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Early renal failure after primary thoracic organ transplantation

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Dialysis;
Heart transplant;
Lung transplant;
Mortality;
Risk factors

This special report from the International Society for Heart and Lung Transplantation (ISHLT) International Thoracic Organ Transplant (TTX) Registry is focused on incidence, risk factors, and mortality risk associated with early posttransplant dialysis among adult and pediatric heart transplant (HT) and lung transplant (LT) recipients. Renal failure including dialysis is a known risk factor for mortality in patients undergoing nontransplant thoracic surgery,[1] and several studies have raised concern among transplant recipients.[2–12] The report includes selected figures and tables from the International Thoracic Organ Transplant Registry's online eslide set available at https://ishltregistries.org/registries/slides.asp. Some slides will be referenced and not shown due to limited space in this report.

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Statistical methods

Data collection, conventions, and statistical methods

The ISHLT TTX Registry was developed using data submitted to the Registry from national and multinational transplant collectives as well as individual transplant centers. Since its inception, the Registry has captured data for transplants performed through June 2018 from 481 HT centers, 260 LT centers, and 184 centers that perform combined heart–lung transplantation. The Registry paused its data submissions due to privacy laws enacted in Europe, specifically the General Data Protection Regulations (GDPR) in 2018, and is presently in the process of relaunching. The Registry required submission of core donor, recipient, and transplant procedure variables at baseline (i.e., at the time of transplantation) and at annual follow-up. Variables that were required have low rates of missingness, while those that depended on voluntary reporting may be more incomplete. The Registry used various quality control

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measures to ensure acceptable data quality and completeness before including data for analyses. Detailed spreadsheets of the data elements collected in the Registry through early 2019 are available at the ISHLT Registry website: (https://www.ishlt.org/education-and-publications/resource/data-fields-look-up-tables-forms).

The cohorts for this special report have been previously described,[13–16] and included all recipients who underwent primary HT or LT between January 1994 and June 2018, with follow-up data in the ISHLT Registry until April 19, 2019. Multi-organ transplants were excluded except for 131 HT/LTs in the pediatric LT group, given the rare occurrence of single-organ LT in this population. Early posttransplant dialysis (or early dialysis) was defined as peritoneal or hemodialysis occurring after transplant surgery anytime between surgical intensive care unit admission and hospital discharge. Prior dialysis was defined as dialysis at the time of transplant without specification of chronicity. De novo dialysis was defined as dialysis occurring after transplant with no prior usage immediately before transplant. Estimated glomerular filtration rate (eGFR) was calculated using the 2021 CKD-EPI formula without race variable[17] for adults and modified Schwartz formula[18] for pediatric transplant recipients. Severe renal dysfunction at follow-up was defined as need for dialysis, renal transplant, or serum creatine >2.5 mg/dl. Baseline characteristics of those with and without early posttransplant dialysis were compared using chi-square tests (for categorical variables) and Wilcoxon's rank-sum tests (for continuous variables). Percentages of recipients on dialysis and/or severe renal dysfunction were calculated at 1 year for recipients with available data. These percentages were compared among early dialysis vs no early dialysis groups using chi-square tests. Multivariable logistic regression models were utilized to determine risk factors for early posttransplant dialysis for each age and organ combination. Patient survival within 1 year of transplant was estimated using the Kaplan–Meier method for transplants performed between January 1994 and June 2017, allowing for 1-year follow-up submission. Records with follow-up beyond 1 year were administratively censored at 1 year. Survival was stratified by early posttransplant dialysis status and by dialysis usage and compared across stratification groups using log-rank tests.

Analytical conventions

Previous Registry reports provided more detail regarding specific donor and recipient characteristics and outcomes.[19–22] For time-to-event analyses, time was censored at the most recent annual follow-up or at retransplantation. We truncated time-to-event graphs (e.g., survival graphs) when the number of individuals at risk was less than 10. As the ISHLT TTX Registry does not have the exact time to event for many morbidity outcomes, the 1-year dialysis or severe renal dysfunction outcome was restricted to recipients who survived 1 year.

Adult and pediatric HT recipients

Baseline characteristics

The current Registry analysis included 50,131 adults and 7,969 pediatric recipients who underwent primary single deceased donor HT between January 1994 and June 2018. The study cohort for this analysis had a high percentage of transplant recipients from North America compared to Europe and other regions. Baseline characteristics at the time of transplant were compared between patients who did and did not require post-HT dialysis during the index hospitalization. Early posttransplant dialysis occurred in 9.9% of adult and 6.3% of pediatric recipients (eSlide 4). Variables associated with early posttransplant dialysis included higher usage of extracorporeal membrane oxygenation (ECMO), mechanical ventilation, pretransplant dialysis at time of transplantation, prior cardiac surgery, longer ischemic times (Table 1, eSlides 6–7), as well as higher usage of mechanical circulatory support (MCS; Figure 1, eSlides 10; Figure 2, eSlide 13). Although the differences in recipient age by early dialysis were statistically significant for adult and pediatric HT recipients, the differences were not clinically meaningful. No statistically significant differences were seen in sex and body mass index (BMI) distribution compared with the nondialysis group in pediatric HT (Table 1, eSlides 6–7). Most adult HT recipients had ischemic and nonischemic cardiomyopathy as the underlying cardiac disease. The early dialysis group was more likely than the nondialysis group to have all other types of underlying heart disease (eSlide 8). Among pediatric HT recipients, the dialysis group was more likely to have congenital heart disease with prior surgery than the nondialysis group (55.8% vs 33.9%; eSlide 11). Adult and pediatric HT recipients requiring early dialysis postoperatively had lower eGFR at time of transplant than the nondialysis group; however, only 11.8% of adult and 21% of pediatrics recipients requiring posttransplant dialysis were already on dialysis at the time of HT surgery (Table 1, eSlides 6–7). Among adult HT recipients, there were significant differences in donor characteristics between dialysis and nondialysis groups. Dialysis group tended to have older donors (median age 34 vs 30 years of age, $p < 0.0001$), slightly more female donors (32.1% vs 29.4%, $p = 0.0001$), and higher frequency of transplants with undersized donor hearts. Among pediatric HT recipients, there were no significant differences in the distribution of donor age, sex, or donor–recipient weight ratio between early dialysis and nondialysis groups.

Risk factors for early posttransplant dialysis

In a multivariable analysis, several recipient and donor factors at the time of transplant were associated with higher risk of early dialysis. Categorical variables associated with higher risk of post-HT dialysis in adult recipients were underlying heart disease (congenital heart disease, restrictive cardiomyopathy, hypertrophic cardiomyopathy, and valvular heart disease compared to nonischemic cardiomyopathy), mechanical ventilator support, MCS support, and ECMO support (Figure 3, eSlide

Table 1 Select Baseline Characteristics Stratified by Early Posttransplant Dialysis for Adult and Pediatric Heart Transplants Performed During January 1, 1994, to June 30, 2018

	Adult heart			Pediatric heart		
Recipient and donor characteristics	No dialysis (n = 45,155)	Dialysis (n = 4,976)	p value[a]	No dialysis (n = 7,468)	Dialysis (n = 501)	p value[a]
Age (years)	55 (27-68)	56 (28-68)	< 0.0001	5 (0.1-17)	5 (0.1-17)	0.0186
Male	75.6%	77.5%	0.0036	55.8%	57.7%	0.407
BMI (kg/m^2)	26.2 (19.5-34.3)	26.9 (19.7-35.0)	< 0.0001	16.4 (12.4-27.1)	16.5 (12.1-26.2)	0.8564
Pretransplant ECMO	0.5%	1.8%	< 0.0001	5.6%	23.4%	< 0.0001
Pretransplant ventilator	2.0%	6.4%	< 0.0001	16.0%	41.7%	< 0.0001
Pretransplant diabetes	22.8%	27.9%	< 0.0001	0.4%	1.0%	0.0523
Pretransplant dialysis	1.4%	11.8%	< 0.0001	1.4%	21.0%	< 0.0001
eGFR[b] (ml/min/1.73 m^2)	69.7 (33.9-115.1)	55.7 (14.0-107.8)	< 0.0001	85.7 (31.2-163.7)	57.8 (14.0-140.4)	< 0.0001
Prior cardiac surgery	45.4%	58.6%	< 0.0001	46.1%	67.5%	< 0.0001
Donor age (years)	30 (16-53)	34 (17-56)	< 0.0001	6 (0-30)	6 (0-38)	0.1599
Donor male	70.6%	67.9%	0.0001	58.9%	57.9%	0.6465
Ischemic time (hours)	3.1 (1.5-4.8)	3.3 (1.6-5.3)	< 0.0001	3.5 (1.6-5.6)	3.9 (2.0-6.5)	< 0.0001
Predicted heart mass difference (%)	0.5 (−23.2 to 37.0)	−0.9 (−24.6 to 34.3)	< 0.0001	N/A	N/A	N/A
Donor–recipient weight ratio	N/A	N/A		1.3 (0.8-2.3)	1.3 (0.8-2.4)	0.4703
Transplant era			< 0.0001			0.4140
1994-2002	15,995 (35.4%)	1,315 (26.4%)		2,125 (28.5%)	145 (28.9%)	
2003-2011	15,546 (34.4%)	1,687 (33.9%)		2,803 (37.5%)	174 (34.7%)	
2012-2018	13,614 (30.1%)	1,974 (39.7%)		2,540 (34.0%)	182 (36.3%)	
Region of transplant center			< 0.0001			< 0.0001
Europe	2,248 (5.0%)	410 (8.2%)		145 (1.9%)	9 (1.8%)	
North America	42,003 (93.0%)	4,340 (87.2%)		7,231 (96.8%)	472 (94.2%)	
Other	904 (2.0%)	226 (4.5%)		92 (1.2%)	20 (4.0%)	

BMI, body mass index; ECMO, extracorporeal membrane oxygenation;eGFR, estimated glomerular filtration rate; N/A, not available.
Definition: Early dialysis included dialysis that occurred posttransplantation from time to surgical intensive care until hospital discharge.
Summary statistics excluded transplants with missing data.
Continuous factors are expressed as median (5th to 95th percentiles).
[a]p-value was calculated using a chi-square (for categorical variables) or Wilcoxon's rank-sum test (for categorical variables).
[b]GFR was estimated using the CKD-EPI formula for adults and modified Schwartz formula for pediatrics.

