DOI: http://dx.doi.org/10.48305/arya.2022.11802.2458

Comparison of Pulmonary Artery Pressure before and after Kidney Transplantation in Kidney Transplant Patients with Pulmonary Hypertension

Sahar Ravanshad[1], Anoush Azarfar[2], Negin Jafarnezhad Sani[1], Maryam Miri[2]
Yalda Ravanshad[3]

Original Article

Abstract

BACKGROUND: Pulmonary hypertension (PH) is a common finding in chronic kidney disease (CKD) and is associated with increased mortality and morbidity. The effect of kidney transplantation on PH is not yet well evaluated. This study aimed to compare pulmonary artery pressure (PAP) before and after kidney transplantation in CKD patients.

METHOD: This longitudinal study was conducted on 33 CKD patients who were candidates for kidney transplantation in a tertiary hospital in Mashhad, Iran. Pulmonary artery pressure and ejection fraction (EF) were assessed using trans-thoracic echocardiography (TTE). Demographic and clinical findings, including age, gender, and body mass index (BMI), as well as laboratory assessments, including hemoglobin, serum calcium and phosphorus level, and parathyroid hormone, were recorded before transplantation. TTE assessment was repeated one year after transplantation.

RESULTS: Mean age of the study patients (17 males and 16 females) was 30.42 ± 9.71 years. The majority of patients (85%) received hemodialysis before transplantation. Compared to before transplantation, PAP significantly decreased (from 33.67 ± 6.78 to 26.06 ± 5.78 mmHg, P<0.001) and EF increased (from 52.85 ± 7.12 to 57.03 ± 4.08, P=0.003) one year after transplantation. A significant positive correlation was found between PAP difference and EF before transplantation.

CONCLUSIONS: The findings of this study showed that kidney transplantation was correlated with improved PAP and EF one year after transplantation and EF before kidney transplantation was correlated with PAP changes.

Keywords: Pulmonary Hypertension; Pulmonary Artery Pressure; Kidney Transplantation; Chronic Kidney Failure

Date of submission: *2021-Jun-22,* ***Date of acceptance:*** *2022-May-24*

Introduction

Pulmonary hypertension (PH) is a progressive disease caused by different etiologies, including cardiac, pulmonary, and vascular diseases. Due to its etiology, PH is associated with increased morbidity and mortality of the patient.[1] High pulmonary pressure is defined as systolic pulmonary pressure above 30 mm Hg. The prevalence of secondary and primary PH has been reported to increase by 90-97% and 5-10%, respectively.[2]

How to cite this article: Ravanshad S, Azarfar A, Jafarnezhad Sani N, Emadzadeh M, Ravanshad Y. **Comparison of Pulmonary Artery Pressure before and after Kidney Transplantation in Kidney Transplant Patients with Pulmonary Hypertension.** ARYA Atheroscler 2022; 18(6): 2458.

1- Department of Internal Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2- Kidney Transplantation Complications Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
3- Department of Community Medicine, Mashhad Branch, Islamic Azad University, Mashhad, Iran
Address for correspondence: Maryam Miri. Kidney Transplantation Complications Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. Email: mirighm@mums.ac.ir

PH is defined as mean pulmonary artery pressure (MPAP) greater than 35 mm Hg which is measured by right heart catheterization, which is the gold standard for PH diagnosis. Because right heart catheterization is an expensive and invasive test, trans-thoracic echocardiography (TTE) has been accepted as the screening test of choice, in which systolic pulmonary artery pressure greater than 35 mmHg is considered as PH.[3] Most patients with chronic kidney disease (CKD) have high blood pressure with diastolic dysfunction, arterial fistulas (AV fistulas), anemia, uremic lung, volume overload with interstitial pulmonary edema and high cardiac output, all of which can lead to increased pulmonary vascular pressure.[4]

