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Should we perform heart retransplantation in early graft failure?

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Summary

Cardiac retransplantation represents the gold standard treatment for a failing cardiac graft but the decision to offer the patient a second chance is often made difficult by both lack of donors and the ethical issues involved. The aim of this study was to evaluate whether retransplantation is a reasonable option in case of early graft failure. Between November 1985 and June 2008, 922 patients underwent cardiac transplantation at our Institution. Of these, 37 patients (4%) underwent cardiac retransplantation for cardiac failure resulting from early graft failure ($n = 11$) or late graft failure (acute rejection: $n = 2$, transplant-related coronary artery disease: $n = 24$). Survival at 1, 5 and 10 years of patients with retransplantation was 59%, 50% and 40% respectively. An interval between the first and the second transplantation of less than ($n = 11$, all in early graft failure) or more than ($n = 26$) 1 month was associated with a 1-year survival of 27% and 73%, and a 5-year survival of 27% and 65% respectively ($P = 0.01$). The long-term outcome of cardiac retransplantation is comparable with that of primary transplantation only in patients with transplant-related coronary artery disease. Early graft failure is a significant risk factor for survival after cardiac retransplantation and should be considered as an exclusion criteria.

Introduction

Cardiac transplantation is the only therapeutic option that ensures long-term survival in patients with end-stage heart disease [1,2]. Despite the consolidated experience and the important improvements in selection criteria, graft preservation, surgical techniques, immunosuppressive therapy, rejection surveillance and treatment of transplant coronary artery disease, some recipients still develop early and late graft failure, thus becoming potential candidates for heart retransplantation. The three main problems leading to this surgical option are early graft failure (EGF; <30 days), acute rejection (AR) and chronic rejection (CR); acute rejection and chronic rejection can be classified as late graft failure (LGF; >30 days). Today, cardiac retransplantation represents 2% of cardiac transplants in adults and 6–7% in pediatric patients (age: 1–17 years) [3], but these numbers are expected to increase with time. In this scenario, challenged by the lack of donors, the consequent supply-demand imbalance and ethical and financial concerns, the crucial question to ask is when a retransplantation is justifiable. In case of chronic rejection the operation can usually be programmed electively, on hemodynamically stable and metabolically balanced recipients. The context is different in case of early graft failure, because of the fact that patients are usually clinically compromised, often with inotropic or mechanical support, and retransplantation is frequently performed in emergency conditions [4]. With these concerns in mind, we retrospectively reviewed our

experience in Pavia with heart retransplantation over the past 23 years. The aim of this study was to evaluate our long-term experience on cardiac retransplantation, focusing the discussion on the merit of such a procedure for patients in early graft failure.

Patients and methods

Patients

During the period between November 1985 and June 2008, 922 cardiac transplantations were performed at our institution for end-stage heart failure. Of these patients, 37 (4%) underwent heart retransplantation for cardiac failure resulting from early graft failure ($n = 11$) or late graft failure ($n = 26$) (acute rejection: $n = 2$, transplant-related coronary artery disease: $n = 24$). There were 29 (78%) male and 8 (22%) female patients, ranging in age from 25 to 67 years (mean age ± standard deviation = 53 ± 10 years). Twenty-two patients were retransplanted in elective conditions (all in LGF) while in 15 cases surgery was performed on very compromised and hemodynamically unstable recipients (EGF: $n = 11$; LGF: $n = 4$). Five patients (EGF: $n = 3$; LGF: $n = 2$) were supported with extra-corporeal membrane oxygenation (ECMO) before retransplantation. The underlying diagnosis for primary transplantation in these patients was: dilated cardiomyopathy ($n = 14$; 38%), ischemic cardiomyopathy ($n = 13$; 35%), end-stage valvular heart disease ($n = 5$; 13.5%), hypertrophic cardiomyopathy ($n = 2$; 5.4%), postpartum cardiomyopathy ($n = 1$; 2.7%), congenital heart disease ($n = 1$; 2.7%) and post myocarditis heart failure ($n = 1$; 2.7%). Selection criteria for retransplantation were similar to those for primary heart transplantation. Contraindications to cardiac retransplantation are listed in Table 1.

