periods in the patients who received general anaesthesia than in those who received neurolept-anaesthesia. However, no anaesthesia-related morbidity or mortality was noted. This suggests that general, neuroleptand spinal anaesthesia do not affect haemodynamic function or postoperative outcome in heart-transplanted recipients undergoing subsequent non-cardiac surgery.

Cet article documente la conduite anesthésique, la fonction hémodynamique et l'évolution de 18 des 86 transplantés cardiaques qui sont revenus pour 32 interventions chirurgicales non cardiaques à l'Hôpital de Toronto de 1985 à 1990. Une anesthésie générale a été administrée pour huit des 27 interventions programmées et pour quatre des cinq interventions d'urgence. Les agents d'induction comprenaient du thiopental (2,0–4,0 mg · kg^{-1}), du fentanyl (1,0–7.0 μg · kg^{-1}) et de la succinylcholine (1,0–1,5 mg · kg^{-1}). L'anesthésie a été entretenue avec une combinaison d'oxygène/protoxyde d'azote et isoflurane ou enflurane. La relaxation musculaire a été maintenue avec du vécuronium ou du pancuronium. On n'a pas observé de réveil retardé ni de ventilation post-opératoire imprévue. Une neuroleptanesthésie a été administrée à 63,0% des interventions programmées et à 20% des interventions urgentes. Les agents étaient du fentanyl (25–100 μg) et du midazolam (0,5–1,5 mg) ou du diazemul (2,5–5 mg). L'anesthésie rachidienne (75 mg de lidocaïne) n'a été administrée qu'à seulement deux des 27 opérations programmées. Dans aucun groupe, on n'a observé de variations hémodynamiques importantes, mais une pression artérielle systolique plus basse a été notée après l'induction et pendant les périodes d'entretien chez les patients qui ont reçu une anesthésie générale par rapport à ceux qui ont reçu une neuroleptanesthésie. On n'a cependant pas enregistré de morbidité ni de mortalité en rapport avec l'anesthésie. Ceci suggère que l'anesthésie générale, la neuroleptanesthésie, ou l'anesthésie rachidienne n'affecte pas la fonction hémodynamique ou l'évolution post-opératoire chez les patients transplantés qui ultérieurement subissent une chirurgie non cardiaque.

Key words
ANAESTHESIA: outcome;
SURGERY: transplantation, heart.

From the Department of Anaesthesia, University of Toronto, The Toronto Hospital, Toronto, Ontario.

This study has been presented in part at the Canadian Anaesthetists' Society Meeting 1991.

Address correspondence to: Dr. D.C.H. Cheng, Department of Anaesthesia, University of Toronto, The Toronto Hospital, Toronto General Division, 200 Elizabeth St., Toronto, Ontario M5G 2C4.

Accepted for publication 23rd June, 1993.

Cardiac transplantation has become the standard therapy for idiopathic dilated cardiomyopathy and end-stage ischaemic heart disease. With the introduction of cyclosporine in the last decade, together with better patient selection, improved perioperative monitoring and care,

the overall survival of recipients has increased to approximately 75% at five years and more than 70% at ten years post transplantation.[1] Cardiac-transplanted patients present anaesthetists with challenging problems related to the pharmacodynamic behaviour and haemodynamic function of the denervated heart and their complex drug therapies. This review documents the anaesthetic management, haemodynamic function and outcome in 18 of the 86 heart-transplanted recipients returning for 32 noncardiac surgical procedures at The Toronto Hospital during 1985–1990. The implications of post-transplantation morbidity on perioperative anaesthetic management are also reviewed.

Methods

With the approval of the institutional ethics committee, medical charts of all patients who underwent cardiac transplantation and subsequent surgery from March 1985 to May 1990 at The Toronto Hospital, Toronto Western Division, were reviewed. Data regarding preoperative demographics and associated diseases, duration of transplanted heart, type of surgery, type and doses of anaesthetics administered, perioperative haemodynamics (BP, HR, SaO_2) and postoperative complications were recorded. Data were expressed as mean ± standard deviation of mean (SD). Repeated measures ANOVA were used to compare differences within anaesthetic groups in a variable over time. One-way ANOVA was used to compare the differences among the treatment groups in a variable over time. Fisher's exact test was applied for comparison of different anaesthetic types between emergency and elective surgery. Statistical significance was denoted as a P value < 0.05.

