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Weight Matching in Infant Heart Transplantation: A National Registry Analysis

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Abstract

Purpose: Infants account for a significant proportion of pediatric heart transplants, but also suffer from a high waitlist mortality. Donor oversizing by weight-based criteria is common practice in transplantation and is prevalent in this group. We sought to analyze the impact of oversizing on outcomes in infants.

Methods: Infant heart transplantations reported to the United Network for Organ Sharing from 01/1994 to 09/2019 were retrospectively analyzed. 2384 heart transplantation recipients were divided into quintiles (Q1-Q5) based on donor-to-recipient weight ratios (DRWR). Multivariate Cox regression was used to estimate the effect of DRWR. The primary endpoint of graft survival at one year.

Results: The median DRWR for each quintile was 0.90 (0.37 to 1.04), 1.17 (1.04 to 1.29), 1.43 (1.29 to 1.57), 1.74 (1.58 to 1.97), and 2.28 (1.97 to 5.00). Pairwise comparisons showed improved survival for Q3 and Q4 over each of the bottom two quintiles and the top quintile, respectively. Regression analyses found that Q3 and Q4 were protective against graft failure when compared to the bottom two quintiles, respectively. There was no difference in hazard amongst the top three quintiles. Significant covariates included primary diagnosis, ischemic time, serum bilirubin, transplant year, mechanical ventilation at transplantation, extracorporeal membrane oxygenation at transplantation. Gender, female-to-male transplantation, and mechanical circulatory support at transplantation were not significant in univariate analyses.

Conclusions: Modest oversizing by DRWR (1.29 to 1.97) is associated with increased survival and lower risk in infant heart transplantation. Additional investigation is needed to establish best practices for size-matching in this population.

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Introduction

Infants listed for heart transplantation face the highest waitlist mortality of any solid organ transplantation population in the United States[1]. It is estimated that over 1 in 4 infants die while waiting for a heart, compared to a waitlist mortality of 15% for children and adolescents[1,2]. Unlike older age groups, congenital heart disease is the primary indication for heart transplantation in this population. Advances in palliative surgery have decreased the proportion of transplants allocated for infants diagnosed with congenital heart disease (CHD) from 80% in the early 1990s to 50–60% in recent decades[3,4]. Despite such advances, the donor pool for this cohort remains extremely limited and 80% of infants listed for heart transplantation are listed as status 1A[5].

Significant strides have been made in an effort to expand the donor pool in the infant population. In 2001, West et al reported the first series of successful ABO incompatible (ABOi) transplantations in 10 infants[6]. ABOi has gained wider acceptance as a treatment in recent years with single-center and multi-institutional studies showing equivalent survival between ABOi and ABO compatible transplant recipients[7]. Multivariable analysis has also shown a greater tolerance for donor-related factors in infants <6 months old, and it has been suggested that there may be a persistent immunological advantage to early transplantation[8]. Further investigation is needed to evaluate the extent to which donors deemed “marginal” by criteria established in the adult and adolescent populations should limit the donor pool in infant heart transplantation. Transplantation continues to be the gold standard treatment for many congenital heart diseases, and the longevity of the transplanted heart is the highest in the infant age group, with a median survival approaching 25 years[9].

Unlike the adult and adolescent populations where size-matching has been evaluated using weight, height, and body surface area, there is little guidance for size-matching in the infant population. Weight is the traditional metric for size-matching and it is the only metric reported to the United Network for Organ Sharing (UNOS). Many institutions have adopted oversizing up to 300% in infants due to a lack of suitable donors while discouraging undersizing due to concerns of cardiac output and pulmonary vascular resistance[10, 11,12]. Yet these guidelines are largely based on single-institution experiences and there is no general consensus for acceptable infant donor-recipient weight ratios (DRWR).

To address this lack of knowledge, we utilize the UNOS database to evaluate DRWR in infant heart transplantation. To the authors’ knowledge, this is the first multi-institutional study of weight-based size-matching in infants.

Methods

This study retrospectively reviewed all infant heart transplantations (<1 years old) reported to the United Network for Organ Sharing/Organ Procurement and Transplantation Network (UNOS/OPTN) from 1/1994 to 9/2019. The UNOS Standard Transplant Analysis and Research File contains data regarding every organ transplanted in the United States since October, 1987. There were 2552 infant heart transplantations reported to UNOS in the study period. We excluded donors or recipients with missing data for graft status (n=8),

weight (n=15), or age in days (n=122) from the analysis. Infants with previous heart transplantations (n=18) were also excluded from the study. Remaining missing covariate data was handled using multiple imputation to avoid list-wise deletion in multivariate analyses. A regression switching approach with predictive mean matching was utilized. Regression coefficients from 20 imputations were pooled according to Rubin's rules.