Operative technique

Donors were brain-dead, beating-heart individuals (mean age 35 ± 15 years) who had suffered from head injuries ($n = 21$; 56.8%) or cerebrovascular accidents ($n = 16$; 43.2%). Allografts were harvested locally or distantly and organ preservation was achieved with a combination of topical hypothermia and cold crystalloid cardioplegic solution. In our series, the mean ischemic time was 131 ± 50 min. All cardiac retransplantations were performed orthotopically, using the technique described by Lower and Shumway ($n = 35$; 94.6%) or the bicaval technique ($n = 2$; 5.4%). The average time needed for cross-clamping was 59 ± 11 min, with a mean cardiopulmonary bypass (CPB) time of 138 ± 85 min.

Table 1. Contraindications to heart retransplantation.

Pulmonary hypertension (wood units/$m^2 \geq 4$ after vasodilator therapy)
Positive donor-specific lymphocyte cross-match
Active infections or sepsis
Patient noncompliance after primary transplantation
Severe parenchymal dysfunction
Renal dysfunction
Hepatic dysfunction
Chronic lung disease
Insulin-dependent diabetes mellitus with end-organ damage
Severe vascular disease

Immunosuppression and rejection surveillance

Our immunosuppressive protocol is based on a triple-therapy with cyclosporine, Azathioprine and corticosteroids. At the time of retransplantation, most patients already have therapeutic cyclosporine levels, which means it can usually be re-administered from the 3rd postoperative day onwards maintaining a serum concentration of 300 ng/ml (radioimmunoassay). Tacrolimus can be used instead of cyclosporine in case of recurrent acute rejections or in young patients gravely disturbed by the secondary minor effects of the cyclosporine. The antithymocyte globulin induction therapy is not used systematically in case of retransplantation as patients are usually already immunosuppressed and as there is a risk of anaphylactic shock. Antithymocyte globulins are administered for the first few days after retransplantation only in patients with severe renal dysfunction; in these cases, the use of mycophenolate mofetil (since 2000) instead of azathioprine is also preferred. Methylprednisolone is administered intraoperatively (500 mg at the end of the aortic cross-clamping) and postoperatively (3 doses of 125 mg every 8 h). Prednisone is then administered at a daily oral dose of 1 mg/kg/day and is gradually tapered over the following months. Finally, since 2005, it has been possible to administer everolimus instead of mycophenolate mofetil in patients retransplanted for graft-related coronary artery disease. Rejection surveillance in case of retransplantation is similar to post primary heart transplant procedures. Acute rejection is diagnosed by frequent systematic echocardiography and endomyocardial biopsy, scored according to the International Society for Heart and Lung Transplantation (ISHLT) grading system. Initially, biopsies are performed weekly for the first month, then every 2 weeks for 2 months, then every month for 3 months, then every 2 months for 6 months, then every 3–6 months for 1 year and finally every 6–12 months thereafter. Grade II or III rejections are treated with intravenous methylprednisolone (500 to 1000 mg daily for 3 days), followed by a bioptic control 1 week after. If rejection persisted even after two courses of methylprednisolone therapy, antithymocyte globulins and/or

tacrolimus can be used. Chronic rejection is monitored by annual coronary angiography to assess the presence and progression of graft atherosclerosis. When a transplant-related coronary artery disease is diagnosed, angiographic controls can be performed every 6 months.

Statistical analysis

The Shapiro-Wilk's test was used to test the normal distribution of quantitative variables. If they were normally distributed, mean and standard deviation (SD) were used to summarize the results; otherwise, we used median and interquartile range (IQR; 25°–75°percentile). Kaplan-Meier cumulative survivals (95% CI) were computed and the log-rank test was used for univariable comparisons. Cox regression analysis was used to identify independent factors for survival. Hazard ratios and 95% CI were calculated. Variables reaching $P < 0.2$ at univariable analysis were included in the multivariable model. $P < 0.05$ was considered statistically significant. All tests were two-sided. Data analysis was performed with STATA statistical package (vers: 9; Stata Corporation, College Station, 2008, TX, USA).

