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Original Article

Evaluation of pulmonary artery pressure variations in end stage renal disease patients before and after renal transplantation

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ABSTRACT

Aims: This study aims to evaluate changes in systolic pulmonary artery pressure (sPAP) in end-stage renal disease (ESRD) patients before and after kidney transplantation, as well as the prevalence and impact of pulmonary hypertension (pHT) on post-transplant outcomes.

Methods: A total of 87 ESRD patients undergoing kidney transplantation at the Nephrology Department of Ankara University Faculty of Medicine were prospectively followed. Demographic data, pretransplant, and posttransplant (3rd and 12th months) serum tests, as well as echocardiographic measurements, were analyzed. Patients with pHT due to non-renal causes were excluded. Mean systolic pulmonary artery pressure was measured echocardiographically and a level of above 30 mmHg was accepted as pHT. Statistical analyses were performed using SPSS, with a p-value <0.05 considered statistically significant.

Results: Among the 87 patients, 40 (45.9%) were male and 47 (54.1%) were female, with a mean age of 42.6±11.7 years. The mean pretransplant sPAP was 36.6±7.97 mmHg, which decreased significantly to 31.7±5.5 mmHg at 3 months and 30.1±6.2 mmHg at 12 months post-transplant (p<0.05). Pretransplant pHT was present in 72.4% of patients, which reduced to 36.7% at 3 months and 22.9% at 12 months post-transplant. Preoperative triglyceride and parathormone levels were significantly correlated with sPAP (p<0.05), while patients with pretransplant sPAP ≥40 mmHg had a higher incidence of early graft dysfunction (p<0.05).

Conclusion: Pulmonary hypertension is prevalent in patients with ESRD but significantly decreases after kidney transplantation. Patients with preoperative sPAP ≥40 mmHg are at higher risk for early graft dysfunction, highlighting the importance of screening for pHT in transplant candidates. Addressing pHT in ESRD patients may improve post-transplant outcomes, reduce morbidity, and enhance overall patient management.

Keywords: Pulmonary hypertension, chronic kidney disease, end stage renal disease, hemodialysis, peritoneal dialysis

INTRODUCTION

End-stage renal disease (ESRD) is associated with high morbidity and mortality, exacerbated by comorbidities such as atherosclerotic heart disease (ASHD), diabetes mellitus, congestive heart failure, and hyperlipidemia. These conditions not only increase the disease burden but also lead to significant healthcare costs, particularly due to dialysis and kidney transplantation.

Pulmonary hypertension (PH), specifically classified as type 5 in ESRD patients, is a notable complication. The global rise in chronic diseases, including chronic obstructive pulmonary disease (COPD), ASHD, and heart failure, has led to an increase in PH prevalence, particularly in older adults. Recent data suggest that hospitalization and mortality rates related to PH have nearly doubled in this population. PH is defined as a mean pulmonary artery pressure ≥25 mmHg or a systolic pulmonary artery pressure (sPAP) ≥35 mmHg, with the latter being a widely recognized threshold for diagnosis.

Several studies have reported an increased incidence of PH in ESRD patients, both in those undergoing dialysis and in transplant recipients, contributing to heightened morbidity and mortality. Despite this, there is limited prospective research examining changes in sPAP before and after kidney transplantation and their effects on graft function.

This study aims to evaluate sPAP in ESRD patients undergoing dialysis and kidney transplantation, investigate factors influencing pulmonary artery pressure, and assess the impact of transplantation on PH. The findings aim to address a gap in the literature by providing prospective data on PH in this patient population.

METHODS

Approval for the study was obtained from the Ankara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 09.03.2015, Decision No: 2015/12). Between 2013 and 2015, patients aged 18 and older who underwent kidney transplantation at Ankara University Medical Faculty Hospitals' Department of Internal Medicine, Nephrology Division were informed about the study. The study followed the requirements given in the Declaration of Helsinki.

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Informed consent was obtained from 87 participants, and their demographic data, comorbidities (e.g., hypertension, diabetes, sleep apnea), and various clinical parameters were collected. The number of patients were determined by the time frame the study was done. Data included age, sex, etiology of kidney disease, duration of kidney disease, dialysis details, medications, and echocardiographic findings at baseline, 3 months, and 12 months post-transplant. Patients under 18 years of age and patients with a follow-up under 12 months were excluded. Patients with non-renal causes of pulmonary hypertension (e.g., heart disease, COPD, chronic pulmonary embolism) were also excluded.