The resulting study cohort of 2384 infant transplant recipients was split into quintiles based on DRWR. The primary endpoint of this study was graft survival at one year. Univariate Cox proportional hazards regression modeling was used to evaluate the effect of patient characteristics previously shown to predict post-transplant survival. Baseline patient demographics between DRWR quintiles were compared using the Kruskal-Wallis rank sum test with Benjamini-Hochberg procedure for continuous variables. Pearson's chi-squared test was used to compare categorical variables. Post-transplant survival was estimated using Kaplan-Meier survival estimator and evaluated using the Mantel-Cox log rank test with Benjamini-Hochberg procedure. A multivariate Cox proportional hazards regression model was constructed to evaluate the independent effect of donor-recipient weight ratios on graft survival. Variable selection was based on literature review and expert clinical input. Schoenfeld residuals were used to evaluate the proportional hazards assumption for each variable in the final (Supplemental Figure 1).

To evaluate the sensitivity of the findings to outliers, a follow-up analysis that excluded recipients with DRWR >3.5 or DRWR <0.8 was performed. An additional analysis excluding older era transplantations (pre-2006) was also performed to corroborate the findings in a modern 15-year period of transplantation. In order to evaluate whether risk increased beyond certain thresholds within the bottom and top quintiles (i.e. determine the homogeneity of risk within the outlying quintiles), further subanalysis of the outlying quintiles was performed using inverse probability weighting via the propensity score. The thresholds analyzed were predetermined. In the bottom quintile, infants with DRWR 0.37 to 0.8 were compared to infants with DRWR 0.8 to 1.04; in the top quintile, infants with DRWR 1.97 to 2.5 were compared to infants with DRWR 2.5 to 5.0. Propensity scores were calculated via logistic regression across all imputed data sets (n=20) and combined using the across method of analysis for multiply imputed propensity scores.

Quintiles are presented with DRWR ranges in parenthesis. Hazard ratios are presented with 95% confidence intervals. Continuous variables are presented as medians with interquartile ranges and categorical variables are presented with percentages. A p-value <0.05 was considered statistically significant. All analyses were conducted in R statistical software (version 4.0.4). The study was approved by the institutional review board and the need for patient consent was waived because the UNOS Standard Transplant Analysis and Research File includes no patient identifiers. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the OPTN or the United States Government.

Results

There were 2552 infant heart transplantations reported to UNOS from 1/1994 to 9/2019. The primary indication for transplantation was CHD in 61.8% of infants and dilated cardiomyopathy (DCM) in 31.1% of infants. 7.1% of patients received transplantation for a diagnosis other than CHD or DCM. Infants diagnosed with DCM had the highest 1-year graft survival of 91.5%, compared to 81.0% for CHD and 81.1% for other diagnoses. The overall 1-year graft survival during the study period was 85.8%. At the time of transplantation, 12.3% of infants were on mechanical circulatory support and 8.3% were supported by extracorporeal membrane oxygenation (ECMO). Transplantations were performed between incompatible ABO blood types in 13.4% of transplantations.

9 of 13 variables were found to be significant predictors of 1 year graft survival in univariate analysis (Table 1). ECMO at transplantation, mechanical ventilation at transplantation, serum bilirubin, and longer ischemic times were associated with worse graft survival. Transplanted year, older recipient age, and diagnosis of DCM were found to be protective against graft failure. Mechanical circulatory support at transplantation, female-to-male transplantation, and ABOi transplantation were not significantly associated with 1-year graft survival in univariate analyses (Table 1).

When transplantations were split into quintiles by DRWR, the median DRWR for each quintile ranged from 0.90 to 2.28 (Figure 1). There were 15 infants with a DRWR below 0.60 in the bottom quintile and 8 infants with a DRWR above 3.5 in the top quintile. The lower four quintiles were largely equivalent in baseline characteristics with the exception of ischemic time, with Q4 (1.58 to 1.97) showing longer ischemic times than Q3 (1.29 to 1.57) (Table 2). Compared to the bottom four quintiles, the top quintile featured younger recipients, longer ischemic times, higher bilirubin, higher creatinine, and older era of transplantation (Table 2). There was no significant difference in utilization of ECMO, ABOi transplantation, or diagnosis (DCM vs CHD vs other) between any of the quintiles.

Pairwise comparisons of Kaplan-Meier survival curves showed superior survival for Q3 (1.29 to 1.57) over each of the bottom two quintiles (Q1: 0.37 to 1.04; Q2: 1.04 to 1.29) respectively and superior survival compared to the top quintile (1.97 to 5.0). Q4 (1.58 to 1.97) also demonstrated superior survival to each of the bottom two quintiles (Q1: 0.37 to 1.04; Q2: 1.04 to 1.29) respectively and the top quintile (1.97 to 5.0) (Figure 2). In multivariate Cox regression, Q3 (1.29 to 1.57) and Q4 (1.29 to 1.57) were protective against 1-year graft failure when compared to each of the bottom two quintiles (Q1: 0.37 to 1.04; Q2: 1.04 to 1.29) (Table 3). Q5 (1.97 to 5.0) was not associated with an increased risk of 1-year graft failure compared to either of the bottom quintiles. There was no statistically significant difference in risk for 1-year graft failure amongst the top three quintiles. Ischemic time, serum bilirubin, and mechanical ventilation or ECMO at transplantation were associated with increased risk of 1-year graft failure while later transplantation year and DCM diagnosis were associated with lower risk of 1-year graft failure in the multivariate regression model.

