2-22-2021

Clinical impact of pre-kidney transplant pulmonary hypertension on post-transplant outcomes

Besher Sadat

Deepthi Tirunagari

Vanji Karthikeyan

Anita Patel

Meredith Van Harn

See next page for additional authors

Authors

Besher Sadat, Deepthi Tirunagari, Vanji Karthikeyan, Anita Patel, Meredith Van Harn, Mariam Saleem, and Karthikeyan Ananthasubramaniam

The International Journal of Cardiovascular Imaging
https://doi.org/10.1007/s10554-021-02182-7

ORIGINAL PAPER

Clinical impact of pre-kidney transplant pulmonary hypertension on post-transplant outcomes

Besher Sadat[1] · Deepthi Tirunagari[2] · Vanji Karthikeyan[3] · Anita Patel[3] · Meredith Van Harn[4] · M. Mariam Saleem[1] · Karthikeyan Ananthasubramaniam[5]

Received: 11 September 2020 / Accepted: 30 January 2021

Abstract

Outcomes of kidney transplant (KT) patients with pre-transplant pulmonary hypertension (PH) are poorly understood. PH patients are often considered high risk and excluded from KT. We investigated the association of pre-transplant PH with KT recipient's outcomes. A single-center, retrospective study that reviewed all patients transplanted from 2010 to 2016, who had a transthoracic echocardiogram (TTE) before KT and at least one TTE post-KT. The TTE closest to the KT was used for analyses. PH is defined as pulmonary artery systolic pressure (PASP) ≥ 40 mm Hg. Of 204 patients, 61 had PASP ≥ 40 mm Hg (with PH) and 143 had PASP < 40 mm Hg (without PH) prior to KT. No statistically significant differences existed between the two groups in baseline demographics, renal failure etiologies, dialysis access type, and cardiovascular risk factors. The mean difference in pre-KT PASP was 18.1 ± 7 mm Hg (P < 0.001). Patients with PH had a statistically significant decrease in PASP post-KT compared to the patients without PH with a mean change of -7.03 ± 12.28 mm Hg vs. + 3.96 ± 11.98 mm Hg (p < 0.001), respectively. Moderate mitral and moderate-severe tricuspid regurgitation were the only factors found to be independently associated with PH (p = 0.001) on multivariable analysis. No statistically significant difference was notable in patient survival, graft function, and creatinine post-KT in both groups. PH pre-KT particularly mild-moderate PH did not adversely affect intermediate (90-day) and long-term allograft and patient survival. Patients with mild-moderate PH should not be excluded from KT.

Keywords Pulmonary hypertension · End-stage kidney disease · Kidney transplant · Survival

Introduction

Pulmonary hypertension (PH) is commonly encountered in patients with underlying chronic kidney disease and end-stage kidney disease (ESKD). Several observations have reported an association between PH and increased morbidity and mortality in this population [1]. The studies on the prevalence of PH in kidney disease is variable with reports ranging from 27 to 58% in ESKD patients on hemodialysis to 17%–32% in patients undergoing evaluation for a kidney transplant (KT) [2–5]. This variability is in part related to different definitions used for PH, but also the variety of contributing elements to PH plays a role, with higher prevalence reported with older age, longer duration on hemodialysis [6], and the presence of cardiovascular comorbidities [1].

Transthoracic echocardiography (TTE) is the most common diagnostic imaging performed as part of the pre-transplant evaluation of patients with chronic kidney disease and ESKD. It is a versatile, readily available test with a wealth

Prior presentation: The work was presented as a poster at the Michigan Chapter of the American College of Cardiology 30th Annual Conference, Detroit, MI, October 26-27, 2018.

✉ Karthikeyan Ananthasubramaniam
kananth1@hfhs.org

1 Department of Hospital Medicine, Henry Ford Hospital, Detroit, MI, USA

2 Department of Cardiology, St. Joseph Mercy Oakland Hospital, Pontiac, MI, USA

3 Department of Nephrology, Henry Ford Hospital, Detroit, MI, USA

4 Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA

5 Heart and Vascular Institute, Henry Ford West Bloomfield Hospital, 6777 West Maple, West Bloomfield, MI 48322, USA

Published online: 22 February 2021

of information on cardiac structure and function. It is also the recommended first-line test to noninvasively assess left ventricular (LV) function and estimate pulmonary artery systolic pressure (PASP) for evaluating PH in pre-transplant candidates by leading societal guidelines [7].

