Coronary artery bypass grafting after orthotopic heart transplantation

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Abstract

Objective: Graft coronary disease (GCD) remains the major determinant of long-term survival after heart transplantation. Therapeutic strategies for the prevention or retardation of GCD in the cardiac allograft are limited, and palliative surgical coronary revascularization has been attempted. The aim of this report was to retrospectively analyze our results of coronary artery bypass grafting after cardiac transplantation. This paper correlates the outcome of patients with the pathohistological and angiographic type of lesion in order to identify transplant recipients who may profit from surgical myocardial revascularization.

Methods: Seven patients with a mean age of 55 years (range 45–61 years) underwent coronary artery bypass grafting as a result of GCD at a mean of 67 months (range 6–128 months) after cardiac transplantation. By the inclusion of the clinical history and the angiographic pattern of GCD lesions, the primary indications for surgical revascularization, operative results, pathohistological studies and follow-ups were examined.

Results: Elective surgery was performed in two patients with proximal, severe triple vessel disease (Type A lesion) and in one patient in whom the primary reason for cardiac surgery was severe tricuspid regurgitation. This patient electively received a tricuspid valve replacement and concomitant single vessel bypass surgery for proximal GCD (Type A lesion). Emergency surgery was performed in four patients; preoperatively three patients post-infarction developed worsening congestive heart failure, which resulted in low cardiac output syndrome. One patient with combined Types A and B/C lesions required emergency surgery for dissection of the right coronary artery (RCA) after an angioplasty procedure. Angiographically all these patients showed diffuse, distal arteriopathy (combined Type B/C lesions). The electively operated patients (n = 3) and the patient with dissection of the RCA (n = 1) had successful operations and survived beyond hospital discharge (overall survival for coronary artery bypass graft (CABG) in GCD patients 4 out of 7; 57%). All three patients with distal arteriopathy, who underwent emergency surgery, died in hospital from left ventricular failure (43%). The four patients discharged from hospital with a mean follow-up of 10 months (range 2–32 months) are all in good clinical condition.

Conclusions: Coronary artery bypass grafting can be successfully performed in a subgroup of cardiac transplant patients with Type A lesions. However, the state of diffusely diseased distal arteries (Type B/C lesions), which is prevalent in this group of patients, limits the use of bypass surgery.

Keywords: Coronary bypass surgery; Graft coronary disease; Heart transplantation

1. Introduction

More than 30 years after the first clinical implantation, orthotopic heart transplantation (HTX) has become a routine operation world-wide for patients with end-stage heart disease [1,2]. Despite this, graft coronary disease (GCD), an unusually accelerated form of coronary artery disease, remains the major determinant of long-term survival. In patients who survive for more than 1 year after transplantation, it is the primary cause of death. Even though many factors have been implicated (Table 1), the etiology of this aggressive and diffuse disease remains unclear [3]. Angiographically the disease is classified as proximal Type A lesions when compared with distally located Type B and C lesions (Table 2).

In the past, when GCD developed in cardiac allografts, retransplantation was thought to be the only surgical option. In the face of organ shortage, poor results of repeat cardiac
transplantation, and the possible recurrence of GCD in the new organs, retransplantation is now regarded as controversial [4,5]. All palliative coronary revascularization procedures that have been reported, such as angioplasty [6], directional coronary atherectomy [7,8] or several anecdotal reports of successful coronary bypass surgery [9–11], were shown to be helpful in the short-term but, because of the rapid and diffuse nature of GCD, long-term results were disappointing. New therapeutic strategies, such as transmyocardial laser revascularization [12–14] or coronary stenting [15,16], are to be proved in the future.

The aim of this report was to retrospectively analyze our results of coronary artery bypass grafting after cardiac transplantation. This paper correlates the outcome of patients with the pathohistological and angiographical type of lesion in order to identify transplant recipients who may profit from surgical myocardial revascularization.

