Long-term experiences on cardiac retransplantation in adults

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Abstract

Background: It remains disputed whether cardiac retransplantation should be performed. This study aimed to evaluate our long-term experiences on cardiac retransplantation in adults.

Patients and methods: Between March 1989 and December 2004, 2% (28/1290) of cardiac retransplantations were performed.

Results: The reasons for cardiac retransplantation were cardiac allograft vasculopathy (n = 13; 47%), primary graft failure (n = 11; 39%), and refractory acute rejection (n = 4; 14%). The 30-day mortality risk was 29% (acute rejection: 50%; primary graft failure: 36%; cardiac allograft vasculopathy: 15%, p = 0.324), compared to 8.5% for primary cardiac transplantation (p < 0.001). The causes of early death were acute rejection (n = 3; 37%), multiorgan failure (n = 3; 37%), primary graft failure (n = 1; 13%), and right ventricular failure (n = 1; 13%). The late mortality rate was 96/1000 patient-years. The causes of late death were acute rejection (n = 4; 50%), cardiac allograft vasculopathy (n = 2; 25%), multiorgan failure (n = 1; 13%), and infection (n = 1; 13%). The 1-, 5-, 10-, and 15-year survival was respectively 78, 68, 54, and 38% (cardiac retransplantation) and 46, 41, 32, and 32% (cardiac transplantation) (p = 0.003). The short-term survival for cardiac retransplantation due to cardiac allograft vasculopathy was likely better than primary graft failure and refractory acute rejection (p = 0.09).

Conclusion: The overall outcomes of cardiac retransplantation are significantly inferior to primary cardiac transplantation. Cardiac retransplantation should be only performed for selected patients.

Keywords: Retransplantation; Cardiac; Adult; Mortality; Survival

1. Introduction

Despite significant improvements in recipient selection criteria, donor organ preservation, new immunosuppressive therapy, better post-transplant care, and increased surgical experiences, patients undergoing cardiac transplantation continue to experience early and late allograft failure. Several therapeutic interventions such as aggressive immunosuppressive therapy, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting, and ventricular assist devices have been proposed; however, cardiac retransplantation remains the gold standard treatment for these patients. Today, it represents nearly 2% of cardiac transplant procedures in adults [1] and 7% in pediatric patients [2].

Despite estimated increasing number of patients requiring cardiac retransplantation [3], only limited centers have reported their experiences with varying outcomes [4–10]. Some studies reported lower survival in cardiac retransplant patients compared with primary cardiac transplant patients [4,5,9], but others [6–8,10] demonstrated promising results. Currently, it remains disputed whether cardiac retransplantation should be performed. This study aimed to evaluate our long-term experiences on cardiac retransplantation in adults.

2. Patients and methods

Between March 1989 and December 2004, 1290 cardiac transplantations in adult patients were performed at the Heart & Diabetes Center North Rhine Westphalia in Bad Oeynhausen, Germany. Twenty-eight (2%) of them were cardiac retransplantations. These patients were compared to those of primary cardiac transplantation. This study was approved by our ethics committee, and the need for individual informed consent was waived. The principles of recipient selection for cardiac retransplantation were similar to those for primary cardiac transplantation. These patients were compared to those of primary cardiac transplantation. This study was approved by our ethics committee, and the need for individual informed consent was waived. The principles of recipient selection for cardiac retransplantation were similar to those for primary cardiac transplantation. These patients were compared to those of primary cardiac transplantation. There were 20 (71%) male (mean age: 52 ± 14 years) and 8 (29%) female (mean age: 46 ± 12 years). The underlying diagnosis for first cardiac transplantation in these patients was dilated...
cardiomyopathy \( (n = 18; 64\%) \), ischemic cardiomyopathy \( (n = 9; 32\%) \), and end-stage valvular heart disease \( (n = 1; 4\%) \).