Results

Between March 1985 to May 1990, 86 patients underwent heart transplantation at our institution. Eighteen of these patients subsequently underwent 32 noncardiac surgical operations requiring an anaesthetic. The recipients (16M:2F) who returned for subsequent surgery ranged in age from 30–58 yr. The number of patients returning for subsequent procedures were distributed according to the following ASA classification: II–10, III–16, IV–5, V–1. The surgical procedures and type of anaesthetics are listed in Table I. All operations were performed between one day and four years following cardiac transplantation.

All patients had received chronic immunosuppression with prednisone, cyclosporine and azathioprine, except for one who received only prednisone and azathioprine. Twenty-seven operations were performed on an elective basis and five as emergency procedures (Table II). Twelve operations were performed under general anaesthesia, of which eight were done on an elective basis and four were emergency cases.

TABLE I Type of noncardiac surgery and anaesthesia in heart-transplanted patients

Surgery	*Anaesthetic*
Cataract surgery	9 (Neurolept)
Pacemaker insertion	3 (Neurolept)
Hickman line insertion	2 (Neurolept)
Vocal cord augmentation	1 (Neurolept)
Scleral buckle	1 (Neurolept)
Stereotactic brain tumour biopsy	1 (Neurolept)
Thrombectomy	1 (Neurolept)
Laparotomy	3 (GA)
Dental extraction	2 (GA)
Cholecystectomy	2 (GA)
Chevron osteotomy	1 (GA)
Closure of ileostomy	1 (GA)
Bronchoscopy	1 (GA)
Open lung resection	1 (GA)
Inguinal herniorraphy	2 (GA–1, Regional–1)
TURP	1 (Regional)

TABLE II Type of anaesthesia in elective and emergency surgery for heart-transplanted patients

Anaesthesia	*Elective surgery (n = 27)*	*Emergency surgery (n = 5)*
General	8	4
Regional	2	0
Neurolept	17	1

Aside from standard intraoperative monitors, five patients (vocal cord augmentation, cholecystectomy, thrombectomy, thoracotomy and laparotomy) had invasive arterial lines inserted. Invasive central venous pressure monitoring were used in two patients (laparotomy and thrombectomy). Invasive monitors were used because of the surgical and preoperative condition of patient (arterial line for thoracotomy and open lung biopsy, and central venous pressure monitoring for emergency laparotomy and small bowel resection). The patients who underwent thrombectomy and vocal cord augmentation were one and four days postheart-transplant, respectively, and still had the lines *in situ*. One patient was in septic shock and had a pulmonary artery catheter inserted preoperatively before undergoing emergency cholecystectomy.

In all the elective cases, anaesthesia was induced with thiopentone (3–4 $mg \cdot kg^{-1}$) and fentanyl (1–3 $\mu g \cdot kg^{-1}$). In the emergency cases, two patients received thiopentone (2 $mg \cdot kg^{-1}$) and fentanyl (3 $\mu g \cdot kg^{-1}$), while two others were given fentanyl (7 $\mu g \cdot kg^{-1}$). The tracheas of all patients were intubated after succinylcholine and only two patients received precurarization. Anaesthesia was

TABLE III Comparison of perioperative haemodynamic and SaO_2 in heart-transplanted patients during general anaesthesia and neurolept-anaesthesia

Anaesthesia	*Pre-induction*	*Post-induction*	*Maintenance*
SBP			
GA	131.0 ± 19.1	116.0 ± 22*	124.5 ± 21.9*
Neurolept	147.6 ± 25.5	148.8 ± 30.3	149.2 ± 30.1
HR			
GA	87.3 ± 20.4	83.7 ± 11.6	82.9 ± 9.5
Neurolept	81.4 ± 16.9	81.2 ± 16.0	79.8 ± 14.7
SaO_2			
GA	99.0 ± 0.7	99.0 ± 0.9	98.6 ± 1.2
Neurolept	98.0 ± 1.5	98.5 ± 1.4	98.8 ± 1.3

Mean ± SD.
*$P < 0.05$ (GA vs neurolept).

maintained with a nitrous oxide/oxygen mixture and isoflurane ($n = 7$) or a nitrous oxide/oxygen mixture and enflurane ($n = 3$) or 100% oxygen and isoflurane ($n = 2$). Muscle relaxants administered were vecuronium ($n = 9$) and pancuronium ($n = 2$). Paralysis was easily reversed with neostigmine with or without atropine. No significant effect on heart rate was recorded. No delayed awakening was noted and none required reintubation or unplanned postoperative ventilation.