2. Patients and methods

Seven patients (six males, one female), with a mean age of 55 years (range 45–61 years), underwent bypass surgery at a mean of 67 months (range 6–128 months) after cardiac transplantation. Demographic and clinical characteristics are given in Table 3 which show that one patient needed bypass surgery very early (6 months) after HTX and that two patients needed bypass surgery after an excess of 10 years (120 and 128 months) after HTX. Four patients had previously undergone unsuccessful angioplasty. The mean time from transplantation to angioplasty was 50 months (range 24–80 months). The mean time to bypass surgery following angioplasty was 9.3 months (range 3–17 months).

2.1. Clinical profile

Seven patients (six males, one female), with a mean age of 55 years (range 45–61 years), underwent bypass surgery at a mean of 67 months (range 6–128 months) after cardiac transplantation. Demographic and clinical characteristics are given in Table 3 which show that one patient needed bypass surgery very early (6 months) after HTX and that two patients needed bypass surgery after an excess of 10 years (120 and 128 months) after HTX. Four patients had previously undergone unsuccessful angioplasty. The mean time from transplantation to angioplasty was 50 months (range 24–80 months). The mean time to bypass surgery following angioplasty was 9.3 months (range 3–17 months).

2.2. Coronary artery bypass surgery and Type of GCD-lesion

Emergency surgery was performed in four patients (group 1; Table 3; numbers 1–4). Preoperatively three patients post-infarction developed worsening congestive heart failure, which resulted in low cardiac output syndrome. Echocardiographically they showed a mean left ventricular ejection fraction of 25% (range 20–30%), and bypass surgery was performed as the ultimate therapeutic treatment. One patient, with combined Types A and B/C lesions required emergency surgery for dissection of the RCA with acute ischemia of the posterior wall after an angioplasty procedure. On this patient bypass surgery was performed on the beating heart. Angiographic studies of these four patients showed predominantly diffuse distal arteriopathy (combined Type B/C lesions), and one patient developed severe stenosis of the left main coronary artery.

The other three patients (group 2; numbers 5–7) were operated on electively and preoperatively they were in a stable clinical condition. In one of these patients the primary reason for cardiac surgery was severe tricuspid regurgitation due to rupture of anterior and posterior leaflet chordae resulting in biventricular heart failure. This patient received a tricuspid valve replacement and concomitant single vessel bypass surgery. Angiographically these three patients showed a predominantly proximal type of GCD (Type A lesion) with one patient having high-risk left main coronary artery atherosclerosis.

Bypass surgery was performed using hypothermic right atrial-aortic cardiopulmonary bypass. The heart was arrested using cold cardioplegic solution (Kirsch solution buffered with sodium bicarbonate and Haes), which was supplemented by a continuous cold pericardial irrigation
system. Grafts were performed using lengths of reversed great saphenous vein (n = 8). In the elective cases left (n = 2) or right internal thoracic artery (n = 1) was used and anastomosed to the left anterior descending coronary artery. Mean aortic clamp time and perfusion time was 38.2 min (32±47 min) and 288.3 (184±465 min) for group 1 and 52.6 min (37–63 min) and 91 min (68–113 min), respectively for group 2.

2.3. Pathohistological studies

Prior to surgery all patients underwent a right heart endomyocardial biopsy, and in all cases no episode of acute rejection was present. In contrast to the angiography, pathohistological studies of all patients showed diffuse arteriopathy with peripheral obliteration of arterioles and capillaries. Histological slices of the paraf®n-embedded right ventricular rejection control samples were stained with immunomarkers for smooth muscles cells (SMCs; α-actin) and endothelial cells (CD 31). They showed intensive wall thickening by proliferation of SMCs of arterioles (Fig. 1) and severe endothelial cell swelling in arterioles and capillaries. Histomorphometric analysis, carried out by counting vessels and SMCs in a test field of 100 compartments, showed no statistical difference between the two groups.

2.4. Outcome

The patients who underwent elective surgery (n = 3; group 2) and the patient with dissection of RCA after angioplasty (n = 1) had successful operations and survived beyond hospital discharge (overall survival 4/7 = 57%). All patients who underwent emergency surgery because of post-infarction unstable angina with preoperatively low-cardiac output (n = 3) died in hospital (1, 2 and 10 pod) from left ventricular failure (43%) despite intraoperative implantation of an intra-aortic balloon pump and a long reperfusion time.