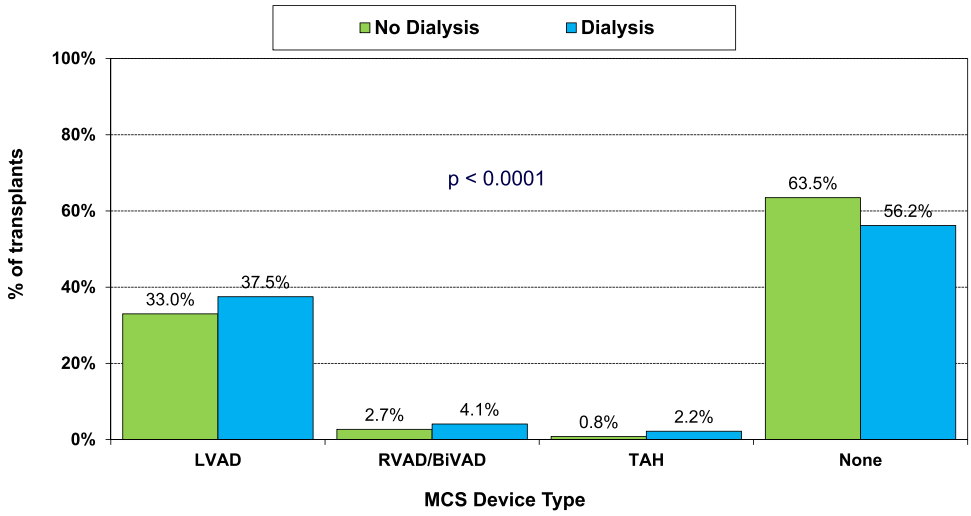

Figure 1 Adult HT: MCS device type at the time of HT stratified by early posttransplant dialysis (transplants: January 2000 to June 2018). BiVAD, biventricular assist device; HT, heart transplant; LVAD, left ventricular assist device; MCS, mechanical circulatory support; RVAD, right ventricular assist device; TAH, total artifical heart.

34). Renal dysfunction at the time of transplant was the most impactful risk factor, with a progressively higher risk in patients with lower eGFR (Figure 4, eSlide 39). For example, patients with eGFR of 20 ml/min/1.73 m^2 and 45 ml/min/1.73 m^2 were 5 and 2 times more likely, respectively, to need early dialysis compared to those with median eGFR of 69 ml/min/1.73 m^2.

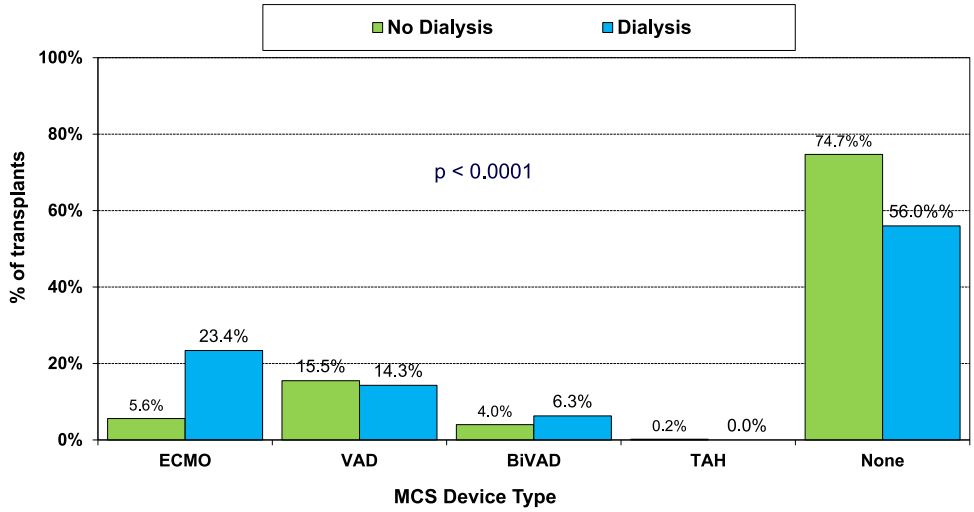

Figure 2 Pediatric HT: MCS device type at time of HT stratified by early posttransplant dialysis (transplants: January 2000 to June 2018). BiVAD, biventricular assist device; ECMO, extracorporeal membrane oxygenation; HT, heart transplant; MCS, mechanical circulatory support; TAH, total artifical heart; VAD, ventricular assist device.

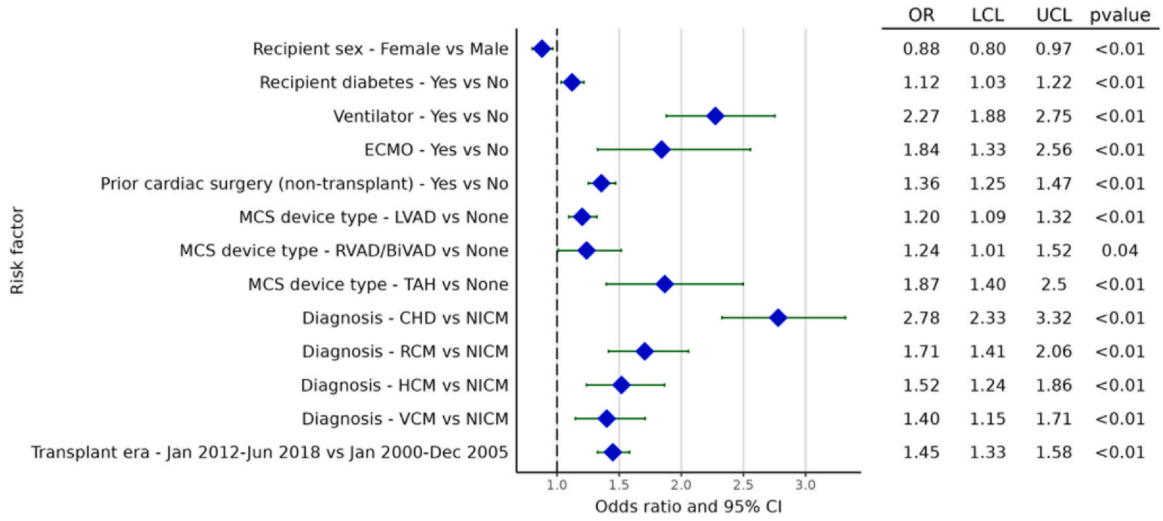

Figure 3 Adult HT: statistically significant categorical risk factors for early posttransplant dialysis with 95% confidence limits (transplants: January 2000 to June 2018). BiVAD, biventricular assist device; CHD, congenital heart disease; ECMO, extracorporeal membrane oxygenation; HCM, hypertrophic cardiomyopathy; HT, heart transplant; LCL, lower confidence limit; LVAD, left ventricular assist device; MCS, mechanical circulatory support; NICM, non ischemic cardiomyopathy; OR, odds ratio; RCM, restrictive cardiomyopathy; RVAD, right ventricular assist device; TAH, total artifical heart; UCL, upper confidence limit; VCM, valvular cardiomyopathy.

Older donor age was also a significant risk factor; for example, donor age of 60 years was associated with 1.7 times higher risk of early dialysis compared to median donor age of 31 years old (eSlide 40). Other significant factors associated with increased risk of early dialysis included male sex, prior cardiac surgery, recipient diabetes mellitus, younger recipient age, obesity (e.g., patients with BMI of 35 kg/m^2 had 1.3 times higher risk than those with median BMI of 27 kg/m^2), hyperbilirubinemia, longer ischemic time, and undersized donor heart based on predicted heart mass (Figure 3, eSlides 34, 36, 37, 38, 41, 42).

In pediatric HT recipients, categorical variables associated with increased risk of early dialysis included recipient diagnosis of congenital heart disease (with or without prior surgery) compared to dilated cardiomyopathy, ventilator support at transplant, and ECMO support at transplant (Figure 5, eSlide 44). Similar to adult HT recipients, lower eGFR at the time of transplant was associated with progressively higher risk of early dialysis (Figure 6, eSlide 46). For example, children with eGFR of 20 ml/min/1.73 m^2 and 45 ml/min/1.73 m^2 were 8.4 and 3.4 times more likely, respectively, to need dialysis compared to those with median eGFR of 87 ml/min/1.73 m^2. Older donor age and longer ischemic time were associated with higher risks of early dialysis, whereas using slightly oversized donors seemed to have a protective effect (eSlides 47–49).

