The echocardiographic course of pretransplant pulmonary hypertension following kidney transplantation and associated outcomes

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Abstract
The post 3 kidney transplant course of pretransplant echocardiographically-defined pulmonary hypertension (PH) was reviewed in 115 patients. Of these 61 patients (the largest cohort reported to date), underwent 160 “for indication” echocardiograms posttransplant (mean echocardiograms per patient: 2.6 ± 2.3). Patients undergoing posttransplant echocardiograms demonstrated greater risks for worse outcomes than those without posttransplant echocardiograms; however, there was no difference in mortality, death-censored graft failure or the composite of death or graft failure between these two groups. Of patients tested, 36 (59%) showed resolution of PH at a median of 37.5 months. Six patients (16.7%) in whom PH resolved (at a median of 29 months), experienced recurrence of PH after an interval of 48 months. No pretransplant demographic or echocardiographic characteristics distinguished those in whom PH persisted versus resolved. Though there was no difference in the risk for mortality or death-censored graft loss between the two groups at 3 and 5 years, there was a higher risk for the composite of mortality or graft loss at three but not at five years in the group with persistent PH. In conclusion, echocardiographically defined PH resolved in 59% of patients following kidney transplantation; but irrespective of resolution there was no clear association with worse outcome.

KEYWORDS
diastolic dysfunction, graft loss, survival
INTRODUCTION

Although “primary pulmonary hypertension,” now referred to as “pulmonary arterial hypertension,” (PAH) has been the focus of significant scientific inquiry and therapeutic developments in the last 20 years, increasingly pulmonary hypertension (PH) has been demonstrated in multiple other systemic disorders, notably left heart failure with and without reduced ejection fraction, and importantly in progressive kidney disease, and in those patients who are dialysis-dependent. In all instances, there is an increased risk of mortality with increasing echocardiographically demonstrated elevation in pulmonary artery pressures. In the latter group (those with end-stage kidney disease with or without dialysis) the prevalence of PH has been reported to be between 13% and 50%.1 PH in candidates for kidney transplantation has been the subject of considerable discussion, with some studies suggesting an adverse outcome,2,3 and even recommending restricting transplantation to living donor kidneys only.4 Increasingly physicians with expertise in PH are being asked to evaluate and or treat such patients before kidney transplantation. In 2020, in the largest series reported to date, risk factors associated with the echocardiographic finding of PH (e.g., race, left ventricular [LV] systolic function, and age at presentation), but not PH itself, were associated by multivariable analysis with observed patient or graft loss.5 The study also indicated that in most cases the PH was associated with features of LV diastolic dysfunction. Because kidney transplantation has been shown to be associated with evidence of LV reverse remodeling,6-8 it was thought reasonable to inquire as to whether kidney transplantation could result in resolution of pre-existing echocardiographically determined PH. The objectives of the present study were to explore, in a cohort of kidney transplant recipients with pretransplant echocardiographically diagnosed PH, the following questions:

1) Does PH resolve or persist following kidney transplantation; and if it resolves, at what frequency and over what time frame?
2) Do any pretransplant demographic or echocardiographic features predict the resolution or persistence of PH?
3) Do outcomes differ between individuals in whom PH persists versus resolves?

METHODS

As part of a quality metric of a large academic renal transplant program, the association of PH with outcomes was assessed. Briefly, the current study was a retrospective cohort review of the electronic health records (EHRs) on all adult patients (≥18 years of age) presenting as renal transplant candidates to the Center’s Medical Review Board and accepted, listed, and transplanted between January 1, 2010 and December 31, 2015. Recipients of prior transplants, multiorgan transplants, and those recipients without an echocardiogram (echo) were excluded from this analysis. PH was defined by echocardiogram using the modified Bernoulli equation9 combined with the estimated value of the right atrial (RA) pressure; kidney transplant recipients were considered to have PH if the pulmonary artery (PA) systolic pressure (PAsys) was ≥35 mmHg. It is generally accepted that <35 mmHg for an estimated PA pressure represents a normal or very low risk of PH.10 The EHR of the hospital system (six hospitals: one academic and five community hospitals) were searched and reviewed for posttransplantation echocardiograms through August 2020, on the cohort identified as having PH. Echocardiograms were undertaken posttransplantation for indication, not as part of a posttransplant protocol. Patients with pretransplant PH without posttransplant echocardiograms were compared for demographics, echocardiographic features and outcomes with those recipients having posttransplant echocardiograms. All echocardiograms, irrespective of the hospital where they were undertaken, were interpreted by the centralized echocardiography service.

Demographic characteristics evaluated in this cohort included: gender, ethnicity, height, body mass index blood group, posttransplant hemoglobin, history of malignancy, comorbidities (diabetes, hypertension, autoimmune disease, genetic diseases, glomerular diseases), creatinine at transplant, human leukocyte antigen mismatch, most recent calculated panel reactive antibodies (cPRA) proximate to transplant, dialysis at presentation (including type, and vintage), viral serostatus (hepatitis B virus [HBV], hepatitis C virus, cytomegalovirus, Epstein –Barr virus, human immunodeficiency virus), donor type (living vs. deceased) and donor characteristics (as per recipient).

Echocardiographic parameters included PAsys, right atrial pressure (RAP), left ventricular ejection fraction (LVEF), qualitative LV diastolic and systolic function, LV filling pressures, LV wall thickness (LVH), wall motion abnormalities, right ventricular (RV) systolic function, qualitative RA and left atrial (LA) size, LV cardiac output, and cardiac index and LA volume indexed for body surface area (BSA; ml/m²).

All analyses were performed using both echocardiograms performed before presentation to the medical review board (at presentation) and those proximate to transplant surgery (Pre-Tx) echocardiograms. When more than one echocardiogram was present before
transplantation, the echo closest to transplant was used for analysis. Presentation echocardiograms were undertaken on scheduled transplant evaluation days, which were nondialysis days. Echocardiograms done proximate to transplant were not usually done close to dialysis as dialysis immediately before transplantation is avoided. All posttransplant echocardiograms (echos) were evaluated for the same parameters as well as the persistence of PH as previously defined. If neither PH nor a PA systolic pressure $\geq 35$ mmHg was noted on the posttransplant echocardiogram, and there were not subsequent echos documenting PH by either criterion, the time of the first PH negative echocardiogram was considered the time of “PH resolution.” In the event, that one or more echocardiograms posttransplant documented PH resolution but subsequent remote echocardiograms reliably and consistently (more than once) reported PH the event was considered “recurrence after resolution of PH.” In the event that any or all posttransplantation echocardiograms demonstrated PH, this occurrence was considered “persistent PH” and the most remote echocardiogram positive for PH was noted as the “duration of persistent PH.”

Outcome data included patient survival, death-censored graft survival, and survival with a functioning graft at 3 and 5 years. The presence of delayed graft function (DGF) defined as the need for dialysis in the first week posttransplantation was included in the analyses as a risk variable.

STATISTICAL ANALYSIS

Demographic and clinical data were reported as frequencies and proportions for categorical variables and as median and interquartile range (IQR) for continuous variables. Differences between groups were determined by $\chi^2$ or Fisher’s exact tests for categorical variables and Kruskal-Wallis test for continuous variables as appropriate. Univariable Cox regression was used to determine the contribution of potential prognostic variables to the patient and death censored graft outcomes, and the composite outcome of either death or death-censored graft loss. Kaplan-Meier curves were used to depict the 3- and 5-year patient and graft survival and survival with a functioning graft. Difference between groups was compared by the log-rank test. Change in posttransplant hemoglobin over time was compared between the PH persisted and PH resolved groups using the generalized linear mixed model and depicted by a line graph. All the analyses were performed using Stata version 17.0 (StataCorp LLC). A $p$ value of $<$0.05 was considered statistically significant.

RESULTS

Of 733 kidney transplant recipients (Figure 1), 115 had pretransplant PH defined by echocardiography, and of these recipients, 54 (47%) had no subsequent posttransplant echocardiograms and 61 (53%) had one or more follow-up echocardiograms posttransplant.

The patients who had posttransplant echocardiograms compared to those recipients who had no posttransplant echocardiograms were respectively: more sensitized (cPRA median: 36.5 [IQR: 4.0, 81.5] vs. 3.0 [IQR: 0.0, 33.0]; $p = 0.001$); had a longer cold ischemic time (16.3 [1.5, 26.0] vs. 9.8 h [1.0, 19.0]; $p = 0.04$); were less likely to have immediate graft function (83.3% vs. 98.1%; $p = 0.01$); were more likely to experience DGF (18.3% vs. 3.7%; $p = 0.01$); and were less likely to be male (45.9% vs. 66.7%); $p = 0.03$. Also, more of the patients who had posttransplant echocardiograms had had additional immediate pretransplant echocardiograms (77.0% vs. 57.4%; $p = 0.02$; Table 1). There were no differences in pretransplant echocardiographic parameters in those individuals who did versus did not have posttransplant echocardiograms; importantly this included median PA systolic pressure, (median 41.0 [IQR: 37.5, 48.0] vs. 41.3 mmHg [IQR: 37.5, 47.0], respectively; $p = 0.99$; Table 2).