The prevalence of PH in CKD varies based on the method of diagnosis. The prevalence of PH among non-dialysis CKD patients was reported to be 32%,[5] while the prevalence of PH among hemodialysis and peritoneal dialysis patients was reported to be up to 40% [6] and 21%,[6,7] respectively. It was also reported that CKD patients with PH based on TTE have a significantly higher mortality risk compared to those without PH (with a relative risk of 2.02).[6,8] Furthermore, patients with PH have a higher risk for heart failure with or without perceived ejection fraction (EF), lower mean hemoglobin level, increased inter-dialytic weight gain, and increased calcium × phosphate products compared to patients without PH. The risk factors for PH in CKD include left ventricular systolic and diastolic failure (reduced EF), calcium phosphate product equal to or higher than 50 and fluid retention as well as obesity, anemia, hypertriglyceridemia, proteinuria, and the extent of reduced glomerular filtration rate.[9]

Kidney transplantation is one of the treatment choices for CKD. It was shown that kidney transplantation results in improved left ventricular function, including left ventricular systolic and diastolic function, left ventricular mass, and right ventricular volume.[10] Therefore, it can be hypothesized that kidney transplantation may result in improved PH in CKD patients. To the best of our knowledge, few studies have assessed the effect of kidney transplantation on pulmonary artery pressure.[11] Moreover, studies have shown that high pulmonary artery pressure before transplantation does not change patients' survival compared to patients without PH.[8] Therefore, further studies are required to assess the effect of the improvement of this complication following kidney transplantation on the survival of these patients. Thus, this study aimed to compare pulmonary artery pressure before and after kidney transplantation in CKD patients.

Materials and Methods

This cross-sectional study was conducted in Mashhad, Montaserieh Hospital, between 2018 and 2019 on 33 patients over 18 years old, who had undergone kidney transplantation during the past year before the study and were reported to have PH. PH was defined as pulmonary artery pressure above 25 mm Hg on transthoracic echocardiography (TTE) before the transplant. Candidate patients for kidney transplantation undergo routine transthoracic echocardiography before transplantation, and patients were selected by reviewing patient records before transplantation.

Vulnerable patients to high PAP due to other causes, including rheumatic diseases, such as systemic lupus erythematous, scleroderma, and chronic lung diseases such as COPD were excluded. In other words, only patients with pulmonary hypertension due to ESRD and hemodialysis were included in this study, and no underlying disease other than renal failure was identified as the cause of hypertensive pulmonary disease. The secondary causes of hypertensive pulmonary disease were excluded by examining the patient's underlying medical history leading to renal failure.

Patient information was extracted from their medical records in Montaserieh Hospital, Mashhad, Iran. Demographic data, laboratory and clinical data, including body mass index(BMI), serum calcium, phosphor, parathyroid hormone (PTH), and hemoglobin were extracted from the patient medical records. During telephone calls, the selected

patients were asked to refer for TTE which was done using Samsung Medison P2- 4BA echocardiography machine to identify ejection fraction (EF) and PAP one year after transplantation.

This study was presented on in the Organizational Ethics Committee of Mashhad University of Medical Sciences with the No. 961818 and approved with the ethics code of IRMUMSMEDICALREC.1397.235.

Statistical analysis: Data analysis was performed using descriptive and inferential statistics in IBM SPSS ver. 23. The characteristics of the subjects were presented by descriptive statistical methods including central indicators, dispersion, and frequency distribution in tables and graphs. Paired t-test was used to compare the results of echocardiography before and after transplantation and the independent t-test or Mann-Whitney U test was used to compare quantitative variables between genders. Spearman and Pearson Correlation tests (according to the type of distribution) were also used to define the correlations between variables. P-values less than 0.05 were considered statistically significant in all tests.

Results

Of the 33 patients studied, 17 (51.5%) were male and 16 (48.5%) were female, 15% underwent peritoneal dialysis and 85% underwent hemodialysis before transplantation. Characteristics of the patients are presented in Table 1. There was no significant difference between gender in terms of age (P= 0.694), BMI (P=0.171), serum levels of phosphorus (P=0.295), calcium (P=0.367), Hb (P=0.312), and PTH (P=0.668**)** (Table 1).

Changes in PAP and EF during the study period are presented in Table 2. PAP (<0.001) was significantly increased and EF (P=0.003) was significantly decreased following transplantation. Changes in PAP and EF values are presented in Figure 1.