Two patients (transurethral resection of the prostate and inguinal hernia repair) received spinal anaesthesia with 75 mg lidocaine without any complications.

Eighteen operations were performed under neurolept-anaesthesia, of which 17 were on an elective basis and one as an emergency case (insertion of a Hickman line). The anaesthetic regimen consisted of fentanyl (25–100 μg) and midazolam (0.5–1.5 mg) or diazemuls (2.5–5.0 mg). Lower SBP was found after induction and during maintenance in patients who had general anaesthesia than in patients who had neurolept-anaesthesia (Table III). There was no anaesthesia-related morbidity and mortality. One patient died of graft rejection 25 days after cholecystectomy (525 days post-transplant) and another died of lower gastrointestinal bleeding 22 days after stereotactic brain tumour biopsy (498 post-transplant).

Discussion

During 1968 and 1969, 20 cardiac transplant procedures were performed in Ontario and Quebec. Most patients died of infection or rejection within one year, but one patient from Quebec survived for over four years before dying of rejection and a cerebrovascular accident. One patient from Ontario survived for over five years.[2] From 1970 until 1980, no further heart transplantation was done in Canada, but in 1981, McKenzie at the University Hospital in London, Ontario, reintroduced cardiac transplantation, and in May 1983, performed Canada's first combined heart and lung transplantation. From April 1981 to September 1985, 81 heart transplants in 80 recipients have been performed. The age of the recipients ranged from 12 to 60 yr.[2]

Heart transplantation has become an established therapeutic modality for patients with end-stage heart disease.[3] With refined transplantation techniques, improved patient selection, cyclosporine immunosuppression, improved anaesthetic management and monitoring techniques, and appropriate postoperative care, the expected survival rate of cardiac-transplanted patients is excellent with approximately 75% at five years and greater than 70% at ten years after transplantation.[1] In addition, the rehabilitation potential for these patients is very good. By three months, most cardiac transplant recipients have returned to NYHA class I functional capacity. As the duration of post-transplant survival has continued to improve, more of these patients require elective or emergency operation.

In 1977, Kanter and Samuels were the first to review the anaesthetic management of 29 cardiac-transplanted patients undergoing additional operations at Stanford University.[4] A follow-up review at the same institution in 1986 reported 80 of 261 cardiac transplant patients (30.6%) who subsequently underwent 136 surgical procedures, both emergency (55%) and elective (45%). Surgery varied from two hours to six years after transplantation. The majority underwent general anaesthesia and only 4.4% of patients received regional anaesthesia. The agents used for general anaesthesia were: nitrous oxide-oxygen and narcotic (35%), narcotic-oxygen only (18%) and inhalational agent (23%), and other *iv* agents: thiopentone (10%) and ketamine (8%).[5] Our post-transplanted non-cardiac surgical procedures were similar to those reported at Columbia University in 1991.[6] Melendez *et al.* reported 28 of 124 cardiac transplant patients (22%) subsequently underwent 35 non-cardiac surgical procedures. They also concluded, within the normal range of dose requirement for *iv* and inhalational agents, muscle relaxants, and local anaesthetics, there was no apparent instance of prolonged anaesthetic action.

The post-transplantation morbidity and anaesthetic implications

DENERVATED HEART

Cardiac transplantation involves removing the diseased heart and leaving an atrial cuff. The aorta and the main pulmonary arteries are transected, the cardiac plexus is interrupted and the heart is denervated. The recipient atrium remains innervated, but haemodynamically un-

important, while the donor atrium is denervated and is responsible for the electrophysiological responses of the transplanted heart. The ECG often contains two P waves, one from the native atrium and the other from the donor atrium. The denervated heart retains its intrinsic control mechanisms which include: a normal Frank-Starling effect demonstrated with volume loading and in response to exercise, normal impulse formation and conductivity and intact alpha- and beta-adrenoreceptors responding normally to circulating catecholamines without evidence of denervation hypersensitivity to exogenous and endogenous catecholamines.[4,5] But the normal respiratory variations or response to carotid sinus massage and Valsalva maneouvres are absent. At rest, the heart rate reflects the intrinsic rate of depolarization at the donor sino-atrial node in the absence of any vagal tone, is faster than normal at about 90–100 beats per minute.[7]

