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Cardiac Surgery after Heart Transplantation: Coronary Artery Bypass Grafting and Heart Valve Replacement

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ABSTRACT

Introduction. Due to increasing need for and a shortage of donor organs, therapeutic procedures such as heart valve replacement for valve insufficiency and coronary artery bypass grafting (CABG) for graft vasculopathy (GVP) must be performed to improve allograft function to avoid retransplantation.

Methods. We performed a retrospective analysis of patients who underwent surgical procedures after orthotopic heart transplantation. Since 1989, we have performed more than 1400 heart transplantation procedures. Valve replacement was necessary in 8 patients and CABG was necessary in 3 patients. Five patients received valve prostheses (3 bioprostheses and 2 mechanical valves) at the tricuspid position. Three patients received a Hancock bioprosthesis at the mitral position. One of the 3 received the valve 3 years after heart transplantation while suffering from mitral regurgitation grade IV, and another patient received the valve 1 year following heart transplantation while suffering from mitral insufficiency grade III due to infective endocarditis. Three patients underwent coronary artery revascularization, 2 patients underwent the procedure 1 and 7 years after heart transplantation because of GVP, 1 patient underwent the procedure simultaneously with heart transplantation because of donor coronary artery disease. One patient received concomitant CABG with heart transplantation because of 75% left anterior descending stenoses in the donor organ, and one patient received CABG 1 year after heart transplantation because of rapidly progressive GVP in the left anterior descending artery. The third patient had 3-vessel disease with 95% left stem and 75% ramus circumflex, ramus marginalis, and ramus diagonalis.

Results. Two patients who underwent CABG and 4 patients who underwent valve replacement are still alive and maintain good clinical performance. One patient with a graft at the mitral position died 9 years after heart transplantation and 6 years after mitral valve replacement. Two patients with a graft at the tricuspid position died 17 and 4 years after heart transplantation (6 and 3 years after valve replacement, respectively). One patient with a bioprostheses at the tricuspid position had to be retransplanted 2 years following valve replacement while suffering from a paravalvular leakage grade III.

Conclusion. Cardiac surgical procedures can be safely performed after heart transplantation. To improve graft and patient survival, such procedures must be carefully performed after heart transplantation to avoid retransplantation. The shortage of donor organs will and must lead to an increase in the number of conventional procedures performed to improve allograft function in transplanted hearts.

INTRODUCTION

Long-term survivors of cardiac transplantation may experience a diverse array of cardiovascular diseases that require late cardiac reoperation. Due to the increasing need for and shortage of donor organs, therapeutic procedures such as heart valve replacement for valve insufficiency and coronary artery bypass grafting (CABG) for graft vasculopathy (GVP) must be performed to improve allograft function to avoid retransplantation.

Among valve dysfunctions after heart transplantation, tricuspid valve abnormalities are the most common [Rees 1993; William 1996]. Studies have estimated that 50% to 90% of recipients experience tricuspid regurgitation (TR) [Angermann 1990; Rees 1993; Huddleston 1994; Alharethi 2006]. Severe TR occurs rarely, but when it does occur it is mostly as a biopsy-related complication in which valvular apparatus injury occurs. Its estimated occurrence is 10% at 5 years and 15% at 10 years [Tucker 1994; Chan 2001], and if it is refractory to medical therapy, surgery is mandatory. Mitral valve incompetence may reach an incidence rate between 55% and 87% after transplantation. Mitral regurgitation may be related to atrial enlargement [Stevenson 1987; Angermann 1990].

Each year, 10% of heart transplant recipients develop coronary artery disease (CAD), and the prevalence of CAD is approximately 40% to 50% by 5 years after heart transplantation [Pennock 1982; Gao 1987; Uretsky 1987;

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Table 1. Demographic Data*

Patient No.	Sex	Diagnosis	Heart Transplantation Age, y	Procedure	Survival	Age, y
1	Male	DCM	71	CABG	Yes	71
2	Male	DCM	63	CABG	Yes	76
3	Male	CAD	49	CABG	No	67
4	Female	DCM	37	TVR	Yes	57
5	Male	DCM	69	TVR	Yes	84
6	Male	DCM	49	MVR	Yes	54
7	Male	DCM	47	TVR	No	64
8	Male	DCM	58	TVR	No	61
9	Male	DCM	59	TVR	No	71
10	Male	CAD	63	MVR	Yes	69
11	Female	CAD	52	MVR	No	61

*DCM indicates dilative cardiomyopathy; CABG, coronary artery bypass grafting; CAD, coronary artery disease; TVR, tricuspid valve replacement; MVR, mitral valve replacement.