Table 1. Comparison of clinical and anthropometric variables before transplantation between men and women

Variable	Total(n=33)	Gender		p
		Male (n=17)	Female (n=16)	
Age (years)	30.42 ± 9.71	29.76 ± 8.94	31.12 ± 10.73	0.694*
BMI (kg/m^2)	21.8 ± 2.71	21.88 ± 2.71	20.43± 3.20	0.171*
Phosphorus (mg/dL)	4.70 ± 1.38	4.70±1.38	5.13±0.86	0.295*
Calcium (mg/dL)	8.71 ± 0.88	8.71± 0.88	8.59±0.87	0.367†
Hb (g/dL)	10.10 ± 1.29	10.10±1.29	9.95±2.02	0.312†
PTH (pg/mL)	259.59 ± 108.18	259.59±108.18	246.25±64.04	0.668*

† The Mann-Whitney test; *Independent Sample t-test

Note: Data are described as Mean ± standard deviation (SD). BMI: Body Mass Index; Hb: Hemoglobin; PTH: Parathyroid hormone

Table 2. Changes in PAP and EF over the study period

Variable		Before transplantation	After transplantation	p
PAP (mmHg)	total	33.67 ± 6.78	26.06 ± 5.78	<0.001*
	Male	33.06 ± 7.13	24.65 ± 6.17	<0.001*
	Female	34.31 ± 6.55	27.56 ± 5.08	<0.001*
		0.6**	0.15**	
EF (%)	total	52.85 ± 7.12	57.03 ± 4.08	0.003*
	Male	53.52 ± 6.06	56.47 ± 4.24	0.004*
	Female	52.12 ± 8.24	57.62 ± 3.95	0.048*
		0.58**	0.425**	

* Significant difference based on paired t-test; **Independent Sample t-test

PAP: Pulmonary Arterial Pressure; **EF:** Ejection Fraction

No significant differences were found in PAP and EF values between genders before and after transplantation (Table 2).

The correlation between study parameters is presented in Table 3. A significant correlation was only found between PAP difference and EF before transplantation (r=0.434, P=0.012), while a significant negative correlation was observed between EF difference and EF before transplantation (r=-0.847, r<0.001) and a positive correlation between EF after transplantation (r=0.374, P=0.032). These findings indicate that increased PAP difference was correlated with higher EF before transplantation, and increased EF difference with lower EF before transplantation and higher EF after transplantation.

Table 3. Correlation between laboratory findings and PAP and EF differences

Variable	Total(n=33)	Gender		p
		Male (n=17)	Female (n=16)	
Age (years)	30.42 ± 9.71	29.76 ± 8.94	31.12 ± 10.73	0.694*
BMI (kg/m^2)	21.8 ± 2.71	21.88 ± 2.71	20.43± 3.20	0.171*
Phosphorus (mg/dL)	4.70 ± 1.38	4.70±1.38	5.13±0.86	0.295*
Calcium (mg/dL)	8.71 ± 0.88	8.71± 0.88	8.59±0.87	0.367†
Hb (g/dL)	10.10 ± 1.29	10.10±1.29	9.95±2.02	0.312†
PTH (pg/mL)	259.59 ± 108.18	259.59±108.18	246.25±64.04	0.668*

BMI: Body Mass Index; Hb: Hemoglobin; PTH: Parathyroid Hormone; PAP: Pulmonary Arterial Pressure; EF: Ejection Fraction. (#: Spearman Correlation Test. Other correlations conducted by Pearson correlation test); r: correlation coefficient; p: p-value

