Late graft dysfunction after heart transplantation: a single centre experience

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Background: Late graft dysfunction (LGD) compromises long-term survival and quality of life after heart transplantation. The pathophysiology of LGD includes both general and transplant specific factors, although the exact mechanisms remain unknown. Many recipients finally develop heart failure with preserved ejection fraction due to a restrictive cardiomyopathy characterized by diffuse interstitial fibrosis. Despite being common, limited information is available on the incidence of and risk factors for LGD.

Purpose: To describe the incidence of LGD in long-term survivors after heart transplantation and determine baseline characteristics associated with the development of LGD.

Methods: We retrospectively analysed pretransplant and 1 year characteristics of all adult heart recipients that were transplanted in our tertiary heart centre, and who underwent elective right heart catheterization (RHC) 10 years post-transplantation. LGD was defined as pulmonary capillary wedge pressure (PCWP) ≥15mmHg.

Results: Three hundred and ten heart transplant recipients were transplanted between 1989 and 2010 and were followed annually, with RHC 10 years postoperatively. A PCWP ≥ 15 mmHg was observed in 138/310 (45%) patients. This percentage increased to 46 and 57% 15 and 20 years after transplantation, respectively. Table 1 shows the differences in pretransplant and first year characteristics between recipients with a PCWP < 15 mmHg and those with a PCWP ≥ 15 mmHg. In the first era (1987-1999) donor age was lower compared to the second post-transplantation era (2000-2010), with a median age of 30 (interquartile range (IQR) 21-39) and 38 (IQR 22-47) years, respectively ($p < 0.001$). On multivariate analysis, donor age and PCWP 3 weeks postoperatively remained independently associated with LGD (table 2).

Conclusion: Our analysis shows a high incidence of LGD 10 years after heart transplantation. Recipients receiving an older donor heart or having a higher PCWP 3 weeks postoperatively are at increased risk of developing LGD. The increased incidence of LGD in the most recent era (58% versus 42%, $p = 0.001$), might be explained by the higher donor age.

Table 1. Baseline characteristics of recipients with and without increased PCWP (≥15mmHg) 10 years after heart transplantation.

	Total population (n=310)	PCWP <15 mmHg (n=172)	PCWP ≥15 mmHg (n=138)	P value
Recipient age, years - median (IQR)	53 (45 – 59)	52 (44 – 60)	55 (46 – 59)	0.153
Male recipient (%)	254 (81.9)	138 (80.2)	116 (84.1)	0.384
Diabetes mellitus pre-transplant (%)	30 (9.7)	17 (9.9)	13 (9.4)	0.891
Ischemic cardiomyopathy (%)	137 (44.3)	76 (44.4)	61 (44.2)	0.966
Era of transplantation				**0.001**
1987 - 1999 (%)	163 (52.6)	105 (61.0)	58 (42.0)	
2000 - 2010 (%)	147 (47.4)	67 (39.0)	80 (58.0)	
Donor age, years - median (IQR)	34 (22 – 43)	29 (20 – 41)	38 (22 – 46)	**0.005**
Male donor (%)	218 (70.3)	121 (70.3)	97 (70.3)	0.991
Cold ischemia time, minutes (SD)	161 (±47)	159 (±49)	163 (±45)	0.499
Creatinine				
3 months, mg/dl (SD)	1.34 (±0.43)	1.31 (±0.34)	1.38 (±0.52)	0.160
6 months, mg/dl (SD)	1.39 (±0.39)	1.35 (±0.34)	1.43 (±0.44)	0.096
12 months, mg/dl (SD)	1.44 (±0.39)	1.44 (±0.39)	1.44 (±0.40)	0.880
Immunosuppressive therapy at 1 year				
Corticosteroids (%)	230 (74.2)	137 (79.7)	93 (67.4)	**0.014**
Azathioprine (%)	146 (47.1)	95 (55.2)	51 (37.0)	**0.001**
Cyclosporine (%)	179 (57.7)	111 (64.5)	68 (49.3)	**0.007**
Tacrolimus (%)	131 (42.3)	61 (35.5)	70 (50.7)	**0.007**
Mycophenolate Mofetil (%)	127 (41.0)	55 (32.0)	72 (52.2)	**<0.001**
Everolimus (%)	5 (1.6)	2 (1.2)	3 (2.2)	0.482
Rejection during first year (%)	41 (13.3)	19 (11.1)	22 (15.9)	0.213
Mean biopsy score	0.521 (±0.304)	0.502 (±0.304)	0.546 (±0.303)	0.221
Cardiac allograft vasculopathy at 1 year				0.706
CAV 0 (%)	263 (85.4)	144 (84.7)	119 (86.2)	
CAV 1-2 (%)	45 (14.6)	26 (15.3)	19 (13.8)	
PCWP ≥15mmHg after 3 weeks (%)	104 (33.5)	43 (25.0)	61 (44.2)	**<0.001**
PCWP ≥15mmHg after 3 months (%)	57 (18.4)	22 (12.8)	35 (25.4)	**0.005**
PCWP ≥15mmHg after 6 months (%)	69 (22.3)	25 (14.5)	44 (31.9)	**<0.001**
PCWP ≥15mmHg after 12 months (%)	63 (20.3)	25 (14.5)	38 (27.5)	**0.005**

CAV: cardiac allograft vasculopathy, PCWP = pulmonary capillary wedge pressure

Table 1

Table 2. Baseline characteristics associated with increased PCWP (≥15mmHg) 10 years after heart transplantation: univariate and multivariate analysis.

	Univariate analysis			Multivariate analysis		
	Unadjusted OR	95% CI	P-value	Adjusted OR	95% CI	P-value
Age recipient	1.013	0.993 – 1.033	0.206			
Age donor	1.028	1.009 – 1.047	**0.003**	1.020	1.001 – 1.040	**0.041**
Era of transplantation	2.162	1.370 – 3.411	**0.001**	1.731	0.756 – 3.967	0.195
Male patient	0.770	0.427 – 1.389	0.385			
Diabetes mellitus	0.948	0.444 – 2.027	0.891			
Cold ischemia time	1.002	0.997 – 1.006	0.498			
Creatinine at 3 months	1.471	0.848 – 2.553	0.169			
Cyclosporine use	0.534	0.338 – 0.843	**0.007**	1.331	0.575 – 3.082	0.505
PCWP at 3 weeks	2.377	1.468 – 3.847	**<0.001**	1.105	1.052 – 1.160	**<0.001**

PCWP = pulmonary capillary wedge pressure

Table 2