All donor hearts were harvested from beating heart, brain-dead individuals through cooperation with Eurotransplant. Graft procurement and preservation was achieved through a combination of topical hypothermia and cold cardioplegia solution (Bretschneider-Custodiol; Kohler Chemie, Alsbach-Hahnlein, Germany). All cardiac retransplant procedures were performed orthotopically, using biatrial technique \[11\] with additional technical considerations as suggested by Mill and Stinson \[12\]. Immunosuppressive protocol and other post-transplant medical care for cardiac retransplantation were identical to that for primary cardiac transplantation, based on initial triple-drug therapy (cyclosporine A, azathioprine, and steroid). Long-term steroid maintenance was preferably avoided. Follow-up was 100% complete.

Statistical analyses were done with SPSS, version 13.0 (Chicago, IL, USA). Results were expressed as mean \( \pm \) standard deviation or median and interquartile range (continuous variable) or counts and percentages (categorical variable). For comparative evaluations, the Pearson \( \chi^2 \)-test or Mann–Whitney U-test were used. The survival was calculated using Kaplan–Meier’s limit-product method. Comparison between groups was assessed by using the log-rank test. A \( p \)-value of less than or equal to 0.05 was considered statistically significant.

3. Results

The reasons for cardiac retransplantation were cardiac allograft vasculopathy \( (n = 13; 47\%) \), primary graft failure \( (n = 11; 39\%) \), and refractory acute rejection \( (n = 4; 14\%) \) (Fig. 1). Twenty-five percent \( (7/28) \) of the patients were bridged with ventricular assist devices to cardiac retransplantation (primary graft failure, \( n = 6 \); cardiac allograft vasculopathy, \( n = 1 \)). The time interval between primary cardiac transplantation and cardiac retransplantation was less than 1 month \( (n = 12; 43\%) \), 1–3 months \( (n = 2; 7\%) \), 3–6 months \( (n = 1; 4\%) \), and greater than 12 months \( (n = 13; 46\%) \). Totally, 16 patients died. Eight patients died within 30-day postoperative, for a mortality risk of 29%, compared to 8.5% in patients undergoing primary cardiac transplantation \( \left( p < 0.001 \right) \). The reasons for cardiac retransplantation in these eight patients were acute rejection \( (n = 2) \), primary graft failure \( (n = 4) \), and cardiac allograft vasculopathy \( (n = 2) \). Four patients were bridged to cardiac retransplantation with ventricular assist devices (primary graft failure, \( n = 3 \); cardiac allograft vasculopathy, \( n = 1 \)). The causes of 30-day death were acute rejection \( (n = 2) \), multiorgan failure \( (n = 1) \), primary graft failure \( (n = 1; 13\%) \), and right ventricular failure \( (n = 1; 13\%) \). The 30-day mortality risk likely differed across the reason for cardiac retransplantation, notably, 50% for refractory acute rejection, 36% for primary graft failure, and 15% for cardiac allograft vasculopathy \( \left( p = 0.324 \right) \).

Other eight patients died during a total follow-up time of 83 patient-years (median: 1 year; interquartile range: 0.5–7.1 years), resulting in 96/1000 patient-years of late mortality rate. The causes of late death were acute rejection \( (n = 4; 50\%) \), cardiac allograft vasculopathy \( (n = 2; 25\%) \), multiorgan failure \( (n = 1; 13\%) \), and infection \( (n = 1; 13\%) \). Table 1 presents the comparison of baseline characteristics between primary

![Image](https://academic.oup.com/ejcts/article-abstract/32/6/923/387977/fig1)

**Fig. 1.** Indications for cardiac retransplantation in adults.

![Image](https://academic.oup.com/ejcts/article-abstract/32/6/923/387977/fig2)