Barnhardt 1988; Constanza 1996; Reedy 2002]. CAD results from a combination of immunologic and nonimmunologic factors that cause endothelial injury, smooth muscle proliferation, intimal thickening, and coronary obstruction [Grewal 2004]. CAD is usually diffuse and is characterized by concentric involvement of both intramyocardial and epicardial vessels mostly at mid and distal segments [Gao 1988; Johnson 1989; Pucci 1990; Mcmanus 1995], differing from classic atherosclerotic CAD in being a very diffuse disease of epicardial and myocardial vessels with intimal proliferative narrowing of all vessels and only occasionally presenting with focal stenoses. However, some patients have focal, proximal disease that is suitable for traditional revascularization.

Transplant recipients are usually afflicted because of symptom-free denervated hearts and face sudden death or silent myocardial infarction. Some cases manifest with congestive heart failure and arrhythmias. In rare occasions, sympathetic reinnervation of the myocardium occurs, leading to afferent neuronal stimulation presenting as angina pectoris.

METHODS

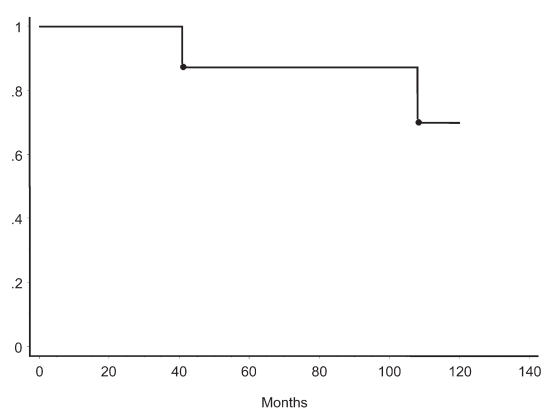
The aim of this report was to retrospectively analyze our single center's experience with the necessity for cardiovascular operations after heart transplantation. Between 1990 and 2006, 8 patients (2 female, 6 male) underwent heart valve replacement after transplantation, and 3 patients underwent coronary artery revascularization. Two patients underwent the procedure 1 and 7 years after heart transplantation because of GVP, and 1 patient underwent the procedure simultaneously with heart transplantation because of donor CAD. Patient age was 56 ± 10 years (range, 37-71 years). Indications for heart transplantation in the valve group were dilative cardiomyopathy (DCM) in 6 patients and CAD 2 patients; in the CABG group, DCM occurred in 2 patients and CAD in 1 patient.

Five patients received valve prostheses (3 bioprostheses and 2 mechanical valves) at the tricuspid position because of biopsy-related endomyocardial damage to the tricuspid valve caused by a ruptured chordae refractory to medical therapy. Three patients received a Hancock-bioprosthesis at the mitral position. One patient received the bioprosthesis while suffering from mitral regurgitation grade IV secondary to GVP-related acute myocardial infarction 3 years after heart transplantation; one patient received the bioprosthesis while suffering from mitral insufficiency grade III due to infective endocarditis 1 month after heart transplantation; and one patient received the bioprosthesis while suffering from myocardial infarction grade III due to left atrium enlargement and annular dilatation 6 years after heart transplantation. Table 1 shows the demographic data of the patients. Significant CAD was detected on coronary angiographies performed 1 and 5 years after heart transplantation. Control coronary angiographies showed disease progression. One patient had local middle-left anterior descending artery (LAD) stenoses and received CABG × 1 of the LAD with the saphenous vein magna 1 year after heart transplantation. Another patient had 3-vessel disease with 95% left stem and 75% ramus circumflex, ramus marginalis, and ramus diagonalis. The lesions were inaccessible for angioplasty.

