Treatment of Left Main Coronary Artery Stenosis with Drug-Eluting Stent Following Heart Transplantation

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Abstract

Cardiac allograft vasculopathy is the leading cause of death after the first year of heart transplantation. The optimal treatment for unprotected left main coronary artery disease in orthotopic heart transplantation (OHT) patients is unknown. Two OHT patients with left main disease following heart transplantation underwent percutaneous coronary intervention (PCI). Technical success was achieved in the patients with drug-eluting stents inserted to cover the lesions in the left main coronary artery. After 16 months follow-up, one patient died of multiorgan failure, the other was alive and free from myocardial infarction or target vessel revascularization. We conclude that the unprotected PCI for the left main coronary artery stenosis in transplanted heart is feasible.

Key words: left main coronary artery, heart transplantation, mortality, percutaneous coronary intervention, stent

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Introduction

Cardiac allograft vasculopathy is a major cause of late death in patients who underwent orthotopic heart transplantation (OHT). There is a linear and steady risk of developing vasculopathy after the first year from transplantation, and by the fifth year, more than 50% of transplanted recipients present some coronary artery disease (1). Currently, there is limited success in pharmacological prevention or treatment of allograft vasculopathy. Possible alternatives include percutaneous coronary intervention (PCI), coronary artery bypass surgery, and repeat OHT. Bypass surgery might not be the best treatment option for patients with allograft vasculopathy owing to the diffuse intimal thickening that commonly involves the distal vessels, in addition to the high perioperative mortality rates of 40% to 80% (2, 3). Retransplantation is limited by the scarcity of donor organs and by the relatively lower survival rate after retransplantation (4).

PCI is a reasonably palliative and occasionally definitive therapy for allograft vasculopathy. However, neither PCI nor bypass surgery is effective when the transplant vasculopathy involves diffuse areas or it affects the distal vessels. PCI with a drug-eluting stent of the unprotected left main coronary artery is currently not recommended as a routine procedure (5). We report the results of two patients who received PCI for left main coronary artery stenosis following OHT.

Case Reports

Case 1

A 37-year-old man received OHT for dilated cardiomyopathy in 2003. The patient developed posttransplant hypertension and hypercholesterolemia which was poorly responsive to dietary modification and pharmacologic therapy. He was on a three-drug immunosuppressive regimen consisting of cyclosporine, mycophenolate mofetil, and steroids. There was no detectable organ rejection or cytomegaloviral infections. Four years after the OHT, he developed renal and liver dysfunction with significant edema in the lower extremities and oliguria. He was subsequently treated with prostaglandin E and a diuretic. Myocardial infarction was diagnosed in 2008, 5 years after OHT, after paroxysmal
Main blood biochemistry findings were total cholesterol 8.6 mmol/L, low density lipoprotein (LDL) cholesterol 4.1 mmol/L, and serum triglycerides 3.2 mmol/L. His serum creatinine level was 2.3 mg/dL. ECG showed atrial flutter, complete right bundle branch block and old inferior wall myocardial infarction (Fig. 1). Echocardiogram showed pulmonary hypertension with a mean pulmonary artery pressure of 30 mmHg, and left ventricular dysfunction with a left ventricular ejection fraction (EF) of 34%.

Quantitative analysis of coronary angiogram was performed in two orthogonal views, and the percentage of the stenosis was calculated as the mean of the values from the two views. There was 95% stenosis in the ostium of the left main coronary artery (LMT), 75% stenosis in the middle segment of the left anterior descending artery (LAD), and 85% stenosis in the left circumflex artery (LCX) (Fig. 2). Diffuse lesions were also found in the distal parts of the left descending and left circumflex coronary arteries.

PCI was attempted in the LMT, which was cannulated with a 7-French guide catheter with side holes. The LCX lesion was crossed with a 0.014-inch guidewire, and the LCX lesion was dilated twice with 2.0x2.0 mm Maverick balloon at 22 atm for 5 sec. The LMT lesion was deployed with a 3.0x14 mm rapamycin eluting stent at 20 atm for 10 sec after pre-dilatation with 2.0x2.0 mm Maverick balloon at 20 atm for 5 sec. The post-PCI result is shown in Fig. 3. There was no residual stenosis and no evidence of complications. The patient was treated with clopidogrel (75 mg daily) and aspirin (100 mg daily) for 12 months. The clopidogrel was discontinued after 12 months, but aspirin was continued. Other medications included oral atorvastatin (10 mg/day), enalapril (10 mg twice daily) and frusemide (20 mg/day). The patient died 16 months after the PCI due to multiorgan failure. The causes for the multiorgan failure were unclear, but progressive heart failure and resultant low perfusion to the vital organs such as kidney and liver may in part be responsible.

