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A Review of the Management of Abdominal Aortic Aneurysms in Patients Following Cardiac Transplantation

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Objectives: *To describe the presentation, preoperative assessment and postoperative management of patients presenting with an infrarenal abdominal aortic aneurysm following a previous cardiac transplant.*
Methods: *The case histories of three patients have been examined and a literature review performed.*
Conclusions: *The majority of patients developing aortic aneurysms had undergone cardiac transplantation for ischaemic cardiomyopathy and thus require detailed assessment of cardiac function preoperatively to exclude accelerated coronary artery disease in the graft. Full invasive cardiac monitoring during surgery is mandatory to maintain haemodynamic stability in patients with a dennervated heart and to avoid postoperative renal failure. The higher incidence of pulmonary and wound complications are discussed, together with protocols for maintaining adequate immunosuppression. Finally, data supporting a higher prevalence and more rapid expansion of aortic aneurysms in immunosuppressed patients is considered and evidence-based recommendations made regarding aneurysm screeening in these patients.*

Key Words: Abdominal aortic aneurysms; Transplantation.

Introduction

Cardiac transplantation is an accepted therapeutic option for selected patients with end-stage cardiac failure, with ischaemic cardiomyopathy (CM) accounting for 39–65% of recipients.[1,2] Life expectancy of transplant patients has improved considerably since the introduction of cyclosporine, with reported survival rates of up to 94%, 79% and 72% at 1, 5 and 10 years, respectively.[1,3] Thus, it is increasingly likely that these patients will develop extra-cardiac manifestations of their atherosclerosis.

This paper reports the elective repair of three infrarenal aortic aneurysms (AAA) in cardiac transplant patients and discusses their preoperative, perioperative and postoperative management. A literature review suggests that the natural history of AAA in these patients may differ from that in non-transplant patients, and thus the role of screening is considered.

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Patients and Methods

Case 1

A 47-year-old male who underwent transplantation (ischaemic cardiomyopathy) in April 1990 had mild aortic dilatation (3.2 cm) prior to surgery. A computed tomography (CT) scan in August 1994 demonstrated a 5.7 cm diameter AAA. His medical history included post-transplantation hypertension, hyperlipidaemia, mild chronic renal insufficiency (serum creatinine 180 umol/l; normal range; 50–140) and reflux oesophagitis. Current medication comprised cyclosporine, azathioprine, prednisolone, nifedipine, captopril, frusemide, aspirin and cimetidine.

The AAA was impalpable due to obesity (wt: 116 kg), although a 2.5 cm left femoral artery aneurysm was noted. The chest X-ray and pulmonary function tests were normal, an ECG showed a sinus rhythm with superadded recipient P-waves, and annual post-transplantation angiography confirmed normal coronary vessels, with no evidence of rejection on endomyocardial biopsy.

Aortography mirrored the CT findings and thus an

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aorto-bifemoral Y-graft was performed. Perioperative monitoring included invasive arterial, central venous and pulmonary artery wedge pressure (PAWP) measurements, and an epidural catheter was employed for postoperative analgesia. Anaesthesia was maintained with low-dose isoflurane and nitrous oxide, whilst nitroglycerin and dopamine infusions were instituted for blood pressure (BP) control and optimisation of renal perfusion (urine output maintained at 1–2 ml/kg/h). Adequate preload was achieved by a CVP of 9–11 mmHg and a PAWP of 18 mmHg.

Antibiotic prophylaxis (cephradine 1 g, 8-hourly i.v.) was continued until all catheters had been removed. Cyclosporine and azathioprine were administered via a nasogastric tube, and i.v. hydrocortisone given in reducing doses to replace oral prednisolone. Serum cyclosporine levels and white cell count were monitored daily. The patient made an uneventful recovery and was discharged on the 14th day. He remains well at 18-months' follow-up.

Case 2

A 55-year-old male had a cardiac transplant in July 1993 (ischaemic cardiomyopathy) following coronary artery bypass surgery 3 years earlier. Pre-transplant ultrasound confirmed a normal aorta (1.9 cm diameter), although angiography in August 1995 (symptoms of calf claudication) demonstrated a saccular infrarenal AAA and left iliac and bilateral superficial femoral artery arteriosclerosis. The AAA (5.2 cm diameter on ultrasonography) was impalpable due to obesity (109 kg). Medical history included insulin-dependent diabetes, mild chronic obstructive airways disease, a minor stroke in 1991, hypertension, hyperlipidaemia, chronic renal insufficiency (serum creatinine 275 umol/l) and gout, for which he was receiving cyclosporine, azathioprine, diltiazem, bendrofluazide, insulin and a ventolin inhaler.

