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Title: Predictors and Clinical Significance of Pericardial Effusions after Pediatric Heart Transplantation

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Author Contributions:

D.M., K.R.S, and D.M.P. designed the study. Data collection performed by D.M., D.M.P, and T.T. Statistical analyses and design of tables and figures performed by S.Y. and R.L. D.M. wrote the manuscript with support from D.M.P., K.R.S., A.D.M., and S.Y. All authors discussed the results, provided critical feedback, and contributed to the final manuscript.

Abbreviations: Body Surface Area (BSA), Heart Transplantation (HT), Interquartile Range (IQR)

Abstract:

Background: We aimed to describe the incidence, risk factors, and clinical outcomes of pericardial effusions within 6 months after pediatric heart transplantation (HT).

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Methods: A single-center retrospective cohort study was performed on all pediatric HT recipients from 2004-2018. Logistic regression was used to identify factors associated with pericardial effusions post-HT and survival was compared using log-rank test.

Results: During the study period, 97 HT were performed in 93 patients. Fifty patients (52%) had a \geq small pericardial effusion within 6 months, 16 of which were, or became, \geq moderate in size. Pericardial drain was placed in 8 patients. In univariate analysis, larger recipient body surface area ($p=0.01$) and non-congenital heart disease ($p=0.002$) were associated with pericardial effusion development. Donor/recipient size ratios, post-HT hemodynamics, and rejection did not correlate with pericardial effusion development. In multivariable analysis, non-congenital heart disease (adjusted odds ratio 3.3, $p=0.01$) remained independently associated with development of pericardial effusion. There were no significant differences in post-HT survival between patients with and without \geq small ($p=0.68$) or \geq moderate pericardial effusions ($p=0.40$).

Conclusions: Pericardial effusions are common after pediatric HT. Patients with cardiomyopathy, or non-congenital heart disease, were at higher risk for post-HT pericardial effusions. Pericardial effusions increased morbidity but had no effect on mortality in our cohort. The risk factors identified may be used for anticipatory guidance in pediatric HT.

Keywords: pediatric heart transplantation, pericardial effusion, heart transplant rejection, heart transplant survival.

Introduction:

Pericardial effusions after heart transplant (HT) are not uncommon. In adult HT recipients, the reported incidence of pericardial effusions ranges from 9-35%.¹⁻⁴ In adult studies, the data regarding risk factors for and the clinical significance of pericardial effusions after HT are conflicting.^{1, 2, 5-8} Though not consistent across studies, previous reports have correlated the development of early pericardial effusions after HT with lack of prior cardiac surgery,^{1, 2} greater recipient weight in comparison to donor weight,¹ and prolonged donor ischemic time.⁴ Presence and severity of rejection have also been correlated with pericardial effusions.⁵⁻⁷

The significance of pericardial effusions after HT in pediatrics has not been well-described. In a large Pediatric Health Information System (PHIS) study of readmissions for pericardial effusion

after cardiac surgery, 2.3% of HT recipients (57/2511) were readmitted for pericardial effusion and 19 of those patients underwent pericardial intervention. The majority of these readmissions occurred within the first 2 weeks after discharge.⁹ An immune-mediated or inflammatory process and donor-recipient size discrepancies have been proposed as possible etiologies for the development of pericardial effusion early on after HT.^{1, 4, 7, 10} One previous study reported low risk of hemopericardium after endomyocardial biopsy, though that remains a potential complication.¹¹

Thus, we aimed to (1) examine the incidence of pericardial effusions in children within 6 months after HT, (2) evaluate for factors associated with the development of pericardial effusions post-HT, and (3) describe the clinical course and survival in patients with pericardial effusions after pediatric HT.

Methods:

We performed a single-center retrospective cohort study including all HT recipients from our institution from 2004-2018. We excluded those who received HT at other institutions. The study was approved by the institutional review board. Patient electronic medical records were reviewed. At our institution, transthoracic echocardiograms are routinely performed post-transplant within the first 3 days, at 1 week, 1 month, 2 months, 3.5 months, 6 months, and as clinically indicated. The presence and qualitative size of pericardial effusions were routinely described by the echocardiographer in all post-HT reports. Effusion size was qualitatively assessed as trivial, small, small-moderate, moderate, moderate-large, or large. For this study, only effusions that were “small” or greater in size were included, given that trivial pericardial effusions may be physiologic. All follow-up echocardiograms within the period were reviewed for changes or resolution of the identified pericardial effusion. “Rejection” was defined as having either acute cellular rejection (\geq Grade 1R)¹² or antibody mediated rejection (\geq Grade pAMR1).¹³