Despite these demographic differences, no difference was observed in patient survival at 3 and 5 years between those with and without posttransplant echocardiograms (89.9% vs. 92.4%, log-rank test $p = 0.62$; and 78.3% vs. 87.1%, log-rank test $p = 0.19$, respectively). Nor was there a difference in the 3- and 5-year posttransplant death censored graft survival between those with or without posttransplant echocardiograms (96.7% vs. 98.1%, log-rank test $p = 0.62$; 91.5% vs. 95.4%, log-rank test $p = 0.43$, respectively). Similarly, survival with a functioning graft...
**TABLE 1** Recipient characteristics in those who did versus did not have posttransplantation echocardiograms

| Recipient demographic and clinical characteristics | Total (N = 115) | No post-tx echo (n = 54) | Had post-tx echo (n = 61) | p Value |
|---------------------------------------------------|----------------|--------------------------|---------------------------|---------|
| **Age at presentation (years), median (IQR)**     | 56.0 (45.0, 64.0) | 51.5 (45.0, 60.0) | 58.0 (46.0, 65.0) | 0.14    |
| **Male gender**                                   | 64 (55.7)       | 36 (66.7)               | 28 (45.9)                | 0.03    |
| **Race/ethnicity**                                |                |                          |                          | 0.16    |
| White                                             | 43 (37.4)       | 18 (33.3)               | 25 (41.0)                |         |
| Black                                             | 36 (31.3)       | 14 (25.9)               | 22 (36.1)                |         |
| Hispanic                                          | 31 (27.0)       | 18 (33.3)               | 13 (21.3)                |         |
| Asian                                             | 5 (4.3)         | 4 (7.4)                 | 1 (1.6)                  |         |
| **BMI, median (IQR)**                             | 27.1 (24.0, 30.6)| 27.2 (23.4, 29.7) | 26.9 (24.5, 30.7) | 0.68    |
| **Smoking**                                       |                |                          |                          | 0.40    |
| No                                                | 81 (70.4)       | 40 (74.1)               | 41 (67.2)                |         |
| Yes                                               | 18 (15.7)       | 9 (16.7)                | 9 (14.8)                 |         |
| Unknown                                           | 16 (13.9)       | 5 (9.3)                 | 11 (18.0)                |         |
| **Malignancy**                                    | 5 (4.3)         | 2 (3.7)                 | 3 (4.9)                  | 0.75    |
| **ABO blood group**                               |                |                          |                          | 0.04    |
| A                                                 | 43 (37.4)       | 25 (46.3)               | 18 (29.5)                |         |
| B                                                 | 7 (6.1)         | 3 (5.6)                 | 4 (6.6)                  |         |
| AB                                                | 6 (5.2)         | 5 (9.3)                 | 1 (1.6)                  |         |
| O                                                 | 59 (51.3)       | 21 (38.9)               | 38 (62.3)                |         |
| **Deceased donor**                                | 71 (61.7)       | 29 (53.7)               | 42 (68.9)                | 0.09    |
| **Primary diagnosis, diabetes**                   | 51 (44.3)       | 22 (40.7)               | 29 (47.5)                | 0.46    |
| **Primary diagnosis, hypertension**               | 112 (97.4)      | 53 (98.1)               | 59 (96.7)                | 0.63    |
| **ESRD cause**                                    |                |                          |                          |         |
| Diabetes                                          | 48 (41.7)       | 21 (38.9)               | 27 (44.3)                | 0.56    |
| Hypertension                                      | 45 (39.1)       | 21 (38.9)               | 24 (39.3)                | 0.96    |
| Autoimmune diseases                               | 7 (6.1)         | 4 (7.4)                 | 3 (4.9)                  | 0.58    |
| Genetic diseases                                  | 5 (4.3)         | 4 (7.4)                 | 1 (1.6)                  | 0.13    |
| Glomerular diseases                               | 5 (4.3)         | 2 (3.7)                 | 3 (4.9)                  | 0.75    |
| Urinary tract problems                            | 1 (0.9)         | 1 (1.9)                 | 0 (0.0)                  | 0.47    |
| Other                                             | 23 (20.0)       | 9 (16.7)                | 14 (23.0)                | 0.40    |
| **Creatinine at transplant, median (IQR)**        | 6.6 (5.0, 8.8)  | 7.2 (5.0, 9.5)          | 6.4 (5.1, 8.3)           | 0.18    |
| HLA mismatch level, median (IQR)                  | 4.0 (3.0, 5.0)  | 4.0 (3.0, 5.0)          | 4.0 (3.0, 5.0)           | 0.41    |
| Most recent cPRA, median (IQR)                    | 23.0 (0.0, 69.0)| 3.0 (0.0, 33.0)         | 36.5 (4.0, 81.5)         | 0.001   |
| **Dialysis at presentation**                      | 99 (86.1)       | 45 (83.3)               | 54 (88.5)                | 0.42    |
| **Dialysis type at presentation**                 |                |                          |                          | 0.52    |
| PD                                                | 9 (9.1)         | 5 (11.1)                | 4 (7.4)                  |         |
| HD                                                | 90 (90.9)       | 40 (88.9)               | 50 (92.6)                |         |
| **Dialysis (overall)**                            | 9 (7.8)         | 4 (7.4)                 | 5 (8.2)                  | 0.88    |
| Yes                                               | 106 (92.2)      | 50 (92.6)               | 56 (91.8)                |         |
**TABLE 1** (Continued)

|                     | Total (N = 115) | No post-tx echo (n = 54) | Had post-tx echo (n = 61) | p Value |
|---------------------|-----------------|--------------------------|---------------------------|---------|
| Dialysis vintage (years), median (IQR) | 3.8 (2.3, 6.2) | 3.6 (2.0, 4.5) | 3.9 (2.6, 6.9) | 0.07 |
| HBV core antibody (+) | 13 (11.3) | 6 (11.1) | 7 (11.5) | 0.95 |
| HbsAg (+) | 1 (0.9) | 1 (1.9) | 0 (0.0) | 0.29 |
| HCV serostatus (+) | 12 (10.4) | 7 (13.0) | 5 (8.2) | 0.40 |
| CMV status (+) | 90 (78.3) | 41 (75.9) | 49 (80.3) | 0.57 |
| EBV serostatus (+) | 105 (95.5) | 50 (94.3) | 55 (96.5) | 0.59 |
| HIV serostatus (+) | 4 (3.5) | 1 (1.9) | 3 (5.0) | 0.36 |

**Kidney transplant procedure type**

|                  | No post-tx echo (n = 54) | Had post-tx echo (n = 61) | p Value |
|------------------|--------------------------|---------------------------|---------|
| Left             | 71 (61.7) | 31 (57.4) | 40 (65.6) | 0.67 |
| Right            | 42 (36.5) | 22 (40.7) | 20 (32.8) | 0.67 |
| En-bloc          | 2 (1.7) | 1 (1.9) | 1 (1.6) | 0.67 |

**Donor characteristics**

|                  | No post-tx echo (n = 54) | Had post-tx echo (n = 61) | p Value |
|------------------|--------------------------|---------------------------|---------|
| Donor age (years), median (IQR) | 39.0 (29.0, 49.0) | 38.0 (24.0, 45.0) | 42.0 (34.0, 51.0) | 0.08 |
| Donor male gender | 46 (40.0) | 23 (42.6) | 23 (37.7) | 0.59 |
| Donor race/ethnicity | 39.0 (29.0, 49.0) | 38.0 (24.0, 45.0) | 42.0 (34.0, 51.0) | 0.59 |
| White        | 60 (52.2) | 30 (55.6) | 30 (49.2) | 0.84 |
| Black        | 20 (17.4) | 8 (14.8) | 12 (19.7) | 0.84 |
| Hispanic/Latino | 32 (27.8) | 15 (27.8) | 17 (27.9) | 0.84 |
| Asian        | 3 (2.6) | 1 (1.9) | 2 (3.3) | 0.84 |
| Donor BMI, median (IQR) | 26.1 (22.5, 29.3) | 26.3 (22.3, 28.1) | 26.1 (22.7, 30.4) | 0.49 |
| HBV core antibody (+), donor | 0 (0.0) | 0 (0.0) | 0 (0.0) | – |
| ABO blood group, donor | 34 (30.4) | 19 (36.5) | 15 (25.0) | 0.45 |
| A            | 34 (30.4) | 19 (36.5) | 15 (25.0) | 0.45 |
| B            | 4 (3.6) | 2 (3.8) | 2 (3.3) | 0.45 |
| AB           | 3 (2.7) | 2 (3.8) | 1 (1.7) | 0.45 |
| O            | 71 (63.4) | 29 (55.8) | 42 (70.0) | 0.45 |
| Kidney cold ischemic time (h), median (IQR) | 12.8 (11.1, 22.8) | 9.8 (10.0, 19.3) | 16.3 (15.1, 26.0) | 0.04 |
| History of smoking, donor | 15 (13.0) | 4 (7.4) | 11 (18.0) | 0.09 |
| History of hypertension, donor | 23 (20.0) | 7 (13.0) | 16 (26.2) | 0.08 |
| History of diabetes, donor | 7 (9.9) | 1 (3.4) | 6 (14.3) | 0.13 |

**Outcomes**

|                  | No post-tx echo (n = 54) | Had post-tx echo (n = 61) | p Value |
|------------------|--------------------------|---------------------------|---------|
| Immediate graft function | 103 (90.4) | 53 (98.1) | 50 (83.3) | 0.01 |
| Delayed graft function | 13 (11.4) | 2 (3.7) | 11 (18.3) | 0.01 |
| Overall mortality | 23 (20.0) | 6 (11.1) | 17 (27.9) | 0.03 |
| Graft failure, not censured for death | 29 (25.2) | 8 (14.8) | 21 (34.4) | 0.02 |
| Graft failure, censured for death | 7 (6.1) | 2 (3.7) | 5 (8.2) | 0.31 |

**Note:** Values are in number and % unless otherwise specified; comparisons between groups were performed by χ² or Fisher exact tests for categorical variables and Kruskal–Wallis for continuous variables. Differences of survival between groups were compared using the log-rank test.

Abbreviations: BMI, body mass index; CMV, cytomegalovirus; cPRA, calculated panel reactive antibodies; EBV, Epstein–Barr virus; ESRD, end-stage renal disease; HBV, hepatitis B virus; HCV, hepatitis C virus; HD, hemodialysis; HIV, human immunodeficiency virus; HLA, human leukocyte antigen; IQR, interquartile range; PD, peritoneal dialysis.
**TABLE 2**  Pretransplant echocardiographic characteristics in kidney transplant recipients who did versus did not have posttransplant echocardiograms

