

Degenerative Mitral Valve Insufficiency Long Term after Heart Transplantation: Clinical and Surgical Considerations

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With the increasing survival of heart transplant recipients, the risk for acquired allograft disease will be augmented. Severe mitral valve insufficiency after heart transplantation is rarely described. Similar to the general population, a degenerative process may affect the allograft mitral valve. Herein are reported two cases of severe mitral valve degen-

eration necessitating mitral valve replacement long term after heart transplantation. The pathophysiology and operative strategy for these patients are discussed.

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Increased allograft survival owing to improvements in heart transplant patient care has resulted in a larger number of patients at risk for acquired cardiac pathologies. Severe mitral valve incompetence refractory to medical therapy is an infrequent structural allograft abnormality. Under such circumstances, conventional surgery for the preservation of cardiac allograft function should be considered. The reported worldwide experience of mitral surgery in heart transplant patients consists of six cases requiring either mitral valve repair or replacement, with or without concomitant tricuspid valve surgery (1-6). Herein are described two cases of severe mitral valve regurgitation long term after heart transplantation. The pathophysiology and operative strategy for these patients are discussed.

The patients underwent an orthotopic heart transplantation using a standard bi-atrial Shumway technique. Post-transplantation transthoracic echocardiography showed no valve regurgitation (Table I), and no significant rejection episode was diagnosed either clinically or through endomyocardial biopsies. Follow up echocardiography showed no mitral valve dysfunction for both patients up to 9.5 and 8.5 years, respectively, after transplantation. Subsequently, both patients experienced a gradual decrease in their exercise capacity, with dyspnea on exertion. Moderate to severe MR was documented on echocardiography. In spite of an optimal medical therapy, both patients showed persistent heart failure symptoms (NYHA class III/IV), with severe MR on transesophageal echocardiography. Anterior leaflet thickening with

Clinical material and methods

Among 100 heart transplant recipients followed at the Quebec Heart Institute (Quebec City, Canada), two male patients were diagnosed with progressive mitral regurgitation (MR) and required surgical treatment at 11.2 and 12.4 years, respectively, after heart transplantation. The patient characteristics are listed in Table I. The donors' echocardiography and the surgical inspection during organ harvesting were inconspicuous.

Table I: Peri-transplantation characteristics of patients.

Parameter	Patient no.	
	1	2
Age at transplant (years)	63	55
Initial cardiomyopathy	Ischemic	Ischemic
Donor age (years)	21	16
Cause of donor death	SAH	MVA
No. of rejections*	0	0
MR at discharge	0	0

*Grade ≥ 2 during follow up.

MVA: Motor vehicle accident; MR: Mitral regurgitation (after heart transplantation); SAH: Subarachnoid hemorrhage.

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Figure 1: Mitral valve exposure via a trans-septal incision (A) through the right atrium (B).

prolapse and annular dilatation were the mechanisms responsible for the severe MR on echocardiography. A concomitant severe tricuspid regurgitation was diagnosed in one patient. The echocardiographic measures are depicted in Table II. Coronary angiography showed no focal coronary artery lesion or distal coronary artery tapering. Both patients had a history of high blood pressure and moderate renal failure (serum creatinine levels 165 and 180 mmol/l, respectively).

Surgical approach

In one patient, mitral valve surgery with concomitant tricuspid valve surgery was considered. The surgical approach was via a re-sternotomy. Both the right and left atria were severely dilated due to the bi-atrial transplant technique and the valve pathologies. The mitral valve was exposed through the right atriotomy with a trans-septal incision (Fig. 1). Mitral valve

inspection confirmed the echocardiographic description consisting of annular dilatation, anterior leaflet thickening and prolapse owing to chordal elongation and posterior leaflet retraction. The diseased tricuspid valve showed a dilated annulus and several ruptured chords on the anterior leaflet which, most likely, was secondary to the endomyocardial biopsies. Owing to the extent of the degenerative process in the mitral valves, both patients underwent mitral valve replacement (MVR) with a mechanical ON-X (Medical Carbon Research Institute, Austin, TX, USA) valve with posterior chordal sparing. The diseased tricuspid valve was replaced with a pericardial Magna (Edwards Lifesciences, Irvine, CA, USA) bioprosthesis.

Postoperative course

The postoperative course was uneventful in one patient, but was complicated by acute renal failure necessitating hemofiltration for three days in the other patient. The patients were discharged from hospital on postoperative days 8 and 14, respectively. Microscopic examination of both mitral valves revealed a myxomatous degeneration, without inflammatory cell infiltration suggestive of rejection. Transthoracic echocardiography at discharge for both patients showed a normal left ventricular diameter and function, without prosthetic valve dysfunction (Table II). At the six-month follow up, both patients were asymptomatic and had resumed their normal lifestyles.