The effect of distal GCD, detected on the arteriogram before bypass surgery, was examined (Table 2). Three (75%) out of four patients with distal arteriopathy (Type B/C lesions) died as opposed to none of the patients without distal arteriopathy (n = 3).

The four patients discharged from hospital with a mean follow-up of 17.7 months (range 9–34 months) are all in good clinical condition. The complications encountered in this group included acute renal failure in one and infection in another patient.

3. Discussion

This paper underlines specifically the problems of bypass surgery in a very special collective of patients. Because of the denervation of the afferent cardiac nervous system, most cardiac transplant recipients do not suffer from the classic symptoms of ischemia. Although there is evidence of partial reinnervation of the cardiac allograft [17], angina pectoris may infrequently occur in heart transplant recipients. Therefore, the first clinical manifestations of allograft ischemia predominantly includes congestive heart failure, ventricular arrhythmias, silent myocardial infarction or sudden cardiac death.

Fig. 1. Histological slice from right ventricular biopsy of a GCD patient stained with an immunomarker for smooth muscle cells (SMC, α-actin). Intensive wall thickening of arterioles is due to proliferation of SMCs.
There have been several anecdotal case reports of successful coronary artery bypass surgery in heart transplant recipients [18,19]. A single-center experience has been reported by Heroux et al. [20], which describes five hospital survivors who underwent bypass surgery very early in the post-transplantation period, i.e. on average 14 ± 10 months. In contrast, two recently published studies that examined the effect of the presence of distal coronary disease on the angiogram before bypass surgery, showed an operative mortality rate of between 33% and 40% [21,22]. In the largest series collected by Halle et al. (1995) in a multicenter review, 12 patients underwent surgery on average at 5 years post-transplantation. The most significant risk factor for mortality in this group was the presence of distal obliterative disease as shown by conventional contrast angiography. Four of the five patients (80%) with distal arteriopathy died as opposed to one of seven patients (14%) without distal arteriopathy.

This report confirms the results of our study, i.e. presence of angiographic distal arteriopathy should be considered a significant factor in patient selection for surgical coronary revascularization. Those patients who could be operated on electively (group 2; n = 3) together with the patient with dissection of RCA (n = 1), angiographically showed predominantly proximal Type A lesions. They had successful operations and an excellent postoperative course. All patients survived beyond hospital discharge and at a mean follow-up of 17.7 months (range 9–34 months) they are all in good clinical condition (Table 3).

Interestingly, the mean time from HTX to bypass surgery for these patients (111 months; range 85–128 months) was significantly longer than for the patients in group 1 (31 months; range 6–55 months).

The significant detrimental influence of distal arteriopathy on patients’ survival in our series is underlined by the fact that all three patients of group 1 angiographically showed predominately combined Type B/C lesions (Table 2). Preoperatively these patients developed worsening congestive heart failure, and the reason for perioperative or postoperative myocardial failure may have been the presence of diffuse disease of the microcirculation which may fail to provide adequate myocardial perfusion during and after cardiopulmonary bypass. Our experience has also confirmed what has been known for a long time, that angiography underestimates the presence and severity of GCD [23,24] and does not give a good impression of the state of the distal arteries. In contrast to the angiography, our pathohistological study showed diffuse arteriopathy with severe peripheral obliteration of arterioles and capillaries in all patients, which shows that perhaps GCD could be diagnosed from endomyocardial biopsies [25,26]. In future, ICUS and use of coronary flow reserve measurements may enable a better judgement of the presence or absence of distal obliterative disease [27], which could improve the results of bypass surgery in GCD patients.

The limitations of our study include the fact that it was a retrospective analysis of only a small number of patients. None of the patients had any functional assessment of the distal vascular bed. The follow-up time was short. Despite these limitations, the present series represents the largest single-center study of bypass surgery in cardiac transplant recipients.