Respiratory function tests confirmed mild, reversible, chronic obstructive airways disease (COAD), whilst an ECG showed a sinus tachycardia, recipient P-waves and a right bundle branch block (RBBB). Coronary angiography and endomyocardial biopsy were normal.

The AAA was repaired with an aorto-bifemoral Y-graft. Anaesthetic management, antibiotic prophylaxis and immunosuppression were as for case 1. Postoperative recovery was complicated by adult respiratory distress syndrome and acute-on-chronic renal failure requiring ventilation and haemodialysis for 7 days. Subsequent recovery was uneventful, and the patient was discharged on day 21 with a creatinine of 250 umol/l. He remains well at 1 year.

Case 3

A 41-year-old male received a cardiac transplantation in September 1990 for ischaemic cardiomyopathy following coronary artery bypass surgery 12 months earlier. Mild aortic dilatation (3.1 cm diameter) was noted prior to surgery, although a saccular infrarenal AAA was demonstrated during coronary angiography (normal coronary vessels, no evidence of rejection) in September 1991 (4.3 × 5 cm on CT scan). His medical history included post-transplantation hypertension, hyperlipidaemia and reflux oesophagitis, and medication included cyclosporine, azathioprine, frumil, aspirin and ranitidine. Renal biochemistry and pulmonary function tests were normal, whilst an ECG showed sinus tachycardia with RBBB.

Although the AAA was successfully replaced with a tube graft (discharged on day 10), the patient was readmitted 6 months later with congestive cardiac failure. Coronary angiography indicated marked progression of coronary atherosclerosis, and the patient died 2 months later despite intensive medical treatment.

Discussion

Patients may be referred to a vascular surgeon for a number of reasons following cardiac transplantation. These include iatrogenic complications of cardiopulmonary bypass and either occlusive or aneurysmal peripheral vascular disease. Although surgical morbidity and mortality may not be increased in these patients, careful consideration of their preoperative, intraoperative and postoperative management is required.

Preoperative management

Cardiovascular assessment. Allograft rejection and accelerated coronary artery disease (CAD) may complicate cardiac transplantation, with CAD occurring in 4–30% of patients within 3 years and accounting for one-third of late deaths.[4,5] These patients do not experience angina (cardiac denervation), and thus preoperative coronary angiography and endomyocardial biopsy are essential.

After cardiac transplantation the ECG often shows a sinus tachycardia (parasympathetic denervation[6]), recipient P-waves, and a right bundle branch block.[7] However, significant tachyarrhythmias may reflect allograft rejection or accelerated CAD,[8] whilst bradyarrhythmias might indicate the need for pre-operative cardiac pacing.[7]

Hypertension occurs in 50–90% of patients after transplantation,[9,10] often being precipitated by immunosuppressive drugs or neuroendocrine abnormalities.[10] Whilst control may be difficult,[11] sodium restriction, diltiazem and angiotensin-converting-enzyme inhibitors are often effective.

Pulmonary function. Whilst severe COAD is a relative contraindication to cardiac transplantation, all of our patients had smoked and were markedly obese. Their immunosuppressive therapy and perhaps impaired exercise tolerance may contribute to the latter. Routine pulmonary function tests should be performed and bronchodilators prescribed for significant reversible bronchospasm.

Renal function. The renal vasoconstrictive effect of cyclosporine, post-transplantation hypertension and the nephrotoxic effect of angiotensin-converting enzyme inhibitors may all contribute to the chronic renal insufficiency after cardiac transplantation.[12] Serum creatinine was elevated in two of our three patients, with the third showing a temporary rise postoperatively. Avoidance of nephrotoxic drugs, adequate pre-operative hydration, peri- and postoperative haemodynamic stability, and optimising renal perfusion with dopamine, may help preserve renal function.

Anaesthetic management

Anaesthetic management requires special consideration,[13] and in particular obesity may pose considerable anaesthetic risks.[14] Furthermore, changes in cardiac output by the denervated heart depend upon the Frank–Starling law, and maintenance of an adequate preload and avoidance of hypovolaemia are critical. This requires invasive monitoring of both CVP and PAWP. Finally, anaesthetic agents which cause minimal myocardial depression should be used.