The normal heart increases its cardiac output via neural stimuli which lead to simultaneous increases in heart rate and contractility. The denervated heart lacks the ability to respond acutely to hypovolaemia or hypotension with reflex tachycardia but responds to stress primarily by an increase in stroke volume. The increases in cardiac output are dependent upon venous return with an initial increase in left ventricular end-diastolic volume (LVEDV), which mediates an increase in stroke volume and ejection fraction by means of the Frank-Starling mechanism. The increases in LVEDV and pressure are not sustained, but the increased cardiac output is maintained by a heart rate which slowly increases over five to six minutes in response to increasing circulating catecholamines. This reflects dependence of the sinus node on direct stimulation by endogenously released catecholamines and the absence of control via neural mechanisms. That is why heart transplant patients are said to be "preload dependent." Thus, increasing preload is useful before anaesthetic maneouvres such as rapid thiopentone induction or high spinal anaesthesia. The heart rate shows no response to drugs like muscle relaxants (pancuronium, gallamine), anticholinergics (atropine, glycopyrrolate and scopolamine), anticholinesterases (neostigmine, edrophonium, pyridostigmine, physostigmine), and digoxin, nifedipine, phenylephrine, or nitroprusside, but will respond to isoproterenol, ephedrine, dopamine or glucagon. It has been suggested that no autonomic reinnervation takes place in humans after transplantation, thus the sympathetic response to laryngoscopy and intubation are absent.[8,9] However, recent evidence indicates that slow development of cardiac reinnervation may be possible.[10]

Cardiac dysrhythmias may occur in heart-transplanted patients, probably due to lack of vagal tone, rejection, and increased endogenous catecholamine concentrations. The sinus node may have an increased refractory period and atrial conduction may be prolonged. Thus, first-degree atrioventricular (AV) block is common. Dual AV nodal pathways are frequently observed, but re-entry dysrhythmias are rare. A 5–10% incidence of incomplete and complete right bundle-branch block has been noted and as many as 20% of heart-transplanted patients require a pacemaker for bradyarrhythmias.[11] At our centre only three of 86 patients (3.5%) required permanent pacemaker insertion. Bradyarrhythmic therapy in these patients should be a direct beta-adrenergic stimulating agent (ephedrine, isoproterenol). Glucagon is also useful as a positive chronotrope and inotrope. Verapamil, procainamide and quinidine are useful for supraventricular tachyarrhythmias of atrial flutter and fibrillation. Lidocaine should be used cautiously in treating ventricular dysrhythmias because of its negative inotropic action.[11]

REJECTION

The majority of rejection episodes occur within the first three months of transplantation with a peak at about four to six weeks. Usually, these episodes resolve with modification of the immunosuppression regimen by augmentation of steroid therapy; however, refractory rejection remains an important cause of early mortality after transplantation. It has been suggested that graft rejection markedly increases intraoperative morbidity,[4] thus it is suggested that endomyocardial biopsy information be available before elective surgery. Also there are several reports of an increasing frequency of atrial, junctional and ventricular arrhythmias in asymptomatic heart transplant recipients, especially in the first six months after transplantation, with the incidence increasing during episodes of rejection.[7] In our series, none of the patients had endomyocardial biopsy information available before their procedures. Nonetheless, there were no perioperative arrhythmias or rejection noted.

INFECTION

Immunosuppressive drugs are continued indefinitely in heart transplant patients and infection remains a major cause of death.[1] It is most prevalent in the first several weeks after transplantation when immunosuppressive therapy is most intense. Early postoperative, bacterial infections (e.g., mediastinitis) and opportunistic infections (e.g., CMV, pneumocystis carinii, toxoplasma and legionella) are the most common. The leading cause of infection is direct contact with contaminated material. Thus, invasive monitoring techniques and all forms of instrumentation should be kept to the minimum consistent with safe anaesthesia. Attention to aseptic technique should be paramount, and it has been recommended that all intravascular and airway equipment be handled with sterile gloves. Intubation via the orotracheal route is pref-

erable to the nasotracheal since the latter is associated with infection by diphtheroids and staphylococcal commensals from the nasopharynx and skin.