Despite KT being the final logical solution for ESKD patients, some studies have shown that moderate to severe PH is associated with worse overall post-transplant outcomes, perioperative complications as well as worse graft survival [1, 8–12]. However, other studies have shown that PH may improve post-KT and may not affect post-KT graft and patient survival [13–15]. Thus overall, PH continues to pose a dilemma with regards to KT listing and outcomes.

We have previously reported our experience in patients with LV dysfunction undergoing KT and demonstrated that patients with preexisting LV dysfunction should not be excluded from listing for KT. A substantial number of these patients had improvement of LV function post-KT [16]. Given that PH is commonly associated with chronic kidney disease and ESKD with or without LV dysfunction, it remains a challenge for pre-KT assessment and transplant listing. Thus, we conducted a retrospective single-center study at our institution to study our experience with PH and KT focusing on graft survival and mortality at our center.

Materials and methods

Study population

We conducted a retrospective chart review at our center from January 2010 until April 2016 with a principal diagnosis of ESKD who underwent KT and had a TTE pre- and post-KT. PH was defined as PASP ≥ 40 mm Hg derived from pre-KT TTE. The maximum tricuspid regurgitation flow obtained by continuous-wave Doppler examination was used in the modified Bernoulli equation to estimate PASP equal to $4V^2$ + plus right atrial pressure [17].

Data collection

Henry Ford Health System Institutional Review Board reviewed and approved the study protocol (IRB no: 12248). Data were collected on patient demographics, medical comorbidities, valvular heart disease, systolic and diastolic heart failure, etiology of ESKD, donor type, and type of dialysis access. TTE specific data included PASP, ejection fraction, and valvular pathology, data were collected through review of clinical reports. We stratified patients into two groups according to the PASP (≥ or < 40 mm Hg). The TTE closest to the KT was used to determine pre-KT PASP. Post-KT PASP was determined from the first available TTE after transplant. If patients had a second TTE post-KT, data were collected from that as well. A univariate comparison on KT patients with and without PH was performed. Additionally, a subgroup analysis of patients with PH who had a drop in PASP ≥ 10 mm Hg after KT on the first TTE compared to those who did not was reported. Finally, we evaluated patients' outcomes and graft function according to follow-up documentation in the medical record.

Statistical analysis

The sample of patients is described using counts and percentages for categorical variables and using means, standard deviations, medians, minimums, and maximums for continuous variables. Univariate two-group comparisons for continuous and categorical variables were carried out using two-group t-tests and chi-square tests, respectively. Multivariable logistic regression models were used to identify independent predictors of pre-KT PH, and results are presented using adjusted odds ratios and their 95% CIs. Models were checked for multicollinearity using correlation coefficients, variance inflation factors, eigenvalues, and condition indices, and no issues were detected. Kaplan–Meier survival estimates were used to determine patient survival with median survival time, calculated as the time at which survival probability reaches 0.50. Statistical significance was set at $p < 0.05$. All analyses are performed using SAS 9.4 (SAS Institute Inc, Cary, NC).

Results

Of the 204 patients (113 male and 91 female), 61 (29.9%) were identified to have pre-KT PH. A summary of the analyzed patients' characteristics is listed in (Table 1).

There was no statistically significant difference between the two groups (PASP ≥ or < 40 mm Hg) in terms of demographics, body mass index, cardiovascular risk factors, etiology of ESKD, transplant type, prevalence of coronary artery disease, systolic and diastolic heart failure, peripheral artery disease, venous disease, or asthma. Patients with PH noted to have a statistically significant difference in valvular heart disease ($p < 0.001$), specifically moderate mitral regurgitation ($p = 0.01$) and moderate to severe tricuspid regurgitation ($p = 0.001$). On multivariate analysis, moderate to severe tricuspid regurgitation was the only factor found to be independently associated with PH ($p = 0.001$) (Table 2).

The mean pre-KT PASP was 35.20 ± 10.7 mm Hg in the entire study group; the group with PH showed a mean PASP of 47.8 ± 7.7 mm Hg compared to 29.7 ± 6.3 mm Hg in the group without PH ($p < 0.001$). The distribution of PASP in each group is illustrated in (Fig. 1). A significant decrease in PASP post-KT ≥ 10 mm Hg was noted in 21.3% (n = 43). Patients in the group with PH had a