|                                      | Total (N = 115) | No post-tx echo (n = 54) | Had post-tx echo (n = 61) | p Value |
|--------------------------------------|----------------|--------------------------|---------------------------|---------|
| PA pressure (mmHg), median (IQR) [range] | 41.0 (37.5, 47.5) | 41.3 (37.5, 47.0) | 41.0 (37.5, 48.0) | 0.99    |
| Presentation echocardiogram results available | 0.49 |
| No                                   | 3 (2.6)        | 2 (3.7)                  | 1 (1.6)                  |         |
| Yes                                  | 112 (97.4)     | 52 (96.3)                | 60 (98.4)                |         |
| LV systolic function, at-presentation | 0.17 |
| Hyperdynamic                         | 8 (7.1)        | 4 (7.7)                  | 4 (6.7)                  |         |
| Normal                               | 95 (84.8)      | 47 (90.4)                | 48 (80.0)                |         |
| Reduced                              | 7 (6.3)        | 1 (1.9)                  | 6 (10.0)                 |         |
| Not reported                         | 2 (1.8)        | 0 (0.0)                  | 2 (3.3)                  |         |
| LVEF (%), at presentation, median (IQR) | 62.0 (57.0, 67.0) | 62.0 (57.0, 67.0) | 62.0 (57.0, 67.0) | 0.49    |
| LV diastolic function, at presentation | 0.65 |
| Normal                               | 9 (8.0)        | 5 (9.6)                  | 4 (6.7)                  |         |
| Reduced                              | 73 (65.2)      | 35 (67.3)                | 38 (63.3)                |         |
| Not reported                         | 30 (26.8)      | 12 (23.1)                | 18 (30.0)                |         |
| LV filling pressure, at presentation | 0.31 |
| Normal                               | 20 (18.3)      | 7 (13.7)                 | 13 (22.4)                |         |
| Elevated                             | 52 (47.7)      | 28 (54.9)                | 24 (41.4)                |         |
| Not reported                         | 37 (33.9)      | 16 (31.4)                | 21 (36.2)                |         |
| LV wall thickness (LVH), at presentation | 0.97 |
| Normal                               | 15 (13.4)      | 7 (13.5)                 | 8 (13.3)                 |         |
| Abnormal                             | 68 (60.7)      | 31 (59.6)                | 37 (61.7)                |         |
| Not reported                         | 29 (25.9)      | 14 (26.9)                | 15 (25.0)                |         |
| LV wall motion abnormality, at presentation | 0.47 |
| No                                   | 81 (75.0)      | 41 (80.4)                | 40 (70.2)                |         |
| Yes                                  | 11 (10.2)      | 4 (7.8)                  | 7 (12.3)                 |         |
| Not reported                         | 16 (14.8)      | 6 (11.8)                 | 10 (17.5)                |         |
| RV systolic function, at presentation | 0.19 |
| Hyperdynamic                         | 98 (87.5)      | 48 (92.3)                | 50 (83.3)                |         |
| Normal                               | 3 (2.7)        | 0 (0.0)                  | 3 (5.0)                  |         |
| Reduced                              | 11 (9.8)       | 4 (7.7)                  | 7 (11.7)                 |         |
| RA size category, at presentation | 0.25 |
| Normal                               | 86 (76.8)      | 43 (82.7)                | 43 (71.7)                |         |
| Dilated                              | 17 (15.2)      | 7 (13.5)                 | 10 (16.7)                |         |
| Not reported                         | 9 (8.0)        | 2 (3.8)                  | 7 (11.7)                 |         |
| LA size category, at presentation | 0.14 |
| Normal                               | 29 (25.9)      | 14 (26.9)                | 15 (25.0)                |         |
| Dilated                              | 75 (67.0)      | 37 (71.2)                | 38 (63.3)                |         |
| Not reported                         | 8 (7.1)        | 1 (1.9)                  | 7 (11.7)                 |         |
TABLE 2 (Continued)

|                             | Total (N = 115) | No post-tx echo (n = 54) | Had post-tx echo (n = 61) | p Value |
|-----------------------------|-----------------|--------------------------|---------------------------|---------|
| IVS diastolic thickness (IVSd, mm), at presentation, median (IQR) | 1.2 (1.1, 1.3) | 1.3 (1.0, 1.3) | 1.2 (1.1, 1.3) | 0.87 |
| Posterior wall thickness (LVPWd, mm), at presentation, median (IQR) | 1.2 (1.0, 1.3) | 1.2 (1.0, 1.3) | 1.2 (1.0, 1.3) | 0.77 |
| LVIDd (mm), at presentation, median (IQR) | 4.7 (4.3, 5.3) | 4.7 (4.4, 5.3) | 4.7 (4.3, 5.2) | 0.51 |
| LV cardiac output (L/min), at presentation, median (IQR) | 5.7 (4.4, 6.8) | 5.8 (4.8, 6.7) | 5.6 (4.4, 6.8) | 0.57 |
| LV cardiac index, at presentation, median (IQR) | 3.0 (2.6, 3.5) | 3.2 (3.0, 3.5) | 2.8 (2.4, 3.5) | 0.11 |
| LA volume indexed to BSA (ml/m²), at presentation, median (IQR) | 39.6 (31.7, 46.3) | 41.9 (31.8, 46.6) | 38.7 (31.7, 45.6) | 0.56 |
| Pre-Tx echocardiogram results available | 0.02 |
| No | 37 (32.2) | 23 (42.6) | 14 (23.0) |
| Yes | 78 (67.8) | 31 (57.4) | 47 (77.0) |
| LV systolic function (pre-Tx) | 0.84 |
| Hyperdynamic | 4 (5.1) | 2 (6.3) | 2 (4.3) |
| Normal | 64 (81.0) | 26 (81.3) | 38 (80.9) |
| Reduced | 10 (12.7) | 4 (12.5) | 6 (12.8) |
| Not reported | 1 (1.3) | 0 (0.0) | 1 (2.1) |
| LVEF (%), pre-Tx, median (IQR) | 62.0 (57.0, 67.0) | 62.0 (57.0, 67.0) | 62.0 (57.0, 67.0) | 0.75 |
| LV diastolic function (pre-Tx) | 0.44 |
| Normal | 7 (8.9) | 4 (12.5) | 3 (6.4) |
| Reduced | 53 (67.1) | 19 (59.4) | 34 (72.3) |
| Not reported | 19 (24.1) | 9 (28.1) | 10 (21.3) |
| LV filling pressure (pre-Tx) | 0.24 |
| Normal | 10 (12.8) | 6 (19.4) | 4 (8.5) |
| Elevated | 43 (55.1) | 14 (45.2) | 29 (61.7) |
| Not reported | 25 (32.1) | 11 (35.5) | 14 (29.8) |
| Wall motion abnormality (pre-Tx) | 0.34 |
| No | 58 (75.3) | 21 (67.7) | 37 (80.4) |
| Yes | 11 (14.3) | 5 (16.1) | 6 (13.0) |
| Not reported | 8 (10.4) | 5 (16.1) | 3 (6.5) |
| RV systolic function (pre-Tx) | 0.90 |
| Hyperdynamic | 71 (89.9) | 29 (90.6) | 42 (89.4) |
| Normal | 6 (7.6) | 2 (6.3) | 4 (8.5) |
| Reduced | 2 (2.5) | 1 (3.1) | 1 (2.1) |
| LA size category (pre-Tx) | 0.18 |
| Normal | 13 (16.5) | 4 (12.5) | 9 (19.1) |
| Dilated | 64 (81.0) | 26 (81.3) | 38 (80.9) |
| Not reported | 2 (2.5) | 2 (6.3) | 0 (0.0) |

(Continues)
did not differ between the two groups at 3 and 5 years (all Figure 2).

A total of 160 posttransplant echocardiograms were performed in 61 patients (echocardiograms per patient: mean: 2.6 ± 2.3; median: 2 [IQR: 1, 3]). Of those patients with posttransplant echocardiograms, 25 (41%) had persistent PH and this was documented to have persisted for a median of 33 months (IQR: 10.0, 50.0). Of the 36 (59%) kidney transplant recipients who showed PH resolution, the PH was deemed to have resolved by a median 37.5 months (IQR: 14.0, 49.5). PH duration was not different between those recipients with or without resolution, \( p = 0.69 \).

In six patients in whom PH was considered to have resolved, resolution occurred at a median of 29 months (IQR: 14.0, 49.5). PH duration was not different between those recipients with or without resolution, \( p = 0.69 \).

In patients with posttransplant persistence versus resolution of pretransplant PH there was no difference at different as follows: median PAsys: 41 (IQR: 38.0, 47.0) versus 40.7 mmHg (IQR: 36.3, 50.0), \( p = 0.77 \); LA volume: 75.1 (IQR: 65.0, 88.8) versus 71.4 mL (IQR: 58.0, 84.3), \( p = 0.36 \); LVEF: 62.0% (IQR 57.0, 62.3) versus 62.0% (IQR: 57.0, 67.0), \( p = .41 \); qualitative LV wall thickness (LVH): abnormal 62.5% versus 61.1%, \( p = 0.99 \); while there were small differences in pretransplant RV systolic function (qualitatively reduced, hyperdynamic or normal) there was no significant difference observed between groups, \( p = 0.26 \); pretransplant RA size (qualitative) dilated 25% versus 11.1%, \( p = 0.34 \); LV filling pressure, (qualitative) elevated 33.3% versus 47.1%, \( p = 0.42 \); LV diastolic function (qualitative) reduced 58.3% versus 66.7%, \( p = 0.53 \) (Table 3). No other statistically significant or clinically meaningful differences were observed in the additional evaluated echocardiographic parameters between those in whom PH persisted or resolved posttransplant. There were no demographic or clinical differences between those with resolution versus persistence of pretransplant PH (Table 4).

In patients with posttransplant persistence versus resolution of pretransplant PH there was no difference at

**Table 2 (Continued)**

|                  | Total (N = 115) | No post-tx echo (n = 54) | Had post-tx echo (n = 61) | \( p \) Value |
|------------------|----------------|-------------------------|---------------------------|--------------|
| RA size category (pre-Tx) |                |                         |                           |              |
| Normal           | 51 (44.3)      | 17 (31.5)               | 34 (55.7)                 | 0.02         |
| Dilated          | 25 (21.7)      | 12 (22.2)               | 13 (21.3)                 |              |
| Not reported     | 39 (33.9)      | 25 (46.3)               | 14 (23.0)                 |              |
| LV wall thickness (LVH) (pre-Tx), median (IQR) |    |                        |                           | 0.79         |
| Normal           | 8 (10.3)       | 3 (9.7)                 | 5 (10.6)                  |              |
| Abnormal         | 52 (66.7)      | 22 (71.0)               | 30 (63.8)                 |              |
| Not reported     | 18 (23.1)      | 6 (19.4)                | 12 (25.5)                 |              |
| IVS diastolic thickness (IVSd, mm) (pre-Tx), median (IQR) | 1.3 (1.1, 1.4) | 1.1 (1.1, 1.4) | 1.3 (1.1, 1.5) | 0.35         |
| Posterior wall thickness (LVPWd, mm) (pre-Tx), median (IQR) | 1.3 (1.1, 1.4) | 1.2 (1.0, 1.4) | 1.3 (1.1, 1.5) | 0.29         |
| LVIDd (pre-Tx, mm), median (IQR) | 5.0 (4.6, 5.3) | 5.1 (4.7, 5.3) | 4.9 (4.3, 5.3) | 0.06         |
| LV cardiac output (pre-Tx, L/mn), median (IQR) | 5.5 (4.5, 6.6) | 5.9 (5.1, 6.7) | 5.2 (4.3, 6.1) | 0.09         |
| LV cardiac index (pre-Tx), median (IQR) | 3.0 (2.6, 3.5) | 3.1 (2.7, 3.7) | 2.9 (2.2, 3.4) | 0.24         |
| LA Volume indexed to BSA (ml/m²) (pre-Tx), median (IQR) | 44.6 (37.1, 53.7) | 47.2 (38.6, 52.4) | 43.9 (36.4, 54.8) | 0.67         |

Notes: Values are in number and % unless otherwise specified; comparisons between groups were performed by \( \chi^2 \) or Fisher exact tests for categorical variables and Kruskal–Wallis for continuous variables; at presentation—at Medical Review Board presentation. Pre-Tx—clinically indicated echocardiogram done before transplantation surgery.