DRUG INTERACTIONS

Chronic steroid treatment may result in an abnormal stress response, so that patients should receive perioperative steroid coverage. Azathioprine has been reported to antagonize the competitive neuromuscular blocking drug by its phosphodiesterase inhibiting properties, therefore larger doses of relaxants may be required.[12] In experimental animals, cyclosporine infusions have been shown to potentiate the neuromuscular blocking effects of atracurium and vecuronium and single doses of cyclosporine may result in increased duration of action of both barbiturates and narcotics.[13,14]

ALLOGRAFT CORONARY ARTERY DISEASE

The denervated heart is vulnerable to an accelerated process of coronary atherosclerosis. Angiographic evidence of allograft CAD is present in 10–20% of patients one year after transplantation and in up to 50% by five years.[15] Even in angiographically normal coronary arteries, coronary luminal narrowing may develop insidiously.[16] The aetiology of allograft CAD is likely multifactorial.[17] Some CAD is transplanted with the donor heart, other factors include immunological or vital injury to vascular endothelium with a resultant proliferative response, ischaemic injury at time of transplantation, and other risk factors such as smoking, hypertension, hyperlipidaemia and diabetes. The lack of afferent innervation renders episodes of myocardial ischaemia silent in these patients. Therefore, diagnostic ECG is essential in the perioperative period.

HYPERTENSION

Nearly 75% of post-transplant recipients develop mild to moderate hypertension as a result of cyclosporine therapy.[17] Current therapy may consist of a calcium channel blocker such as diltiazem. However, diltiazem will interact and increase cyclosporine levels, therefore dosage adjustment may be required. Nifedipine may be less tolerated by these patients because of its prominent vasodilator effect. When necessary, an angiotensin-converting enzyme inhibitor may be added. Because cardiac responsiveness during exercise is dependent on circulating catecholamines, beta blockers are best avoided after heart transplantation.[18]

RENAL DYSFUNCTION

Due to the nephrotoxic effects of cyclosporine, serum creatinine concentrations gradually increase after cardiac transplantation, but generally plateau around 170–180 $mmol \cdot L^{-1}$.[17] Co-administration of nephrotoxic drugs, e.g., non-steroidial anti-inflammatory drugs or trimethoprim-sulphamethoxazole, or agents which elevate cyclosporine blood concentrations, e.g., erythromycin or diltiazem, must be monitored closely to avoid acute deterioration of renal function. Anaesthetic drugs that are excreted mainly by renal clearance should be avoided. Hyperuricaemia commonly resulted from decreased renal urate clearance caused by cyclosporine. When allopurinol is used to treat gout, toxic accumulation of azathioprine can develop with resultant bone marrow depression as azathioprine is metabolized via the xanthine oxidase pathway which is inhibited by allopurinol.[19]

Our study suggests that these patients have similar monitoring and anaesthetic requirements to non-transplant patients undergoing similar procedures. This review confirms recent reports that a minimum amount of monitoring is needed for these patients.[6] The patients in our series had invasive monitoring because these were needed in keeping with giving a safe anaesthetic for a particular procedure (i.e., arterial line for thoracotomy and open lung biopsy, central venous pressure monitor for small bowel resection) or because the patient was unstable preoperatively. Smooth and safe anaesthesia is contingent upon careful preoperative assessment which may reduce the need for invasive monitoring with all its attendant risks. Adequate preload must be ascertained preoperatively and intravascular volume status maintained intraoperatively because these patients are "preload dependent" and the denervated heart is unable to mount a rapid tachycardic response.

The majority of the patients received neuroleptanaesthesia, although the patients who received general anaesthesia had a combination of N_2O/O_2/narcotic/relaxant technique with low doses of volatile agents as described in most series. The patients had normal requirements for intravenous and inhalational agents, muscle relaxants and local anaesthetics. There was no prolonged action of any anaesthetic agents. Although all the patients in this study were receiving chronic immunosuppresants with known drug interactions, the potential problems were not observed. Despite reports of cyclosporine-enhanced neuromuscular blockade by vecuronium and atracurium,[14] it does not appear that patients on cyclosporine have decreased requirements for nondepolarizing muscle relaxants. In terms of postoperative monitoring, most patients were sent to the postanaesthetic care unit (PACU) for routine monitoring and stay. No anaesthetic-related morbidity was observed and no prolonged PACU stay or unplanned intubation reported. However, this study is a retrospective chart review and a well controlled prospective study would be needed to assess properly this issue.