One-year incidence of dialysis and severe renal dysfunction

Among adult and pediatric HT recipients with 1-year data available for analysis, 18.5% of adult and 14.2% of pediatric HT recipients with early posttransplant dialysis were on dialysis 1 year after HT compared to < 1% adult and pediatric HT recipients in the nondialysis group (Figure 7A,

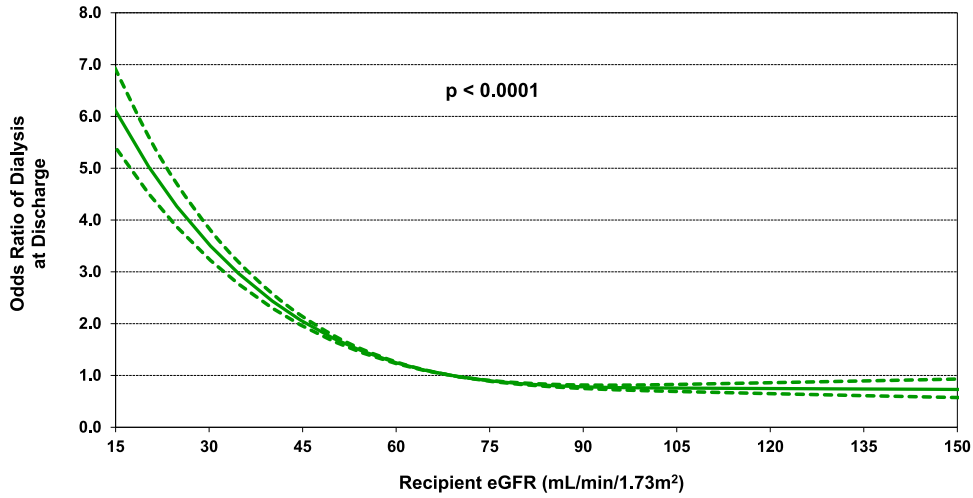

Figure 4 Adult HT: adjusted odds ratio of early posttransplant dialysis based on recipient eGFR at transplant with 95% confidence limits (transplants: January 2000 to June 2018). eGFR, estimated glomerular filtration rate; HT, heart transplant.

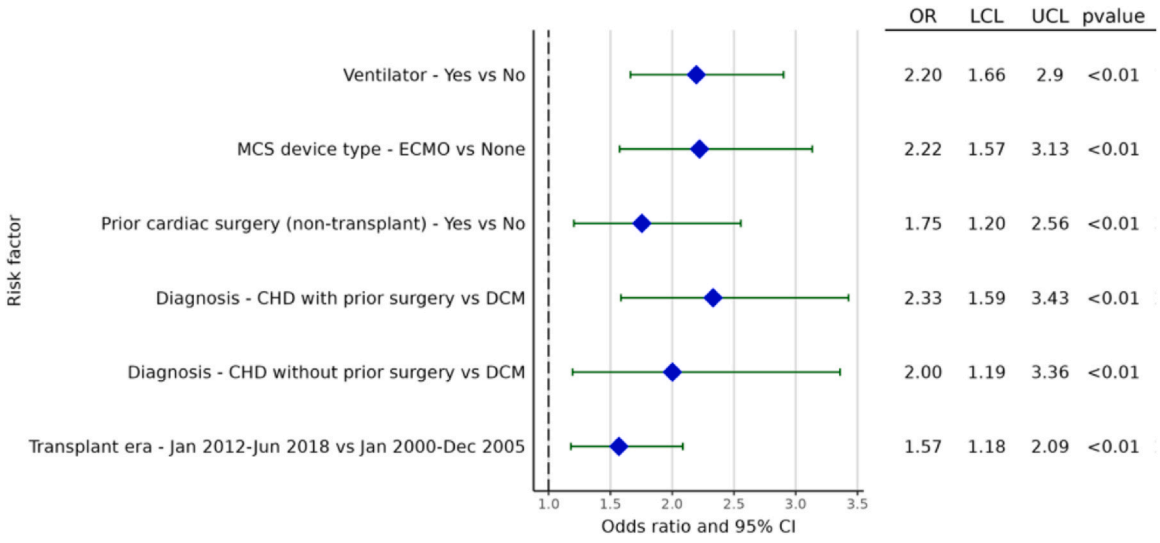

Figure 5 Pediatric HT: statistically significant categorical risk factors for early posttransplant dialysis with 95% confidence limits (transplants: January 2000 to June 2018). CHD, congenital heart disease; DCM, dilated cardiomyopathy; ECMO, extracorporeal membrane oxygenation; HT, heart transplant; LCL, lower confidence limit; MCS, mechanical circulatory support; OR, odds ratio; UCL, upper confidence limit.

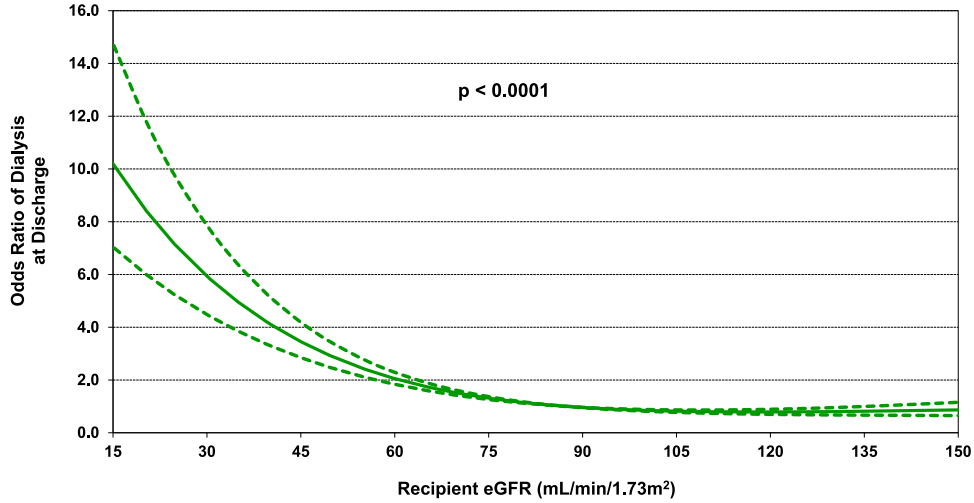

Figure 6 Pediatric HT: adjusted odds ratio of early posttransplant dialysis based on recipient eGFR at transplant with 95% confidence limits (transplants: January 2000 to June 2018). eGFR, Estimated glomerular filtration rate; HT, heart transplant.

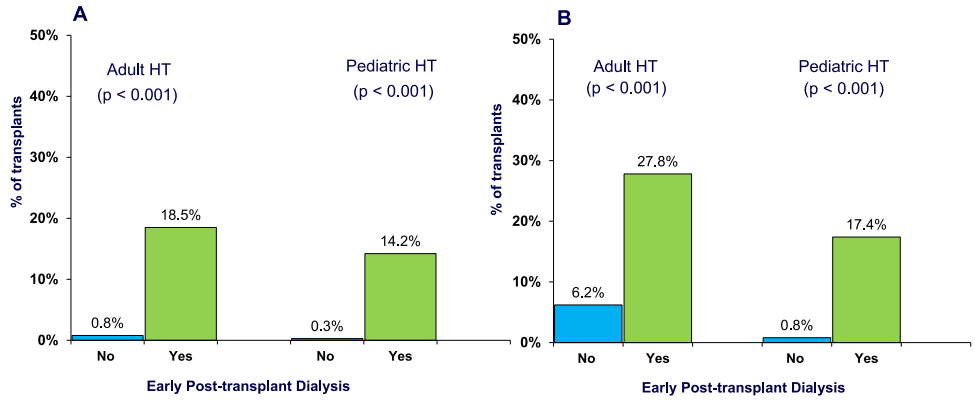

Figure 7 HT: incidence of (A) dialysis within 1 year and (B) severe renal dysfunction within 1 year (transplants: January 2000 to June 2017). HT, heart transplant.

eSlide 61). Severe renal dysfunction was present in 27.8% of adult and 17.4% of pediatric HT recipients in the early dialysis group and 6.2% of adult and 0.8% of pediatric recipients in the nondialysis group at 1 year after transplant (Figure 7B, eSlide 61).

Patient survival (freedom from death)

There were significant differences in 1-year patient survival (freedom from death) in adult and pediatric HT recipients who developed early posttransplant dialysis compared to those who did not. Among adult HT recipients (Figure 8, eSlide 64), early dialysis was associated with lower survival at all times up to 1 year when compared to the nondialysis group (77.5% vs 96.5% at 30 days, 69.2% vs 95.7% at 60 days and 56.4% vs 91.7% at 1 year). Similarly, pediatric HT recipients with early dialysis had lower survival when compared to the nondialysis group (75.1% vs 96.8% at 30 days survival, 63.0% vs 96.0% at 60 days survival, 46.0% vs 91.9% at 1 year; Figure 9, eSlide 65). When comparing patient survival based on dialysis pre- (regardless of early posttransplant dialysis usage) vs early dialysis posttransplantation, the de novo early dialysis posttransplant group had the lowest survival compared to nondialysis and predialysis groups (Figures 10 and 11, eSlides 66–67).

Adult and pediatric LT recipients

Baseline characteristics

The current Registry report included 34,510 adult and 1,185 pediatric LT recipients who underwent primary single deceased donor LT between January 1994 and June 2018. In the pediatric LT cohort only, 131 dual-organ HT/LT were included. Baseline characteristics at the time of transplant were separated into renal categories based on usage of postoperative dialysis during index LT hospitalization. Early renal failure requiring dialysis occurred posttransplantation in 6.1% of adult and 5.6% of pediatric LT recipients (eSlide 4) and was associated with need for ECMO support, mechanical ventilation, pretransplant dialysis, lower eGFR, and higher pulmonary capillary wedge pressures at the time of transplant (Table 2, eSlides 14–15).