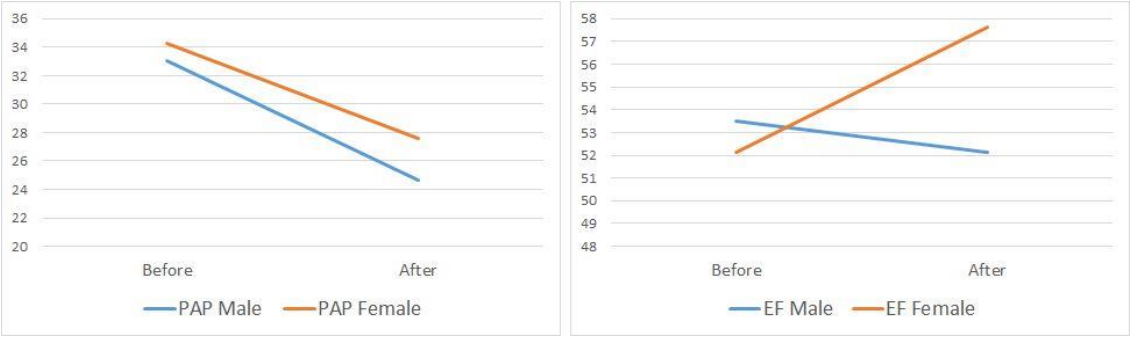

Figure 1. Changes in PAP and EF before and after transplantation as per gender

Discussion

Our study indicated that the EF of patients was significantly improved after transplantation compared with before transplantation. Also, pulmonary pressure was significantly decreased after transplantation. These findings are helpful in decision-making on the justifiability of kidney transplantation in end-stage renal disease (ESRD) patients with severe cardiovascular damage and the potentially increased surgical risk in these patients.

The present study showed that PAP was significantly decreased one year after transplantation compared to before transplantation, which is supported by previous studies that reported a significant decrease in PAP after transplantation.[12]

Results of the present study also showed that EF was significantly increased one year after transplantation compared to before transplantation, which is consistent with the finding of another study that assessed PH one year after kidney transplantation using radionuclide ventriculography gated blood pool (MUGA) scan.[13] Reddy et al. (2013) studied 124 CKD patients who underwent kidney transplantation from 2001 to 2007 and reported that PAP significantly decreased after transplantation while EF did not significantly change after transplantation.[14] This difference may have occurred due to the difference in the mean EF before transplantation between the studies. In the present study, the mean EF was 52.85% before transplantation, which increased to 57.03% one year after transplantation. In contrast, in Reddy et al.'s study, the mean EF was 61% before transplantation which was higher than the highest achievable EF in our study, showing that the majority of the subjects in their study had a normal cardiac function. Furthermore, a significant positive correlation was found between EF before transplantation and PAP difference in the present study, indicating that higher EF before transplantation is correlated with an increased PAP improvement after transplantation, which further supports that the difference between the findings of the present study and Reddy et al.'s study which included patients with higher EF compared to the present study.

The present study also showed that EF before transplantation was correlated with PAP changes. Left ventricular heart failure has been proven as a risk factor for PH in CKD patients.[15] To the best of our knowledge, previous studies did not assess the correlation between EF and PAP in CKD; however, the results of previous studies showed that patients with low EF before transplantation experienced an increase in EF along with reduced PAP.[13, 14] Therefore, it can be hypothesized that left heart dysfunction might be strongly associated with PAP both as a risk factor and as an outcome of improved PAP. Further investigations are required to assess the mechanism of the reciprocal effects of PAP and EF.

Besher Sadat et al. study in 2021 showed that mild to moderate hypertension before kidney transplantation does not negatively affect the survival of patients after kidney transplantation[16] supporting the results of the present study that patients with PH should not be excluded from kidney transplantation. Due to the evident pulmonary artery pressure reduction after transplantation, survival is assumed to be potentially improved.

The effect of hemodialysis on PAP is affected by dialysis duration. Nevertheless, the information regarding the duration of hemodialysis before transplantation was not available in the present study; thus, the confounding effect of dialysis duration could not be assessed in this study. On the other hand, the findings of the present study indicated that regardless of dialysis duration, EF could be an indicator of PAP difference. Therefore, EF can be assumed as an independent indicator for the extent of improvement in PAP in CKD patients with PH undergoing kidney transplantation.

Limitations

Limitations of the present study included the impossibility of performing right heart catheterization to accurately determine pulmonary artery pressure, lack of access to transesophageal echocardiography (TEE), and lack of information regarding the duration of hemodialysis before transplantation.