The time interval from heart transplantation to heart valve replacement was 71 ± 58 months (range, 1-141 months); for aortocoronary venous bypass, the time interval was 34 ± 49 months (range, 0-89 months). Table 2 shows the time intervals. Technically, the operation was similar to a normal redo operation. Median sternotomy was used in all patients. Dense adhesions were present. Because of previous sternotomies and long-term steroid therapy, bilateral internal mammary artery grafting was not considered in our cohort. Patients were weaned from cardiopulmonary bypass without difficulty. There were no differences concerning intensive care unit duration and hospital stay in comparison to the patients who had not received heart transplants. The myocardial biopsy specimens showed no histological evidence of acute rejections. Patients underwent close follow-up with regular echocardiography and coronary angiographies. Risk factors were controlled medically. Three patients developed steroid-resistance acute rejections, necessitating OKTIII therapy. No thromboembolic episodes or prosthetic or native valve infections were observed during the follow-up period.

Table 2. Time Intervals between Heart Transplantation and Additional Procedure

	Mean	SD	Range
Coronary artery bypass grafting, mo	34	49	0-89
Valve replacement, mo	71	58	1-141
Total, mo	60	56	0-141



Kaplan Meier analysis survival curve.

There was no perioperative mortality. Six patients are still alive and maintain good clinical performances. One patient died 18 years after heart transplantation, which was 11 years after aortocoronary venous bypass. One patient with a graft at the mitral position died 9 years after heart transplantation, which was 6 years after mitral valve replacement. Three patients with a graft at the tricuspid position died 17, 8, and 4 years after heart transplantation (6 months, 2 months, and 3 years after valve replacement, respectively). The Figure shows a Kaplan Meier analysis survival curve. All patients with bioprosthetic tricuspid valves were free from structural valve deterioration except for 1 patient with a Biocor bioprostheses (Bethesda, MD, USA) at the tricuspid position. This patient had to undergo retransplantation 13 years following the original heart transplantation, which was 2 years following valve replacement, while suffering from a paravalvular leakage grade III. None of the deaths were valve related. Hospital morbidity included acute renal failure requiring hemodialysis in 1 patient.

Study Limitations

The present study is retrospective. The CABG and valve groups are rather small. Clinical endpoints such as ventricular function and exercise capacity were not assessed. Despite these limitations, the present study represents a unique attempt to collect and analyze single-center results of cardiovascular operations after heart transplantation.

DISCUSSION

Valve dysfunctions have several hypothetical etiologies as well as iatrogenic causes such as endomyocardial biopsy. TR is supposed to increase with time. TR is believed to be caused by biatrial anastomosis techniques performed when an enlarged right atrium is present, left ward rotation leading to distortion of tricuspid valve annulus in DCM patients receiving small donor hearts, and pulmonary hypertension [Haverich 1991; Soares 1994].

Managing CAD involves prevention and the control of risk factors. We perform angiography routinely 1 year after transplantation then yearly if CAD is detected or after 5 years if it is not. The disease in allografts varies from proximal lesions (type A) to diffuse and distal lesions (type C). Angioplasty and CABG can be performed successfully in patients with type A lesions without distal arteriopathy, which shows progression and has symptomatic reversible ischemia with worsening heart failure. Coronary angiography is the standard method for diagnosing GVP. The prevalence of any angiographically visible CAD 1, 2, and 4 years after heart transplantation is 11%, 22%, and 45%, respectively [Constanza 1996]. Intracoronary ultrasound has shown intimal thickening in as many as 85% of patients 1 year after heart transplantation [Musci 1998].