These findings were corroborated by multivariate sensitivity analysis which excluded undersized infants with DRWR <0.6 (n=15) and oversized infants with DRWR >3.5 (n=8) from the analysis. There was no change in the statistical significance of covariates included in the multivariate model when these outliers were excluded. Additional sensitivity analysis restricting the study to a modern 15-year period (2006–2019) corroborated the protective effect associated with Q3 (1.29 to 1.57) compared to Q1 (0.37 to 1.04) and Q2 (1.04 to 1.29), respectively. Infants transplanted after 2006 in Q5 (1.97 to 5.0) and Q1 (0.37 to 1.04) had lower levels of serum bilirubin and serum creatinine compared to their counterparts in the pre-2006 period. Additionally, ischemic time decreased for infants in Q1 (0.37 to 1.04) in the modern period while utilization of mechanical ventilation increased for infants in Q5 (1.97 to 5.0) (Table 4).

Threshold analysis using inverse probability weighting via propensity scores demonstrated higher risk of 1-year graft survival associated with oversizing beyond a DRWR of 2.5 in the top quintile (hazard ratio, 1.59; 95% confidence interval: 1.01 to 2.52; p=0.04) and higher risk associated with undersizing below a DRWR of 0.8 in the bottom quintile (hazard ratio, 1.67; 95% confidence interval: 1.05 to 2.65; p=0.03). Differences in baseline characteristics between the most undersized infants (DRWR <0.8) or most oversized infants (DRWR >2.5) compared to the remainder of their respective quintiles summarized in Table 5 and Table 6.

Discussion

Size match in heart transplantation is most commonly evaluated using weight, yet there is little guidance for acceptable DRWR thresholds in the infant population. Infants are often transplanted with greater size mismatches compared to older adolescents or adults, and some centers report oversizing up to 300%[10, 11,12]. Despite this practice, the risk associated with undersizing or oversizing to varying degrees has not been quantified in the infant population, making it difficult for clinicians to accurately weigh the risk of size mismatch. We sought to leverage the national UNOS registry to quantify the risk associated with varying degrees of DRWR mismatch in the infant population.

The findings of this study demonstrate a protective effect associated with modest oversizing from DRWR 1.29 to 1.97 in infants. Quintiles in this range (Q3, Q4) were associated with higher rates of 1-year graft survival compared to undersized (Q1) or approximately size-matched (Q2) infants. The protective effect of modest oversizing persisted even after controlling for confounding variables. Although the top quintile (1.97 to 5.0) demonstrated inferior 1-year graft survival compared to Q3 (1.29 to 1.57) and Q4 (1.58 to 1.97), it was not associated with increased risk after controlling for differences in baseline characteristics such as ischemic time and serum bilirubin. This suggests that a DRWR in the 1.97 to 5.0 range may be a surrogate marker for higher-than-average risk in recipients, rather than being a risk factor for graft failure in its own right.

Further threshold analysis of the bottom quintile revealed a 67% increase in hazard associated with undersizing below a DRWR of 0.8 compared to the remainder of the bottom quintile (0.8 to 1.04). Although recipients with DRWR <0.8 were associated with higher levels of serum creatinine, such differences in baseline characteristics were controlled

for using inverse probability weighting via propensity scores (Table 5). The 67% increase in hazard with undersizing below DRWR 0.8 may be indicative of a limit below which undersized hearts struggle to provide adequate cardiac output. Similar threshold analysis of the top quintile revealed a 59% increase in hazard to oversizing beyond a DRWR of 2.5 (Table 6). This suggests an upper limit to oversizing; that is, aggressively oversizing beyond a DRWR of 2.5 may be an intrinsic risk rather than a surrogate marker for more critical recipient status.

The worse baseline characteristics in recipients the top quintile (1.97 to 5.0) likely reflect a reluctance to oversize beyond a DRWR of 2.0 at many institutions. Recipients in the top quintile were more likely to have end organ dysfunction at the time of surgery (as reflected by higher bilirubin levels and higher creatinine levels) and had longer ischemic times. Infants in Q5 were also disproportionately composed of early era transplantations, which was a risk factor for graft failure in both univariate and multivariate analyses. In comparison, recipients in the bottom quintile featured equivalent baseline characteristics compared to the middle three quintiles (1.04 to 1.97) (Table 2). These differences in baseline characteristics were controlled for in our multivariate analyses.