Postoperative management.

Immunosuppressive therapy. This should be maintained with cyclosporine and azathioprine administered either intravenoulsy or via the nasogastric tube, with daily monitoring of serum cyclosporine levels and the white blood cell count. For patients taking prednisolone, appropriate high doses of i.v. hydrocortisone are given, but are reduced over 3–5 days to the maintenance dose.

Infection risk. Immunosuppression increases susceptibility to infection and strict asepsis should be observed during insertion of indwelling catheters. These should be removed as soon as possible postoperatively and prophylactic antibiotics administered until this time.

Significant weight gain following transplantation is common,[15] and both obesity and long-term corticosteroids increase the risks of pulmonary and wound complications.[16] Despite meticulous wound care, two of our three patients developed significant wound problems.

Complications. Perioperative myocardial infarction, an important complication of routine aortic aneurysm surgery, is unusual following cardiac transplantation if annual coronary angiography has demonstrated normal coronary arteries. Pulmonary complications are common in these patients, who have usually smoked and may have underlying respiratory disease. Furthermore, obesity may limit postoperative mobility, thus necessitating vigorous postoperative physiotherapy. Epidural analgesia may also reduce the risk of pulmonary complications,[17] although the catheter should be removed within 72 h because of the risk of sepsis.

Natural History of Aortic Aneurysms in Cardiac Transplant Patients

The majority of AAAs after transplantation occur in patients who presented with ischaemic cardiomyopathy (Table 1) – an extracardiac manifestation of their atherosclerosis. Furthermore, these aneurysms appear to expand more rapidly (0.74–1.75 cm/year)[1,18] than other AAAs (0.2–0.5 cm/year),[19,20] and this is apparently confirmed by our report (1.35 cm/year). Thus, combined data from all series indicate a mean aneurysm growth rate of 1.10 ($\pm$0.61) cm/year (Table 2). This phenomenon might be explained by factors which promote or accelerate atherosclerosis in transplant patients, including hyperlipidaemia and immunosuppressive therapy. Furthermore, experimental evidence suggests that corticosteroids may promote both the development and rupture of aortic

Table 1. Previous series describing the development of AAA in cardiac transplantation patients.

Authors	Indication for cardiac transplantation	AAA symptom	AAA surgery	Shape of AAA	Sex	Age at AAA repair (year)	Interval between cardiac and aortic surgery	Size of AAA at repair (cm)	Op. mortality
Infrarenal AAA									
Reitz *et al.*[2]	Ischaemic CM	Pain	Elective	Fusiform	Male	50/51	5 year+8 month	8	No
	Ischaemic CM	Pain	Elective	?	Male	51	4 year+2 month	12	No
Reichman *et al.*[32]	Ischaemic CM	Pain (NR)	Emergency	?	Male	61	2 year	11	No
	Ischaemic CM	Pain	Elective	?	Male	61	2 year	5.2	No
Piotrowski *et al.*[1]	Ischaemic CM	Asympt.	Elective	Fusiform	Male	55	2 year+4 month	5.5	No
	Ischaemic CM	Pain (NR)	Emergency	?	Male	66	2 year	5.9	No
	Ischaemic CM	Ruptured	Emergency	?	Male	60	2 month	4	Died
	Ischaemic CM	Asympt.	Elective	?	Male	56/57	18 month	4.8	No
	Ischaemic CM	Pain (NR)	Emergency	?	Male	55	3 year	4.1	No
MacIntyre *et al.*[5]	Ischaemic CM	Asympt.	Elective	?	Male	57	2 year+6 month	6.5	No
Bull *et al.*[33]	Ischaemic CM	Rupture	Emergency	?	?	?	2 month	?	Died
	Ischaemic CM (six patients)	Asympt.	Elective	?	?	?	?	?	No
Benvenisty *et al.*[28]	Ischaemic CM	Pain (NR)	Emergency	?	Male	52	4 month	?	No
	Ischaemic CM	Asympt.	Elective	?	Male	52	5 year	?	No
Shenaq *et al.*[34]	Ischaemic CM	Asympt.	Elective	?	Male	63	3 month	?	?
	Ischaemic CM	Asympt.	Elective	?	Male	59	6 month	?	?
Chandrasekar *et al.*[35]	Ischaemic CM	Rupture	Emergency	?	Male	61	6 year	5.0	No
Defraigne *et al.*[18]	Valvular CM	Asympt.	Elective	?	Male	63	4 year	5.3	No
	Idiopathic CM	Asympt.	Elective	?	Male	63	1 year	6.5	No
	Ischaemic CM	Asympt.	Elective	?	Male	64	2 year	5.3	No
Ammori *et al.* (this paper)	Ischaemic CM	Asympt.	Elective	Fusiform	Male	51	4 year+4 month	5.7	No
	Ischaemic CM	Asympt.	Elective	Saccular	Male	57	2 year+1 month	5.2	No
	Ischaemic CM	Asympt.	Elective	Saccular	Male	42	1 year	5.0	No
Suprarenal AAA									
Benvenisty *et al.*[28]	Ischaemic CM	Rupture	Emergency	?	Male	44	13 month	?	No
Oz *et al.*[36]	?	?	Elective	?	Male	45	?	8.5	No