Echocardiograms were performed using a continuous-wave Doppler (Toshiba Applio 400) probe. The pulmonary artery pressure (PAB) was calculated using the modified Bernoulli equation. Care was taken to ensure patients were in a euvolemic state post-dialysis to avoid elevated PAB due to volume overload. Additionally, high-risk patients underwent preoperative respiratory function tests. Patients who did not sign the consent form or had severe psychiatric disorders were excluded from the study.

Statistical Analysis

Data were analyzed using IBM SPSS for Windows ver. 18.0. Descriptive statistics included mean±standard deviation for normally distributed variables and median (minimum-maximum) for non-normally distributed ones. Counts (n) and percentages (%) were used for categorical variables.

For continuous variables, a paired T test was used for normal distributions; otherwise, the Wilcoxon test was applied. For multiple follow-ups, repeated measures ANOVA or the Friedman test was used based on distribution normality.

For two groups, the T test assessed mean differences, while the Mann-Whitney test evaluated median differences. For more than two groups, ANOVA and the Kruskal-Wallis test were used. Nominal variables were assessed with Pearson chi-square or fisher exact tests.

Spearman correlation was used for non-normally distributed continuous variables, and pearson correlation for normally distributed ones. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 87 patients were included in the study, comprising 40 men (46%) and 47 women (54%). The average age was 42.6±11.7 years, with no significant gender differences. Among the patients, 26 (29.9%) were current smokers, while 61 (70.1%) had never smoked or had quit. Kidney transplants were performed in 63 patients (72.4%) from living donors and 24 patients (27.6%) from cadaveric donors (**Table**).

Table. Demographics	
Male/female	40/47 (46%/54%)
Median age	(31-54)
Median chronic kidney disease duration	118.6 months
Smoking	
Yes/no	26/61 (29.9%/70.1%)
Graft source	Living/cadaveric: 63/24 (72.4%/27.6%)
Comorbidities	
Hypertension	71 (81.6%)
Left ventricular hypertrophy	29 (33.3%)
Diabetes mellitus	24 (27.6%)
Atherosclerotic heart disease	10 (11.5%)
Obstructive sleep apnea	1 (1.1%)
Chronic obstructive pulmonary disease	1 (1.1%)

The Causes of ESRD Included

- **Chronic glomerular and tubular diseases:** 28 (32.4%)
- **Amyloidosis:** 13 (14.9%)
- **Hypertensive nephropathy:** 11 (12.6%)
- **Diabetes mellitus:** 11 (12.6%)
- **Polycystic kidney disease:** 9 (10.3%)
- **Unknown:** 10 (11.5%)

Pretransplant Data

- 24 patients (27.6%) received pre-emptive transplants without dialysis.
- 54 patients (62.1%) underwent chronic hemodialysis, while 2 (2.3%) received peritoneal dialysis. A total of 63 patients (72.4%) were on chronic dialysis.
- Average duration of chronic kidney disease was 118.6 months, with one patient on record for 30 years.
- Average dialysis duration for those on chronic dialysis was 49.1 months.

Preoperative respiratory function tests showed no significant airway obstruction, ruling out COPD. Transplant compatibility based on HLA was recorded, with varying degrees of matches among the recipients.

Patients underwent echocardiographic assessment and sPAB measurements in the early and late post-transplant periods (3 months and 12 months), and laboratory data were recorded. The mean sPAB value for patients in the early post-transplant period (3 months) was found to be 31.7±5.5 mmHg (min 25-max 65 mmHg). The mean sPAB measured during the pre-transplant period was 36.6±7.97 mmHg. A statistically significant difference was found between the mean sPAB values measured during the pre-transplant period and at 3 months post-transplant ($p=0.002$).

In the late post-transplant period (12 months), the average sPAB was found to be 30.1 mmHg±6.2 (min 20-max 65). It was determined that the average sPAB value measured at the 12th month post-transplant was lower than the average 36.6±7.97 mmHg sPAB value measured in the pre-transplant period. As a result, a statistically significant decrease in average sPAB was observed when comparing the pre-transplant period to the average sPAB measured at the 12th month post-transplant ($p<0.05$). The frequency of pulmonary hypertension at 3 months post-transplant was observed in 32 patients (36.7%), while at 12 months post-transplant, it decreased to 20 patients (22.9%) ($p<0.05$).

The average pre-transplant sPAB value for patients who underwent preemptive transplantation was found to be 36.6±8.8 mmHg. In patients receiving chronic dialysis treatment, the pre-transplant average sPAB was 36.61±6.7 mmHg, with no statistically significant difference between the

two groups (p=0.57). When comparing the average pulmonary artery pressures at the third month post-transplant for these two patient groups, values were measured as 30.4±3.51 mmHg and 32.2±6.1 mmHg, respectively. The average sPAB values at the twelfth month post-transplant were also measured as 28.8±3.8 mmHg and 30.7±6.9 mmHg, respectively, with no statistically significant difference found (p=0.1 and p=0.379).