Data are presented as frequency with percentage for categorical variables and median with interquartile range (IQR) or mean \pm standard deviation for continuous variables. Univariate comparisons of patient and clinical characteristics between patients with and without development of \geq small pericardial effusion within 6 months of HT were made using Chi-square test or Fisher’s exact test for categorical variables and Wilcoxon rank sum test or two-sample t-

test for continuous variables. Variables found to be significantly associated with development of \geq small pericardial effusion in the univariate analyses ($p < 0.05$) were considered to be included in the multivariable logistic regression. Multicollinearity among candidate variables included in the multivariable analysis was examined using Spearman correlation coefficient (r), two-sample t -test, and Variance inflation factor. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) from the multivariable analysis were reported. Similarly, patient and clinical characteristics between patients with and without development of \geq moderate pericardial effusion within 6 months of HT were compared using Chi-square test or Fisher's exact test for categorical variables and Wilcoxon rank sum test or two-sample t -test for continuous variables. Due to relatively small number of patients with \geq moderate pericardial effusion within 6 months of HT, a multivariable analysis was not performed. Survival was generated using Kaplan-Meier curve and compared between groups using log-rank test. A p value < 0.05 was considered statistically significant. All analyses were performed using SAS Version 9.4 (SAS Institute Inc, Cary, NC).

Results:

There were 97 HT performed in 93 patients, including 4 re-transplants, during the study period. Demographics, transplant, and post-transplant characteristics of the study cohort were reported (Table 1). Median age at HT was 10.4 years (IQR 1.6-15 years). Median time to first pericardial effusion detected was 10 days (IQR 3-27 days) (Table 2). Of 97 HT, 50 (52%) developed a \geq small pericardial effusion within 6 months of HT, 6 of which were \geq moderate at the initial recognition of an effusion. Of the 44 initially small or small-moderate pericardial effusions, 10 (23%) increased to \geq moderate in size. Overall, 16/97 pediatric HT patients (16%) therefore had a moderate or large effusion within 6 months of HT (Supplemental Table 1). For the patients with \geq moderate pericardial effusions that did not undergo pericardiocentesis, median time to resolution was 45.5 days (IQR 15-125). Eight of the 97 patients (8%) had pericardiocentesis with pericardial drain placement performed within 6 months of HT. Details pertinent to their interventions are documented in Table 3. Pulsus paradoxus was not documented in any of these patients. In three patients, there were other signs and symptoms concerning for cardiac tamponade (decreased cardiac output, significant respiratory variation of the mitral inflow doppler, and symptoms including dizziness, chest pain and dyspnea). The other five patients had persistent and/or enlarging pericardial effusions without obvious evidence of cardiac tamponade

which prompted drain placement. One patient underwent immediate surgery to repair cardiac perforation during attempted pericardial drain placement.

In univariate analysis, older and larger recipients and donors, shorter ischemic time, and non-congenital heart disease were associated with \geq small pericardial effusion development (Table 4). Donor/recipient weight ratio, donor/recipient BSA ratio, crossmatch results, and post-transplant hemodynamics were not associated with pericardial effusion development. There was no difference in pericardial effusions across time when the cohort was divided into three evenly spaced eras ($p=0.43$). In the cardiomyopathy cohort alone, donor/recipient weight ratio ($p=0.41$), left ventricular end diastolic diameter by echocardiogram (LVEDd, $p=0.93$) and LVEDd z-scores ($p=0.85$) were not correlated with pericardial effusion development. Of 10 patients with protein losing enteropathy, 8 developed \geq small pericardial effusions ($p=0.09$). A total of 46 patients (47%) experienced rejection within 6 months of HT. Rejection was not associated with having a \geq small pericardial effusion within 6 months of HT (26 [52%] having \geq small pericardial effusion vs. 20 [43%] without, $p=0.35$) or having a \geq moderate pericardial effusion within 6 months of HT (5 [31%] having \geq moderate pericardial effusion vs. 41 [51%] without, $p=0.16$). Limiting the analysis to more significant rejection ($\geq 2R$ cellular rejection and $\geq pAMR1$) did not reveal a significant association ($p=1.0$). Only non-congenital heart disease ($p=0.0004$) and no prior cardiac surgery ($p=0.004$) were associated with development of \geq moderate sized pericardial effusions (Supplemental Table 2).