Table 1 Demographic data

Characteristic	N (%) (N = 204)
Gender	
Male	113 (55.5)
Race	
Caucasian	69 (34.0)
African American	120 (59.1)
Other	15 (6.9)
Kidney donor	
Deceased	130 (64.0)
Living	73 (35.9)
Etiology of ESKD	
Hypertension	70 (34.3)
Diabetes mellitus	64 (31.4)
Glomerulonephritis	13 (6.4)
Polycystic kidney disease	12 (5.9)
Interstitial nephritis	6 (2.9)
Hepatorenal syndrome	9 (4.4)
Retransplant	10 (4.9)
Other	19 (9.3)
Peripheral vascular occlusive disease	33 (16.3)
Coronary artery disease	61 (29.9)
Hypertension	192 (94.6)
Diabetes mellitus	110 (54.2)
Cardiomyopathy	61 (29.9)
Diastolic heart failure	12 (5.9)
Systolic heart failure	25 (12.3)
Asthma	1 (0.5)

ESKD, end-stage kidney disease

Table 2 Multivariable model of pre-transplant pulmonary hypertension

Variable	OR (95% CI)	P Value
Valvular heart disease (all/any)	0.39 (0.04–3.50)	0.397
Moderate/Severe MR	4.87 (0.52–46.10)	0.167
Moderate/Severe TR	40.67 (4.21–393.18)	0.001
Diastolic heart failure	2.51 (0.69–9.11)	0.160
Systolic heart failure	0.35 (0.10–1.28)	0.112
Diabetes mellitus	1.23 (0.60–2.50)	0.573
AVF or AVG	0.82 (0.41–1.63)	0.572

AVF arteriovenous fistula, *AVG* arteriovenous graft, *MR* mitral regurgitation, *OR* odds ratio, *TR* tricuspid regurgitation

statistically significant decrease in their PASP, with 47.5% (n = 29) of patients dropping PASP by at least 10 mm Hg after transplant compared to 9.9% (n = 14) of patients in the group without PH (p < 0.001), and these changes persisted on second follow-up TTE (p < 0.001) (Table 3). Figure 2 is showing an example of the change in a patient's tricuspid regurgitation signal from pre- to post-KT.

The mean time interval from pre-KT TTE to transplant was 13.62 ± 13.9 months (without PH) vs. 12.55 ± 12.5 months (with PH) (p = 0.606). Time from the KT to first TTE was 23.08 ± 26.53 months (without PH) vs. 21.91 ± 26.29 months (with PH) (p = 0.773), and for the KT to second TTE it was 39.32 ± 29.62 months (without PH) vs. 33.86 ± 24.75 months (with PH) (p = 0.371). The median ejection fraction was 53% ± 9.60%, with no statistically significant changes after KT documented between the groups on the first and second TTE. (Fig. 3) depicts the difference in left ventricular size pre- and post-KT in a patient with pre-KT PH.

A subgroup analysis was performed among a subset of pre-KT PH patients who had a significant decrease (PASP drop ≥ 10 mm Hg) in their PASP on the first post-KT TTE. These patients had a higher pre-KT PASP with a mean difference of + 4.2 ± 0.14 mm Hg (p = 0.029), and more significant post-KT PASP drop with a mean difference of -14.92 ± 4.5 mm Hg (p < 0.001). They also had a longer duration of dialysis with a mean difference + 0.95 ± 1.3 years (p = 0.036), and a more prevalent arteriovenous graft dialysis access (p = 0.009) despite no differences in valvular heart disease.

The mean creatinine post-KT for the entire group was 2.01 ± 1.63 mg/dL, graft failure happened in 26.5% (n = 54) with no significant difference in graft function, or graft failure noted between the groups or the subgroup with PASP drop post-KT.

The mean follow-up period was 77.9 ± 36.12 months, with no significant difference between the groups. Overall mortality was 32.8% (n = 67) at the end of the follow-up period, with 30.7% mortality in the group without PH versus 37.7% in the group with PH (p = 0.334) (Fig. 4).

Discussion

The main findings of this study can be summarized as follows: First, PH is commonly encountered in pre-KT evaluation, with a 29.9% prevalence in this study population; second, a substantial number of patients with PH (47.5%) dropped their PASP significant post-KT; and third, mild to moderate Pre-KT PH had no adverse effects on overall survival or graft loss post-KT regardless of the severity of PH or the duration of dialysis.