Case 2

A 45-year-old man received OHT in 2006 for dilated cardiomyopathy. The patient was treated with a three-drug immunosuppressive regimen of cyclosporine, mycophenolate mofetil, and steroids, and suffered no organ rejection. Post-transplant hypertension, hypercholesterolemia and obesity
were detected and were poorly controlled by dietary modification and pharmacologic therapy. Increasing levels of fatigue and decreasing levels of exercise tolerance had been noticed by the patient 4 years after the transplantation. On admission, his blood pressure and heart rate was 172/110 mmHg and 85 beats/min, respectively. Main blood biochemistry findings were total cholesterol 8.9 mmol/L, LDL cholesterol 4.7 mmol/L, and serum triglycerides 4.0 mmol/L. His fasting blood glucose level was 10.3 mmol/L. His admission ECG showed rS morphology on leads II, III and aVF (Fig. 4). Echocardiogram showed a left ventricular EF of 42%. He was treated with a combination of short and intermediate insulin (24 units/day), simvastatin (20 mg/day), spironolactone (50 mg/day), digoxin (0.125 mg/day) and low molecular heparin (20 mg/day). Coronary angiogram showed 80% stenosis in the ostial of the LMT (Fig. 5). PCI was attempted in the LMT, which was cannulated with a 6-French guide catheter with side holes. The LMT lesion was deployed with 3.0×14 mm sirolimus eluting stent at 18 atm for 10 sec after twice pre dilatation with 2.0×2.0 mm Maverick balloon® at 15 atm for 5 sec (Fig. 6). There was no residual stenosis and no evidence of complications (Fig. 7). The patient was treated with clopidogrel and aspirin for 12 months, together with the other medications which had been initiated prior to PCI. He underwent a follow up angiogram 6 months after PCI, which showed no evidence of restenosis of the LMT. Echocardiogram at 12 months showed improvement in the left ventricular EF (48%) and the patient reported a marked improvement in his ability to perform physical exercise.

**Discussion**

Allograft vasculopathy represents a main obstacle to long-term survival after heart transplantation, as up to 42% of the patients develop this disease within 5 years of OHT (1). Once three-vessel disease or severe vasculopathy develops, the risk of death or retransplantation is extremely high within one year after the diagnosis (2).

Allograft vasculopathy is related to a number of causes.
Many risk factors for cardiovascular disease have been identified, including hypertension, hyperlipidemia, diabetes mellitus, donor’s age, cytomegalovirus infection, specific human leukocyte antigen immunologic serologies, and the occurrence of humoral or cellular rejection (6-9). The onset of allograft vasculopathy can be insidious, as the transplanted heart is denervated, and patients may not experience the classic symptoms of ischemia. Instead, the only clinical manifestations of allograft vasculopathy may be congestive heart failure, ventricular arrhythmias, silent ischemia, myocardial infarction and sudden death (9, 10). The diagnosis of allograft vasculopathy is not easily performed because of the silent ischemia and the low sensitivity of non-invasive stress testing. Coronary angiogram helps to confirm the diagnosis. Furthermore, intravascular ultrasound (IVUS) is more sensitive than angiogram in detecting early atherosclerotic disease, and allows the evaluation of both the lumen and the vessel wall. However, only proximal vessels can be approached by IVUS, and this limits its value in detecting diffuse diseases such as allograft vasculopathy (11, 12).

The optimal treatment for allograft vasculopathy in OHT patients is unknown, but PCI appears to be a therapeutic option. One of the main concerns of PCI in OHT patients is re-stenosis, as the allografted coronary vessel is in a pro-inflammatory state, which influences vessel remodeling (13-16). Multivariate analysis revealed that in allograft vasculopathy, the use of stents decreased the risk of restenosis (odds ratio 0.34, p<0.05) compared with cutting balloon or other PCI methods (10, 17). PCI allows a high level of primary success with a low procedural-complication rate (9). In addition, the restenosis rate with drug-eluting stents is reported to be 15-19%, which is lower than bare metal stent (31%) (10, 17).

PCI has been used in the treatment of unprotected left main coronary disease following OHT. In a follow-up study on five patients who received drug-eluting stents for left main disease, all survived after a follow up of 518 days (range 124-990 days) with no major adverse cardiac events (18). In a multicenter retrospective analysis on 21 patients with allograft vasculopathy involving the left main coronary artery, angiographic success was achieved in 100% of patients. At a mean follow-up of 4.9±3.2 years, three patients (14%) had died, one patient (5%) had myocardial infarction, and four patients (19%) had target lesion revascularization (19). Follow-up angiography showed a restenosis rate of 19%. In the present report, PCI was associated with excellent short-term results on the left main lesions and without complication from the procedures. One patient died of multiorgan failure 16 months after PCI, and the other remained in good condition both clinically and angiographically 6 months after PCI.

In conclusion, PCI with drug-eluting stents seems feasible in treating unprotected left main coronary disease following OHT. The procedure is safe but the long-term outcomes require further investigation.

The authors state that they have no Conflict of Interest (COI).

References