AAA, abdominal aortic aneurysm; CM, cardiomyopathy; NR, non-ruptured.

Table 2. Expansion rate of reported AAA in cardiac transplant patients.

Authors	Infrarenal aortic diameter (cm)			
	Pre-cardiac transplant	Post-cardiac transplant	At AAA repair	Growth rate (cm/year)
Piotrowski *et al.*[1]	3.4	—	5.5	0.84
	4.5	—	5.9	0.80
	3.5	—	4.0	0.50
	3.5	—	4.8	0.67
	1.5	—	4.1	0.87
Chandrasekar *et al.*[35]	—	3.2 cm at 3 year	5	0.60
Defraigne *et al.*[18]	—	3.0 cm at 2 year	5.4	1.20
	4.0	—	6.5	2.50
	3.0	—	5.3	1.15
Ammori *et al.* (this paper)	3.2	—	5.7	0.57
	1.9	—	5.2	1.58
	3.1	—	5.0	1.9

aneurysms,[21] whilst aneurysmal disease appears more common, and develops 10 years earlier, in patients receiving steroids for autoimmune diseases.[22] Finally, increased aortic haemodynamic stress following a rise in cardiac ejection fraction[1,18] and systemic hypertension may accelerate aneurysm enlargement[23–25] and promote rupture.[26,27]

It might be considered unusual that two of our patients had saccular aneurysms, although Benvenisty *et al.*[28] have also reported the development of a saccular aneurysm of the descending aorta after transplantation. Unfortunately, aneurysm morphology is not described in any other reports (Table 1). However, given the possibility that saccular aneurysms may be more common in these patients, it is worth considering their natural history. Thus, whilst Ouriel *et al.*[29]

reported that saccular aneurysms rupture less often than fusiform aneurysms, Faggioli *et al.*[30] have suggested that saccular outpouchings in the aneurysm wall increase the risk of early rupture. Thus, early repair of saccular aneurysms may be justified.

In view of the foregoing discussion it is logical to consider the role of aneurysm screening in transplant patients, particularly as the overall incidence of aneurysm development is 4.3%, increasing to 10.5% in patients undergoing transplantation for ischaemic cardiomyopathy. This compares to a prevalence of 2% in males aged 65–74 years, in the general population.[31]

It is also apparent that AAA in transplant patients may be impalpable due to obesity, and thus routine ultrasonography is required for screening. However, because there are no reports of aneurysm development in female patients (Table 1), it might be reasonable to restrict screening to males.

Finally, the role of endovascular aneurysm repair might be considered in this group of patients. Certainly a reduced aortic occlusion time might be beneficial from the cardiac point of view. Similarly, avoidance of an abdominal wound and early mobilisation should reduce pulmonary complications, while the absence of a postoperative ileus allows easy administration of immunosuppressive therapy. However, current techniques for stent-grafting require groin incisions which are more susceptible to infection than abdominal wounds, and this could increase the risk of graft infection, particularly when performed in the angiography suite where sterility may be inferior to that of an operating theatre.

In summary, aortic aneurysms in cardiac transplant patients should be considered for early repair, as they appear to have a rapid expansion rate and concomitant corticosteroid therapy may increase the risk of rupture. Such a policy should be relatively safe, because these patients usually have relatively normal cardiac functions and this almost certainly explains the absence of mortality for elective aneurysm repair in the published series.

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