Cardiovascular factors

The definition of PH varies in the literature, with most defining it as PASP ≥ 35 or 40 mm Hg. Our analysis showed a comparable prevalence of pre-KT PH to previous literature

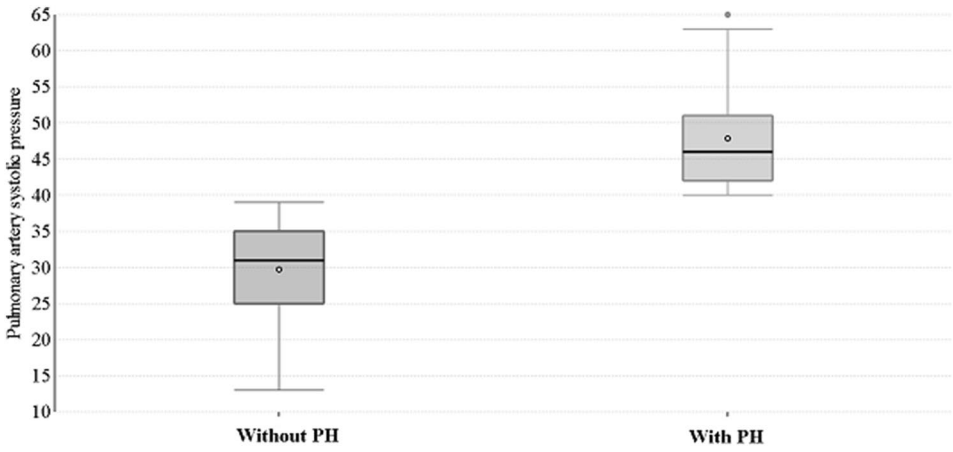

Fig. 1 Boxplot of the pulmonary artery systolic pressure in groups with and without PH

Table 3 PASP comparison between groups with and without PH

Covariate (mm Hg)	Statistics	PH		Parametric P value
		No	Yes	
Pre-KT PASP	Mean ± SD	29.73 ± 6.33	47.84 ± 7.77	< 0.001
Post-KT PASP TTE 1	Mean ± SD (N)	33.59 ± 12.35 (143)	40.8 ± 13.25 (61)	< 0.001
Drop in PASP from pre-KT to post-KT TTE 1		3.96 ± 11.98	− 7.03 ± 12.28	< 0.001
Post-KT PASP TTE 2	Mean ± SD (N)	36.3 ± 11.23 (60)	43.27 ± 14.72 (33)	0.012
Drop in PASP from post-TTE 1 to 2		1.33 ± 13.68	2.55 ± 15.96	0.701
Drop in PASP from pre-KT to post-KT TTE 2		5.95 ± 12.52	− 5.03 ± 14.06	< 0.001

KT kidney transplant, *PASP* pulmonary artery systolic pressure, *PH* pulmonary hypertension, *SD* standard deviation, *TTE* trans-thoracic echocardiogram

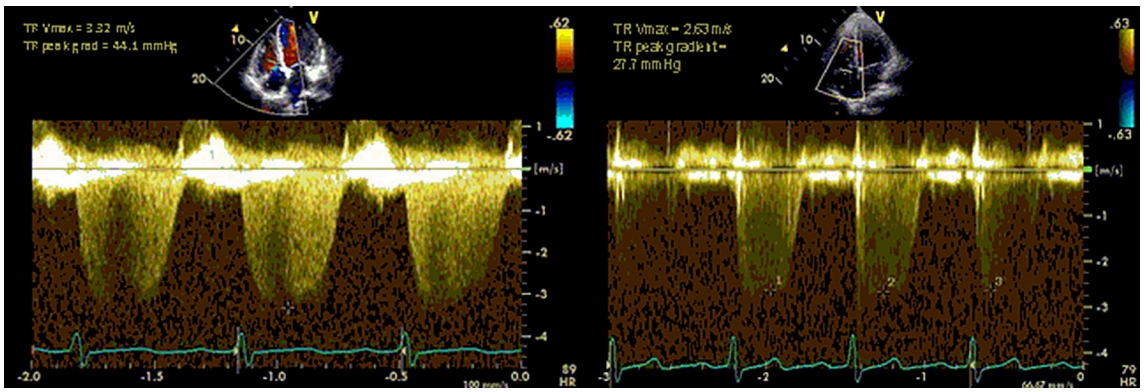

Fig. 2 Tricuspid regurgitation velocity and gradient pre-KT (left) and post-KT (right) in a patient with pre-KT PH; illustrating a drop of TR peak gradient by 16.4 mm Hg

[12, 14]. Several studies demonstrated a link between PH and mortality, with two meta-analyses finding a remarkable association between PH and cardiovascular event rate and increased mortality in chronic kidney disease and ESKD patients, with risks being proportional to the stage of chronic kidney disease [1, 18]. While some studies suggested that PH is an independent risk factor for all-cause mortality after adjusting for cardiovascular variables [19], other studies did not confirm PH and worse outcomes post KT. Rather LV dysfunction and race were factors associated with worse outcome [15].