Results

In our study population, the time interval between the two transplants ranged from 1 day to 17 years (median 5.3 years, IQR 0.04–9.3 years). The median durations between transplants for patients undergoing retransplantation for EGF, AR and CR were 4 days, 2.3 months and 8.3 years respectively. Median follow-up time for the entire cohort was 15.9 months (IQR = 0.4–70.2) (mean ± SD = 48 ± 61 months). The actuarial survival at 1, 5 and 10 years of patients undergoing retransplantation was 59% (95% CI: 0.41–0.73), 50% (95% CI: 0.31–0.66) and 40% (95% CI: 0.21–0.57) respectively, while survival of primary transplanted patients was 85% (95% CI: 0.83–0.87), 76% (95% CI: 0.73–0.79) and 60% (95% CI: 0.56–0.64) respectively ($P < 0.001$). Therefore, survival rates were significantly lower in the retransplantation group, and these findings are even more accentuated if we compare primary transplantations with retransplantations for EGF ($P < 0.0001$) (Fig. 1). On the other hand, the difference in the actuarial survival was not statistically significant ($P = 0.15$) between patients undergoing primary transplantations and patients retransplanted who were not in EGF (Fig. 1). In fact, if we consider the time interval between the two procedures, an interval between first and second transplantation of less than ($n = 11$) or more than ($n = 26$) 1 month was associated with a 1-year survival of 27% and 73%, and a 5-year survival of 27% and 65% respectively ($P = 0.01$). Most deaths occurred in the perioperative period: the overall hospital mortality rate was 38%, varying from 64% for the EGF group to 27% for the LGF series. After 12 months, the actuarial curves tended to parallel one other (Fig. 1). Patient characteristics at retransplantation are presented in Table 2. Six patients (EGF: $n = 4$; LGF: $n = 2$) were supported with ECMO after retransplantation. Of these patients, five died in hospital and in only one case (patient no.°8, re-transplanted in early graft failure) the ECMO assistance was removed on the 6th postoperative day and the patient was still alive at follow up. Surgical revision for bleeding was necessary in three patients. The main causes of hospital death after retransplantation were: low output syndrome (EGF: $n = 1$; LGF: $n = 4$), multiorgan failure (EGF: $n = 2$; LGF: $n = 1$), early graft failure (EGF: $n = 3$) and infection (EGF: $n = 1$; LGF: $n = 2$). The main causes of late death were: chronic rejection (EGF: $n = 1$; LGF: $n = 2$) and cancer (LGF: $n = 2$). The univariate analysis of the risk factors affecting outcome after cardiac retransplantation is presented in Table 3. Early graft failure ($P = 0.01$) and cardiopulmonary bypass time ($P = 0.04$)

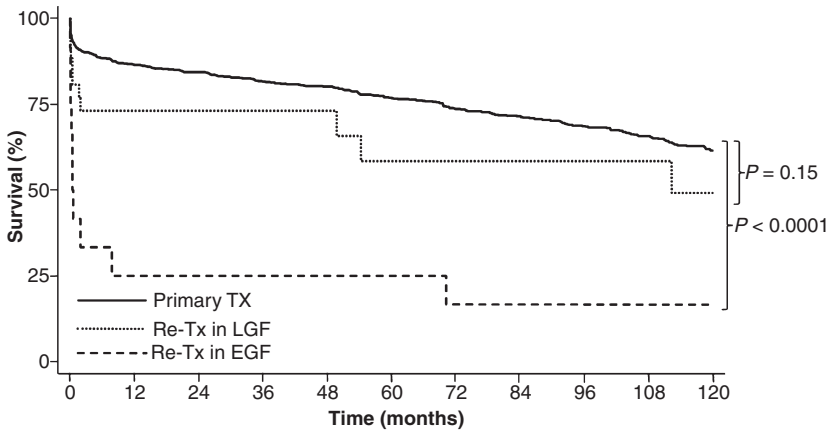

Figure 1 Actuarial survival of patients undergoing primary cardiac transplantation versus patients undergoing cardiac retransplantation for early graft failure (at an interval of less than 30 days after the first transplant) or late graft failure (at an interval of more than 30 days after the first transplant). Tx, transplantation; Re-Tx, retransplantation; EGF, early graft failure; LGF, late graft failure.