We further evaluated the protective effect of modest oversizing (1.29 to 1.58) by performing a sensitivity analysis that restricted the study cohort to a modern 15-year period (2006–2019). This reduced the influence of early era transplantation, particularly with regards to less aggressive surgical strategy for complex CHD. Limiting the study to a modern cohort also had the effect of reducing the differences in baseline characteristics between the top quintile and the bottom four quintiles, particularly for ischemic time, serum creatinine, and serum bilirubin (Table 4). The results from this sensitivity analysis corroborate the findings from our analysis of the entire study period, with the middle quintile (1.29 to 1.58) demonstrating a protective effect to both Q1 and Q2 respectively.

Finally, we also reviewed the individual cases of the most oversized and the most undersized infants. The three most oversized infants ranged from DRWR 4.1 to 5.0. Notably, the most oversized recipient with DRWR 5.0 had been followed for 8328 days (22.8 years) without graft failure. The next most oversized recipient with DRWR 4.5 experienced graft failure at 1 days due to cardiac arrest. The following most oversized recipient with DRWR 4.1 experienced graft failure due to cerebrovascular hemorrhage at 495 days. The three most undersized cases ranged from DRWR 0.37 to 0.48. The most undersized infant was free of graft failure at 8379 days (23.0 years). However, the next two most undersized infants with DRWR 0.46 and 0.48 experienced graft failure within 18 days of transplantation with a cardiovascular cause of death.

The 20+ years of graft survival in recipients with DRWR 0.37 and DRWR 5.0 demonstrate that extremely size mismatched organs can be successfully transplanted with long graft survival times. However, these individual cases do not negate the increase in risk and decreased graft survival attendant with undersizing below DRWR 0.8 or oversizing above DRWR 2.5. The unadjusted 1-year graft survival in recipients undersized with DRWR <0.8 was 70.2% and the 1-year graft survival rate in recipients oversized beyond DRWR 2.5 was

75.7%, lower than any of the 5 quintiles (Table 7). However, these 1-year graft survival rates should be interpreted within the context of an infant waitlist mortality exceeding 25%.

The findings from this study should be interpreted within the limitations of a retrospective multi-institutional review. It therefore cannot establish causality and DRWR comparisons made between quintiles should be interpreted as trends rather than as exact threshold values. The lack of granularity in such a registry-based study prevented evaluation of risk factors such as pulmonary hypertension or pulmonary vascular bed anomalies. Nonetheless, this review benefits from a large sample size allowing for quantification of risk and broad generalizability to the infant transplantation population.

In conclusion, the findings from this retrospective review suggest that modest oversizing (DRWR 1.29 to 1.97) is the optimal size-match in infant heart transplantation. Undersizing below a DRWR of 0.8 or oversizing above a DRWR of 2.5 is more hazardous compared to better size-matched recipients. These recommendations should not be interpreted as strict contraindications but as estimations of risk associated with increasing degrees of size-mismatch. The decision to accept organs with larger DRWR mismatches should be evaluated within the context of clinical factors and an infant waitlist mortality exceeding 25%. Further investigation is needed to evaluate best donor-recipient matching practices in the infant population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

[1]. Mah D, Singh TP, Thiagarajan RR, et al. Incidence and risk factors for mortality in infants awaiting heart transplantation in the USA. J Heart Lung Transplant. 2009;28(12):1292–1298. doi:10.1016/j.healun.2009.06.013 [PubMed: 19782580]

[2]. Kirk R, Dipchand AI, Davies RR, et al. ISHLT consensus statement on donor organ acceptability and management in pediatric heart transplantation. J Heart Lung Transplant. 2020;39(4):331–341. doi:10.1016/j.healun.2020.01.1345 [PubMed: 32088108]

[3]. Chinnock RE, Bailey LL. Heart transplantation for congenital heart disease in the first year of life. Curr Cardiol Rev. 2011;7(2):72–84. doi:10.2174/157340311797484231 [PubMed: 22548030]

[4]. Rossano JW, Singh TP, Cherikh WS, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Twenty-second pediatric heart transplantation report – 2019; Focus theme: Donor and recipient size match. J Hear Lung Transplant. 2019;38(10):1028–1041. doi:10.1016/j.healun.2019.08.002

[5]. Almond CSD, Thiagarajan RR, Piercey GE, et al. Waiting list mortality among children listed for heart transplantation in the United States. Circulation. 2009;119(5):717–727. doi:10.1161/CIRCULATIONAHA.108.815712 [PubMed: 19171850]

[6]. West LJ, Pollock-Barziv SM, Dipchand AI, et al. ABO-Incompatible Heart Transplantation in Infants. N Engl J Med. 2001;344(11):793–800. doi:10.1056/nejm200103153441102 [PubMed: 11248154]