Hypertension and diabetes accounted for 65% of ESKD etiologies in our study. Studies have linked diabetes to PH [20], worse graft survival [21], and lower patient survival

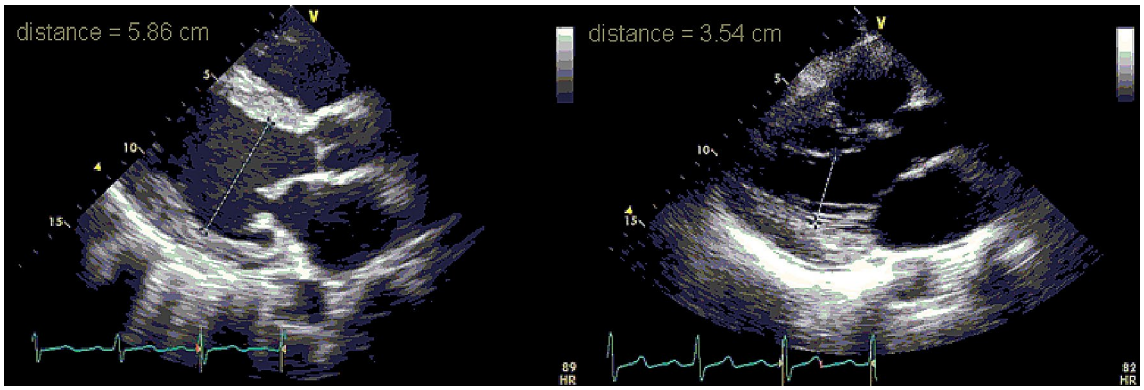

Fig. 3 Left ventricular size pre-KT (left) and post-KT (right) in a patient with pre-KT PH

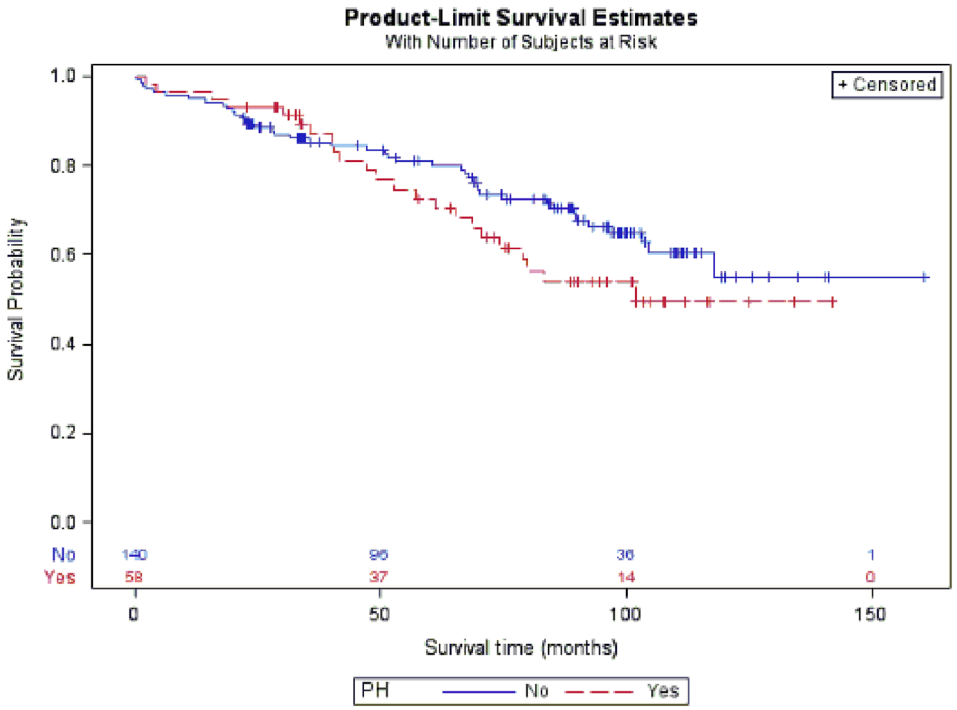

Fig. 4 Kaplan–Meier curves of overall survival by a group. The difference in survival is not statistically significantly different (p = 0.220). *PH* pulmonary hypertension

post-KT [22]. However, the last finding is challenged with better post-KT glycemic control and accountancy of other cardiovascular risk factors. Our study groups had similar cardiovascular risk factors distribution in both the main groups and the subgroups analysis.

In line with our previous finding, pre-KT LV dysfunction does not affect graft failure or survival of KT recipients [16]. Another study documented improvements in LV TTE parameters post-KT [13]. In contrast, systolic dysfunction in KT recipients with pre-KT PH was found to be associated with worse graft outcomes [15]. Our findings showed LV systolic and diastolic dysfunction were evenly distributed in both groups and did not predict pre-transplant PH in our evaluation.