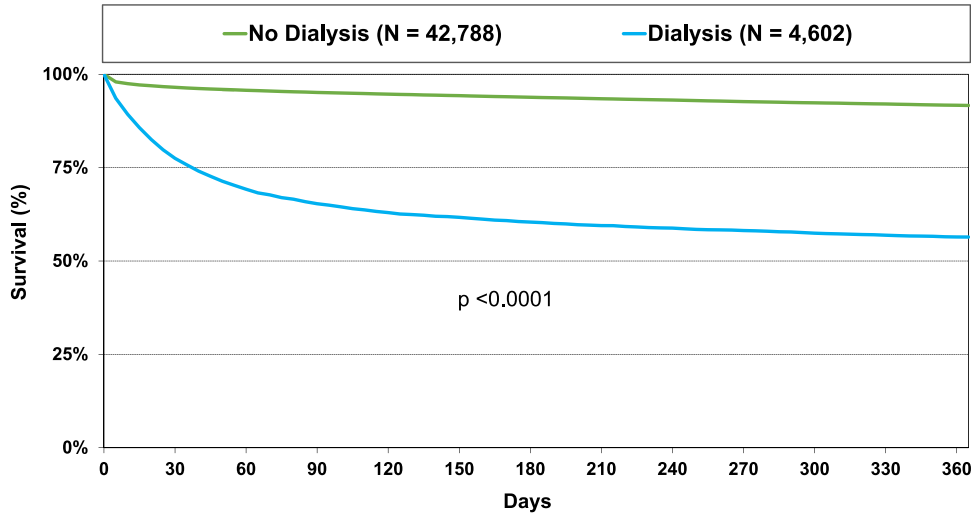

Figure 8 Adult HT: Kaplan–Meier survival stratified by early posttransplant dialysis (transplants: January 1994 to June 2017). HT, heart transplant.

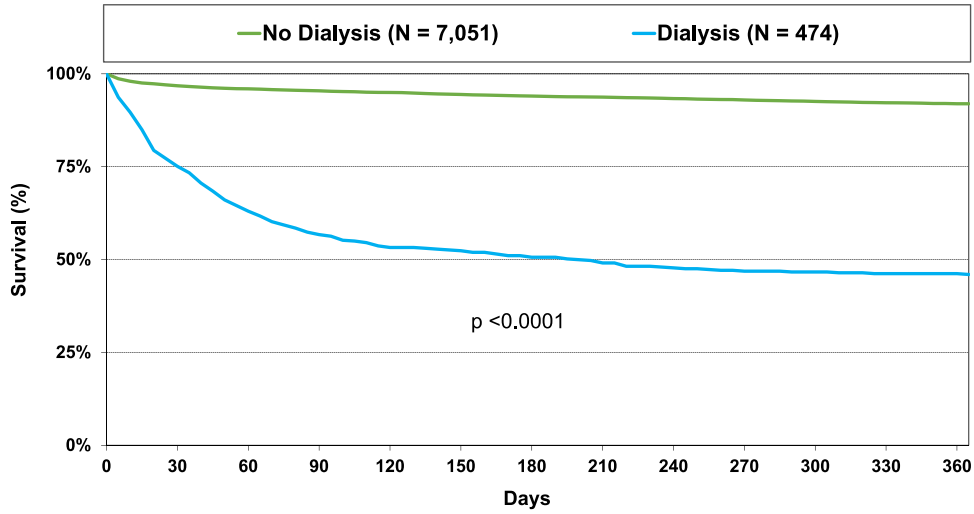

Figure 9 Pediatric HT: Kaplan–Meier survival stratified by early posttransplant dialysis (transplants: January 1994 to June 2017). HT, heart transplant.

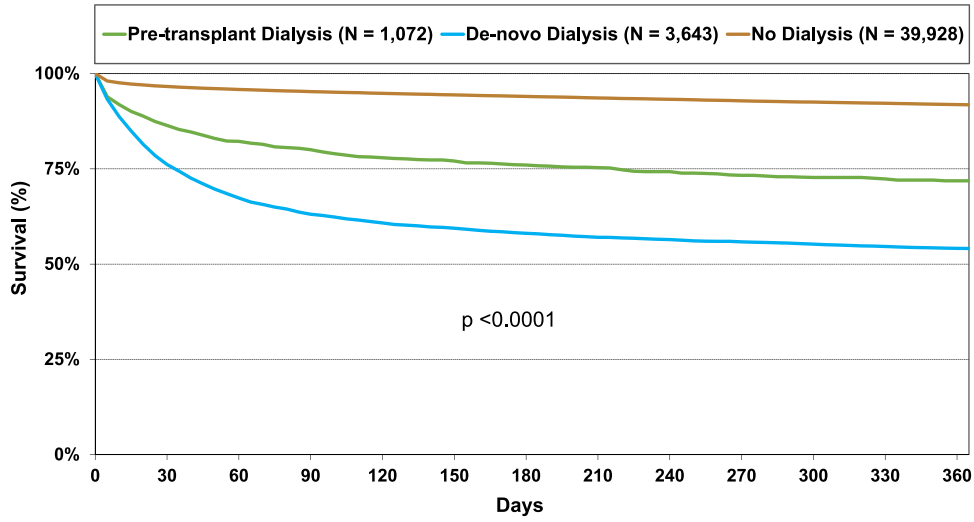

Figure 10 Adult HT: Kaplan–Meier survival stratified by usage of dialysis (pretransplant dialysis, de novo posttransplant dialysis, or no dialysis; transplants: January 1994 to June 2017). HT, heart transplant.

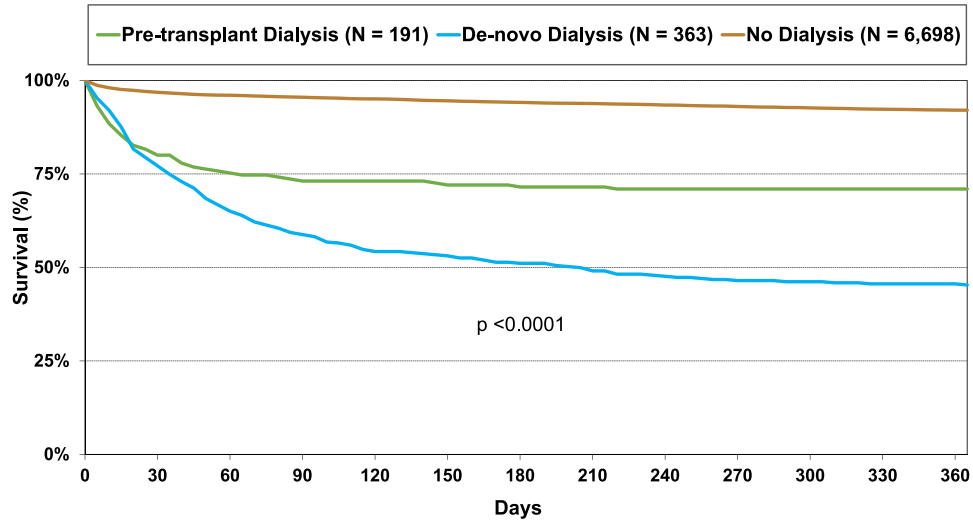

Figure 11 Pediatric HT: Kaplan–Meier survival stratified by usage of dialysis (pretransplant dialysis, de novo posttransplant dialysis, or no dialysis; transplants: January 1994 to June 2017). HT, heart transplant.

Table 2 Select Baseline Characteristics Stratified by Early Posttransplant Dialysis for Adult and Pediatric Lung Transplants Performed During January 1, 1994, to June 30, 2018

	Adult lung			Pediatric lung[a]		
Recipient and donor characteristics	No dialysis ($n = 32,412$)	Dialysis ($n = 2,098$)	p-value[b]	No dialysis ($n = 1,119$)	Dialysis ($n = 66$)	p-value[b]
Age (years)	57 (25-69)	56 (25-69)	< 0.0001	13 (0-17)	12 (0-17)	0.0341
Male	56.6%	57.3%	0.5492	42.7%	36.4%	0.3101
BMI (kg/m²)	24.8 (17.6-32.2)	25.6 (17.8-33.2)	< 0.0001	17.0 (13.1-24.3)	17.3 (12.0-24.8)	0.5858
Pretransplant ECMO	1.9%	8.5%	< 0.0001	3.7%	22.7%	< 0.0001
Pretransplant ventilator	4.2%	11.6%	< 0.0001	16.2%	40.6%	< 0.0001
Pretransplant diabetes	15.3%	19.9%	< 0.0001	14.9%	12.5%	0.5949
Pretransplant dialysis	0.3%	3.7%	< 0.0001	0.4%	7.7%	< 0.0001
eGFR[c] (ml/min/1.73 m^2)	98.3 (57.9-129.6)	93.4 (40.5-128.5)	< 0.0001	121.4 (60.4-219.4)	93.2 (14.0-293.0)	0.0006
Prior lung surgery	17.5%	18.9%	0.135	17.3%	34.5%	0.001
PCW (mm/Hg)	25.0 (14.0-49.0)	28.0 (15.0-62.0)	< 0.0001	11.0 (4.0-28.0)	14.0 (7.0-46.0)	0.0084
Donor age (years)	32 (16-59)	35 (17-61)	< 0.0001	12 (0-43)	7 (0-48)	0.1329
Donor male	60.30%	56.20%	0.0002	52.00%	40.90%	0.0795
Ischemic time (hours)	4.8 (2.4-7.4)	5.3 (2.6-7.8)	< 0.0001	5.3 (2.9-7.6)	5.7 (3.1-7.7)	0.0663
Donor–recipient height ratio	1.0 (0.9-1.1)	1.0 (0.9-1.1)	< 0.0001	1.0 (0.9-1.2)	1.0 (0.9-1.3)	0.4278
Transplant era						
1994–2002	7025 (21.7%)	403 (19.2%)	< 0.0001	389 (34.8%)	16 (24.2%)	0.2117
2003–2011	12,410 (38.3%)	753 (35.9%)		443 (39.6%)	31 (47.0%)	
2012–2018	12,977 (40.0%)	942 (44.9%)		287 (25.6%)	19 (28.8%)	
Region of transplant center			< 0.0001			0.0057
Europe	1,045 (3.2%)	100 (4.8%)		28 (2.5%)	6 (9.1%)	
North America	30,882 (95.3%)	1,920 (91.5%)		1,079 (96.4%)	60 (90.9%)	
Other	485 (1.5%)	78 (3.7%)		12 (1.1%)	0 (0.0%)	