Abbreviations: BSA, body surface area; IQR, interquartile range; IVS, interventricular septum; LA, left atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; PA, pulmonary artery; RA, right atrial; RV, right ventricular.
at 3 and 5 years was 92% versus 100%, \( p = 0.09 \); and 82.8% versus 96.4%, \( p = 0.12 \), respectively. However, survival with a functioning graft was significantly lower at three years in those with persistent versus resolved PH (76.0% vs. 94.4%; \( p = 0.04 \), respectively; although this difference was no longer evident at 5 years (64.6% vs. 75.9%; \( p = 0.29 \); Figure 3). In a separate analysis (not shown) of all outcomes at six-monthly intervals following transplantation, only survival with a functioning graft was significantly lower between those with persistent versus resolved PH and only at the 36 months date.

In addition to the persistence vs resolution of PH, other echocardiographic, donor and recipient demographic variables were assessed as risk factors for the outcomes of interest by univariable analysis: mortality, death censored graft failure, or the composite outcome of death or graft loss (Table 5). Small numbers of adverse outcomes precluded multivariable analyses.

The following features were associated with increased risk of mortality: recipient age at presentation (hazard ratio [HR]: 1.06; 95% confidence interval [CI]: 1.01, 1.1; \( p = 0.01 \)); malignancy (HR: 4.57; 95% CI: 1.34, 15.64; \( p = 0.02 \)); interventricular septal diastolic thickness (HR: 7.84, 95% CI: 1.00, 61.31; \( p = 0.049 \)); and donor blood type AB versus reference type O (HR: 6.47, 95% CI: 1.42, 29.37; \( p = 0.02 \)). Two features were associated with decreased risk: Hispanic race/ethnicity (HR: 0.20, 95% CI: 0.04, 0.87; \( p = 0.02 \)); and duration of PH persistence post-transplant (HR: 0.96, 95% CI: 0.93, 0.99; \( p = 0.003 \)). The latter presumably because patients with longer lasting posttransplantation PH had to have lived longer.

Death censored graft failure was associated, by univariable analysis, with: recipient blood group B (HR: 15.26, 95% CI: 1.38, 168.75; \( p = 0.02 \)); HBV core antibody positivity, (HR: 9.64, 95% CI: 1.94, 47.91; \( p = 0.01 \)); and en-bloc kidney transplant procedure, (HR: 28.47, 95% CI: 2.52, 321.82; \( p = 0.01 \)); hyperdynamic LV systolic function (vs. normal systolic function as reference) (HR: 14.28, 95% CI: 1.18, 149.58; \( p = 0.04 \)); and reduced RV systolic function versus normal (HR: 10.06, 95% CI: 1.42, 71.41; \( p = 0.02 \)).

The composite outcome of death or graft loss was associated by univariable analysis with: age at presentation (HR: 1.03, 95% CI: 1.00, 1.07; \( p = 0.04 \)); HBV core antibody positivity (HR: 3.33, 95% CI: 1.33, 8.37; \( p = 0.01 \)); presence of dilated RA size on repeat echocardiogram done proximate to transplant (vs. normal) (HR: 3.24, 95% CI: 1.21, 8.72; \( p = 0.02 \)) This latter analysis though statistically significant is limited by a small number of patients (47) due to missing data. The small but significant association (HR: 1.04) of RA size in impacting graft outcome has been previously reported although not in patients specifically with pretransplant

**FIGURE 2** Kaplan–Meier curves for posttransplant (a) patient survival (b) death-censored graft survival (c) freedom from composite events (survival with a functioning graft) at 3 and 5 years comparing those with versus without posttransplant echocardiograms.
TABLE 3  Pretransplant echocardiographic features in kidney transplant recipients with follow up echocardiograms: Comparing those in whom PH persisted versus resolved posttransplantation

|                        | Total (N = 61) | PH persisted (n = 25) | PH resolved (n = 36) | p Value |
|------------------------|---------------|-----------------------|----------------------|---------|
| PA pressure (mmHg), median (IQR) [range] | 41.0 (37.5, 48.0) | 41.0 (38.0, 47.0) | 40.7 (36.3, 50.0) | 0.77   |
|                        | [35.0–70.0]   | [35.5–70.0]           | [35.0–68.0]          |         |
| PH persistent duration (months), median (IQR) [range] | 36.0 (12.0, 50.0) | 33.0 (10.0, 50.0) | 37.5 (14.0, 49.5) | 0.69   |
|                        | [0.03–108]    | [0.03–108]            | [0.5–76]             |         |
| Prepresentation echocardiogram results available |              |                      |                      | 0.23   |
| No                     | 1 (1.6)       | 1 (4.0)               | 0 (0.0)              |         |
| Yes                    | 60 (98.4)     | 24 (96.0)             | 36 (100.0)           |         |
| LV systolic function at presentation |              |                      |                      | 0.64   |
| Hyperdynamic           | 4 (6.7)       | 2 (8.3)               | 2 (5.6)              |         |
| Normal                 | 48 (80.0)     | 20 (83.3)             | 28 (77.8)            |         |
| Reduced                | 6 (10.0)      | 2 (8.3)               | 4 (11.1)             |         |
| Not reported           | 2 (3.3)       | 0 (0.0)               | 2 (5.6)              |         |
| LVEF (%), at presentation, median (IQR) | 62.0 (57.0, 67.0) | 62.0 (57.0, 62.3) | 62.0 (57.0, 67.0) | 0.41   |
| LV diastolic function, at presentation |              |                      |                      | 0.53   |
| Normal                 | 4 (6.7)       | 1 (4.2)               | 3 (8.3)              |         |
| Reduced                | 38 (63.3)     | 14 (58.3)             | 24 (66.7)            |         |
| Not reported           | 18 (30.0)     | 9 (37.5)              | 9 (25.0)             |         |
| LV filling pressure, at presentation |              |                      |                      | 0.42   |
| Normal                 | 13 (22.4)     | 5 (20.8)              | 8 (23.5)             |         |
| Elevated               | 24 (41.4)     | 8 (33.3)              | 16 (47.1)            |         |
| Not reported           | 21 (36.2)     | 11 (45.8)             | 10 (29.4)            |         |
| LV wall thickness (LVH), at presentation |              |                      |                      | 0.99   |
| Normal                 | 8 (13.3)      | 3 (12.5)              | 5 (13.9)             |         |
| Abnormal               | 37 (61.7)     | 15 (62.5)             | 22 (61.1)            |         |
| Not reported           | 15 (25.0)     | 6 (25.0)              | 9 (25.0)             |         |
| LV wall motion abnormality, at presentation |              |                      |                      | 0.68   |
| No                     | 40 (70.2)     | 17 (70.8)             | 23 (69.7)            |         |
| Yes                    | 7 (12.3)      | 2 (8.3)               | 5 (15.2)             |         |
| Not reported           | 10 (17.5)     | 5 (20.8)              | 5 (15.2)             |         |
| RV systolic function, at presentation |              |                      |                      | 0.26   |
| Hyperdynamic           | 50 (83.3)     | 22 (91.7)             | 28 (77.8)            |         |
| Normal                 | 3 (5.0)       | 0 (0.0)               | 3 (8.3)              |         |
| Reduced                | 7 (11.7)      | 2 (8.3)               | 5 (13.9)             |         |
| RA size category, at presentation |              |                      |                      | 0.34   |
| Normal                 | 43 (71.7)     | 16 (66.7)             | 27 (75.0)            |         |
| Dilated                | 10 (16.7)     | 6 (25.0)              | 4 (11.1)             |         |
| Not reported           | 7 (11.7)      | 2 (8.3)               | 5 (13.9)             |         |
| TABLE 3  (Continued) | Total (N = 61) | PH persisted (n = 25) | PH resolved (n = 36) | p Value |
|-----------------------|----------------|----------------------|---------------------|--------|
| **LA size category, at presentation** | | | | 0.60 |
| Normal | 15 (25.0) | 5 (20.8) | 10 (27.8) | |
| Dilated | 38 (63.3) | 17 (70.8) | 21 (58.3) | |
| Not reported | 7 (11.7) | 2 (8.3) | 5 (13.9) | |
| **IVS diastolic thickness (IVSd, mm), at presentation, median (IQR)** | 1.2 (1.1, 1.3) | 1.2 (1.1, 1.3) | 1.2 (1.1, 1.4) | 0.74 |
| **Posterior wall thickness (LVPWd, mm), at presentation, median (IQR)** | 1.2 (1.0, 1.3) | 1.2 (1.1, 1.3) | 1.2 (1.0, 1.3) | 0.55 |
| **LVIDd (mm), at presentation, median (IQR)** | 4.7 (4.3, 5.2) | 4.9 (4.2, 5.1) | 4.6 (4.3, 5.6) | 0.69 |
| **LV cardiac output (L/min), at presentation, median (IQR)** | 5.6 (4.4, 6.8) | 5.2 (3.9, 5.6) | 6.4 (4.6, 6.9) | 0.11 |
| **LV cardiac index, at presentation, median (IQR)** | 2.8 (2.4, 3.5) | 2.7 (2.1, 2.9) | 3.0 (2.5, 3.8) | 0.15 |
| **LA volume indexed to BSA (ml/m²), prepresentation, median (IQR)** | 38.7 (31.7, 45.6) | 38.4 (34.0, 45.8) | 38.9 (31.2, 45.6) | 0.83 |
| **Pre-Tx echocardiogram results available** | | | | 0.87 |
| No | 14 (23.0) | 6 (24.0) | 8 (22.2) | |
| Yes | 47 (77.0) | 19 (76.0) | 28 (77.8) | |
| **LV systolic function (pre-Tx)** | | | | 0.15 |
| Hyperdynamic | 2 (4.3) | 2 (10.5) | 0 (0.0) | |
| Normal | 38 (80.9) | 13 (68.4) | 25 (89.3) | |
| Reduced | 6 (12.8) | 3 (15.8) | 3 (10.7) | |
| Not reported | 1 (2.1) | 1 (5.3) | 0 (0.0) | |
| **LVEF (%), pre-Tx, median (IQR)** | 62.0 (57.0, 67.0) | 62.0 (57.0, 67.0) | 60.0 (55.0, 62.0) | 0.34 |
| **LV diastolic function (pre-Tx)** | | | | 0.10 |
| Normal | 3 (6.4) | 1 (5.3) | 2 (7.1) | |
| Reduced | 34 (72.3) | 11 (57.9) | 23 (82.1) | |
| Not reported | 10 (21.3) | 7 (36.8) | 3 (10.7) | |
| **LV filling pressure (pre-Tx)** | | | | 0.09 |
| Normal | 4 (8.5) | 1 (5.3) | 3 (10.7) | |
| Elevated | 29 (61.7) | 9 (47.4) | 20 (71.4) | |
| Not reported | 14 (29.8) | 9 (47.4) | 5 (17.9) | |
| **Wall motion abnormality (pre-Tx)** | | | | 0.47 |
| No | 37 (80.4) | 13 (72.2) | 24 (85.7) | |
| Yes | 6 (13.0) | 3 (16.7) | 3 (10.7) | |
| Not reported | 3 (6.5) | 2 (11.1) | 1 (3.6) | |
| **RV systolic function (pre-Tx)** | | | | 0.42 |
| Hyperdynamic | 42 (89.4) | 16 (84.2) | 26 (92.9) | |
| Normal | 4 (8.5) | 2 (10.5) | 2 (7.1) | |
| Reduced | 1 (2.1) | 1 (5.3) | 0 (0.0) | |