When comparing the average sPAB values pre-transplant, at early post-transplant (3 months), and late post-transplant (12 months) for our patients, regardless of whether the donor was living or cadaveric, it was observed that there was a decrease in average sPAB values during the post-transplant period for all patients, and this decrease progressively increased during the late follow-up at 12 months.

DISCUSSION

End-stage kidney disease is a critical health condition that significantly impacts morbidity and mortality rates, adversely affecting patients' quality of life. The presence of comorbid conditions such as coronary artery disease, diabetes mellitus and chronic kidney disease exacerbates the morbidity and mortality associated with ESRD. Moreover, the high costs of dialysis and kidney transplantation put a considerable financial burden on national healthcare systems.

Recent studies have indicated an increasing prevalence of pulmonary hypertension (PH) among patients with ESRD.[1-3] According to the World Health Organization's (WHOs) 2013 classification of pulmonary hypertension, PH associated with ESRD falls into group 5,[4] which highlights this unique etiology linked to kidney disease. The mechanisms underlying the development of PH in ESRD patients are multifactorial, including left heart failure, increased cardiac output due to arteriovenous fistulas, endothelial dysfunction, anemia, hypervolemia, and various metabolic and hormonal disturbances related to kidney disease.[3,5]

Kidney transplantation is known to improve both the longevity and quality of life for ESRD patients and can significantly reduce treatment costs. Despite the existing literature emphasizing the prevalence and clinical significance of PH in chronic hemodialysis (HD) and renal transplant patients, there remains a lack of prospective studies evaluating the changes in pulmonary artery pressure (sPAB) and the relationship between kidney graft function and PH in post-transplant periods.[6]

The prevalence of PH among CKD patients has been reported varying widely, from 12.5% to 58.6%. For instance, a study by Yigla et al.[7] found an 8% prevalence of PH in patients with ESRD without any cardiac or pulmonary diseases, suggesting a direct link between ESRD and the development of PH, potentially exacerbated by prolonged HD.

In our study, we aimed to prospectively assess the sPAB levels in patients with ESRD awaiting kidney transplantation, using echocardiographic evaluations. We excluded patients with severe heart failure, chronic pulmonary diseases, or any conditions that could cause PH unrelated to kidney disease. Our findings revealed that 72.4% of the patients had PH, indicating that these patients likely belonged to the WHOs group 5 classification of PH.[4]

Consistent with existing literature, our study found no significant correlation between the presence of PH and gender. Furthermore, no significant age difference was noted between patients with and without PH, although this might be attributed to the low proportion of patients with normal sPAB levels.

The relationship between the duration of dialysis and PH has been previously documented, with studies indicating that prolonged HD correlates with increased sPAB values. However, our findings did not show a statistically significant correlation between dialysis duration and the presence of PH.

In terms of the relationship between PH and hemoglobin levels, we observed a significant negative correlation, suggesting that anemia could contribute to the development of high-output heart failure and subsequent PH. Additionally, a correlation between hypoalbuminemia and PH was identified, potentially pointing to an increased risk of hypervolemia or chronic hypervolemic states contributing to PH.

We also evaluated the impact of kidney transplantation on sPAB levels. Our results demonstrated a statistically significant reduction in sPAB values from the pre-transplant phase to the 3rd and 12th months post-transplant, indicating an improvement in pulmonary hemodynamics following transplantation.

Interestingly, no significant difference was observed in graft function between patients with and without PH after transplantation, nor did the source of the donor (living or cadaveric) influence graft function stability.

CONCLUSION

Research has shown that the presence of PH, regardless of its cause, serves as a risk factor that heightens morbidity and mortality among patients with ESRD. PH not only deteriorates the patients' quality of life but also leads to increased treatment costs. Therefore, close monitoring of patients with ESRD who have PH, as well as addressing the underlying causes of PH, is crucial. Our analysis indicated that AV fistula presence correlates significantly with PH, further supporting the hypothesis that high-output heart failure and PH can arise from the increased blood flow through these fistulas. The existing literature also suggests a correlation between PH and echocardiographic indicators of left ventricular dysfunction, but we chose not to include patients with evident left ventricular failure to maintain a homogeneous study group. Ultimately, our study highlights the importance of monitoring PH in ESRD patients, especially those awaiting kidney transplantation. By understanding the dynamics of sPAB levels and their implications on both pre- and post-transplant outcomes, we can better address the management of these patients to enhance their overall health and quality of life. Our results are open to be confirmed by larger prospective studies.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 09.03.2015, Decision No: 2015/12).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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