Since age at HT and recipient and donor weight, height, and BSA at HT were all strongly correlated ($r>0.8$) with each other, recipients' BSA at HT was the representative variable selected for inclusion in the multivariable analysis. Non-congenital heart disease was also included. Ischemic time was not included as it was highly correlated with congenital heart disease. In multivariable analysis, non-congenital heart disease (AOR 3.3, 95% CI 1.4-7.9; $p=0.01$) remained independently associated with development of \geq small pericardial effusion after HT. Recipient BSA at HT was nearly significant (AOR 2.2, 95% CI 0.99-4.7; $p=0.052$).

The overall survival was 93.6%, 85.0%, and 71.0% at 1 year, 5 years, and 10 years after HT, respectively. There were no significant differences in post-HT survival in patients with or

without \geq small ($p=0.68$, Figure 1a) or \geq moderate pericardial effusions ($p=0.40$, Figure 1b), with the knowledge that pericardial drains were utilized in some patients.

Discussion:

In this study, we found that pericardial effusions were common after pediatric HT at our institution. Over half of HT had a small or greater pericardial effusion within 6 months after HT. A pericardial drain was placed in 8 of these patients for persistent pericardial effusions. Patients with cardiomyopathy and no prior surgery were more likely to develop pericardial effusions post-HT. The presence of early pericardial effusions was not associated with post-HT hemodynamics, rejection, or mortality in our cohort.

Our findings showed that 8% of patients required an intervention for their pericardial effusion. A previous PHIS analysis reported a lower percentage of intervention in children readmitted for pericardial effusion after HT (0.8%, 19/2454).⁹ This difference is most likely due to the fact that the PHIS study did not look at interventions occurring during the initial transplant hospitalization. The incidence of cardiac perforation after endomyocardial biopsy requiring pericardial drain was previously reported to be quite rare in one pediatric study.¹¹ Although still uncommon, there were 3 patients that were found to have larger pericardial effusions on routine post-biopsy surveillance that ultimately underwent pericardial drainage in this cohort. The effusion size increase in these patients was in comparison to their prior echocardiogram, and the temporal relationship to the biopsy is uncertain given the lack of constant echocardiographic surveillance. A recently published small series of adult patients described the development of constrictive pericarditis after heart transplant and 3/8 had associated pericardial effusions.¹⁴ No patients in our study cohort were diagnosed with constrictive pericarditis.

Our study also identified children that might be at greater risk for developing a pericardial effusion after HT. We found that non-congenital heart disease, or cardiomyopathy diagnosis, was independently associated with the development of pericardial effusion. This association also could explain, at least in part, the univariate correlations of pericardial effusion with shorter ischemic time and larger and older recipients and donors. Of note, 8 of the 10 patients with protein losing enteropathy had a \geq small pericardial effusion within 6 months after HT, which

may be related to their unique underlying pathology and lymphatic derangements. In addition to HT itself, older age, larger size, Fontan operation, and first cardiac surgery were also identified as risk factors for significant pericardial effusion after pediatric cardiac surgery in two other large studies.^{9, 15} Many of these effusions, including those occurring after HT in our study, could reflect post-pericardiotomy syndrome as this process is one of the most commonly implicated causes of pericardial effusion after surgery. Factors such as older age and first surgery may increase the risk of developing this exaggerated inflammatory reaction.

We also hypothesize that some pericardial effusions in non-congenital heart disease patients could reflect pre-HT cardiomegaly that may be more pronounced in dilated cardiomyopathy patients as compared with those with congenital heart disease. Unfilled space from pre-HT cardiomegaly could theoretically result in increased likelihood of pericardial effusion after HT. We did not, however find a statistically significant correlation using available measurements to directly support this hypothesis. This lack of statistical correlation likely reflects our small and heterogenous sample size and inaccurate proxies for cardiac size. In the future, more precise methods of donor-recipient sizing using cardiac CT or MRI may help centers consider larger donors and expand the limited pediatric donor pool, especially in candidates with dilated cardiomyopathy and significant cardiomegaly.^{16, 17}

Hauptman et al noted that a larger weight difference (recipient weight > donor weight) was associated with increased risk for post-HT pericardial effusion in adults, and we had hypothesized that the same might be true in children.¹ However, we found that donor/recipient BSA ratio and donor/recipient weight ratio were not associated with pericardial effusion development within 6 months. In children, patient measurements alone may not correctly reflect heart size, especially in the setting of pre-HT cardiomegaly, which further supports the need for more accurate methods of sizing as noted in the abovementioned studies.