Table 2. Patient characteristics at retransplantation.

Patient number	Gender	Age (year)	Cause of Re-Tx	Delay between first Tx and Re-Tx (days)	Ischemic time (min)	Hemodynamic instability at Re-Tx	Delay between Re-Tx and death (days)	Cause of death
1	M	44	EGF	15	130	+	2135	REV
2	M	41	EGF	18	110	+	1	EGF
3	F	31	EGF	8	133	+	4582	CR
4	M	62	EGF	1	110	+	13	MOF
5	M	57	EGF	1	156	+	20	LOS
6	M	62	EGF	1	155	+	239	Infection
7	F	56	EGF	6	148	+	3	EGF
8	M	25	EGF	1	180	+	Still alive	———
9	M	55	EGF	5	180	+	9	MOF
10	M	59	EGF	4	175	+	3	EGF
11	M	64	EGF	3	115	+	13	RHF
12	M	51	LGF	33	123	+	52	Infection
13	M	52	LGF	107	147	–	4	LOS
14	M	48	LGF	320	120	–	5242	CR
15	M	31	LGF	1209	122	–	Still alive	———
16	M	53	LGF	1479	145	–	Still alive	———
17	M	55	LGF	2319	180	–	3413	CR
18	M	65	LGF	2315	216	–	61	MOF
19*	M	59	LGF	3707	117	–	Still alive	———
20	M	55	LGF	3071	110	–	Still alive	———
21	F	51	LGF	1940	52	–	7	LOS
22	M	62	LGF	1008	119	–	1652	Cancer
23	M	65	LGF	2767	107	–	15	Infection
24	M	65	LGF	2000	80	–	Still alive	———
25	F	43	LGF	2906	180	–	Still alive	———
26	F	60	LGF	5099	60	–	1514	Cancer
27	M	63	LGF	3179	174	+	Still alive	———
28	F	48	LGF	1522	40	–	Still alive	———
29	M	59	LGF	3802	70	–	Still alive	———
30	M	64	LGF	6139	230	–	Still alive	———
31	M	53	LGF	4176	61	–	4	LOS
32	M	67	LGF	5847	230	–	Still alive	———
33	M	44	LGF	4955	48	–	13	LOS
34	M	41	LGF	4057	180	+	Still alive	———
35	M	66	LGF	3867	180	+	Still alive	———
36	F	47	LGF	3416	90	–	Still alive	———
37	F	55	LGF	3035	105	–	Still alive	———

*Combined heart-kidney transplant.

TX, transplantation; Re-TX, retransplantation; EGF, early graft failure; LGF, late graft failure; REV, rupture of esophageal varices; MOF, multiorgan failure; LOS, low output syndrome; RHF, right heart failure.

were shown as significant risk factors for death after retransplantation, whereas other variables were not statistically significant. Multivariate analysis (Table 4) revealed only early graft failure ($P = 0.02$) as an independent predictor of mortality after retransplantation.

Discussion

The increasing number of patients undergoing heart transplantation worldwide has inevitably led to an increasing number of recipients that may eventually require cardiac retransplantation. In fact, despite the important advancements in various medical fields and the consequent improved survival of heart transplanted patients, some recipients still develop early and late graft failure, thus becoming potential candidates for heart retransplantation. This scenario, hindered by the shortage of donors, has raised ethical and financial concerns regarding the appropriateness of a second cardiac transplant. Although different surgical and medical options have been proposed to overcome end-stage heart failure, such as coronary artery bypass graft (CABG) surgery, partial left ventriculoplasty, coronary angioplasty, laser myocardial therapy, mechanical assistance and new

Table 3. Univariate analysis for predictors of mortality.