(Continues)
PH. There was an inverse relationship with hemoglobin (g/dl) and the composite of death or graft loss (HR: 0.77, 95% CI: 0.60, 0.98, p = 0.03; all Table 5).

PH persistence versus resolution was not associated with mortality, death censored graft failure, nor the composite of death or graft failure (Table 5). Similarly, persistence versus resolution of PH was not associated with change in hemoglobin posttransplantation over time.

DISCUSSION

Prior reports of the impact of pretransplant PH on outcomes following kidney transplantation have been contradictory. The single largest report of carefully characterized single organ primary kidney transplant recipients\(^5\) found that echo-defined PH (PA systolic pressure of ≥35 mmHg) was present in 15.6% of patients. That study by Obi et al.\(^5\) was the single largest report of demographics and outcomes of echocardiographically defined PH in a kidney transplant population and reported that, by multivariable analyses, the presence of PH while associated with other risk factors for worse outcome (notably dialysis vintage, race, and age) was not itself a risk factor for a poorer outcomes (mortality, death censored graft loss, or the composite of death or graft loss).\(^5\) This lack of adverse impact of pretransplant PH on outcomes following kidney transplantation contrasts sharply with the increased mortality seen in patients with liver disease-associated PAH,\(^12\) and in heart transplant candidates and recipients with PH.\(^13\) The Obi study also demonstrated the association of PH with echocardiographic features of diastolic dysfunction. In the absence of coronary artery disease, prior literature has suggested that “uremic cardiomyopathy” can resolve in the milieu of a functioning kidney.\(^14,15\) The present report, the first to examine the course of pretransplant...
| Recipient demographic and clinical characteristics | Total (N = 61) | PH persisted (n = 25) | PH resolved (n = 36) | p Value |
|---------------------------------------------------|---------------|-----------------------|---------------------|---------|
| Age at presentation (years), median (IQR)         | 58.0 (46.0, 65.0) | 58.0 (50.0, 65.0) | 59.0 (44.5, 64.0) | 0.83    |
| Male gender                                        | 28 (45.9)      | 12 (48.0)             | 16 (44.4)           | 0.78    |
| Race/ethnicity                                     |               |                       |                     | 0.73    |
| White                                              | 25 (41.0)      | 9 (36.0)              | 16 (44.4)           |         |
| Black                                              | 22 (36.1)      | 10 (40.0)             | 12 (33.3)           |         |
| Hispanic                                           | 13 (21.3)      | 6 (24.0)              | 7 (19.4)            |         |
| Asian                                              | 1 (1.6)        | 0 (0.0)               | 1 (2.8)             |         |
| BMI, median (IQR)                                  | 26.9 (24.5, 30.7) | 25.4 (24.2, 30.1) | 27.7 (25.2, 30.9) | 0.20    |
| Smoking                                            |               |                       |                     | 0.57    |
| No                                                 | 41 (67.2)      | 16 (64.0)             | 25 (69.4)           |         |
| Yes                                                | 9 (14.8)       | 3 (12.0)              | 6 (16.7)            |         |
| Unknown                                            | 11 (18.0)      | 6 (24.0)              | 5 (13.9)            |         |
| Malignancy                                         | 3 (4.9)        | 1 (4.0)               | 2 (5.6)             | 0.78    |
| ABO blood group                                    |               |                       |                     | 0.53    |
| A                                                  | 18 (29.5)      | 6 (24.0)              | 12 (33.3)           |         |
| B                                                  | 4 (6.6)        | 1 (4.0)               | 3 (8.3)             |         |
| AB                                                 | 1 (1.6)        | 0 (0.0)               | 1 (2.8)             |         |
| O                                                  | 38 (62.3)      | 18 (72.0)             | 20 (55.6)           |         |
| Deceased donor                                     | 42 (68.9)      | 17 (68.0)             | 25 (69.4)           | 0.90    |
| Primary diagnosis, diabetes                        | 29 (47.5)      | 12 (48.0)             | 17 (47.2)           | 0.95    |
| Primary diagnosis, hypertension                    | 59 (96.7)      | 24 (96.0)             | 35 (97.2)           | 0.79    |
| ESRD cause                                         |               |                       |                     |         |
| Diabetes                                           | 27 (44.3)      | 12 (48.0)             | 15 (41.7)           | 0.62    |
| Hypertension                                       | 24 (39.3)      | 10 (40.0)             | 14 (38.9)           | 0.93    |
| Autoimmune diseases                                | 3 (4.9)        | 1 (4.0)               | 2 (5.6)             | 0.78    |
| Genetic diseases                                   | 1 (1.6)        | 0 (0.0)               | 1 (2.8)             | 0.40    |
| Glomerular diseases                                | 3 (4.9)        | 2 (8.0)               | 1 (2.8)             | 0.35    |
| Urinary tract problems                             | 0 (0.0)        | 0 (0.0)               | 0 (0.0)             | –       |
| Other                                              | 14 (23.0)      | 5 (20.0)              | 9 (25.0)            | 0.65    |
| Creatinine at transplant, median (IQR)             | 6.4 (5.1, 8.3) | 6.4 (4.5, 7.2)        | 6.4 (5.7, 8.6)      | 0.20    |
| HLA mismatch level, median (IQR)                   | 4.0 (3.0, 5.0) | 4.0 (3.0, 5.0)        | 4.0 (3.0, 5.0)      | 0.48    |
| Most recent cPRA, median (IQR)                      | 36.5 (4.0, 81.5) | 40.0 (0.0, 86.0) | 36.5 (11.5, 71.0) | 0.85    |
| Dialysis at presentation                           | 54 (88.5)      | 23 (92.0)             | 31 (86.1)           | 0.48    |
| Dialysis type at presentation                      |               |                       |                     | 0.46    |
| PD                                                  | 4 (7.4)        | 1 (4.3)               | 3 (9.7)             |         |
| HD                                                  | 50 (92.6)      | 22 (95.7)             | 28 (90.3)           |         |

(Continues)
**TABLE 4** (Continued)

|                           | Total (N = 61) | PH persisted (n = 25) | PH resolved (n = 36) | p Value |
|---------------------------|---------------|-----------------------|----------------------|---------|
| Dialysis (overall)        |               |                       |                      |         |
| No                        | 5 (8.2)       | 1 (4.0)               | 4 (11.1)             | 0.32    |
| Yes                       | 56 (91.8)     | 24 (96.0)             | 32 (88.9)            |         |
| Dialysis vintage (years), median (IQR) | 3.9 (2.6, 6.9) | 3.7 (3.1, 7.4) | 4.3 (2.4, 6.0) | 0.90    |
| HBV core antibody (+)     | 7 (11.5)      | 4 (16.0)              | 3 (8.3)              | 0.36    |
| HbsAg (+)                 | 0 (0.0)       | 0 (0.0)               | 0 (0.0)              | –       |
| HCV serostatus (+)        | 5 (8.2)       | 1 (4.0)               | 4 (11.1)             | 0.32    |
| CMV status (+)            | 49 (80.3)     | 21 (84.0)             | 28 (77.8)            | 0.55    |
| EBV serostatus (+)        | 55 (96.5)     | 21 (91.3)             | 34 (100.0)           | 0.08    |
| HIV serostatus (+)        | 3 (5.0)       | 1 (4.2)               | 2 (5.6)              | 0.81    |
| Kidney transplant procedure type |       |                       |                      | 0.41    |
| Left                      | 40 (65.6)     | 15 (60.0)             | 25 (69.4)            |         |
| Right                     | 20 (32.8)     | 9 (36.0)              | 11 (30.6)            |         |
| En-bloc                   | 1 (1.6)       | 1 (4.0)               | 0 (0.0)              |         |
| Most recent hemoglobin (g/dl) | 10.3 (8.9, 11.9) | 10.1 (8.9, 11.2) | 10.5 (8.9, 11.9) | 0.73    |