Echocardiography

Like most transplant centers, right heart catheterization was not the standard of care in our pre-KT evaluation. The selection of patients who need catheterization to evaluate PH usually involves a multidisciplinary decision from cardiology and pulmonology. The use of TTE to estimate PASP has been described in a meta-analysis examining 29 studies. TTE had a sensitivity and specificity of 83% (95% CI 73%–90%) and 72% (95% CI 53%–85%), respectively, to diagnose PH, with a correlation coefficient of 0.70 when compared to right heart catheterization [23]. Other observations have suggested that PASP > 35 mm Hg is abnormal regardless of the fluid status, reasoning that TTE possibly underestimates and rarely overestimates the value of PASP

[11]. It is worth noting that the PASP changes reported on our first post-KT TTE were persistent on a second post-KT TTE.

Dialysis duration and access

There was an association between longer duration on hemodialysis with both the severity of PH and ventricular dysfunction [12, 13, 20]. Concordantly, the presence of arteriovenous fistula access correlated with a higher PASP [20, 24]. In one report it was pointed out that underlying functional abnormalities of the pulmonary circulation likely contribute to the inability to accommodate the increase in cardiac output related to the arteriovenous fistula leading to PH [13].

Although our groups did not differ in the duration of dialysis or vascular access, we noticed a longer duration of dialysis in patients with PH who dropped their PASP significantly ≥ 10 mm Hg post-KT on the subgroup analysis. This significant drop was not related to dialysis access closure after KT and may have been related to fluid overload status seen in patients with ESKD. Equally important, the outcomes of these patients were the same at the end of the follow-up period.

Graft and patient survival

Prior studies have suggested that Pre-KT PH significantly increased the risk of delayed graft function and early graft dysfunction in deceased donor recipients. Yet, this effect was not seen in living donor recipients [11, 25]. Other evidence proposed the association of severe pre-KT PH (PASP > 50 mm Hg) with worse post-transplant survival [12]. Our study found a more significant drop in PASP in patients with worse pre-KT PH. Two-thirds of our patients received a KT from a deceased donor and no disparity in survival, graft dysfunction or follow-up creatinine was noted in our groups.

A summary of the existing evidence on the outcome of KT recipients with pre-KT PH is listed in Table 4.

Limitations

The major limitation of the study pertains to the retrospective single-center setup. The study populations were

Table 4 Retrospective studies on the association of pre-KT PH and post-KT outcomes

Study	Studied population	Outcomes of transplanted patients with PH
Issa et al. [12]	215 KT recipients 32% with PH, defined by pre-transplant RVSP > 35 mm Hg on TTE	RVSP of 50 mm Hg or greater was independently associated with an increased risk of post-transplant death Time on dialysis was the strongest correlate of an elevated RVSP
Zlotnick et al. [11]	55 KT recipients 38% with PH, defined by PASP > 35 mm Hg on TTE	Early graft dysfunction was more common in deceased kidney recipients with PH, specifically if PASP > 45 mm Hg
Casas-Aparicio et al. [13]	35 KT recipients 48.6% with PH, defined by PASP ≥ 40 mm Hg on TTE	PASP decreased significantly by 12 months post-transplantation, with a reduction in PH in 14.3% of the study population (P = 0.01)
Jarmi et al. [25]	363 KT recipients, 36.08% with PH, PASP measured through RHC at time of transplantation	Two groups according to PASP with cut-off of 35 mm Hg. Group with PASP ≥ 35 mm Hg showed a significant decrease in survival (hazard ratio 1.98; 95% CI 1.042–3.74, P = 0.037) after adjustment for comorbidities. Graft failure assessed by Kaplan–Meier analysis showed graft failure probabilities for both PASP groups were increased at similar rates, "deceased subjects were included in this analysis" (hazard ratio 0.34; 95% CI 0.12–1.01, P = 0.05)
Wang et al. [14]	192 KT recipients, 26% with PH, defined by PASP ≥ 37 mm Hg on TTE	Mild and moderate pre-KT PH does not affect post-KT mortality and graft loss at 4 years. However, it was associated with post-KT decline in estimated glomerular filtration rate at first and second years
Obi et al. [15]	773 KT recipients, 18% with PH, defined by PASP ≥ 35 mm Hg on TTE	Reduced patient and graft survival were seen in recipients with pre-transplant PH. However, this was not attributable to PH, but rather to age, black race and left ventricular systolic dysfunction