Variable	Hazard ratio	95% Confidence interval	*P* value
Recipient			
Age	1.03	0.98, 1.07	0.18
Gender	1.03	0.34, 3.09	0.95
Diabetes mellitus	1.53	0.35, 6.68	0.57
CMV	1.61	0.64, 4.06	0.31
BMI	0.98	0.87, 1.10	0.76
Wood units	0.93	0.57, 1.50	0.75
ICM at 1st transplantation	2.11	0.87, 5.11	0.09
Early graft failure	3.15	1.30, 7.63	0.01
ECMO before retransplantation	0.76	0.17, 3.31	0.72
Hemodynamic instability	2.41	0.99, 5.86	0.05
Donor			
Age	1.01	0.97, 1.04	0.59
Gender	1.85	0.71, 4.85	0.21
Perioperative factors			
Ischemic time	0.99	0.98, 1.01	0.82
Cardiopulmonary bypass time	1.01	1.00, 1.01	0.04

CMV, cytomegalovirus; BMI, body mass index; ICM, ischemic cardiomyopathy; ECMO, extra-corporeal membrane oxygenation.

Table 4. Multivariate analysis for predictors of mortality.

Variable	Hazard ratio	95% Confidence interval	*P* value
Early graft failure	2.81	1.10, 7.11	0.02
Cardiopulmonary bypass time	1.00	0.99, 1.01	0.27

pharmacologic regimens [5–10], heart retransplantation remains the only therapy which can achieve the long-term survival of these patients. Since the first case, performed by Copeland and colleagues in 1977 [11], several centers have reported their results on cardiac retransplantation [4,12–17]. From our experience, the overall survival of cardiac retransplantation was significantly lower compared with that of primary transplantation ($P < 0.001$). However, such poor survival was directly related to the higher perioperative mortality of patients retransplanted in early graft failure and with an interval shorter than 1 month between the first and second transplantation. In fact, if we compare the outcome of patients undergoing primary transplantations and patients retransplanted in LGF (or with an interval between the two procedures of more than 1 month), the difference in actuarial survival was not statistically significant ($P = 0.15$). These findings are similar to those reported by other centers [12,14,15,17] and by the ISHLT registry report [3], even though, in their experience, a worse survival rate was seen when the interval between the first transplantation and the retransplantation was less than 6-to-12 months. Several factors may be related to the worse survival rate in recipients with a short interval between transplantations: heavy immunosuppression, hemodynamic instability, intensive pharmacologic or mechanical support, lack of time to recover from the first operation. Moreover, considering the usually urgent conditions of these patients, the possibility of accepting less than optimal donors can be tempting. This, however, is an option that can often lead to disastrous results. In our experience, because of the extremely compromised condition of the recipient, the decision was made to accept a marginal donor for one patient in EGF. This decision, made before we had much experience, ended up being a wrong one and resulted in the rapid rejection of the retransplant and death of the patient, as this added a further risk to an already difficult situation. Conversely, in the case of late graft failure, the retransplantation can be often programmed electively, on hemodynamically stable and metabolically balanced recipients, who can wait for an optimal graft. In this situation, the operative survival rate approaches that of primary transplant. Consequently, the explanation of our hospital mortality rate of 38% must be looked for in the fact that the EGF group represented as much as 30% of our whole population, which is considerably higher when compared with the reported experience of other centers (Columbia University 4.6%, Stanford University 13.6%, La Pitié Paris 16.6%) [12,14,15]. Our statistical analysis of the risk factors affecting outcome after cardiac retransplantation showed that only early graft failure ($P = 0.02$) was an independent predictor of mortality after retransplantation. Although in these cases the only chance for survival could be a salvage retransplantation, the poor outcome in this subgroup of patients calls into question whether or not it