As reported by Koyanagi et al [1999], we have extended the donor criteria at our institute because of the shortage of suitable donor organs. Donors more than 50 years of age, donors receiving an infusion of considerably high-dose catecholamines (dopamine >10 μg/kg per minute; epinephrine >1 μg/kg per minute), donors with a graft ischemic time longer than 4 hours, or donor hearts with possible coronary artery sclerosis are accepted after taking the individual recipient's prolonged waiting period and deteriorating hemodynamic status into consideration [Koyanagi 1999]. Coronary angiography was applied to patients suspected of having 1-vessel CAD by inspection and palpation at explantation. If more than 2-vessel disease was suspected, we rejected it as a donor heart. Baseline coronary angiography was performed in transplant recipients who received a heart from a donor older than 50 years of age, with previous cardiopulmonary resuscitation, or who had been administered OKTIII due to ongoing rejection 1 month after heart transplantation [Koyanagi 1999].

In patients with elevated serum creatinine levels, there was an increased concern regarding the risk of exposure of the patient to even small amounts of contrast material at the time of coronary angiography. Dobutamine stress echocardiography was used as an alternative to angiography because of its high sensitivity for the detection of coronary allograft vasculopathy. If the results were negative, coronary angiography was usually not performed [Reedy 2002].

Percutaneous transluminal coronary angioplasty has an excellent success rate of 84%, similar to classic atherosclerotic CAD, but restenosis rates as high as 67% make it an option only for postponing retransplantation [Halle 1995; Parry 1996; Koyanagi 1999]. Recipients with at least 70% stenosis in a primary coronary vessel have a 46%, 13%, and 13% actuarial survival rate at 1, 2, and 5 years after diagnosis, respectively [Halle 1995]. The presence of distal coronary disease on the angiogram before bypass surgery results in an operative mortality rate between 33% and 40% [Halle 1995; Parry 1996]. Operative mortality rates ranged between 33% and 43% [Halle 1995; Ono 2003].

In the past, retransplantation was the only choice for management because of limited donor organs and poor outcomes compared with initial heart transplantation. Retransplantation is a choice for patients with symptoms of heart failure and severely compromised left ventricular function and whose CAD is so diffuse that no intervention possibilities exists.

Reports with retransplantation mortality rates of 45% at 1 year, 75% at 2 years, and 90% at 5 years have been published [Hosenpud 1994; Smith 1995; Schnetzler 1998; John 1999]. Furthermore, 20% to 30% of these patients died while still on the waiting list [Reedy 2002]. The International Society of Heart and Lung Transplantation Registry has reported 4 factors that are predictive of survival after repeat heart transplantation: accelerated CAD as the cause of allograft failure, an interval greater than 6 months between procedures, no need for mechanical ventilatory assistance before retransplantation, and retransplantation after 1985 [Gallo 1997].

CONCLUSION

As the transplant population ages and longer survival becomes possible, several surgical procedures may be used in addition to retransplantation. Because of the current shortage of donor hearts, these procedures appear to be feasible and safe in terms of overall survival and they seem to provide reasonably effective long-term palliation. The key to treatment must be prevention. It is important to make the optimal therapeutic choice and choose the correct time for reoperation [Goenen 1991].

Retransplantation is the only definitive therapy for GVP, but the survival rate is inferior to that for initial heart transplantation, and the incidence of recurrent GVP in the second graft is high [Gao 1988]; therefore, coronary angioplasty appears to be the method of choice to treat focal stenoses of CAD.

Coronary angioplasty is advisable for type A lesions, but an increased rate of restenosis makes CABG the gold standard for selected patients. CABG can be successfully performed for type A lesions, and quality of life improves following revascularization in the heart transplant recipient. Despite the increased risk of endocarditis in an immunosuppressed patient and the need for anticoagulation in a patient with corticotherapy, the shortage of donor organs often leads to the application of valve replacement.

In our study, the selection of a prosthesis was influenced by the recipient's age, life expectancy, and the necessity of anticoagulation [Rao 2000]. Mechanical prosthesis are reported to have no mechanical valve complications, especially in the tricuspid position, but they would prevent endomyocardial biopsy and right ventricle catheterization [Ichikawa 2000]; therefore, tissue valves are the most commonly used valves, allowing for an endomyocardial biopsy to be performed with a minimal risk of biopsy-related injuries [Alharethi 2006; Filsoufi 2006].

Cardiac surgical procedures can be safely performed after heart transplantation. To improve graft and patient survival, such procedures must be carefully performed after heart transplantation to spare retransplantation.

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