**Fig. 2.** Survival comparison between primary cardiac transplantation and cardiac retransplantation.

### Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>PCTx ((n = 1262))</th>
<th>Re-CTx ((n = 28))</th>
<th>(p)-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age (years)</td>
<td>54 ± 11</td>
<td>50 ± 14</td>
<td>0.07</td>
</tr>
<tr>
<td>Recipient gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1065 (84)</td>
<td>20 (71)</td>
<td>0.07</td>
</tr>
<tr>
<td>Female</td>
<td>197 (16)</td>
<td>8 (29)</td>
<td></td>
</tr>
<tr>
<td>Donor age (years)</td>
<td>38 (25–48)</td>
<td>34 (21–42)</td>
<td>0.18</td>
</tr>
<tr>
<td>Donor gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>635 (50)</td>
<td>16 (57)</td>
<td>0.57</td>
</tr>
<tr>
<td>Female</td>
<td>627 (50)</td>
<td>12 (43)</td>
<td></td>
</tr>
<tr>
<td>Ischemia time (min)</td>
<td>195 ± 40</td>
<td>191 ± 41</td>
<td>0.73</td>
</tr>
<tr>
<td>CPB (min)(^b)</td>
<td>103 (83–131)</td>
<td>121 (95–156)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

CPB, cardiopulmonary bypass; PCTx, primary cardiac transplantation; Re-CTx, cardiac retransplantation. Values are count (percentage) unless otherwise indicated.

\(^a\) Mean \( \pm \) standard deviation.

\(^b\) Median (interquartile range).
cardiac transplantation and cardiac retransplantation. Except cardiopulmonary bypass time (p = 0.03), there were no significant differences in other characteristics. The 1-, 5-, 10-, and 15-year survival was respectively 78, 68, 54, and 38% for primary cardiac transplantation, and 46, 41, 32, and 32% for cardiac retransplantation (p = 0.003) (Fig. 2). The short-term survival for cardiac retransplantation due to cardiac allograft vasculopathy was likely better than primary graft failure and refractory acute rejection (p = 0.09) (Fig. 3).

4. Discussion

Cardiac retransplantation remains a controversial procedure. The worldwide increased shortage of donor hearts, the documented poor outcomes from earlier studies and the increased number of patients awaiting primary cardiac transplantation have raised medical conflict, ethical-moral, and social concerns regarding the merits and fairness of cardiac retransplantation. The escalating cost related to cardiac retransplantation has also raised an interesting question of who should pay for this advanced surgical option, and whether it should be available on demand. In our experience, cardiac retransplantation in adults represents nearly 2% of all cardiac transplant procedures, a similar proportion as currently practiced worldwide [1].

Compared to Smith et al. [9], we found that primary graft failure, refractory acute rejection, and cardiac allograft vasculopathy are the reasons for cardiac retransplantation. Our results reveal that the overall survival of cardiac retransplantation is significantly lower than primary cardiac transplantation. Such poor survival could be partly explained by the high early mortality risk in the cardiac retransplant patients, especially when it is performed due to refractory acute rejection and primary graft failure. This might reflect the commitment and sense of responsibility of the cardiac transplant team to salvage the very ill patients. Surprisingly, Topkara et al. [10] recently reported a very low mortality risk after cardiac retransplantation. Using a cohort of 41 cardiac retransplant patients in a total of 766 cardiac transplant procedures, they demonstrated an overall early mortality risk of 4.9% compared to 6.2% in those of primary cardiac transplantation (p = 0.730). However, most of the cardiac retransplantations in their study (90%) were performed electively due to cardiac allograft vasculopathy.

Currently, our priority for cardiac retransplantation is given to the patients with irreversible allograft failure due to cardiac allograft vasculopathy. We find that cardiac retransplantation based on this reason has better outcomes than primary graft failure and refractory acute rejection, although the small sample size in our study make the survival difference insignificant between the sub-groups. Long-term follow-up with a larger study population may better ensure this result.

In conclusion, the overall outcomes of cardiac retransplantation are significantly inferior to primary cardiac transplantation. Therefore, cardiac retransplantation should be only performed for selected patients, especially for patients with irreversible allograft failure due to cardiac allograft vasculopathy.

References