is justifiable to use resources and precious organs for patients with EGF [4,14]. A hypothetical solution for these patients, especially in the context of lack of donors, could be to use a ventricular assist device (VAD) as a bridge to retransplantation. Several centers have reported their experience in this field [8,18–21], but unfortunately the results achieved with this approach are far from satisfactory. Ventricular assist devices can be helpful for late retransplantation but do not improve poor survival in case of early retransplantation [21]. At our center, the policy is to avoid implanting VAD into immunosuppressed patients because of the fact that the already high risk of infection with the device alone is dangerously higher in the case of transplanted patients and the high cost of VADs do not justify this risk. What should be done, therefore, for these patients? Many ethical and financial concerns have been raised on the merits of such a procedure in connection with the severe lack of donors [22–24], and some authors have suggested that cardiac retransplantation should not be allowed, in any case, even in the case of chronic rejection [25]. We can understand the concerns about 'organ wasting' when we look at the lower survival rate for patients undergoing retransplantation as compared with first-time transplant recipients. We share the doubts about the fairness of allowing some individuals to get multiple transplants while others die awaiting their first. We also acknowledge that hospital expenses can be two or three times higher in the case of retransplantation. However, we do feel a commitment to patients on whom we have already performed a cardiac transplantation and who have no chance for survival other than by a salvage retransplantation. We believe that cardiac transplantation cannot be considered a 'one-time treatment option' for all patients. In our experience, in view of the encouraging long-term survival achieved, it can clearly be justified in the case of late retransplantation in otherwise healthy recipients. In fact the difference in the actuarial survival rate was not statistically significant ($P = 0.15$) when compared with that of patients undergoing primary transplantation (Fig. 1). The situation is different in case of early retransplantation for EGF (less than 1 month between the procedures): recipients are usually very compromised, often with inotropic or ECMO support and, in our series, survival was significantly worse ($P < 0.0001$). For this reason, we feel that EGF should be considered an exclusion criteria for retransplantation. Consequently, at our Institution, priority for cardiac retransplantation has been given, over the years, to the patients with transplant-related coronary artery disease.

In conclusion, the overall survival rate of cardiac retransplantation is significantly lower than that of primary transplantation. This result is related to the higher perioperative mortality of patients retransplanted in early graft failure and with an interval of less than 1 month between the first and the second transplantation. Early graft failure is, in effect, an independent predictor of mortality after cardiac retransplantation and should therefore be considered an exclusion criterion, in order to avoid dissipation of resources and waste of organs. On the other hand, the long-term survival after retransplantation in patients with late graft failure is comparable with that of primary transplantation. Therefore heart retransplantation is clearly justified in the case of late rejection, on condition that rigorous selection criteria are applied.

Authorship

NV: study design, study performance, data collection, data analysis and paper writing. CP: study design, study performance and paper writing. MA: study design, study performance and data collection. AA: study performance and data collection. CM study performance. BC: study performance. CT: data analysis and statistical analysis. AMDA: study performance. MV: study design, study performance and paper writing.

References

1. Kaye MP. The Registry of the International Society for Heart and Lung Transplantation: tenth official report-1993. *J Heart Lung Transplant* 1993; **12**: 541.
2. Reemtsma K, Berland G, Merril J, *et al.* Evaluation of surgical procedures: changing patterns of patient selection and costs in heart transplantation. *J Thorac Cardiovasc Surg* 1992; **104**: 1308.
3. Taylor DO, Edwards LB, Aurora P, *et al.* Registry of the International Society for Heart and Lung Transplantation: twenty-fifth official adult heart transplant report-2008. *J Heart Lung Transplant* 2008; **27**: 943.
4. Martinelli L, Rinaldi M, Goggi C, *et al.* Emergency and elective cardiac transplantation. *Eur J Cardiothorac Surg* 1993; **7**: 587.
5. Musci M, Pasic M, Meyer R, *et al.* Coronary artery bypass grafting after orthotopic heart transplantation. *Eur J Cardiothorac Surg* 1999; **16**: 163.
6. Frazier OH, Kadipasaoglu KA, Radovancevic B, *et al.* Transmyocardial laser revascularization in allograft coronary artery disease. *Ann Thorac Surg* 1998; **65**: 1138.
7. Halle AA, Wilson RF, Massin EK, *et al.* Coronary angioplasty in cardiac transplant patients: results of a multicenter study. *Circulation* 1992; **86**: 458.
8. Tenderich G, Koerner MM, Stuettgen B, *et al.* Mechanical circulatory support after orthotopic heart transplantation. *Int J Artif Organs* 1998; **21**: 414.
9. Klauss V, Konig A, Spes C, *et al.* Cyclosporine versus tacrolimus (FK 506) for prevention of cardiac allograft vasculopathy. *Am J Cardiol* 2000; **85**: 266.