BMI, body mass index; ECMO, extracorporeal membrane oxygenation; eGFR, estimated glomerular filtration rate.
Definition: Early dialysis included dialysis that occurred posttransplantation from time to surgical intensive care until hospital discharge.
Summary statistics excluded transplants with missing data.
Continuous factors are expressed as median (5th to 95th percentiles).
[a]Pediatric lung numbers included pediatric heart/lung transplants.
[b]p-value was calculated using a chi-square (for categorical variables) or Wilcoxon's rank-sum test (for categorical variables).
[c]GFR was estimated using the CKD-EPI formula for adults and modified Schwartz formula for pediatrics.

There were no clinically meaningful differences in recipient age among adult and pediatric LT recipients by early dialysis. No statistically significant differences were seen in sex distribution for adult and pediatric LT by early posttransplant dialysis (Table 2, eSlides 14–15). Early dialysis in adult LT was also associated with recipient diabetes mellitus, older donors, and longer ischemic times and in pediatric LT recipients with prior lung surgery. LT recipients with idiopathic pulmonary arterial hypertension (IPAH) and "other" causes of lung disease were more likely to develop posttransplant dialysis compared to COPD (eSlide 16). COPD and IPF were more common underlying lung diseases in single LT compared to double LT. When data were further stratified by transplant procedure, the differences between dialysis and nondialysis groups were similar to those found for the total LT cohort (Figure 12, eSlide 17). In double LT, IPF, IPAH, and "other" causes were more likely to be in the early dialysis group, similar to those findings in the total LT cohort apart from IPF. Among pediatric LT recipients, the majority had CF and pulmonary vascular disease (PVD) as the underlying disease with the dialysis group more likely to have PVD (Figure 13, eSlide 19). Undersizing LT based on donor/recipient height ratio was more common for the dialysis group compared to the nondialysis group. For pediatric and adult LT, size mismatching was more common in pediatric LT recipients (eSlides 18, 20).

Early posttransplant dialysis risk factors

Abnormal renal function at the time of transplant was the strongest risk factor for early dialysis with higher risk seen in lower eGFR. For example, adult LT patients with eGFR of 30 ml/min/1.73 m^2 and 45 ml/min/1.73 m^2 were 3.5 and 2.6 times more likely, respectively, to have early dialysis compared to those with baseline eGFR of 98 ml/min/1.73 m^2 (Figure 17, eSlide 55). Several other recipient, donor, and surgical variables were associated with early post-LT dialysis in the multivariable models. Recipient factors associated with early dialysis for adult LT recipients included the underlying lung disease (IPAH, CF, and "other" diagnoses compared to COPD), usage of ECMO, mechanical ventilator, higher BMI, and higher recipient bilirubin at the time of transplant (Figure 14, eSlide 51; Figure 15, eSlide 53; Figure 16, eSlide 54). Other significant risk factors included recipient sex, recipient diabetes mellitus, donor age, and ischemic time (Figure 14,

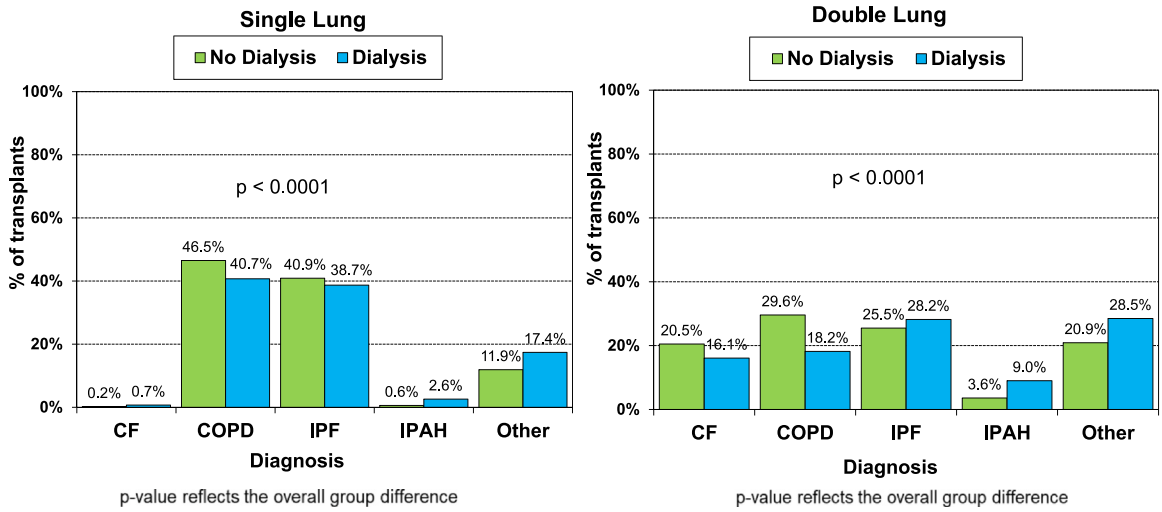

Figure 12 Adult LT: underlying lung disease stratified by single vs double lung transplant and usage of early posttransplant dialysis (transplants: January 1994 to June 2018). CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease; IPAH, idiopathic pulmonary arterial hypertension; IPF, idiopathic pulmonary fibrosis; LT, lung transfer.

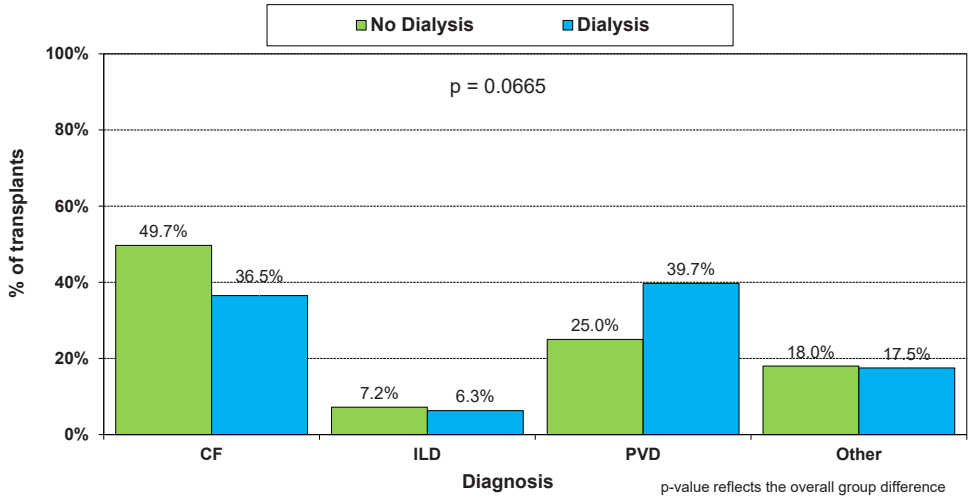

Figure 13 Pediatric LT: underlying lung disease stratified by usage of early posttransplant dialysis (transplants: January 1994 to June 2018). CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease; IPAH, idiopathic pulmonary arterial hypertension; IPF, idiopathic pulmonary fibrosis; LT, lung transfer.

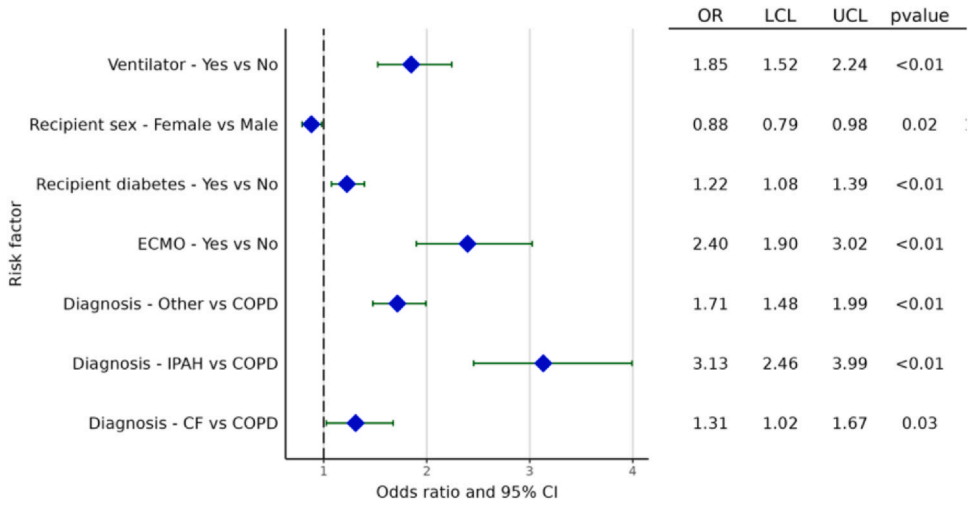

Figure 14 Adult LT: statistically significant categorical risk factors for early posttransplant dialysis with 95% confidence limits (transplants: January 2000 to June 2018). CF, cystic fibrosis; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; IPAH, Idiopathic pulmonary arterial hypertension; LCL, lower confidence limit; LT, lung transplant; OR, odds ratio; UCL, upper confidence limit.