Quin et al did not find an association between effusion presence within 3 months of HT and survival in their adult cohort.² Similarly, Hauptman et al did not find a statistically significant difference at 1 year survival for those with or without pericardial effusions within 1 year post-HT.¹ Pericardial effusions within 6 months of HT in our pediatric cohort were not associated

with post-HT survival, though may have if there were no invasive interventions undertaken. Further research with longitudinal follow-up in pediatric HT recipients is needed to determine if new onset effusions >1 year post-HT are more likely to be associated with increased mortality as has been shown in adult data.⁸

There are important limitations to this study. These data are subject to the inherent limitations of retrospective study designs. Since this was a single center report with a limited number of subjects, we may have been underpowered to detect certain associations. There may have been some variability in the qualitative echocardiographer reports of pericardial effusion size. Nevertheless, our findings were consistent when we repeated the analysis looking at only \geq moderate effusions, which are less likely to be misclassified. We aimed to focus on pericardial effusions detected early post-HT. Effusions occurring several months to years after HT likely reflect a different process such as graft failure or rejection and were not the focus of this analysis. Although there was not an appreciable difference in the incidence of pericardial effusions over time at our center, there may have been changes in practice over the study period that influenced our findings.

In this study, over half of pediatric patients developed a small or greater pericardial effusion after HT. The majority of these were inconsequential and self-limited, but some were refractory and needed to be intervened upon. In our cohort, early pericardial effusion did not correlate with hemodynamics, rejection, or mortality. Patients with cardiomyopathy, or non-congenital heart disease, were more likely to develop pericardial effusions post-HT.

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Table 1. Demographics and transplant/post-transplant characteristics (N=97 transplants)

Male sex	53 (54.6)
Caucasian Race	75 (77.3)
Age at Transplant, years	10.4 (1.6-15.0)
Weight at Transplant, kg	32.8 (10.4-53.0)
Height at Transplant, cm	143 (78.8-159)
BSA at Transplant, m ²	1.13 (0.48-1.51)
Number of prior cardiac surgery (including previous transplants)	
0	36 (37.1)
1	21 (21.6)
2	13 (13.4)
3	12 (12.4)
≥ 4	15 (15.5)
Non-congenital heart disease	40 (41.2)
Protein losing enteropathy	10 (10.3)
Plastic bronchitis	2 (2.1)
Chylothorax	4 (4.1)
Positive crossmatch	17/96 (17.7)
Ischemic time, minutes	212 ± 58.2

Donor Age, years	12.4 (2.8-16.2)
Donor Weight, kg	50.0 (13.4-67.1)
Donor Height, cm	152 (91-169)
Donor BSA, m ²	1.45 (0.57-1.78)
Donor/Recipient Weight ratio	1.36 (1.11-1.71)
Donor/Recipient Height ratio	1.09 (1.00-1.16)
Donor/Recipient BSA ratio	1.22 (1.08-1.38)

Post-Transplant

Catheterization post-transplant ≤ 14 days from transplant	73 (75.3)
Mean right atrial pressure, mmHg (N=71)	8 (5-13)
Pulmonary capillary wedge pressure, mmHg (N=71)	14 (10-17.5)
Cardiac index (N=65)	3.13 ± 0.79
Mean PA pressure, mmHg	22 (17-26)
Hospital length of stay since transplant, days	17 (14-34)
Rejection episode(s) within 6 months of transplant	46 (47.4)
Time to 1 st rejection episode since transplant, days	11 (9-44)
Rejection grade: Cellular	
0	1/46 (2.2)
1R	39/46 (84.8)
2R	5/46 (10.9)
3R	1/46 (2.2)
Antibody mediated	
0	28/46 (60.9)
pAMR 1	3/46 (6.5)
pAMR 2	2/46 (4.3)
pAMR 3	1/46 (2.2)
Unknown	12/46 (26.1)
Duration of follow-up since transplant, years	5.1 (2.3-7.4)
Death post-transplant	19 (19.6)

Data are presented as N (%) for categorical variables and Median (interquartile range) or Mean ± Standard deviation for continuous variables.

Table 2. Pericardial Effusions within 6 months of transplant (N=50 transplants)

Size of (first) pericardial effusion	
Small	36 (72.0)
Small to Moderate	8 (16.0)
Moderate	5 (10.0)
Moderate to Large	0 (0.0)
Large	1 (2.0)
Time to (first) pericardial effusion since transplant, days	10 (3-27)
Duration of (first) pericardial effusion, days	23 (8-63)
Intervention(s) performed	
None	25 (50.0)
Diuretics	18 (36.0)
Pericardial drain placed	8 (16.0)
Catheterization most proximal to (first) pericardial effusion within 6 months of transplant	44 (88.0)
Mean right atrial pressure, mmHg. (N=43)	7 (5-13)
Pulmonary capillary wedge pressure, mmHg. (N=43)	14 (11-19)
Cardiac index (N=40)	3.30 ± 0.78
Mean PA pressure, mmHg	21 (18-29.5)
Progressed to Moderate or greater (as 1 st pericardial effusion was < Moderate)	10/44 (22.7)
Progressed to a larger size (as 1 st pericardial effusion was Small)	7/36 (19.4)
Any pericardial effusion (except Large at first) progressed to a larger size	12/49 (24.5)

Data are presented as N (%) for categorical variables and Median (interquartile range) or Mean ± Standard deviation for continuous variables.