**Donor characteristics**

|                                            |               |                       |                      |         |
|--------------------------------------------|---------------|-----------------------|----------------------|---------|
| Donor age (years), median (IQR)            | 42.0 (34.0, 51.0) | 44.0 (32.0, 52.0) | 41.0 (34.5, 49.5) | 0.72    |
| Donor male gender                          | 23 (37.7)     | 8 (32.0)              | 15 (41.7)            | 0.44    |
| Donor race/ethnicity                       |               |                       |                      | 0.37    |
| White                                      | 30 (49.2)     | 11 (44.0)             | 19 (52.8)            |         |
| Black                                      | 12 (19.7)     | 7 (28.0)              | 5 (13.9)             |         |
| Hispanic/Latino                            | 17 (27.9)     | 7 (28.0)              | 10 (27.8)            |         |
| Asian                                      | 2 (3.3)       | 0 (0.0)               | 2 (5.6)              |         |
| Donor BMI, median (IQR)                    | 26.1 (22.7, 30.4) | 28.7 (23.8, 31.8) | 25.7 (22.2, 27.9) | 0.09    |
| HBV core antibody (+), donor               | 0 (0.0)       | 0 (0.0)               | 0 (0.0)              | –       |
| ABO blood group, donor                     |               |                       |                      | 0.36    |
| A                                         | 15 (25.0)     | 5 (20.0)              | 10 (28.6)            |         |
| B                                         | 2 (3.3)       | 0 (0.0)               | 2 (5.7)              |         |
| AB                                        | 1 (1.7)       | 0 (0.0)               | 1 (2.9)              |         |
| O                                         | 42 (70.0)     | 20 (80.0)             | 22 (62.9)            |         |
| Kidney cold ischemic time (h), median (IQR) | 16.3 (1.5, 26.0) | 16.0 (2.8, 25.1) | 16.5 (1.3, 26.5) | 0.86    |
| History of smoking, donor                  | 11 (18.0)     | 7 (28.0)              | 4 (11.1)             | 0.09    |
| History of hypertension, donor             | 16 (26.2)     | 6 (24.0)              | 10 (27.8)            | 0.74    |
| History of diabetes, donor                 | 6 (14.3)      | 3 (17.6)              | 3 (12.0)             | 0.61    |

**Outcomes**

|                                    |               |                       |                      |         |
|-------------------------------------|---------------|-----------------------|----------------------|---------|
| Immediate graft function            | 10 (16.7)     | 5 (20.0)              | 5 (14.3)             | 0.56    |
| Delayed graft function              | 11 (18.3)     | 6 (24.0)              | 5 (14.3)             | 0.34    |
| Overall mortality                   | 17 (27.9)     | 8 (32.0)              | 9 (25.0)             | 0.55    |
PH following kidney transplantation, describes findings in 61 of 115 kidney transplant recipients with echocardiographically defined pretransplant PH on whom posttransplant echocardiograms were available for examination. The study documents that PH can resolve following renal transplantation (59% resolve) and that even in those in whom resolution does not occur, the outcome is not different in the longer term.

Prior reports of PH outcomes in patients with pretransplant PH undergoing evaluation and or kidney transplant have been limited by very small numbers and no or limited review of the subsequent posttransplant echocardiographic features. In a report by Issa et al. of 215 kidney transplant recipients, 146 (68%) had a PA systolic of <35 mmHg (considered normal), and 69 has PA pressures of ≥35 mmHg (in contrast to the 115 kidney transplant recipients with PH in the present cohort). That publication provided no echocardiographic posttransplantation data. Similarly, data from a single US center registry (University of North Carolina) reported 97 patients with PH out of a cohort of 778 patients screened for kidney transplant. While this group reported a higher mortality in patients with PH the review was largely an evaluation of pretransplant mortality on the kidney transplant wait list, as only 15 patients with pretransplant echocardiographically defined PH underwent kidney transplantation and no posttransplantation echocardiographic data was reported. The only prior paper to date that described posttransplant echocardiographic changes and included data on patients with PH was a review of 232 patients undergoing kidney transplantation at the Cleveland Clinic. The objective of that report was to assess the changes in echocardiographic findings in those 232 patients undergoing kidney transplants many of whom (28%) had reduced LVEF and most of whom (65%) had an abnormal LV mass normalized to BSA. The authors demonstrated improvement in both these indices of LV dysfunction consistent with their hypothesis that resolution of the uremic milieu, improvement in anemia and fluid balance was associated with reverse cardiac remodeling. Their cohort included only 35 patients with a baseline right ventricular systolic pressure (RVSP/PAsys of ≥40 mmHg) (mean 48 ± 8 mmHg). In this small cohort, clearly meaning the definition of PH by echo they demonstrated a significant improvement in mean RVSP (posttransplantation 38 ± 15 mmHg, p < 0.0001). However, the number of patients achieving resolution of PH, the time frame over which this occurred and whether those recipients with pretransplant PH with resolution experienced different outcomes was not addressed in the paper or the data. Hence, the current study is the first to clearly address issues of frequency of resolution, outcomes with resolution, time of resolution, and potential for echocardiographic recurrence of PH.

A recent publication using the International Classification of Diseases (ICD-9/10) codes to identify pretransplant and posttransplant PH reported that ICD9/10 codes for PH were present in 8.2% of kidney transplant recipients at some point in the 2 years before transplantation. In addition, while posttransplant mortality was reported to be substantially higher in those with posttransplant PH, this finding is driven largely by those who develop PH (again by ICD-9/10 code definition) following kidney transplantation. While hypothesis generating, the use of ICD-9/10 codes to define clinical PH has been demonstrated to be fraught with risk of substantial misinterpretation and misrepresentation as the authors themselves cautioned in their manuscript. The development of PH posttransplant in the latter study demonstrated that new-onset posttransplant PH was significantly associated with mortality and graft loss at 3 years. It was less clear that pretransplant persistent PH was associated with posttransplant mortality; resolution defined by ICD-9/10 codes appeared to have occurred in approximately 50% of those with pretransplant PH. However 2/3 of those with posttransplant PH had developed PH de novo, thus the majority of patients with posttransplant PH had developed PH de novo. The statistical analyses of outcomes

| PH persisted | PH resolved |
|--------------|-------------|
| 21 (34.4)    | 10 (27.8)   |
| 5 (8.2)      | 1 (2.8)     |

*p Value*
were only performed on the cohort with posttransplant ICD9/10 code-defined PH and in those newly diagnosed with posttransplant PH, not in the category of those with pretransplant PH whether it persisted or resolved following transplantation.

The pretransplant echocardiographic and demographic variables associated with poorer outcomes in the analysis presented herein, mirrored those seen in previous reports and in the Scientific Registry of Transplant Recipients\textsuperscript{20} databases namely recipient age at presentation, and race/ethnicity (protection conferred by Hispanic race).

Unlike the salutary association of change in hemoglobin posttransplantation with LVEF reported by Hawaa et al.,\textsuperscript{6} no association was seen in the present study between the change in hemoglobin over time and persistence or the resolution of PH. However, there was a significant negative association between the change in hemoglobin over time and the composite outcome of death or graft loss.

The apparent statistically significant association between duration of posttransplant PH and decreased likelihood of mortality probably simply reflects the fact that persistent PH posttransplant does not affect survival, and hence those recipients with the longest follow-up must have lived the longest.

PH resolved in the cohort reported herein in 36 (59\%) patients, a proportion similar to the number inferred from the data in the manuscript by Lentine et al.\textsuperscript{16} (50\%). Herein it is reported that PH resolution occurred at a median of 37.5 months posttransplant. While there was no difference in mortality, or death censored graft loss between those in whom PH resolved versus persisted at 3 and 5 years, there was a significant increase in the composite of death or graft loss at 3 years in those with persistent PH, a difference that was no longer present at 5 years. Though the biggest study to date, the relatively small numbers and infrequent adverse events might confound a meaningful difference. In six patients in whom PH had resolved, it recurred at a median of 48 months from the date of initial resolution. These data suggest that the risks associated with both the underlying etiologies of end-stage renal disease, the metabolic derangements imposed by chronic kidney disease (CKD) and dialysis, or factors posttransplant (calcineurin inhibitors, hypertension, new-onset diabetes) may account for the de novo PH reported by Lentine et al.\textsuperscript{16} and the recurrence of PH reported herein. The small numbers (6) of patients in our cohort with echocardiographically confirmed recurrent PH preclude meaningful evaluation of outcomes or possible associated risk factors.

Limitations of this report include: PH pressure was estimated from echocardiographic features (tricuspid regurgitant jet and estimated RAP), and as such is an estimate; that posttransplantation echocardiograms were not available on all patients who had pretransplant echocardiographically defined PH; and the echocardiograms reported herein were all performed for indication.
### TABLE 5  Potential prognostic variables for outcomes in those with posttransplant echocardiograms