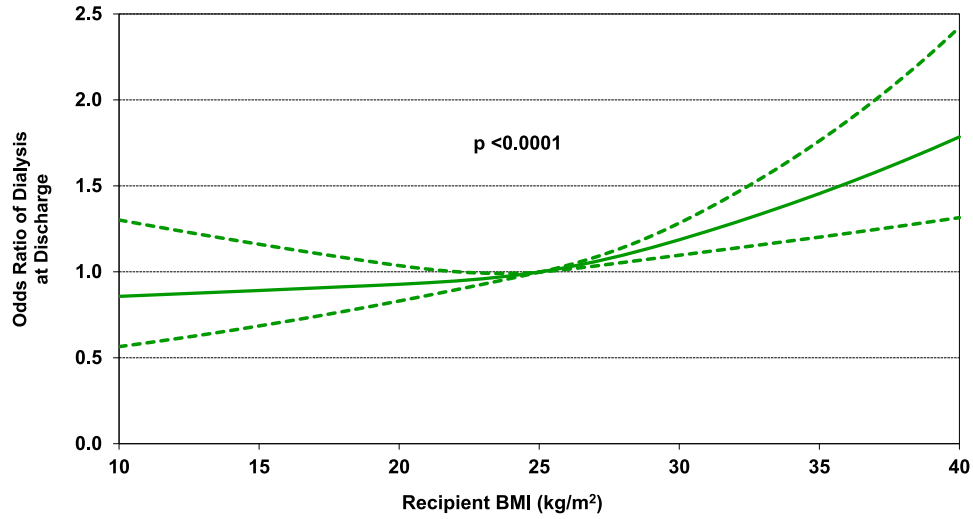

Figure 15 Adult LT: adjusted odds ratio of early posttransplant dialysis based on recipient BMI with 95% confidence limits (transplants: January 2000 to June 2018). BMI, body mass index; LT, lung transplant.

eSlides 51, 56–57). Female patients had a decreased risk of early dialysis, while older donors and longer ischemic time were associated with an increased risk. Among pediatric LT recipients, ECMO was the only risk factor for early dialysis, but this had wide confidence intervals due to the small cohort size (Figure 18, eSlide 59).

One-year incidence of dialysis and severe renal dysfunction

Among adult and pediatric LT recipients with 1-year data available, 22.7% of adult and 5.3% of pediatric LT recipients with early posttransplant dialysis were on dialysis at 1 year after LT compared to 1.3% of adults and 0.7% of pediatric recipients in the nondialysis group (Figure 19A-19B, eSlide 62). Severe renal dysfunction was present in 31.1% of adults and 31.6% of pediatric LT recipients in the early dialysis group compared to 6.0% of adult and 2.1% of pediatric LT recipients in the nondialysis group at 1 year after LT.

Patient survival (freedom from death)

There were differences in patient survival (freedom from death) within 1 year in adult and pediatric LT recipients based on usage of early posttransplant dialysis (Figure 20, eSlide 68; Figure 21, eSlide 69). Among adult LT recipients, early dialysis was associated with much higher mortality when compared to the nondialysis group, with 50% vs 8% mortality at 180 days and 57.6% vs 13.0% mortality at 1 year. These differences were apparent early after LT with 30-day patient survival of 76.0% in dialysis vs 96.8% in nondialysis groups and a 60-day survival of 64.7% in dialysis vs 95.5% in the nondialysis groups. Among pediatric LT recipients, early dialysis was also associated with significantly lower survival. The dialysis vs

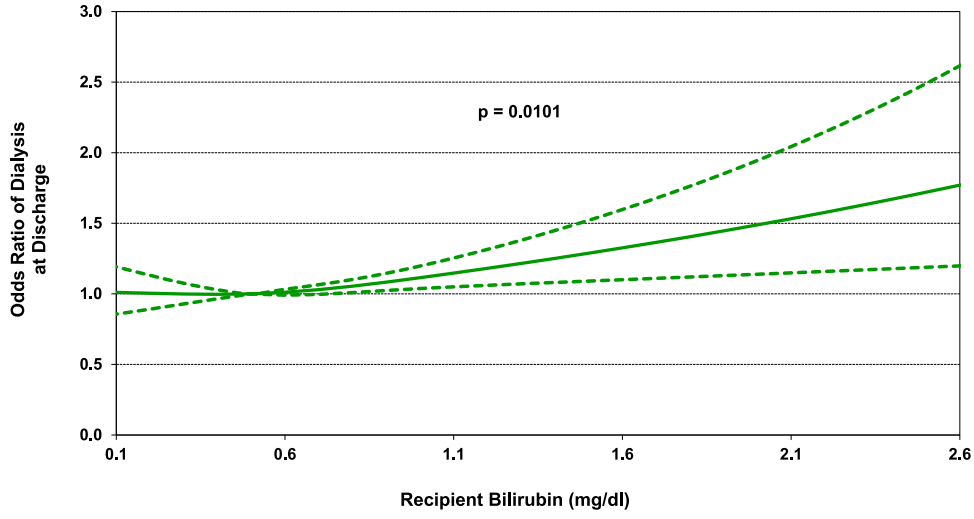

Figure 16 Adult LT: adjusted odds ratio of early posttransplant dialysis based on recipient bilirubin with 95% confidence limits (transplants: January 2000 to June 2018). LT, lung transfer.

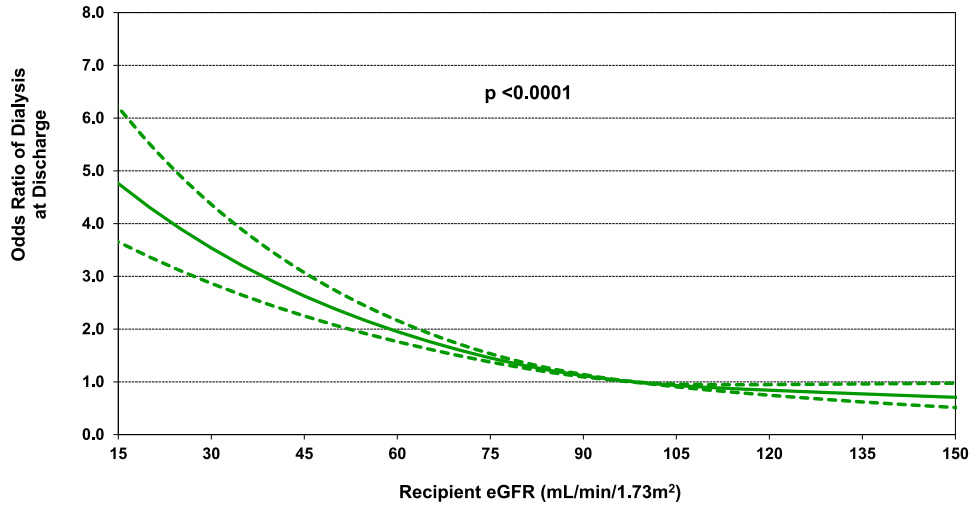

Figure 17 Adult LT: adjusted odds ratio of early posttransplant dialysis based on recipient eGFR at transplant with 95% confidence limits (transplants: January 1994 to June 2018). eGFR, estimated glomerular filtration rate; LT, lung transfer.

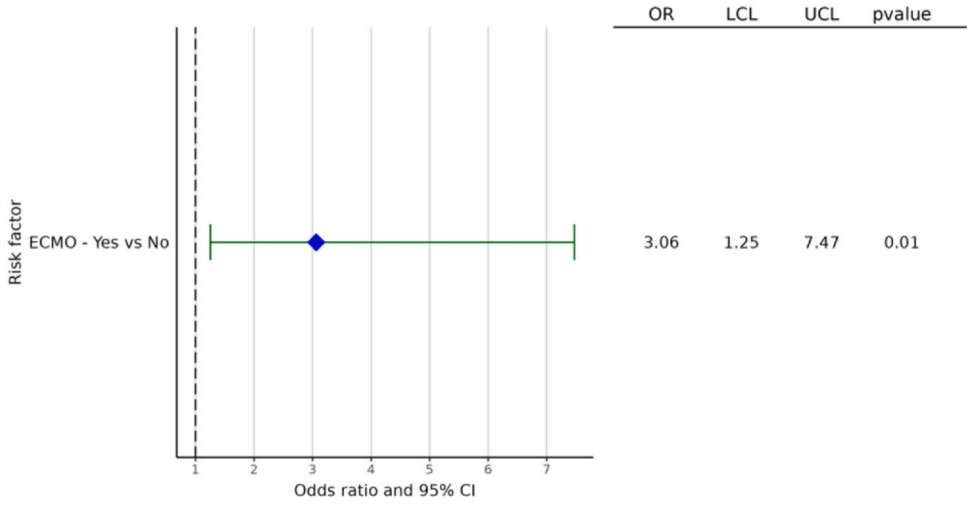

Figure 18 Pediatric LT: statistically significant categorical risk factors for early posttransplant dialysis with 95% confidence limits (transplants: January 2000 to June 2018). CI, confidence interval; ECMO, extracorporeal membrane oxygenation; LCL, lower confidence limit; LT, lung transplant; OR, odds ratio; UCL, upper confidence limit.