[7]. Dipchand AI, Pollock Barziv SM, Manlhiot C, West LJ, Vandervliet M, McCrindle BW. Equivalent outcomes for pediatric heart transplantation recipients: ABO-blood group incompatible versus ABO-compatible. Am J Transplant. 2010;10(2):389–397. doi:10.1111/j.1600-6143.2009.02934.x [PubMed: 20041867]

[8]. Dipchand AI, Kirk R, Mahle WT, et al. Ten yr of pediatric heart transplantation: A report from the Pediatric Heart Transplant Study. Pediatr Transplant. 2013;17(2):99–111. doi:10.1111/petr.12038 [PubMed: 23442098]

[9]. Guleserian KJ, Schechtman KB, Zheng J, et al. Outcomes after listing for primary transplantation for infants with unoperated-on non-hypoplastic left heart syndrome congenital heart disease: A multi-institutional study. J Hear Lung Transplant. 2011;30(9):1023–1032. doi:10.1016/j.healun.2011.03.020

[10]. Fullerton DA, Gundry SR, De Begona JA, et al. The effects of donor-recipient size disparity in infant and pediatric heart transplantation. J Thorac Cardiovasc Surg. 1992;104(5):1314–1319. doi:10.1016/s0022-5223(19)34624-0 [PubMed: 1434712]

[11]. Camarda J, Saudek D, Tweddell J, et al. MRI validated echocardiographic technique to measure total cardiac volume: A tool for donor-recipient size matching in pediatric heart transplantation. Pediatr Transplant. 2013;17(3):300–306. doi:10.1111/petr.12063 [PubMed: 23489637]

[12]. O'Connell JB, Bourge RC, Costanzo-Nordin MR, et al. Cardiac transplantation: Recipient selection, donor procurement, and medical follow-up: A statement for health professionals from the Committee on Cardiac Transplantation of the Council on Clinical Cardiology, American Heart Association. Circulation. 1992;86(3):1061–1079. doi:10.1161/01.CIR.86.3.1061 [PubMed: 1516181]

[13]. Marijianowski MMH, van der Loos CM, Mohrschladt MF, Becker AE. The neonatal heart has a relatively high content of total collagen and type I collagen, a condition that may explain the less compliant state. J Am Coll Cardiol. 1994;23(5):1204–1208. doi:10.1016/0735-1097(94)90612-2 [PubMed: 8144790]

[14]. Tang L, Du W, Delius RE, L'Ecuyer TJ, Zilberman MV. Low donor-to-recipient weight ratio does not negatively impact survival of pediatric heart transplant patients. Pediatr Transplant. 2010;14(6):741–745. doi:10.1111/j.1399-3046.2010.01300.x [PubMed: 20214744]