|                                 | Mortality Univariable HR (95% CI) | Death-censored graft failure Univariable HR (95% CI) | Composite outcome Univariable HR (95% CI) |
|---------------------------------|-----------------------------------|-----------------------------------------------|-------------------------------------|
|                                 | p Value                           | p Value                                     | p Value                             |
| PH resolution                   |                                   |                                              |                                     |
| PH resolved                     | (Reference)                       | (Reference)                                 | (Reference)                         |
| PH persisted                    | 1.18 (0.43, 3.21)                 | 5.52 (0.60, 51.14)                          | 1.49 (0.61, 3.64)                  |
| PH persistent duration (months) | 0.96 (0.93, 0.99)                 | 0.99 (0.96, 1.03)                           | 0.97 (0.94, 0.99)                  |
| Recipient demographic and clinical characteristics |   |                                              |                                     |
| Age at presentation (years)     | 1.06 (1.01, 1.10)                 | 0.99 (0.93, 1.05)                           | 1.03 (1.00, 1.07)                  |
| Male gender                     | 1.46 (0.61, 3.49)                 | 0.63 (0.14, 2.87)                           | 1.29 (0.60, 2.77)                  |
| Race/ethnicity                  |                                   |                                              |                                     |
| White                           | (Reference)                       | (Reference)                                 | (Reference)                         |
| Black                           | 0.69 (0.28, 1.74)                 | 2.51 (0.23, 27.69)                          | 0.89 (0.38, 2.07)                  |
| Hispanic                        | 0.20 (0.04, 0.87)                 | 4.05 (0.42, 38.96)                          | 0.51 (0.18, 1.43)                  |
| Asian                           | –                                 | 8.22 (0.50, 135.02)                         | 0.59 (0.08, 4.56)                  |
| Black                           | 1.16 (0.47, 2.84)                 | 0.94 (0.18, 4.83)                           | 1.14 (0.52, 2.52)                  |
| BMI                             | 1.03 (0.95, 1.13)                 | 0.90 (0.76, 1.08)                           | 1.00 (0.93, 1.08)                  |
| Smoking                         |                                   |                                              |                                     |
| No                              | (Reference)                       | (Reference)                                 | (Reference)                         |
| Yes                             | 0.59 (0.14, 2.57)                 | 1.49 (0.16, 13.74)                          | 0.77 (0.23, 2.61)                  |
| Unknown                         | 0.48 (0.11, 2.07)                 | 2.22 (0.40, 12.15)                          | 0.85 (0.29, 2.49)                  |
| Malignancy                      | 4.57 (1.34, 15.64)                | –                                            | 3.32 (0.99, 11.09)                 |
| ABO blood group                 |                                   |                                              |                                     |
| A                               | 1.12 (0.46, 2.70)                 | 5.47 (0.61, 49.17)                          | 1.37 (0.62, 3.06)                  |
| B                               | –                                 | 15.26 (1.38, 168.75)                         | 1.27 (0.28, 5.68)                  |
| AB                              | 2.17 (0.48, 9.89)                 | –                                            | 2.01 (0.45, 9.04)                  |
| O                               | (Reference)                       | (Reference)                                 | (Reference)                         |
| Deceased donor                  | 1.05 (0.44, 2.50)                 | 3.60 (0.43, 29.97)                          | 1.29 (0.58, 2.85)                  |
| Primary diagnosis, diabetes     | 1.36 (0.58, 3.16)                 | 2.07 (0.44, 9.70)                           | 1.42 (0.67, 3.03)                  |
| Primary diagnosis, hypertension | –                                 | –                                            | –                                   |
| ESRD cause                      |                                   |                                              |                                     |
| Diabetes                        | 1.51 (0.65, 3.51)                 | 1.24 (0.27, 5.73)                           | 1.35 (0.64, 2.88)                  |
| Hypertension                    | 1.94 (0.84, 4.51)                 | 1.12 (0.25, 5.05)                           | 1.84 (0.87, 3.87)                  |
| Autoimmune diseases             | 0.66 (0.09, 4.93)                 | 2.68 (0.32, 22.33)                          | 1.13 (0.27, 4.75)                  |
| Genetic diseases                | 0.78 (0.10, 5.78)                 | –                                            | 0.60 (0.08, 4.43)                  |
| Glomerular diseases             | –                                 | 4.94 (0.58, 42.45)                          | 1.06 (0.14, 7.82)                  |
| Urinary tract problems          | –                                 | –                                            | –                                   |
| Other                           | 0.70 (0.21, 2.36)                 | 0.72 (0.09, 5.97)                           | 0.72 (0.25, 2.08)                  |
| Creatinine at transplant        | 1.04 (0.90, 1.19)                 | 0.91 (0.67, 1.23)                           | 1.02 (0.90, 1.16)                  |
| HLA mismatch level              | 1.02 (0.80, 1.29)                 | 0.96 (0.64, 1.43)                           | 1.05 (0.84, 1.30)                  |

(Continues)
TABLE 5  (Continued)

| Mortality | Death-censored graft failure | Composite outcome |
|-----------|-----------------------------|-------------------|
| Univariable HR (95% CI) | Univariable HR (95% CI) | Univariable HR (95% CI) |
| **p Value** | **p Value** | **p Value** |
| Most recent cPRA | 1.00 (0.99, 1.01) | 1.00 (0.98, 1.02) | 1.00 (0.99, 1.01) |
| Dialysis at presentation | 0.71 (0.24, 2.11) | 0.94 (0.32, 2.72) |
| **Dialysis type at presentation** | | |
| PD (Reference) | (Reference) | (Reference) |
| HD | 0.50 (0.11, 2.23) | 0.38 (0.04, 3.27) | 0.45 (0.13, 1.55) |
| **Dialysis (overall)** | | |
| No (Reference) | – | – | (Reference) |
| Yes | 0.50 (0.15, 1.70) | 0.66 (0.20, 2.21) |
| Dialysis vintage (years) | 0.93 (0.80, 1.09) | 0.95 (0.84, 1.08) |
| HBV core antibody (+) | 1.88 (0.55, 6.41) | 9.64 (1.94, 47.91) | 3.33 (1.33, 8.37) |
| HbsAg (+) | – | – | – |
| HCV serostatus (+) | 0.91 (0.21, 3.92) | 1.60 (0.19, 13.69) | 1.11 (0.33, 3.71) |
| CMV status (+) | 0.95 (0.35, 2.59) | 1.66 (0.20, 13.80) | 1.30 (0.49, 3.42) |
| EBV serostatus (+) | 0.50 (0.12, 2.14) | 0.66 (0.16, 2.79) |
| HIV serostatus (+) | – | – | – |
| **Kidney transplant procedure type** | | |
| Left (Reference) | (Reference) | (Reference) |
| Right | 0.98 (0.41, 2.33) | 3.33 (0.61, 18.26) | 1.17 (0.54, 2.52) |
| En-bloc | – | 28.47 (2.52, 321.82) | 4.02 (0.53, 30.54) |
| **Delayed graft function** | | |
| No (Reference) | (Reference) | (Reference) |
| Yes | 0.55 (0.07, 4.15) | 5.17 (0.93, 28.59) | 1.39 (0.42, 4.64) |
| Most recent hemoglobin (g/dl) | 0.80 (0.62, 1.04) | 0.72 (0.43, 1.21) | 0.77 (0.60, 0.98) |
| **Echocardiographic parameters** | | |
| PA pressure (mmHg) [range] | 1.01 (0.96, 1.06) | 1.04 (0.96, 1.12) | 1.02 (0.98, 1.06) |
| At presentation echo results available | | |
| No (Reference) | (Reference) | (Reference) |
| Yes | 0.64 (0.09, 4.81) | 0.15 (0.02, 1.28) | 0.73 (0.10, 5.42) |
| LV systolic function, at presentation | | |
| Hyperdynamic | 1.31 (0.17, 10.23) | – | 0.98 (0.13, 7.44) |
| Normal (Reference) | – | (Reference) |
| Reduced | 1.16 (0.26, 5.17) | – | 0.85 (0.20, 3.72) |
| Not reported | – | – | – |
| LVEF (%), at presentation | 0.98 (0.94, 1.03) | 0.96 (0.89, 1.04) | 0.98 (0.94, 1.01) |
| LV diastolic function at presentation | | |
| Normal (Reference) | – | (Reference) |
| Reduced | 0.84 (0.10, 6.81) | – | 1.12 (0.14, 8.77) |
| Not reported | 0.85 (0.10, 7.55) | – | 0.95 (0.11, 8.23) |
| TABLE 5  (Continued) | Mortality | Death-censored graft failure | Composite outcome |
|------------------------|-----------|-----------------------------|-------------------|
|                         | Univariable HR (95% CI) | p Value | Univariable HR (95% CI) | p Value | Univariable HR (95% CI) | p Value |
| LV filling pressure at presentation | | | | | | |
| Normal (Reference) | – | – | (Reference) | | | |
| Elevated | 1.13 (0.22, 5.72) | 0.89 | – | – | 1.49 (0.31, 7.17) | 0.62 |
| Not reported | 1.51 (0.30, 7.71) | 0.62 | – | – | 1.95 (0.40, 9.41) | 0.41 |
| LV wall thickness (LVH), at presentation | | | | | | |
| Normal (Reference) | – | – | (Reference) | | | |
| Abnormal | 0.88 (0.23, 3.36) | 0.85 | – | – | 1.27 (0.34, 4.68) | 0.72 |
| Not reported | 0.76 (0.14, 4.01) | 0.75 | – | – | 1.14 (0.24, 5.54) | 0.87 |
| LV wall motion abnormality, pat presentation | | | | | | |
| No (Reference) | – | – | (Reference) | | | |
| Yes | 1.18 (0.26, 5.41) | 0.83 | – | – | 0.88 (0.20, 3.90) | 0.87 |
| Not reported | 0.98 (0.21, 4.51) | 0.98 | 2.09 (0.19, 23.12) | 0.55 | 1.17 (0.33, 4.18) | 0.81 |
| RV systolic function, at presentation | | | | | | |
| Hyperdynamic (Reference) | – | – | (Reference) | | | |
| Normal | 1.35 (0.17, 10.57) | 0.78 | – | – | 1.13 (0.15, 8.73) | 0.90 |
| Reduced | 1.38 (0.30, 6.22) | 0.68 | 3.80 (0.34, 42.02) | 0.28 | 1.74 (0.49, 6.12) | 0.39 |
| RA size category, at presentation | | | | | | |
| Normal (Reference) | – | – | (Reference) | | | |
| Dilated | 0.78 (0.17, 3.52) | 0.75 | – | – | 0.62 (0.14, 2.72) | 0.52 |
| Not reported | 1.29 (0.28, 5.87) | 0.74 | 3.29 (0.30, 36.47) | 0.33 | 1.60 (0.45, 5.65) | 0.47 |
| LA size category, at presentation | | | | | | |
| Normal (Reference) | – | – | (Reference) | | | |
| Dilated | 5.24 (0.67, 40.79) | 0.11 | 1.02 (0.09, 11.47) | 0.99 | 3.21 (0.72, 14.37) | 0.13 |
| Not reported | 11.95 (1.20, 118.85) | 0.03 | 4.79 (0.25, 93.37) | 0.30 | 8.44 (1.47, 48.34) | 0.02 |
| IVS diastolic thickness (IVSd, mm), at presentation | | | | | | |
| Normal | 7.84 (1.00, 61.31) | 0.049 | 0.23 (0.00, 15.98) | 0.49 | 3.68 (0.58, 23.49) | 0.17 |
| Posterior wall thickness (LVPWd, mm), at presentation | | | | | | |
| Normal | 1.07 (0.11, 10.11) | 0.95 | 6.02 (0.08, 448.35) | 0.42 | 1.55 (0.22, 11.20) | 0.66 |
| LVIDd (mm), at presentation | | | | | | |
| Normal | 0.63 (0.29, 1.36) | 0.24 | 1.62 (0.42, 6.25) | 0.48 | 0.79 (0.41, 1.53) | 0.49 |
| LV cardiac output (L/mn), at presentation | | | | | | |
| Normal | 1.00 (1.00, 1.01) | 0.03 | 0.90 (0.39, 2.06) | 0.80 | 1.00 (1.00, 1.01) | 0.04 |
| LV cardiac index, at presentation | | | | | | |
| Normal | 1.12 (0.45, 2.77) | 0.81 | 0.84 (0.13, 5.52) | 0.86 | 1.05 (0.46, 2.38) | 0.91 |
| LA volume indexed to BSA (ml/m²), at presentation | | | | | | |
| Normal | 1.01 (0.96, 1.06) | 0.61 | 1.03 (0.93, 1.04) | 0.55 | 1.02 (0.97, 1.06) | 0.42 |
| Pre-Tx echocardiogram results available | | | | | | |
| No (Reference) | – | – | (Reference) | | | |
| Yes | 1.91 (0.72, 5.10) | 0.19 | 6.33 (0.64, 62.47) | 0.11 | 2.30 (0.93, 5.68) | 0.07 |
| LV systolic function (pre-Tx) | | | | | | |
| Hyperdynamic | – | – | 13.28 (1.18, 149.58) | 0.04 | 4.13 (31.13, 0.00) | 0.49 |