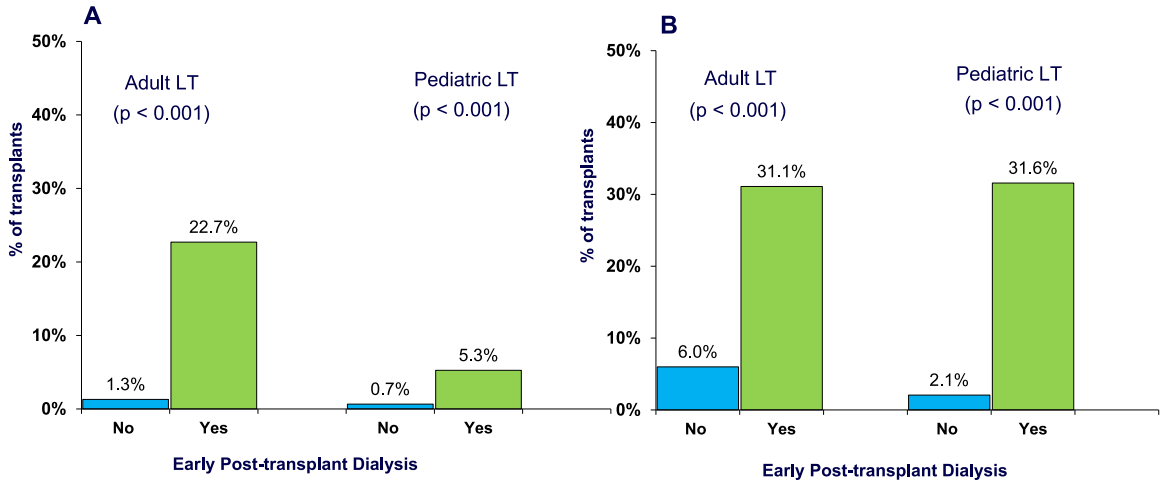

Figure 19 LT: incidence of (A) dialysis within 1 year and (B) severe renal dysfunction within 1 year (transplants: January 2000 to June 2017).

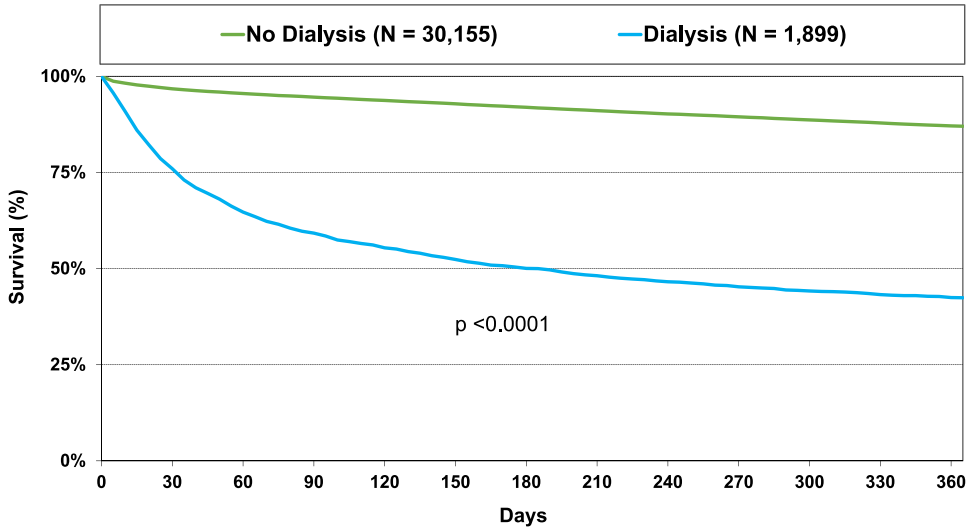

Figure 20 Adult LT: Kaplan–Meier survival stratified by early posttransplant dialysis (transplants: January 1994 to June 2017). LT, lung transplant.

nondialysis patient survival was the following: 71.8% vs 95.8% at 30 days, 54.7% vs 94.6% at 60 days, and 38.7% vs 85.3% at 1 year. When comparing patient survival based on dialysis pre-LT (regardless of early dialysis usage) vs post-LT early dialysis, de novo early dialysis had much worse survival. For instance, survival within 135 days in adult LT recipients with de novo dialysis was 50% vs 74.7% in adult LT recipients with pretransplant dialysis (Figure 22, eSlide 70). Survival rate was also worse in pediatric LT recipients with de novo dialysis (50% at 60 days Figure 23, eSlide 71).

Discussion

In this International Thoracic Organ Transplant Registry special report, we focused on early dialysis among primary thoracic transplant recipients and noted 3 crucial findings: (1) early postoperative dialysis is needed in < 10% of adult and pediatric transplant recipients, (2) risk factors include the severity of illness at the time of transplant, and (3) almost half of all recipients with early posttransplant dialysis die within 1 year posttransplant. These findings are of importance when evaluating patients for thoracic organ transplant candidacy, in optimizing health before transplantation, and in guiding posttransplant decisions around kidney transplantation.

The survival differences between those with and without early posttransplant dialysis occur early and continue to diverge for a few months posttransplantation. Among those needing early dialysis, mortality occurred in 31% of adult HT, 37% of pediatric HT, 35% of adult LT, and 45% of pediatric LT recipients at 60 days posttransplantation. Will a kidney transplant really improve survival, or should we instead focus on recovering renal function before thoracic transplantation? If safety nets are used, what is the ideal recovery time postthoracic organ transplant to wait for kidney transplant knowing high perioperative mortality rates associated with early dialysis and high 1-year renal

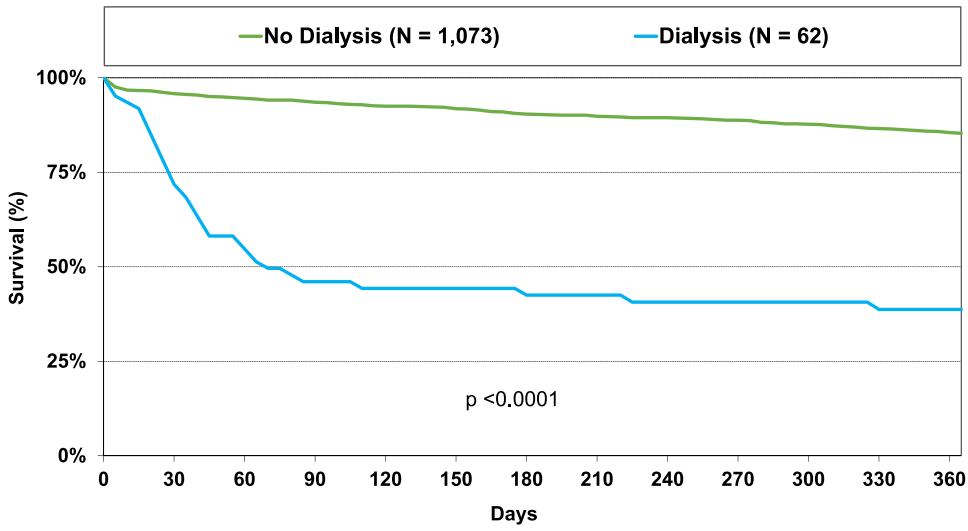

Figure 21 Pediatric LT: Kaplan–Meier survival stratified by early posttransplant dialysis (transplants: January 1994 to June 2017). LT, lung transplant.

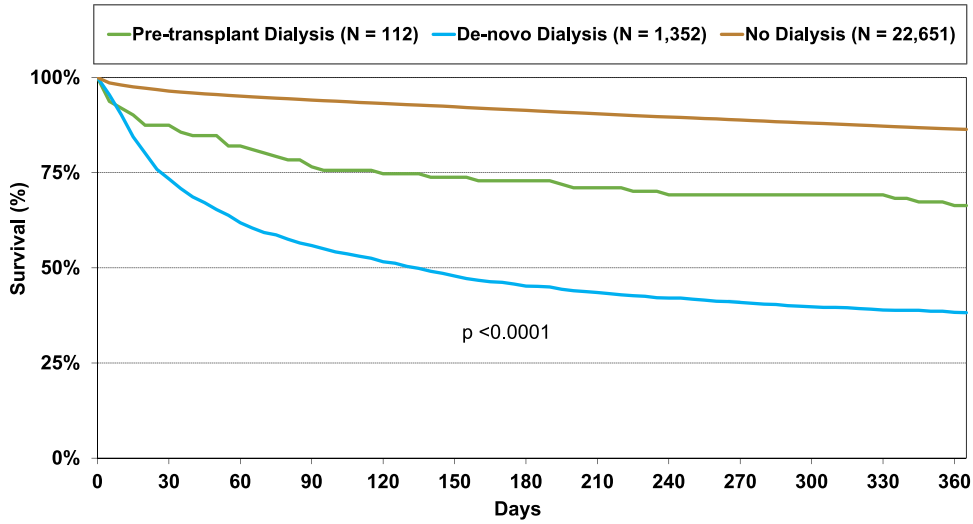

Figure 22 Adult LT: Kaplan–Meier survival stratified by usage of dialysis (pretransplant dialysis, de novo posttransplant dialysis, or no dialysis; transplants: January 1994 to June 2017). LT, lung transplant.