Table 3. Pericardial Effusions within 6 Months Post-Heart Transplantation Managed with Pericardial Drain Placement

Patient	Post-HT Day Drain Placed	Indications for Intervention
1	17	Persistent large pericardial effusion with evidence low clinical cardiac output in the intensive care unit which improved after pericardiocentesis. No echocardiographic or other clinical evidence of tamponade.
2	6	Increasing moderate pericardial effusion which prompted drain to be placed during scheduled routine surveillance endomyocardial biopsy. No echocardiographic or clinical evidence of tamponade.
3	46	Markedly increased large pericardial effusion with diastolic collapse of the right ventricle and significant respiratory variation of the mitral inflow doppler. Associated with dizziness but no other documented clinical evidence of tamponade.
4	34	New, increasing moderate pericardial effusion with diastolic collapse of right atrium found after endomyocardial biopsy (mostly sanguineous effusion thought to be related to biopsy).
5	9	Large pericardial effusion with significant respiratory variation of the mitral inflow doppler associated with chest pain and dyspnea. Drain placed during scheduled routine surveillance endomyocardial biopsy.
6	45	New, increasing large pericardial effusion found after endomyocardial biopsy with right ventricular collapse by echocardiogram. No obvious clinical evidence of tamponade.
7	8	Increasing moderate pericardial effusion with no echocardiographic or clinical evidence of tamponade which prompted drain to be placed during scheduled routine surveillance endomyocardial biopsy. Drain placement was complicated by left ventricular

		perforation which required emergent surgical repair.
8	11	New, slowly increasing moderate pericardial effusion found after endomyocardial biopsy with diastolic collapse of right atrium and right ventricle. No clinical evidence of tamponade.

Table 4. Univariate comparison of demographics and transplant/post-Transplant characteristics between presence and absence of \geq small pericardial effusions within 6 months of transplant (N=97 transplants)

Characteristics	\geq Small pericardial effusions within 6 months of transplants		P-value†
	Yes (N=50)	No (N=47)	

Male sex	26 (52.0)	27 (57.4)	0.59
Caucasian Race	39 (78.0)	36 (76.6)	0.87
Age at Transplant, years	12.7 (4.8-15.7)	5.6 (0.9-14.5)	0.02
Weight at Transplant, kg	42.6 (16.0-54.5)	16.8 (8.0-46.6)	0.01
Height at Transplant, cm	152 (101-160)	103 (68.0-154)	0.02
BSA at Transplant, m ²	1.35 (0.67-1.57)	0.69 (0.39-1.45)	0.01
Prior cardiac surgery (including previous transplants)	27 (54.0)	34 (72.3)	0.06
Non-Congenital heart disease	28 (56.0)	12 (25.5)	0.002
Protein losing enteropathy	8 (16.0)	2 (4.3)	0.09
Plastic bronchitis	0 (0.0)	2 (4.3)	0.23
Chylothorax	2 (4.0)	2 (4.3)	1.00
Positive crossmatch	10/50 (20.0)	7/46 (15.2)	0.54
Ischemic time, minutes	198 ± 53.6	228 ± 59.5	0.01
Donor Age, years	15.1 (6.6-17.2)	8.5 (1.3-14.5)	0.003
Donor Weight, kg	57.1 (23.1-75.2)	21.5 (10.0-62.5)	0.01
Donor Height, cm	160 (117-170)	124 (78.7-168)	0.02
Donor BSA, m ²	1.60 (0.79-1.92)	0.86 (0.47-1.65)	0.01
Donor/Recipient Weight ratio	1.40 (1.09-1.61)	1.32 (1.12-1.72)	0.68
Donor/Recipient Height ratio	1.09 (1.00-1.15)	1.10 (0.99-1.20)	0.43
Donor/Recipient BSA ratio	1.22 (1.08-1.35)	1.22 (1.07-1.43)	0.68
Post-Transplant			
Catheterization post-transplant ≤ 14 days from transplant	41 (82.0)	32 (68.1)	0.11
Mean right atrial pressure, mmHg (N=71)	8 (5.5-13)	7 (4-12)	0.34
Pulmonary capillary wedge pressure, mmHg. (N=71)	14 (10.8-19)	13 (10-16)	0.25
Cardiac index (N=65)	3.08 ± 0.83	3.20 ± 0.74	0.57
Mean PA pressure, mmHg	22 (18-28)	21 (16-24)	0.22
Hospital length of stay since transplant, days	18.5 (15-36)	17 (12-27)	0.22
Rejection episode(s) within 6 months of transplant	26 (52.0)	20 (42.6)	0.35
Time to 1 st rejection episode since transplant, days	21 (10-49)	9.5 (8.5-28.5)	0.03
Rejection grade: Cellular			
0	1/26 (3.8)	0/20 (0.0)	
1R	22/26 (84.6)	17/20 (85.0)	
2R	2/26 (7.7)	3/20 (15.0)	
3R	1/26 (3.8)	0/20 (0.0)	