KT kidney transplant, *PASP* pulmonary artery systolic pressure, *PH* pulmonary hypertension, *RHC* right heart catheterization, *RVSP* right ventricular systolic pressure, *TTE* trans-thoracic echocardiogram

predominantly African American, limiting its generalizability. Patients with PH who were excluded from transplant on initial evaluation were not included in the analysis, these patients might have been sicker compared to PH patients who underwent KT. Given our sample mostly involved patients with mild-moderate PH, our current findings are difficult to extend to patients with severe PH with "PASP > 60 mm Hg". The diagnosis of PH and its contributors were not directly validated by right heart catheterization. The study population with PH may have had combined pre and post capillary PH which was not separately evaluated and could be associated with worse prognosis when associated with right ventricular dysfunction. At the time of study routine detailed analysis of right heart quantitative parameters were not done consistently for PH patients which prevents us from factoring in right heart function which we acknowledge as an important variable. Utilizing TTE's clinical report impact the accuracy of the PASP measurements, as the clinicians were neither blinded nor followed a standard protocol during measurement. Besides, the timing of PASP measurement pre-KT in relation to volume status was lacking and was not standardized. Furthermore, the level of hemoglobin level and the presence of AVF might have affected PASP measurement, making the flow state a challenging confounding variable which was not formally evaluated by right heart catheterization given the retrospective nature of study. However since 2015 we have instituted right heart protocol echocardiography doing detailed analysis of right heart function but is not applicable to this study population. Finally, the role of endothelial-derived molecules, including endothelin-1, thromboxane, and nitric oxide, was not analyzed in this study.

Conclusion

Despite prior evidence showing that PH is a worrisome sign in recipients of a KT, this study showed no impact on post-transplant survival and graft function. Based on these findings, patients with preexisting mild to moderate PH should not be excluded from KT evaluation. Optimization of cardiovascular care, proper pre-transplant PH evaluation, and perioperative management team collaboration, should better support triaging PH patients.

Author contributions KA, VK, BS, DT had full access to all of the data in the study and assume the responsibility for the integrity of the data and the accuracy of the analysis. BS, DT contributed substantially to the study design, data collection, data interpretation, and the writing and editing of this manuscript. KA, VK, MS, AP contributed to the study design and data collection. MVH contributed to statistical analysis. Stephanie Stebens contributed to the editing and formatting of this manuscript.

Funding No funding was used in the preparation of this work.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of Henry Ford Health System approved this study.

References

1. Tang M, Batty JA, Lin C, Fan X, Chan KE, Kalim S (2018) Pulmonary hypertension, mortality, and cardiovascular disease in CKD and ESRD patients: a systematic review and meta-analysis. Am J Kidney Dis 72:75–83
2. Sise ME, Courtwright AM, Channick RN (2013) Pulmonary hypertension in patients with chronic and end-stage kidney disease. Kidney Int 84:682–692
3. Yigla M, Nakhoul F, Sabag A, Tov N, Gorevich B, Abassi Z, Reisner SA (2003) Pulmonary hypertension in patients with end-stage renal disease. Chest 123:1577–1582
4. Tarrass F, Benjelloun M, Medkouri G, Hachim K, Benghanem MG, Ramdani B (2006) Doppler echocardiograph evaluation of pulmonary hypertension in patients undergoing hemodialysis. Hemodial Int 10:356–359
5. Foderaro AE, Baird GL, Bazargan-Lari A, Morrissey PE, Gohh RY, Poppas A, Klinger JR, Ventetuolo CE (2017) Echocardiographic pulmonary hypertension predicts post-transplantation renal allograft failure. Transplant Proc 49:1256–1261
6. Bozbas SS, Akcay S, Altin C, Bozbas H, Karacaglar E, Kanyilmaz S, Sayin B, Muderrisoglu H, Haberal M (2009) Pulmonary hypertension in patients with end-stage renal disease undergoing renal transplantation. Transplant Proc 41:2753–2756
7. Lentine KL, Costa SP, Weir MR, Robb JF, Fleisher LA, Kasiske BL, Carithers RL, Ragosta M, Bolton K, Auerbach AD, Eagle KA, American Heart Association Council on the Kidney in Cardiovascular Disease and Council on Peripheral Vascular Disease, American Heart Association; American College of Cardiology Foundation (2012) Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific statement from the American Heart Association and the American College of Cardiology Foundation: endorsed by the American Society of Transplant Surgeons, American Society of Transplantation, and National Kidney Foundation. Circulation 126:617–663
8. Reich DL, Wood RK Jr, Emre S, Bodian CA, Hossain S, Krol M, Feierman D (2003) Association of intraoperative hypotension and pulmonary hypertension with adverse outcomes after orthotopic liver transplantation. J Cardiothorac Vasc Anesth 17:699–702
9. Ramakrishna G, Sprung J, Ravi BS, Chandrasekaran K, McGoon MD (2005) Impact of pulmonary hypertension on the outcomes of noncardiac surgery: predictors of perioperative morbidity and mortality. J Am Coll Cardiol 45:1691–1699