### 4. Conclusions

From the experience described above, and together with other recent reports, our current policy, based on annual clinical and angiographic reviews, is that coronary angioplasty is to be considered as a method of treatment for severe, local stenoses. This method may be applied in this

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**Table 3**

Demographic and clinical profile of patients undergoing bypass surgery after heart transplantation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time HTX-PTCA (months)</th>
<th>Time HTX-CABG (months)</th>
<th>Time PTCA-CABG (months)</th>
<th>GCD type of lesion</th>
<th>Preoperative status</th>
<th>Operation</th>
<th>Postoperative follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Male, 55 years ICMP</td>
<td>24</td>
<td>32</td>
<td>8</td>
<td>n = 3 B/C</td>
<td>CHF</td>
<td>RITA:LAD, SVG:CX</td>
<td>IABP, 1 pod</td>
</tr>
<tr>
<td>2 Male 50 years ICMP</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>n = 3 B/C</td>
<td>CHF</td>
<td>SVG:LAD, CX</td>
<td>IABP, 10 pod</td>
</tr>
<tr>
<td>3 Male, 61 years DCMP</td>
<td>52</td>
<td>55</td>
<td>3</td>
<td>n = 2 LMC – B/A/C</td>
<td>MI, CHF</td>
<td>SVG:LAD, CX</td>
<td>IABP, 2 pod</td>
</tr>
<tr>
<td>4 Male, 69 years DCMP</td>
<td>44</td>
<td>44</td>
<td>3</td>
<td>n = 3 B/A/C/A</td>
<td>PTCA-dissection</td>
<td>SVG:RCA</td>
<td>14 months</td>
</tr>
<tr>
<td>5 Male, 47 years ICMP</td>
<td>80</td>
<td>120</td>
<td>17</td>
<td>n = 3 A/B/C</td>
<td>Stable</td>
<td>LITA:LAD, SVG:RCA</td>
<td>9 months</td>
</tr>
<tr>
<td>6 Female, 45 years DCMP</td>
<td>128</td>
<td>128</td>
<td>3</td>
<td>n = 2 A</td>
<td>TR stable</td>
<td>SVG:LAD, TVR</td>
<td>39 months</td>
</tr>
<tr>
<td>7 Male, 60 years ICMP</td>
<td>85</td>
<td>85</td>
<td>3</td>
<td>n = 2 LMC – A/B/C</td>
<td>Stable</td>
<td>LITA:LAD</td>
<td>9 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total 6 males, 1 female, mean 54.8 years</th>
<th>mean</th>
<th>mean</th>
<th>mean</th>
<th>n = 4 diffuse, n = 4 unstable, n = 3 stable</th>
<th>mean 17.7 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>67.1</td>
<td>9.3</td>
<td>3 proximal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
selected group of cardiac transplant recipients since comparable primary success and complication rates to routine angioplasty have been found [6].

Coronary artery bypass grafting can successfully be performed in a subgroup of cardiac transplant patients predominantly with Type A lesions. However, the state of diffusely diseased distal arteries (Type B/C lesions), which were prevalent in this group of patients, limits the use of bypass surgery. In this group of patients bypass surgery should only be used cautiously. Long-term follow-up is obviously necessary in order to truly assess the impact of coronary artery bypass surgery on allograft coronary disease.

Acknowledgements

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References


Appendix A. Conference discussion

Dr A. Ritchie (Cambridge, UK): You’ve got some of the patients in your group who are coming to revascularization at 2±4 months. Are these not patients in whom the original donor organ is one with coronary artery disease which has been missed? And what are you actually saying about the long-term ACAD patients? I mean these patients have essentially an immunological burn which makes all of the coronary arteries smoothly small. You’re never going to achieve revascularization in that group.

Dr Musci: Yes, you’re right. I thought long about taking these patients in this group. I wanted to fulfill them. This patient, after 4 months, certainly can be one of those who received coronary artery disease from a donor. But what I wanted to focus on is that bypass surgery is to be done on these patients with proximal stenosis and you should be attentive.

Dr Wheatley (Glasgow, UK): But you would allow that Dr Ritchie’s got a point?

Dr Musci: Totally, yes.
Dr E. Wolner (Vienna, Austria): In your PTCA group, are there also included patients in which the cardiologists have used the stents? And do you have, with the stents, the same high restenosis rate, or is there a difference between simple PTCA and stent use?

Dr Musci: In the PTCA group we have eight patients with stents, but the follow-up time is too short yet to make any worthwhile discussion.