Antibody mediated			
0	14/26 (53.8)	14/20 (70.0)	
pAMR 1	2/26 (7.7)	1/20 (5.0)	
pAMR 2	2/26 (7.7)	0/20 (0.0)	
pAMR 3	0/26 (0.0)	1/20 (5.0)	
Unknown	8/26 (30.8)	4/20 (20.0)	
Duration of follow-up since transplant, years	4.9 (2.2-7.6)	5.1 (2.9-7.1)	0.89
Death post-transplant	11 (22.0)	8 (17.0)	0.54

Data are presented as N (%) for categorical variables and Median (interquartile range) or Mean \pm Standard deviation for continuous variables.

† P-values from Chi-square test or Fisher's exact test for categorical variables and Wilcoxon rank sum test or two-sample t-test for continuous variables.

Figure 1. Post-HTx Survivals between patients with and without presence of \geq Small pericardial effusions (1a) and \geq Moderate pericardial effusions (1b) within 6 months of transplants (N=93 patients)

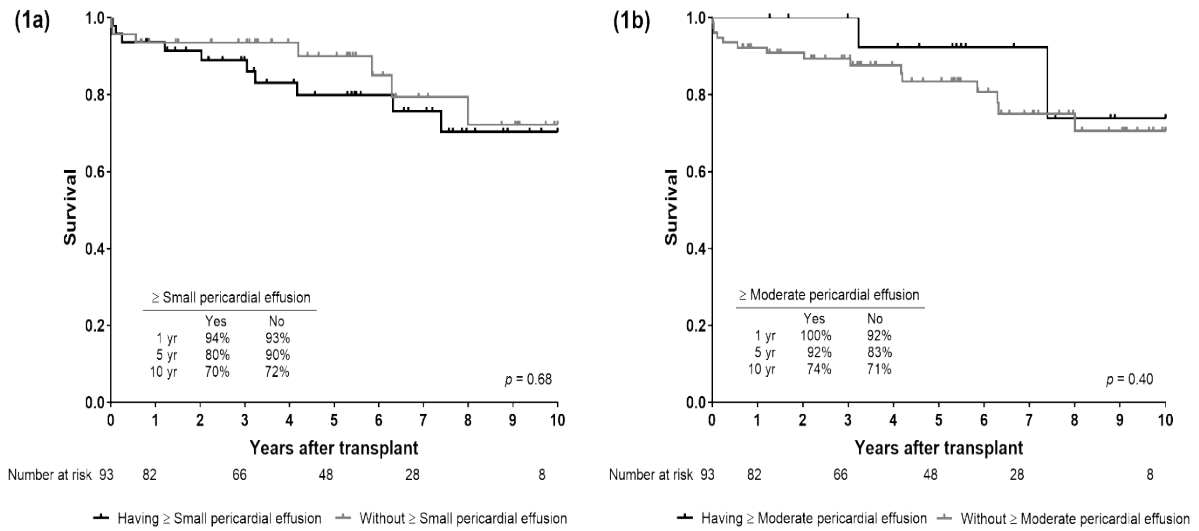


Table 1. Demographics and transplant/post-transplant characteristics (N=97 transplants)