Discussion

Mild mitral valve incompetence is not an infrequent finding in heart transplant recipients, with up to 55% (7) of mild MR cases having been documented immediately after heart transplantation. Multiple etiologies

Table II: Transthoracic echocardiographic measures of patients before and after mitral valve replacement (MVR).

Parameter	Patient no.			
	1		2	
	Preoperative	Postoperative	Preoperative	Postoperative
Age at last MVR (years)	74	-	67	-
Tx-MVR interval (years)	12.4	-	11.2	-
LVEF (%)	70	65	45	45
LVEDD (mm)	51	43	55	53
LVESD (mm)	28	28	46	32
PAP (mmHg)	68+CVP	45+CVP	38+CVP	25+CVP
MR grade	4/4	Trivial	3-4/4	Trivial
TR grade	3-4/4	Trivial	1-2/4	1/4

CVP: Central venous pressure; LVEDD: Left ventricular end-diastolic dimension; LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic dimension; MR: Mitral regurgitation; MVR: Mitral valve replacement; PAP: Pulmonary artery pressure; TR: Tricuspid regurgitation; Tx: Heart transplantation.

have been proposed to explain the MR in heart transplant recipients, including structural mitral valve abnormalities, mitral valve endocarditis and allograft vasculopathy with secondary mitral valve regurgitation (1-6). Although the bi-caval implantation technique has been shown to impact favorably on tricuspid valve competence (8), the influence of the operative technique on the mitral valve remains much more the subject of investigation. In contrast to the tricuspid valve, De Simone et al. (7) have shown that the severity of MR does not correlate with the atrial distortion observed in the bi-atrial technique. In the present two patients, the progressive mitral valve incompetence which occurred several years after heart transplantation suggests that the implantation technique did not contribute to the genesis of the MR.

Echocardiographic, operative and pathologic findings in these patients were suggestive of myxomatous degeneration of the mitral valve. Degenerative mitral valve prolapse (MVP), which occurs in more than 3% of the adult population, is usually a benign condition. Although severe MR develops in 2-5% of affected persons (9), the likelihood of developing a severe MR increases with age and is considerably greater in men than in women with MVP. By the age of 75 years, about 1.5-2% of women with MVP and 5.5% of affected men will develop significant MR requiring either surgical valve repair or replacement. In addition to the non-modifiable risk factors of age and gender, there is some evidence that high blood pressure and body weight may also promote the progression of MR (10). Both of the present patients had high blood pressure and were slightly overweight.

Histologically, the mitral valve tissue is composed largely of collagen in younger individuals, but with increasing age the collagen content falls, to be replaced by glycosaminoglycans (GAGs) and elastin (11). Despite the young donor ages for these transplant recipients (16 and 21 years), the 'aging process' of the atrioventricular valve may be accelerated in an older recipient, in conjunction with long-term immunosuppressive treatment. In addition to the possible increase of GAGs in cardiac valve tissue, it could be hypothesized that accelerated apoptosis or undetected rejection might play a role in this valvular degeneration. The evolution toward severe MR within 11 years after transplantation, in a mild myxomatous, non-regurgitant donor mitral valve without remarkable thickening on the initial post-transplant echocardiogram, may support an accelerated degenerative process in the present two patients. In contrast, Vaturi et al. (12) suggested that the allograft left-sided valves are less prone to degeneration. However, a mean follow up of only 3.8 years in their patients was significantly less than in the present patients, and may have been insuf-

ficient to evaluate degeneration of the mitral valve after transplantation. It also emphasizes the need for a more careful analysis of donor valves by using echocardiography and surgical observation at the time of transplantation to detect minor valve abnormality.

The surgical approach to the mitral valve in the transplanted heart should take into account the operative technique utilized during the transplantation. Although a right thoracotomy may be proposed to approach the mitral valve, the present authors suggest using a re-sternotomy, especially as the inter-atrial groove and the vena cavae may be distorted and scarred following transplantation. With the bi-atrial technique, the mitral valve may easily be exposed through a trans-septal incision owing to the enlarged atria. This approach is especially useful when the tricuspid valve requires concomitant treatment. In the presence of a previous bi-caval transplantation technique, a standard left atriotomy or a trans-septal approach should be selected in light of the adhesions in the atrial groove and the superior and inferior vena cavae. Similar to the non-transplant patient, standard principles of mitral valve surgery - including valve repair techniques - should be applied. In the present cases, the degenerative process of the anterior leaflet was extensive and the decisions were taken to replace the valves. The selection of the type of valve remains controversial but, as the survival of heart transplant patients remains limited, a bioprosthetic valve may be favored. However, especially in the presence of large atria, secondary to a bi-atrial approach, anticoagulation would still be highly recommended postoperatively. Thus, a mechanical MVR was selected with preservation of the posterior leaflet in both patients.

In conclusion, in severe degenerative mitral valve insufficiency late after cardiac transplantation, although the principles of mitral surgery in non-transplanted patients should be applied, the operative technique and valve selection should tapered according to allograft anatomy and the patient's expected survival.

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