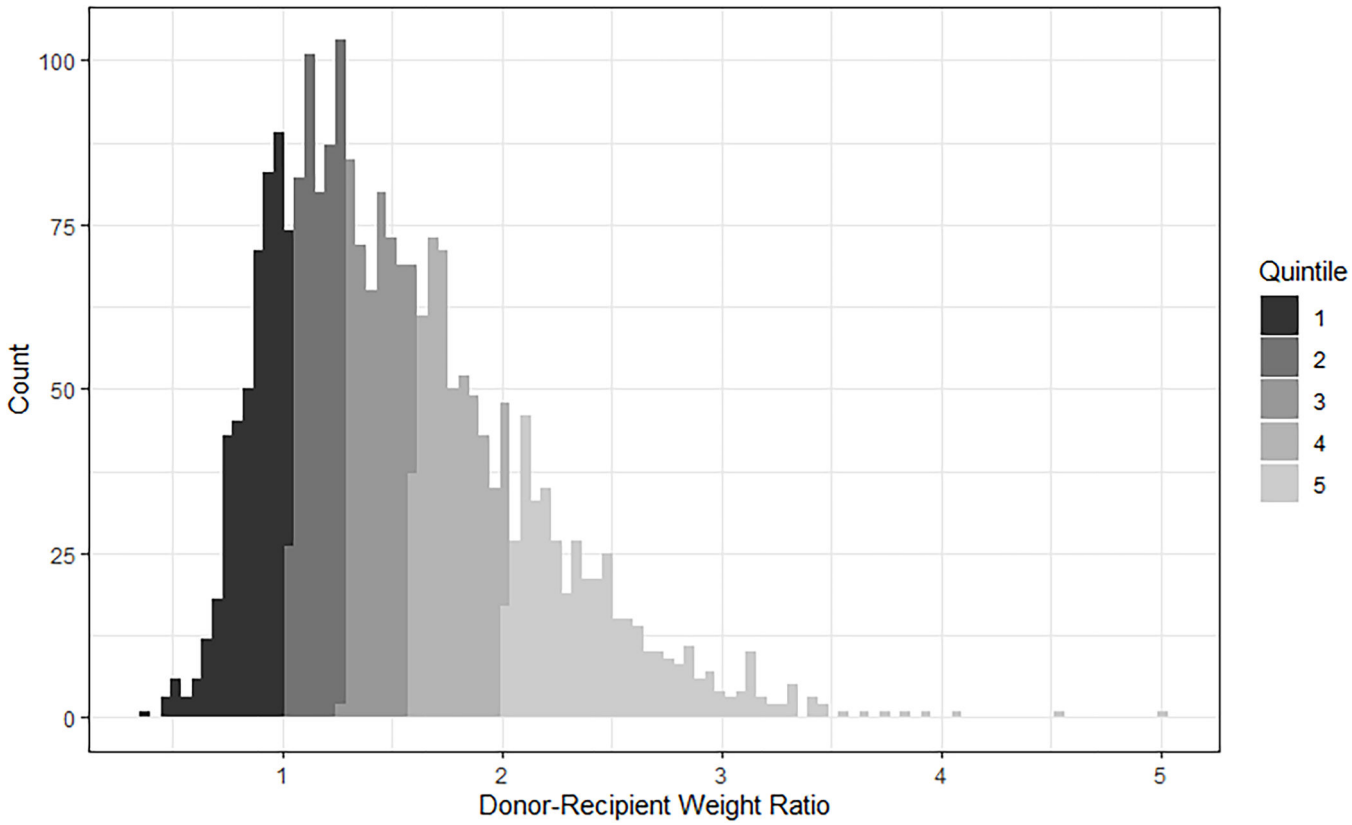

Figure 1:
Distribution of donor-recipient weight ratios in 2384 infants transplanted from 1994 to 2019

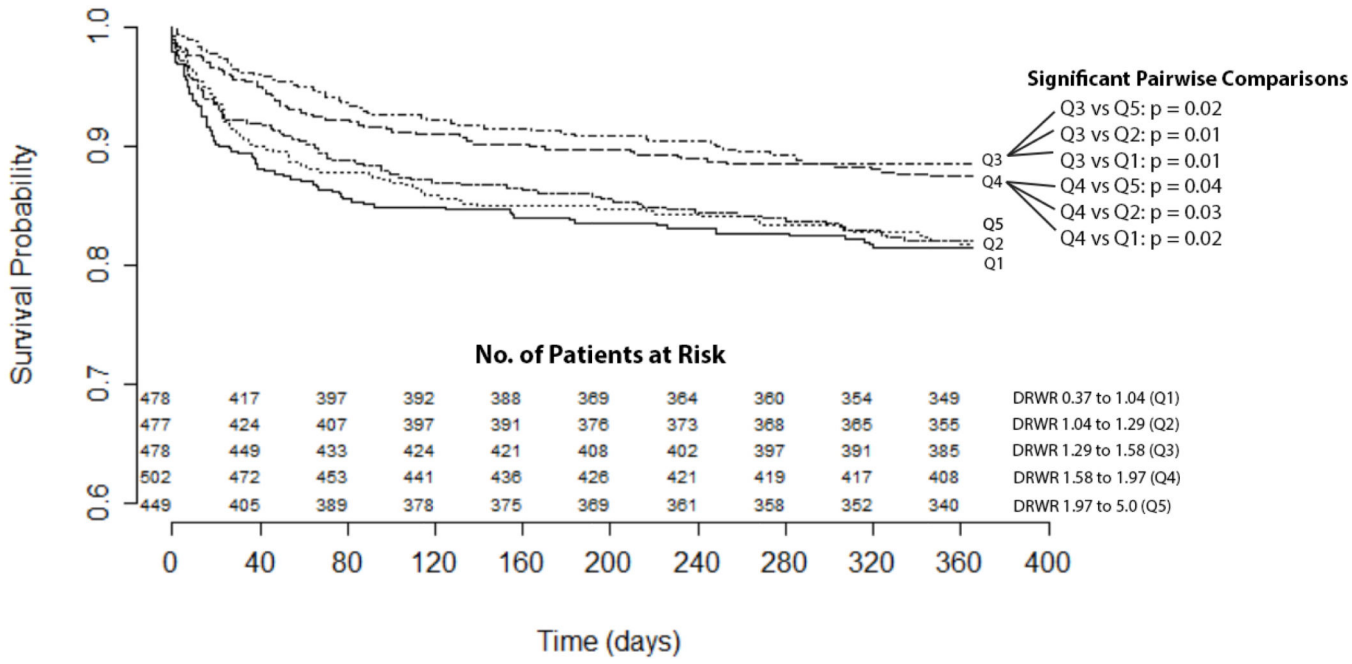

Figure 2:

Kaplan-Meier survival curves stratified by donor-recipient weight ratio (DRWR) quintiles. Pairwise comparisons of survival curves are made using the log-rank test with Benjamini-Hochberg correction