10. Zuckermann AO, Aliabadi AZ. Calcineurin-inhibitor minimization protocols in heart transplantation. *Transpl Int* 2009; **22**: 78.
11. Copeland JG, Griepp RB, Bieber CP, *et al.* Successful retransplantation of the human heart. *J Thorac Cardiovasc Surg* 1977; **73**: 242.
12. John R, Chen JM, Weinberg A, *et al.* Long-term survival after cardiac retransplantation: a twenty-year single-center experience. *J Thorac Cardiovasc Surg* 1999; **117**: 543.
13. Topkara VK, Dang NC, John R, *et al.* A decade experience of cardiac retransplantation in adult recipients. *J Heart Lung Transplant* 2005; **24**: 1745.
14. Smith JA, Ribakove GH, Hunt SA, *et al.* Heart retransplantation: the 25-year experience at a single institution. *J Heart Lung Transplant* 1995; **14**: 832.
15. Schnetzler B, Pavie A, Dorent R, *et al.* Heart retransplantation: a 23-year single-center clinical experience. *Ann Thorac Surg* 1998; **65**: 978.
16. Tjang YS, Tenderich G, Hornik L, Wlost S, Bairaktaris A, Körfer R. Long-term experiences on cardiac retransplantation in adults. *Eur J Cardiothorac Surg* 2007; **32**: 923.
17. Karwande SV, Ensley DR, Renlund DG, *et al.* Cardiac retransplantation: a viable option? *Ann Thorac Surg* 1992; **54**: 840.
18. Kawaguchi AT, Cabrol C, Gandjbakhch I, Pavie A, Bors V, Muneretto C. Preoperative risk analysis in patients receiving Jarvik-7 artificial heart as bridge to transplantation. *Eur J Cardiothoracic Surg* 1991; **5**: 509.
19. Oaks TE, Pae WE, Miller MA, Pierce WS. Combined registry for the clinical use of mechanical ventricular assist pump and the total artificial heart in conjunction with heart transplantation: fifth official report. *J Heart Transplant* 1990; **10**: 621.
20. Pavie A, Muneretto C, Aupart M, *et al.* Prognostic indices of survival in patients supported with temporary devices (TAH, VAD). *Int J Artif Organs* 1991; **14**: 280.
21. Noirhomme P, D'Udekem Y, Jacquet L, *et al.* Is mechanical circulatory support helpful before cardiac retransplantation? *Cardiovasc Surg* 1997; **5**: 584.
22. Spaderna H, Smits JM, Rahmel AO, Weidner G. Psychosocial and behavioural factors in heart transplant candidates-an overview. *Transpl Int* 2007; **20**: 909.
23. Ubel PA, Arnold RM, Caplan AL. Rationing failure. The ethical lessons of the retransplantation of scarce vital organs. *JAMA* 1993; **270**: 2469.
24. Evans RW, Manninem DL, Dong FB, McLynne DA. Is retransplantation cost effective? *Transplant Proc* 1993; **25**: 1694.
25. Collins EG, Mozdzierz GJ. Cardiac retransplantation: determining limits. *Heart Lung* 1993; **22**: 206.