10. Lai HC, Lai HC, Wang KY, Lee WL, Ting CT, Liu TJ (2007) Severe pulmonary hypertension complicates postoperative outcome of non-cardiac surgery. Br J Anaesth 99:184–190
11. Zlotnick DM, Axelrod DA, Chobanian MC, Friedman S, Brown J, Catherwood E, Costa SP (2010) Non-invasive detection of pulmonary hypertension prior to renal transplantation is a predictor of increased risk for early graft dysfunction. Nephrol Dial Transplant 25:3090–3096
12. Issa N, Krowka MJ, Griffin MD, Hickson LJ, Stegall MD, Cosio FG (2008) Pulmonary hypertension is associated with reduced patient survival after kidney transplantation. Transplantation 86:1384–1388
13. Casas-Aparicio G, Castillo-Martínez L, Orea-Tejeda A, Abasta-Jiménez M, Keirns-Davies C, Rebollar-González V (2010) The effect of successful kidney transplantation on ventricular dysfunction and pulmonary hypertension. Transplant Proc 42:3524–3528
14. Wang SC, Garcia R, Torosoff M, Fein SA, Ashar A, Chandolias N, Conti D, Lyubarova R (2019) Influence of mildly and moderately elevated pulmonary artery systolic pressure on post-renal transplantation survival and graft function. Echocardiography 36:22–27
15. Obi C, Frost AE, Graviss EA, Nguyen DT, Gaber AO, Suki WN (2020) The association of pretransplant pulmonary hypertension with patient and graft survival after kidney transplantation: a retrospective cohort study. Transplant Proc. https://doi.org/10.1016/j.transproceed.2020.05.003
16. Karthikeyan V, Chattahi J, Kanneh H, Koneru J, Hayek S, Patel A, Goggins M, Ananthasubramaniam K (2011) Impact of pre-existing left ventricular dysfunction on kidney transplantation outcomes: implications for patient selection. Transplant Proc 43:3652–3656
17. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon SD, Louie EK, Schiller NB (2010) Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 23:685–713
18. Bolignano D, Pisano A, Coppolino G, Tripepi GL, D'arrigo G, (2019) Pulmonary hypertension predicts adverse outcomes in renal patients: a systematic review and meta-analysis. Ther Apher Dial 23:369–384
19. Reque J, Garcia-Prieto A, Linares T, Vega A, Abad S, Panizo N, Quiroga B, Collado Boira EJ, López-Gómez JM (2017) Pulmonary hypertension is associated with mortality and cardiovascular events in chronic kidney disease patients. Am J Nephrol 45:107–114
20. Mehta KS, Shirkande AK, Bhurke SP, Pajai AE, Swami RS, Jadhav SN (2019) Pulmonary hypertension in various stages of chronic kidney disease in Indian patients. Indian J Nephrol 29:95–101
21. Tokodai K, Amada N, Kikuchi H, Haga I, Takayama T, Nakamura A (2012) Outcomes of renal transplantation after end-stage renal disease due to diabetic nephropathy: a single-center experience. Transplant Proc 44:77–79
22. Lim WH, Wong G, Pilmore HL, Mcdonald SP, Chadban SJ (2017) Long-term outcomes of kidney transplantation in people with type 2 diabetes: a population cohort study. Lancet Diabetes Endocrinol 5(1):26–33
23. Janda S, Shahidi N, Gin K, Swiston J (2011) Diagnostic accuracy of echocardiography for pulmonary hypertension: a systematic review and meta-analysis. Heart 97:612–622
24. Nakhoul F, Yigla M, Gilman R, Reisner SA, Abassi Z (2005) The pathogenesis of pulmonary hypertension in haemodialysis patients via arterio-venous access. Nephrol Dial Transplant 20:1686–1692
25. Jarmi T, Doumit E, Makdisi G, Mhaskar R, Miladinovic B, Wadei H, Rumbak M, Aslam S (2018) Pulmonary artery systolic pressure measured intraoperatively by right heart catheterization is a predictor of kidney transplant recipient survival. Ann Transplant 23:867–873