TABLE 1

Univariate Analysis

Characteristic	HR	95% CI	*P* Value
Female-to-male transplantation	1.08	0.86–1.35	.50
Ischemia time, h	1.15	1.07–1.23	<.001
Serum bilirubin level, mg/dL	1.04	1.03–1.05	<.0001
Serum creatinine level, mg/dL	1.05	1.00–1.10	.04
Mechanical ventilation at transplantation	2.36	1.94–2.87	<.0001
ECMO at transplantation	3.52	2.78–4.47	<.0001
Transplantation year	0.95	0.94–0.96	<.0001
Recipient age, y	0.36	0.24–0.54	<.0001
Donor age, y	0.86	0.77–0.96	.008
Diagnosis CHD (vs DCM)	2.46	1.87–3.22	<.0001
Diagnosis other (vs DCM)	3.38	2.33–4.90	<.0001
ABO incompatible	0.88	0.63–1.21	.43
Mechanical circulatory support at transplantation	0.90	0.66–1.24	.53

CHD, congenital heart disease; DCM, dilated cardiomyopathy; ECMO, extracorporeal membrane oxygenation; HR, hazard ratio.

TABLE 2

Baseline Characteristics

Characteristic	Q1 (n = 432)	Q2 (n = 432)	Q3 (n = 430)	Q4 (n = 432)	Q5 (n = 430)	*P* value	Adjusted *P* Value
DRWR (range)	0.90 (0.37–1.04)	1.17 (1.04–1.29)	1.43 (1.29–1.57)	1.74 (1.58–1.97)	2.28 (1.97–5.0)		
Ischemia time, h	3.6 (3.0–4.3)	3.6 (3.0–4.3)	3.6 (2.9–4.2)	3.7 (3.1–4.5)	3.8 (3.0–4.6)	.005	Q5 vs Q1 : .04 Q5 vs Q3: .02 Q4 vs Q3: .04
Serum bilirubin level, mg/dL	0.5 (0.3–1.0)	0.5 (0.3–1.0)	0.5 (0.3–1.1)	0.5 (0.3–1.2)	0.7 (0.3–2.1)	<.001	Q5 vs Q1 : <.001 Q5 vs Q2: <.001 Q5 vs Q3: <.001 Q5 vs Q4: .002
Creatinine level, mg/dL	0.30 (0.22–0.40)	0.30 (0.24–0.40)	0.30 (0.25–0.40)	0.30 (0.25–0.40)	0.36 (0.27–0.50)	.004	Q5 vs Q1 : .005 Q5 vs Q2: .04 Q5 vs Q3: .03 Q5 vs Q4: .01
Transplantation year	2011 (2005–2015)	2011 (2006–2015)	2011 (2005–2015)	2010 (2005–2015)	2008 (1999–2015)	<.001	Q5 vs Q1 : .002 Q5 vs Q2: <.001 Q5 vs Q3: <.001 Q5 vs Q4: .01
Recipient age, d	140 (73–221)	137 (62–222)	152 (86–231)	129 (69–223)	111 (56–188)	<.001	Q5 vs Q1 : <.001 Q5 vs Q2: .003 Q5 vs Q3: <.001 Q5 vs Q4: .00126
Diagnosis DCM	31	34	31	34	28	.46	
Diagnosis CHD	62	58	64	59	64		
Diagnosis other	7	8	6	7	8		
ECMO at transplantation	11	7	9	7	10	.14	
Mechanical ventilation at transplantation	35	37	32	33	41	.05	
ABO incompatible	12	15	16	14	15	.49	

CHD, congenital heart disease; DCM, dilated cardiomyopathy; DRWR, donor-to-recipient weight ratio; ECMO, extracorporeal membrane oxygenation. Continuous variables are presented as median (interquartile range) unless otherwise indicated. Categorical variables are presented as percentage.

TABLE 3

Multivariate Analysis

Characteristic	HR	95% CI	*P* Value
Ischemia time, h	1.11	1.03–1.20	.007
Serum bilirubin level, mg/dL	1.04	1.02–1.06	<.0001
Serum creatinine level, mg/dL	1.05	0.99–1.12	.13
ECMO at transplantation	3.09	3.01–5.07	<.0001
Mechanical ventilation at transplantation	1.85	1.48–2.30	<.0001
Transplantation year	0.96	0.94–0.97	<.0001
Recipient age, y	0.91	0.55–1.51	.71
Donor age, y	1.00	0.87–1.16	.96
DCM reference			
Diagnosis CHD	2.20	1.64–2.95	<.0001
Diagnosis other	1.82	1.17–2.83	.008
Q1 reference			
Q5	0.72	0.49–1.03	.07
Q4	0.57	0.40–0.82	.002
Q3	0.55	0.39–0.78	.0009
Q2	0.92	0.68–1.25	.60
Q2 reference			
Q5	0.77	0.53–1.10	.14
Q4	0.62	0.44–0.87	.007
Q3	0.60	0.42–0.84	.004
Q1	1.08	0.80–1.46	.61
Q3 reference			
Q5	1.28	0.87–1.89	.21
Q4	1.05	0.72–1.52	.82

CHD, congenital heart disease; DCM, dilated cardiomyopathy; ECMO, extracorporeal membrane oxygenation; HR, hazard ratio.