Conclusion

The findings of our study showed the improvement of both PAP and EF one year after kidney transplantation and proposed EF before transplantation as a potential independent indicator of PAP improvement after transplantation. However, further studies are still required to assess the prognostic value of EF in predicting PAP after kidney transplantation.

Reference

1. Bolignano D, Rastelli S, Agarwal R, Fliser D, Massy Z, Ortiz A, et al. Pulmonary hypertension in CKD. Am J Kid Dis 2013; 61(4): 612-22.

2. Di Lullo L, Floccari F, Rivera R, Barbera V, Granata A, Otranto G, et al. Pulmonary hypertension and right heart failure in chronic kidney disease: new challenge for 21st-century cardionephrologists. Cardiorenal Med 2013; 3(2): 96-103.
3. Li Z, Liang X, Liu S, Ye Z, Chen Y, Wang W, et al. Pulmonary hypertension: epidemiology in different CKD stages and its association with cardiovascular morbidity. PloS One 2014; 9(12): e114392.
4. Thenappan T. Pulmonary hypertension in chronic kidney disease: a hemodynamic characterization. Pulm Circ 2017; 7(3): 567-8.
5. Shang W, Li Y, Ren Y, Li W, Wei H, Dong J. Prevalence of pulmonary hypertension in patients with chronic kidney disease without dialysis: a meta-analysis. Int Urol Nephrol 2018; 50(8): 1497-504.
6. Schoenberg NC, Argula RG, Klings ES, Wilson KC, Farber HW. Prevalence and mortality of pulmonary hypertension in ESRD: a systematic review and meta-analysis. Lung 2020; 198(3): 535-45.
7. Tang M, Batty JA, Lin C, Fan X, Chan KE, Kalim S. Pulmonary hypertension, mortality, and cardiovascular disease in CKD and ESRD patients: a systematic review and meta-analysis. Am J Kid Dis 2018; 72(1): 75-83.
8. Rabih F, Holden RL, Vasanth P, Pastan SO, Fisher MR, Trammell AW. Effect of pulmonary hypertension on 5-year outcome of kidney transplantation. Pulm Circ 2022; 12(1): e12010.
9. Suresh H, Arun BS, Moger V, Vijayalaxmi PB, Mohan KM. A prospective study of pulmonary hypertension in patients with chronic kidney disease: a new and pernicious complication. Indian J Nephrol 2018; 28(2): 127-134.
10. Hawwa N, Shrestha K, Hammadah M, Yeo PS, Fatica R, Tang WW. Reverse remodeling and prognosis following kidney transplantation in contemporary patients with cardiac dysfunction. J Am Coll Cardiol 2015; 66(16): 1779-87.
11. Alhamad EH, Al-Ghonaim M, Alfaleh HF, Cal JP, Said N. Pulmonary hypertension in end-stage renal disease and post renal transplantation patients. J Thorac Dis 2014; 6(6): 606-16.
12. Sise ME, Courtwright AM, Channick RN. Pulmonary hypertension in patients with chronic and end-stage kidney disease. Kidney Int 2013; 84(4): 682-92.
13. Hawwa N, Shrestha K, Hammadah M, Yeo PS, Fatica R, Tang WW. Reverse remodeling and prognosis following kidney transplantation in contemporary patients with cardiac dysfunction. J Am Coll Cardiol 2015; 66(16): 1779-87.
14. Reddy YN, Lunawat D, Abraham G, Matthew M, Mullasari A, Nagarajan P, et al. Progressive pulmonary hypertension: another criterion for expeditious renal transplantation. Saudi J Kidney Dis Transpl 2013; 24(5): 925-9.
15. Zhang Q, Wang L, Zeng H, Lv Y, Huang Y. Epidemiology and risk factors in CKD patients with pulmonary hypertension: a retrospective study. BMC Nephrol 2018; 19(1): 70.
16. Sadat B, Tirunagari D, Karthikeyan V, Patel A, Van Harn M, Saleem MM, et al. Clinical impact of pre-kidney transplant pulmonary hypertension on post-transplant outcomes. Int J Cardiovasc Imaging 2021; 37(6): 1979-86.