In summary, heart-transplanted patients present anaesthetists with unique and challenging problems. In our heart-transplanted population, 21% of these patients subsequently returned for 32 non-cardiac surgeries over five years. General, neurolept- and regional anaesthesia used in this series did not adversely affect haemodynamic function at induction of anaesthesia or postoperative outcome in these patients. This report suggests that the cardiac-transplanted patient presents an acceptable anaesthetic risk for noncardiac surgery. However, the anaesthetic implications of post-transplantation morbidity in the denervated heart, rejection, infection, drug interactions, allograft coronary artery disease, hypertension, hyperlipidaemia and renal dysfunction must be considered carefully for the optimal perioperative care of these patients.

References

1 *Shaw IH, Kirk AJB, Conacher ID.* Anaesthesia for patients with transplanted hearts and lungs undergoing non-cardiac surgery. Br J Anaesth 1991; 67: 772–8.

2 *Modry DL, Kaye MP.* Heart and heart-lung transplantation: the Canadian and world experience from December 1967 to September 1985. Can J Surg 1986; 29: 275–9.

3 *Frazier OH, Cooley DA.* Cardiac transplantation. Surg Clin North Am 1986; 66: 477–89.

4 *Kanter SF, Samuels SI.* Anesthesia for major operations on patients who have transplanted hearts, a review of 29 cases. Anesthesiology 1977; 46: 65–8.

5 *Demas K, Wyner J, Mihm FG, Samuels S.* Anaesthesia for heart transplantation. A retrospective study and review. Br J Anaesth 1986; 58: 1357–64.

6 *Melendez JA, Delphin E, Lamb J, Rose E.* Noncardiac surgery in heart transplant recipients in the cyclosporine era. J Cardiothorac Vasc Anesth 1991; 5: 218–20.

7 *Shroeder JS, Berke DK, Graham AF, Rider AK, Harrison DC.* Arrhythmias after cardiac transplantation. Am J Cardiol 1974; 33: 604–7.

8 *Firestone L.* Heart transplantation. Int Anesthesiol Clin 1991; 29: 41–58.

9 *Baumgartner WA, Reitz BA, Oyer PE, Stinson EB, Shumway NE.* Cardiac homotransplantation. Curr Probl Surg 1979; 16: 1–61.

10 *Wilson RF, Christensen BV, Olivari MT, Simon A, White CW, Laxson DD.* Evidence for structural sympathetic reinnervation after orthotopic cardiac transplantation in humans. Circulation 1991; 83: 1210–20.

11 *Stein KL, Darby JM, Grenvik A.* Intensive care of the cardiac transplant recipient. J Cardiothorac Anesth 1988; 2: 543–53.

12 *Eisenkraft JB, Dimich I, Sachdev VD.* Anesthesia for major noncardiac surgery in a patient with a transplanted heart. Mt Sinai J Med 1981; 48: 116–20.

13 *Cirella VN, Pantuck CB, Lee YJ, Pantuck EJ.* Effects of cyclosporine on anesthetic action. Anesth Analg 1987; 66: 703–6.

14 *Gramstad LL, Gjerløw JA, Hysing ES, Rugstad HE.* Interaction of cyclosporin and its solvent, Cremaphor with atracurium and vecuronium. Br J Anaesth 1986; 58: 1149–55.

15 *Uretsky BF, Murali S, Reddy PS, et al.* Development of coronary artery disease in cardiac transplant patients receiving immunosuppressive therapy with cyclosporine and prednisone. Circulation 1987; 76: 827–34.

16 *O'Neill BJ, Pflugfelder PW, Singh NR, Menkis AH, McKenzie FN, Kostuk WJ.* Frequency of angiographic detection and quantitative assessment of coronary arterial disease one and three years after cardiac transplantation. Am J Cardiol 1989; 63: 1221–6.

17 *Miller LW.* Long-term complications of cardiac transplantation. Prog Cardiovasc Dis 1991; 33: 229–82.

18 *Rudas L, Pflugfelder PW, Kostuk WJ.* Comparison of hemodynamic responses during dynamic exercise in the upright and supine postures after orthotopic cardiac transplantation. J Am Coll Cardiol 1990; 16: 1367–73.

19 *Lin HY, Rocher LL, McQuillan MA, Schmaltz S, Palella TD, Fox IH.* Cyclosporine-induced hyperuricemia and gout. N Engl J Med 1989; 321: 287–92.