(Continued)
|                     | Mortality  | Death-censored graft failure | Composite outcome |
|---------------------|------------|-----------------------------|-------------------|
|                     | Univariable HR (95% CI) | p Value | Univariable HR (95% CI) | p Value | Univariable HR (95% CI) | p Value |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| Reduced             | 2.31 (0.62, 8.61) | 0.21 | –               | –       | 1.16 (6.39, 0.00) | 0.49 |
| Not reported        | –          | –         | –                   | –       | –                   | –       |
| LVEF (%), pre-Tx    | 0.97 (0.93, 1.02) | 0.20 | 0.97 (0.91, 1.03) | 0.32 | 0.97 (0.93, 1.00) | 0.07 |
| LV diastolic function (pre-Tx) |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| Reduced             | –          | –         | 0.22 (0.02, 2.17) | 0.20 | 0.74 (0.09, 5.75) | 0.77 |
| Not reported        | –          | –         | –                   | –       | 0.39 (0.04, 4.35) | 0.44 |
| LV filling pressure (pre-Tx) |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| Elevated            | 0.84 (0.10, 7.00) | 0.87 | –               | –       | 1.19 (0.15, 9.43) | 0.87 |
| Not reported        | 0.84 (0.09, 8.22) | 0.88 | –               | –       | 1.19 (0.13, 10.77) | 0.87 |
| Wall motion abnormality (pre-Tx) |
| No (Reference)      |            |            | (Reference)            |         |            |         |
| Yes                 | 3.01 (0.77, 11.81) | 0.11 | –               | –       | 2.17 (0.58, 8.06) | 0.25 |
| Not reported        | 5.22 (0.60, 45.81) | 0.14 | 9.11 (0.80, 103.43) | 0.08 | 6.78 (1.37, 33.46) | 0.02 |
| RV systolic function (pre-Tx) |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| Reduced             | 1.65 (0.20, 13.47) | 0.64 | 10.06 (1.42, 71.41) | 0.02 | 3.89 (1.05, 14.42) | 0.04 |
| Not reported        | 14.81 (1.52, 144.17) | 0.02 | –               | –       | 10.60 (1.21, 92.93) | 0.03 |
| LA size category (pre-Tx) |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| Dilated             | 0.48 (0.12, 1.90) | 0.30 | –               | –       | 0.95 (0.31, 2.87) | 0.93 |
| RA size category (pre-Tx) |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| Dilated             | 2.80 (0.93, 8.40) | 0.07 | 3.51 (0.47, 26.28) | 0.22 | 3.24 (1.21, 8.72) | 0.02 |
| Not reported        | 0.62 (0.14, 2.69) | 0.52 | 0.38 (0.02, 6.75) | 0.51 | 0.64 (0.17, 2.46) | 0.52 |
| LV wall thickness (LVH) (pre-Tx) |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| Abnormal            | 0.09 (0.02, 0.48) | 0.01 | –               | –       | 0.56 (0.16, 1.98) | 0.37 |
| Not reported        | 0.33 (0.07, 1.52) | 0.16 | –               | –       | 0.35 (0.09, 1.27) | 0.11 |
| IVS diastolic thickness (IVSd, mm) (pre-Tx) |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| Posterior wall thickness (LVPWd, mm) (pre-Tx) |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| Abnormal            | 0.42 (0.07, 2.62) | 0.35 | 1.45 (0.08, 26.71) | 0.80 | 0.57 (0.12, 2.79) | 0.49 |
| Not reported        | 1.42 (0.65, 3.13) | 0.38 | 2.52 (0.78, 8.08) | 0.12 | 1.85 (0.96, 3.58) | 0.07 |
| LV cardiac output (pre-Tx, L/mn) |
| Normal (Reference)  |            |            | (Reference)            |         |            |         |
| LV cardiac index (pre-Tx) |
(as studies done for routine per protocol follow up are not reimbursable) suggesting that the reported cohort might have been at higher risk for adverse outcomes. However, the mortality did not differ between those with or without follow-up echocardiograms despite significant differences in risk factors of concern in those who did have follow-up echos (such as higher cPRA, greater incidence of DGF, a longer cold ischemic time, and a lower percentage of patients with immediate graft function). Although this is the largest echocardiographically documented outcomes analysis of the course of PH post kidney transplantation, the number reported herein is still relatively small, with few adverse events, and all undertaken at a single center. Our findings, while not statistically significant, should be interpreted with caution as we cannot rule out the possibility of underpower due to low patient number. This points to the need for a more robust, prospective multicenter echocardiographically studied cohort of PH patients with analyses of outcomes following kidney transplantation.

A strength of this paper is that it reports actual echocardiographic data rather than data inferred from ICD9/10 codes. A hemodynamically measured mean PA > 20 mmHg has been shown to be clearly associated with increased mortality risk in general patients, and in those with connective tissue disease. An echocardiographically estimated PA systolic of ≥35 mmHg has been repeatedly associated with greater risk for mortality in those with CKD on dialysis and ESRD. The reported data herein represents the largest series yet reporting the

| TABLE 5 (Continued) | Mortality | Death-censored graft failure | Composite outcome |
|----------------------|-----------|----------------------------|------------------|
|                      | Univariable HR (95% CI) | p Value | Univariable HR (95% CI) | p Value | Univariable HR (95% CI) | p Value |
| LA volume indexed to BSA (ml/m²) (pre-Tx) | 1.02 (0.98, 1.06) | 0.28 | 1.03 (0.93, 1.14) | 0.55 | 1.02 (0.97, 1.06) | 0.42 |
| Donor characteristics | | | | | | |
| Donor age (years) | 1.02 (1.00, 1.06) | 0.10 | 1.00 (0.95, 1.05) | 0.98 | 1.02 (0.99, 1.05) | 0.13 |
| Donor male gender | 1.15 (0.50, 2.66) | 0.75 | 1.04 (0.23, 4.67) | 0.96 | 1.05 (0.50, 2.23) | 0.89 |
| Donor race/ethnicity | | | | | | |
| White (Reference) | | | | | | |
| Black | 0.81 (0.23, 2.85) | 0.75 | 1.01 (0.11, 9.18) | 0.99 | 0.88 (0.30, 2.64) | 0.82 |
| Hispanic/Latino | 0.56 (0.19, 1.72) | 0.31 | 1.07 (0.20, 5.89) | 0.93 | 0.71 (0.28, 1.81) | 0.48 |
| Asian | 1.63 (0.21, 12.55) | 0.64 | – | – | 1.30 (0.17, 9.85) | 0.80 |
| Donor race/ethnicity, Black | 0.93 (0.27, 3.15) | 0.90 | 1.02 (0.12, 8.54) | 0.99 | 0.96 (0.33, 2.79) | 0.95 |
| Donor BMI | 1.06 (0.99, 1.13) | 0.09 | 1.02 (0.90, 1.16) | 0.75 | 1.04 (0.98, 1.11) | 0.18 |
| HBV core antibody (+), donor | – | – | – | – | – | – |
| ABO blood group, donor | | | | | | |
| A | 1.16 (0.46, 2.94) | 0.76 | 0.99 (0.18, 5.43) | 0.99 | 1.18 (0.52, 2.70) | 0.69 |
| B | – | – | 3.38 (0.37, 30.59) | 0.28 | 0.91 (0.12, 6.91) | 0.93 |
| AB | 6.47 (1.42, 29.37) | 0.02 | – | – | 4.90 (1.11, 21.64) | 0.04 |
| O (Reference) | | | | | | |
| Kidney cold ischemic time (h) | 1.01 (0.97, 1.04) | 0.64 | 1.04 (0.98, 1.11) | 0.16 | 1.02 (0.99, 1.05) | 0.25 |
| History of smoking, donor | 0.85 (0.25, 2.91) | 0.80 | – | – | 0.61 (0.18, 2.05) | 0.42 |
| History of hypertension, donor | 1.40 (0.51, 3.83) | 0.52 | 2.19 (0.40, 11.99) | 0.37 | 1.34 (0.54, 3.35) | 0.53 |
| History of diabetes, donor | 1.34 (0.30, 6.00) | 0.70 | – | – | 0.96 (0.22, 4.15) | 0.95 |

Notes: Cox proportional hazard modeling. Composite outcome = composite of patient mortality or graft failure. Abbreviations: –, unable to calculate due to small number; BMI, body mass index; CI, confidence interval; CMV, cytomegalovirus; cPRA, calculated panel reactive antibodies; EBV, Epstein–Barr virus; ESRD, end-stage renal disease; HBV, hepatitis B virus; HCV, hepatitis C virus; HD, hemodialysis; HIV, human immunodeficiency virus; HLA, human leukocyte antigen; HR, hazard ratio; IQR, interquartile range; IVS, interventricular septum; LA, left atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; PA, pulmonary artery systolic pressure; PD, peritoneal dialysis; PH, pulmonary hypertension; RA, right atrial; RV, right ventricular.
course of pre-existing PH in individuals following kidney transplantation, as derived from actual posttransplant echocardiograms.

In conclusion, echocardiographically defined PH present before kidney transplantation resolves following transplantation in approximately 60% of patients in a median of 37 months. Importantly, even if PH persists posttransplantation, it does not appear to be clearly associated with adverse outcomes.

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CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

ETHICS STATEMENT
Data acquisition and analysis approved under quality metric for hospital transplant program. Deidentified data were analyzed and the study is approved as part of Quality Metric by the Houston Methodist Hospital.

AUTHOR CONTRIBUTIONS
Adaani E. Frost, Wadi N. Suki conceived the protocol, reviewed the data, and authored the manuscript. Edward A. Graviss and Duc T. Nguyen undertook statistical analyses; Linda W. Moore, Miguel Valdivia e Alvarado, A. Graviss and Duc T. Nguyen undertook statistical review and final approval of the manuscript. Edward A. Graviss and Chizoba Obi contributed to data retrieval, entry, and analyses; Linda W. Moore, Miguel Valdivia e Alvarado, A. Graviss and Duc T. Nguyen undertook statistical review and final approval of the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher’s website.

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