Male sex	53 (54.6)
Caucasian Race	75 (77.3)
Age at Transplant, years	10.4 (1.6-15.0)
Weight at Transplant, kg	32.8 (10.4-53.0)
Height at Transplant, cm	143 (78.8-159)
BSA at Transplant, m ²	1.13 (0.48-1.51)
Number of prior cardiac surgery (including previous transplants)	
0	36 (37.1)
1	21 (21.6)
2	13 (13.4)
3	12 (12.4)
≥ 4	15 (15.5)
Non-congenital heart disease	40 (41.2)
Protein losing enteropathy	10 (10.3)
Plastic bronchitis	2 (2.1)
Chylothorax	4 (4.1)
Positive crossmatch	17/96 (17.7)
Ischemic time, minutes	212 ± 58.2
Donor Age, years	12.4 (2.8-16.2)
Donor Weight, kg	50.0 (13.4-67.1)
Donor Height, cm	152 (91-169)
Donor BSA, m ²	1.45 (0.57-1.78)
Donor/Recipient Weight ratio	1.36 (1.11-1.71)
Donor/Recipient Height ratio	1.09 (1.00-1.16)
Donor/Recipient BSA ratio	1.22 (1.08-1.38)
Post-Transplant	
Catheterization post-transplant ≤ 14 days from transplant	73 (75.3)
Mean right atrial pressure, mmHg (N=71)	8 (5-13)
Pulmonary capillary wedge pressure, mmHg (N=71)	14 (10-17.5)
Cardiac index (N=65)	3.13 ± 0.79
Mean PA pressure, mmHg	22 (17-26)
Hospital length of stay since transplant, days	17 (14-34)
Rejection episode(s) within 6 months of transplant	46 (47.4)

Time to 1 st rejection episode since transplant, days	11 (9-44)
Rejection grade: Cellular	
0	1/46 (2.2)
1R	39/46 (84.8)
2R	5/46 (10.9)
3R	1/46 (2.2)
Antibody mediated	
0	28/46 (60.9)
pAMR 1	3/46 (6.5)
pAMR 2	2/46 (4.3)
pAMR 3	1/46 (2.2)
Unknown	12/46 (26.1)
Duration of follow-up since transplant, years	5.1 (2.3-7.4)
Death post-transplant	19 (19.6)
Data are presented as N (%) for categorical variables and Median (interquartile range) or Mean \pm Standard deviation for continuous variables.	

Table 2. Pericardial Effusions within 6 months of transplant (N=50 transplants)

Size of (first) pericardial effusion	
Small	36 (72.0)
Small to Moderate	8 (16.0)
Moderate	5 (10.0)
Moderate to Large	0 (0.0)
Large	1 (2.0)
Time to (first) pericardial effusion since transplant, days	10 (3-27)
Duration of (first) pericardial effusion, days	23 (8-63)
Intervention(s) performed	
None	25 (50.0)
Diuretics	18 (36.0)
Pericardial drain placed	8 (16.0)
Catheterization most proximal to (first) pericardial effusion within 6 months of transplant	44 (88.0)
Mean right atrial pressure, mmHg. (N=43)	7 (5-13)
Pulmonary capillary wedge pressure, mmHg. (N=43)	14 (11-19)
Cardiac index (N=40)	3.30 ± 0.78
Mean PA pressure, mmHg	21 (18-29.5)
Progressed to Moderate or greater (as 1 st pericardial effusion was < Moderate)	10/44 (22.7)
Progressed to a larger size (as 1 st pericardial effusion was Small)	7/36 (19.4)
Any pericardial effusion (except Large at first) progressed to a larger size	12/49 (24.5)
Data are presented as N (%) for categorical variables and Median (interquartile range) or Mean ± Standard deviation for continuous variables.	

Table 3. Pericardial Effusions within 6 Months Post-Heart Transplantation Managed with Pericardial Drain Placement

Patient	Post-HT Day Drain Placed	Indications for Intervention
1	17	Persistent large pericardial effusion with evidence low clinical cardiac output in the intensive care unit which improved after pericardiocentesis. No echocardiographic or other clinical evidence of tamponade.
2	6	Increasing moderate pericardial effusion which prompted drain to be placed during scheduled routine surveillance endomyocardial biopsy. No echocardiographic or clinical evidence of tamponade.
3	46	Markedly increased large pericardial effusion with diastolic collapse of the right ventricle and significant respiratory variation of the mitral inflow doppler. Associated with dizziness but no other documented clinical evidence of tamponade.
4	34	New, increasing moderate pericardial effusion with diastolic collapse of right atrium found after endomyocardial biopsy (mostly sanguineous effusion thought to be related to biopsy).
5	9	Large pericardial effusion with significant respiratory variation of the mitral inflow doppler associated with chest pain and dyspnea. Drain placed during scheduled routine surveillance endomyocardial biopsy.
6	45	New, increasing large pericardial effusion found after endomyocardial biopsy with right ventricular collapse by echocardiogram. No obvious clinical evidence of tamponade.
7	8	Increasing moderate pericardial effusion with no echocardiographic or clinical evidence of tamponade which prompted drain to be placed during scheduled routine surveillance endomyocardial biopsy. Drain placement was complicated by left ventricular perforation which required emergent surgical repair.
8	11	New, slowly increasing moderate pericardial effusion found after endomyocardial biopsy with diastolic collapse of right atrium and right ventricle. No clinical evidence of tamponade.