TABLE 4

Patient Characteristics by Transplantation Era in Outlying DRWR Quintiles

Characteristic	Bottom Quintile (Q1)			Top Quintile (Q5)		
	1994–2005	2006–2019	*P* Value	1994–2005	2006–2019	*P* Value
Ischemia time, h	3.7	3.5	.04	4.0	3.7	.3
Serum bilirubin level, mg/dL	0.8	0.5	<.0001	1.1	0.6	<.0001
Serum creatinine level, mg/dL	0.4	0.3	<.0001	0.4	0.3	<.0001
Mechanical ventilation at transplantation, %	39	34	.3	34	46	.009
ECMO at transplantation, %	8	12	.2	9	11	.5

DRWR, donor-to-recipient weight ratio; ECMO, extracorporeal membrane oxygenation.

TABLE 5

Baseline Characteristics of the Most Undersized Infants

Characteristic	Before Matching			After Matching		
	DRWR 0.37–0.8 (n = 112)	DRWR 0.8–1.04 (n = 366)	SMD	DRWR 0.37–0.8 (n = 112.0)	DRWR 0.8–1.04 (n = 365.5)	SMD
Ischemia time, h	3.8 (1.2)	3.7 (1.2)	0.12	3.7 (1.1)	3.7 (1.2)	0.03
Serum bilirubin level, mg/dL	1.5 (2.6)	1.4 (3.1)	0.02	1.3 (2.4)	1.4 (3.1)	0.05
Serum creatinine level, mg/dL	0.6 (1.1)	0.4 (0.7)	0.17	0.5 (0.8)	0.5 (0.9)	0.01
ECMO at transplantation, %	12	10	0.08	9	10	0.02
Mechanical ventilation at transplantation, %	38	33	0.10	31	33	0.05
Transplantation year	2007 (8)	2009 (7)	0.37	2009 (8)	2009 (8)	0.01
Recipient age, y	0.3 (0.3)	0.4 (0.3)	0.39	0.4 (0.3)	0.4 (0.3)	0.02
Diagnosis DCM, %	27	32	0.12	33	31	0.04
Diagnosis CHD, %	64	61		60	62	
Diagnosis other, %	9	7		7	7	

CHD, congenital heart disease; DCM, dilated cardiomyopathy; DRWR, donor-to-recipient weight ratio; ECMO, extracorporeal membrane oxygenation; SMD, standardized mean difference.

TABLE 6

Baseline Characteristics of the Most Oversized Infants

Characteristic	Before Matching			After Matching		
	DRWR 2.5–5.0 (n = 151)	DRWR 1.97–2.5 (n = 298)	SMD	DRWR 2.5–5.0 (n = 298.4)	DRWR 1.97–2.5 (n = 150.9)	SMD
Ischemia time, h	4.1 (1.4)	3.8 (1.2)	0.20	3.9 (1.3)	3.9 (1.2)	0.02
Serum bilirubin level, mg/dL	2.6 (5.6)	2.1 (3.9)	0.11	2.2 (5.0)	2.3 (4.3)	0.03
Serum creatinine level, mg/dL	0.5 (0.9)	0.4 (0.2)	0.15	2.2 (5.0)	2.3 (4.3)	0.07
ECMO at transplantation, %	7	9	0.05	8	8	0.004
Mechanical ventilation at transplantation, %	36	40	0.08	39	38	0.01
Transplantation year	2005 (8)	2007 (8)	0.22	2006 (9)	2006 (8)	0.01
Recipient age, y	0.3 (0.2)	0.4 (0.3)	0.31	0.3 (0.2)	0.4 (0.3)	0.02
Diagnosis DCM, %	23	31	0.24	29	28	0.02
Diagnosis CHD, %	70	59		62	63	
Diagnosis other, %	7	10		9	9	

CHD, congenital heart disease; DCM, dilated cardiomyopathy; DRWR, donor-to-recipient weight ratio; ECMO, extracorporeal membrane oxygenation; SMD, standardized mean difference.

TABLE 7

One-Year Graft Survival Rates by DRWR Range

DRWR	1-Year Graft Survival Rate (%)
>2.5	75.7
1.97–5.0 (Q5)	82.0
1.58–1.97 (Q4)	87.4
1.29–1.58 (Q3)	88.5
1.04–1.29 (Q2)	81.8
0.37–1.04 (Q1)	81.5
<0.8	70.2

DRWR, donor-to-recipient weight ratio.