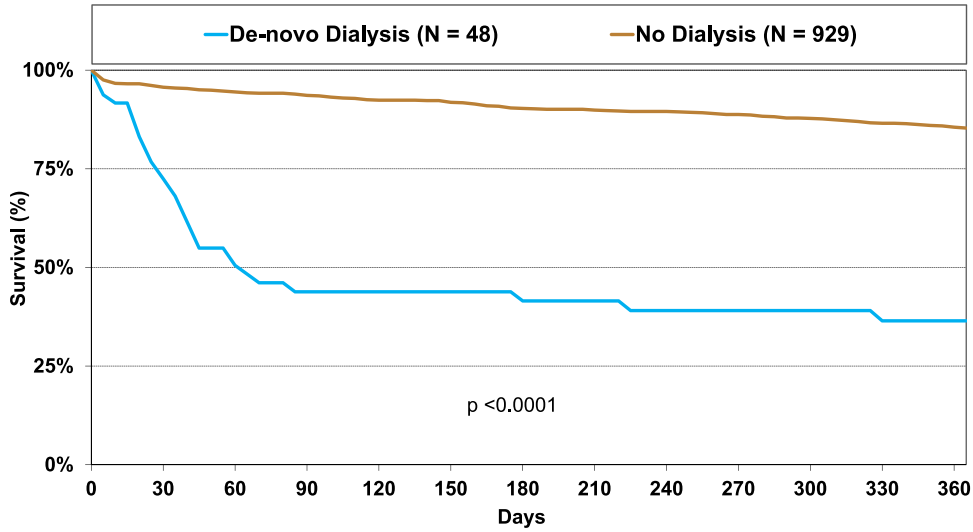

Figure 23 Pediatric LT: Kaplan-Meier survival stratified by usage of dialysis (de novo posttransplant dialysis or no dialysis; transplants: January 1994 to June 2017). LT, lung transplant.

recovery in survivors? These questions are important and difficult to answer. Our analyses and review of the literature will hopefully address some of these issues.

Preoperative renal function and risk of postoperative dialysis

Preoperative renal function is a well-known risk factor for postoperative early dialysis in adult cardiac and noncardiac surgeries[1] and has been identified but considered a less significant risk factor in pediatric cardiac surgery.[23,24] Severe renal dysfunction has also been shown to be a strong risk factor for early dialysis and mortality in adult thoracic transplant recipients[6,12,25] and pediatric HT recipients.[8,9] Among adult HT, adult LT, and pediatric HT transplant recipients in our analysis, eGFR at the time of transplant was the strongest early dialysis risk factor, and small changes in eGFR < 60 ml/min/1.73 m^2 at time of transplant were associated with exponential differences in early dialysis risk. Although many other factors may contribute to postoperative acute kidney injury (AKI) such as hypotension and vasopressors use,[26] the likelihood of dialysis has been shown by our analyses to be significantly associated with eGFR at the time of surgery, making it worth optimizing renal function when possible before transplant, especially given the finding that small differences in abnormal eGFR significantly impact risk.

Postoperative AKI and mortality

The high mortality associated with early dialysis after thoracic transplantation is comparable to mortality after other cardiovascular operations. According to the 20th International Consensus Conference of the Acute [Renal] Disease Quality Initiative, renal replacement therapy after cardiovascular surgery in adults is associated with 40% to 70% mortality[26] and postoperative AKI in noncardiac surgery defined as occurring

within 7 days of an operation is also associated with higher short- and long-term mortality.[27] Based on a global international prospective registry that included 36,357 patients from 26 countries undergoing elective inpatient operations, postoperative mortality was strongly associated with the severity of AKI (stage 1: adjusted odds ratio [OR] 2.57 [1.3-5.0]; stage 2: aOR 8.6 [5.0-15.1]; stage 3: aOR 30.1 [18.5-49.0]) with stage 3 AKI more frequently associated with abdominal surgeries (30%) and cardiothoracic operations (25%).[1] Among pediatric patients undergoing cardiac surgery, AKI is common and also associated with higher risk of mortality. In 1 retrospective study that included 3,620 children from 3 hospitals undergoing cardiovascular surgery, in-hospital mortality was 2.5 times greater in children with postoperative AKI and the mortality risk also increased with severity of AKI adjusted for age, sex, race, preoperative serum creatine, cardiopulmonary bypass time, aortic cross-clamp time, and STAT risk score category (transient AKI with adjusted hazard ratio [aHR] 1.4 [95% confidence interval (CI) 1.02-2.0], $p = 0.04$; acute kidney disease with aHR 3.7 [95% CI 1.7-7.9], $p = 0.001$; and persistent AKI with aHR 22.4 [95% CI 10.2-49.2], $p < 0.0001$).[28] There is limited data on frequency of AKI after pediatric noncardiac surgeries[29–32] with 1 retrospective single-center neonatal study correlating mortality with severity of perioperative renal injury.[32]

Thoracic transplant with and without simultaneous kidney transplant

Changes in the survival of dual organ transplants with policy changes and comparisons to isolated organ transplants provide unique opportunities to study the importance of kidney disease. ISHLT Registry data from 1995 to 2011 showed better survival among simultaneous heart–kidney transplant (SKHT) than HT when transplant recipients had stages 4 to 5 kidney disease before surgery.[33] In the United States, survival for SHKT was similar to isolated HT recipients and even better than isolated HT when evaluating those with eGFR < 60 ml/min/1.73 m^2 at the time of transplant. However, after change in HT allocation in 2018 from 3 to 6 tiers to better prioritize urgent transplantation, 1-year survival was significantly worse in the SHKT cohort, and incidence of renal failure requiring dialysis increased when comparing pre- to post-HT 2018 allocation change (29.5% vs 39.4%, $p = 0.001$).[34–37] In fact, the main cause for this change in outcome was the development of early dialysis since there was no significant difference in 2-year survival for SHLKT pre- and post-HT allocation when data were limited to a cohort without early dialysis (pre-2018: 91.8% [95% CI: 89.1%-93.9%] vs post-2018 HT: 86.5% [79.2%-91.4%]).[35] When comparing to isolated kidney transplant from the same donor in the 3-tiered HT allocation system between January 1, 2005, and April 10, 2018, kidney allograft survival was worse among SHKT recipients (14.7% vs 4.5% at 1 year; HR: 1.7 [95% CI: 1.4-2.1]) despite more isolated kidney transplant recipients on chronic dialysis at the time of transplant. This finding suggests that it is not merely the presence of renal disease at the time of transplant affecting outcome but rather other factors such as the hemodynamic stability of the recipient.[34] Fewer studies have been published for lung–kidney transplantation, with the largest study involving 108 simultaneous lung–kidney transplantation (SLKT) compared to 34,935 LT recipients in the United States transplanted between 2005 and 2022 (a time span that utilized the lung allocation score policy). This study stratified recipients by renal function at the time of transplant and noted better survival for SLKT if the recipient had dialysis or eGFR < 30 ml/min/1.73 m^2 at the time of transplant (aHR 0.59 [95% CI, 0.38-0.92]), no difference in survival between dual vs isolated LT when eGFR > 30 ml/min/1.73 m^2 and worse survival when dual organ transplants were compared to isolated kidney transplant recipients that received the contralateral kidney at the time of SLKT (aHR 3.27 [95% CI 1.22-8.78])[12] raising concern about ethical issues regarding allocation of donor kidneys. More thoracic transplant policies in the United States have been recently implemented (i.e., safety net policy implemented in 2023 and continuous distribution of LT implemented March 9, 2023), but not enough time has passed to determine the outcome.

Study limitations

There are several limitations worth mentioning, including possible inaccuracy of the clinical data, limited granularity, potential errors in data entry that exist for all large databases, and lack of data for transplants after June 2018. Despite this pause in the Registry to comply with the GDPR, this remains the largest HT and LT registry to date with unmatched power to answer clinical questions. This specific analysis had a high percentage of cohort subjects from North America but does not reflect the distribution of transplants in the larger ISHLT Registry. Granularity of data collected is a major limitation for this focused report with eGFR based on single data at the time of transplant with no information regarding indication for dialysis, chronicity, or evidence of structural kidney abnormalities. Relevant factors known to cause AKI postoperatively were also not captured, including pre- and post-operative vasoplegia, right-sided heart failure, and vasopressor usage. Duration of dialysis postoperatively was also not available with early dialysis defined as anytime postoperatively between time of admission to surgical intensive care and hospital discharge posttransplantation. Since the Registry only captured transplants through June 2018, a more contemporary cohort that includes US allocation policy changes is not available for analysis. We have instead summarized the existing contemporary literature and acknowledge that no data are currently available to determine the impact of the June 2023 US thoracic–kidney allocation policy change.[38]

Conclusions

In this focused Registry report, we found early dialysis was associated with higher mortality among adult and pediatric HT and LT recipients with 1-year mortality > 40%. Most deaths occurred early and postoperative de novo dialysis was associated with higher mortality than dialysis at the time of transplant, suggesting that factors other than

dialysis contributed to poor outcome. Although our analysis was limited, recipient factors at the time of transplant, including severity of illness (i.e., eGFR, bilirubin, mechanical ventilation, ECMO) and complexity of surgery (i.e., congenital heart disease, time on cardiopulmonary bypass), best predicted early dialysis, while small differences in eGFR < 60 ml/min/1.73 m^2 at the time of transplant significantly affected outcome. The high mortality associated with early dialysis postthoracic transplantation is a concern, and we hope the Registry analyses combined with existing and future literature will generate discussion among the international thoracic transplant community regarding how to best manage renal failure before and after transplantation.

Disclosure statement

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Rebecca Cogswell serves on the speaker's bureau for Abbott Lab, Medtronic: Spousal employment.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.healun.2024.11.042.

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