Table 4. Univariate comparison of demographics and transplant/post-Transplant characteristics between presence and absence of \geq small pericardial effusions within 6 months of transplant (N=97 transplants)

Characteristics	\geq Small pericardial effusions within 6 months of transplants		P-value [†]
	Yes (N=50)	No (N=47)	
Male sex	26 (52.0)	27 (57.4)	0.59
Caucasian Race	39 (78.0)	36 (76.6)	0.87
Age at Transplant, years	12.7 (4.8-15.7)	5.6 (0.9-14.5)	0.02
Weight at Transplant, kg	42.6 (16.0-54.5)	16.8 (8.0-46.6)	0.01
Height at Transplant, cm	152 (101-160)	103 (68.0-154)	0.02
BSA at Transplant, m ²	1.35 (0.67-1.57)	0.69 (0.39-1.45)	0.01
Prior cardiac surgery (including previous transplants)	27 (54.0)	34 (72.3)	0.06
Non-Congenital heart disease	28 (56.0)	12 (25.5)	0.002
Protein losing enteropathy	8 (16.0)	2 (4.3)	0.09
Plastic bronchitis	0 (0.0)	2 (4.3)	0.23
Chylothorax	2 (4.0)	2 (4.3)	1.00
Positive crossmatch	10/50 (20.0)	7/46 (15.2)	0.54
Ischemic time, minutes	198 \pm 53.6	228 \pm 59.5	0.01
Donor Age, years	15.1 (6.6-17.2)	8.5 (1.3-14.5)	0.003
Donor Weight, kg	57.1 (23.1-75.2)	21.5 (10.0-62.5)	0.01
Donor Height, cm	160 (117-170)	124 (78.7-168)	0.02
Donor BSA, m ²	1.60 (0.79-1.92)	0.86 (0.47-1.65)	0.01
Donor/Recipient Weight ratio	1.40 (1.09-1.61)	1.32 (1.12-1.72)	0.68
Donor/Recipient Height ratio	1.09 (1.00-1.15)	1.10 (0.99-1.20)	0.43
Donor/Recipient BSA ratio	1.22 (1.08-1.35)	1.22 (1.07-1.43)	0.68
Post-Transplant			
Catheterization post-transplant \leq 14 days from transplant	41 (82.0)	32 (68.1)	0.11
Mean right atrial pressure, mmHg (N=71)	8 (5.5-13)	7 (4-12)	0.34
Pulmonary capillary wedge pressure, mmHg. (N=71)	14 (10.8-19)	13 (10-16)	0.25
Cardiac index (N=65)	3.08 \pm 0.83	3.20 \pm 0.74	0.57
Mean PA pressure, mmHg	22 (18-28)	21 (16-24)	0.22
Hospital length of stay since transplant, days	18.5 (15-36)	17 (12-27)	0.22

Rejection episode(s) within 6 months of transplant	26 (52.0)	20 (42.6)	0.35
Time to 1 st rejection episode since transplant, days	21 (10-49)	9.5 (8.5-28.5)	0.03
Rejection grade: Cellular			
0	1/26 (3.8)	0/20 (0.0)	
1R	22/26 (84.6)	17/20 (85.0)	
2R	2/26 (7.7)	3/20 (15.0)	
3R	1/26 (3.8)	0/20 (0.0)	
Antibody mediated			
0	14/26 (53.8)	14/20 (70.0)	
pAMR 1	2/26 (7.7)	1/20 (5.0)	
pAMR 2	2/26 (7.7)	0/20 (0.0)	
pAMR 3	0/26 (0.0)	1/20 (5.0)	
Unknown	8/26 (30.8)	4/20 (20.0)	
Duration of follow-up since transplant, years	4.9 (2.2-7.6)	5.1 (2.9-7.1)	0.89
Death post-transplant	11 (22.0)	8 (17.0)	0.54

Data are presented as N (%) for categorical variables and Median (interquartile range) or Mean \pm Standard deviation for continuous variables.

[†] P-values from Chi-square test or Fisher's exact test for categorical variables and Wilcoxon rank sum test or two-sample t-test for continuous variables.

