

Prospective Comparative Evaluation of Lung Function in ESKD Patients Undergoing Hemodialysis Versus Kidney Transplantation

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Introduction. Chronic kidney disease (CKD) is a global health problem with an increasing prevalence. Retrospective studies have shown associations between CKD and several pulmonary complications. This study was conducted to compare lung function in ESKD patients receiving kidney transplantation versus undergoing maintenance hemodialysis.

Methods. This prospective comparative study included 50 patients with ESKD. Patients were divided into two groups: those undergoing routine hemodialysis and those who underwent kidney transplantation. Demographic data were recorded, and participants underwent spirometry at baseline. The same measures were repeated after six months and compared.

Results. Spirometry parameters including Forced Expiratory Volume (FEV1), Forced Vital Capacity (FVC), FEV1/FVC, Peak Expiratory Flow Rate (PEFR), Forced Expiratory Flow between 25% and 50% of the vital capacity (FEF_{25-75%}) were compared between hemodialysis group and kidney transplantation group. The PEFR parameter was the only index that significantly increased in the hemodialysis group compared to kidney transplantation group both at baseline and six-month follow-up. It was observed that all the parameters significantly increased after six-month follow-up in hemodialysis group. In contrast, only three parameters FEV1, FVC and FEV1/FVC improved significantly in the six-month follow-up in the kidney transplantation group.

Conclusion. Spirometric parameters including FEV1, FVC, FEV1/FVC, PEFR, and FEF_{25-75%} improved significantly after six months of maintenance hemodialysis, whereas FEV1, FVC, and FEV1/FVC improved significantly six months following kidney transplantation. These findings suggest that both treatment modalities may be associated with improvement in pulmonary function, although the pattern of improvement differs.

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INTRODUCTION

Chronic kidney disease (CKD) is a global health problem that affects more than 497 million adults

aged 20 years and older worldwide.¹ According to the latest Global Burden of Disease report, the prevalence of CKD has increased by 19.6% over the

past decade, a significant increase driven by the spread of underlying chronic noncommunicable diseases.^{2,3} Current data on CKD are limited to developed countries, and information on the disease in developing countries is much more limited.⁴

Compared with the general population, patients with CKD, especially in the end-stage kidney disease (ESKD), have a significantly reduced quality of life. Common complications affecting these patients include chronic heart failure, lung disease, or various cancers.^{5,6} ESKD also affects lung function with very common complications such as pulmonary edema and pleural effusion.⁷ Previous studies have also shown a clear association between CKD and pulmonary complications such as pulmonary fibrosis and calcification, pulmonary hypertension, hemosiderosis, and pleural fibrosis.^{8,9} Hypoxemia due to partial obstruction of pulmonary capillary blood flow due to leukocyte sequestration is a well-known problem in hemodialysis patients.¹⁰ Such lung damage in patients with renal impairment causes an additional burden on the patients. Since hemodialysis is time-consuming, these complications predispose the patients to conditions such as impaired PFT, atelectasis, pneumonia, and bacterial bronchitis.¹¹

Kidney transplantation is recognized as a major advance in modern medicine, offering improved quality of life for patients with ESKD worldwide. It is now a routine surgical procedure in more than 80 countries. The beneficial effects of transplantation on quality of life and various systemic complications are well documented.¹¹

Studies investigating pulmonary function in ESKD patients are very limited and their results are highly heterogeneous.¹² Also, in the case of lung capacity, the parameters examined are still mostly limited to retrospective studies. The prospective study regarding kidney transplantation is exceedingly limited.¹³⁻¹⁶

In general, after six months following transplantation various lung capacity parameters are expected to be improved, and obstructive and restrictive lung failure decrease at the same time.¹⁷ However, studies have shown that patients on routine dialysis retain a significant proportion of these abnormalities even after receiving a kidney transplantation. These abnormalities are likely to be related to the underlying disease or to the dialysis itself.¹⁸ Critically, no adequately

powered prospective study has directly compared the trajectory and magnitude of lung function recovery between patients remaining on maintenance hemodialysis and those receiving a kidney transplant. The aim of this study was to prospectively evaluate and compare changes in comprehensive spirometry in ESKD patients before and after initiation of hemodialysis versus after kidney transplantation.

MATERIALS AND METHODS

A prospective observational comparative study was conducted on ESKD patients during 2023 in Shahid Modarres Hospital, Tehran, Iran. This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1402.300).

The sample size was determined using G*Power software. Assuming an effect size of 0.80 based on Cohen's method, a two-tailed α level of 0.05, and a statistical power of 80%, the required sample size was calculated to be 25 participants per group. The study population included 50 patients with ESKD who were candidates for hemodialysis or kidney transplantation, and the sampling was purposive. Patients aged between 18 and 80 years with CKD leading to ESKD at baseline were included in the study. Patients were divided into two groups of kidney transplantation and hemodialysis. All procedures involving patients were performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Exclusion criteria for study participants included transplant rejection, history of pulmonary disease independent of the patient's renal problem such as Chronic Obstructive Pulmonary Disease (COPD), life-threatening complications and intensive care unit (ICU) admission, presence of any malignancy, presence of abnormal findings on chest radiography performed at baseline, and presence of neuromuscular disease. Patients who used inhalers, had lung infections, or were taking medications that affect lung function were also excluded from the study. All kidney transplant recipients received a standard triple maintenance immunosuppressive regimen consisting of tacrolimus, mycophenolate mofetil, and prednisolone. Tacrolimus was administered at a daily dose of 1–3 mg and adjusted to maintain a target trough blood concentration of

5–7 ng/mL. Mycophenolate mofetil (CellCept®) was administered at a dose of 500 mg every 8 hours. Prednisolone was administered at a maintenance dose of 5 mg once daily throughout the study period.

Demographic and clinical information of patients before kidney transplantation or hemodialysis was collected. This information included age, sex, history of underlying diseases, history of medications, smoking history, duration of dialysis, and the main cause of renal failure.

After entering to the study, patients were divided into two groups, one group of 25 patients who underwent transplantation and the other group of 25 patients who underwent hemodialysis. All patients underwent maintenance hemodialysis three times weekly. All patients in the hemodialysis group had adequate dialysis, defined as a $Kt/V \geq 1.2$. All enrolled hemodialysis patients had adequate dialysis ($Kt/V \geq 1.2$). The same type of filter was used in all hemodialysis patients. Diabetic patients in both groups had no neuropathy. The steroid dose used was the same for all kidney transplant patients. The waiting time for kidney transplantation in all transplant candidate patients was less than seven months and all of them were from deceased donors.

Spirometry was conducted following the 2019 ATS/ERS technical standards, incorporating Global lung function Initiative (GLI) reference equations to interpret results. Participants sat upright wearing a nose clip to minimize air leakage. After maximal inhalation, they performed forced expiration as rapidly and completely as possible into a calibrated spirometer through a disposable mouthpiece. At least three reproducible maneuvers were recorded, with the highest FVC and FEV₁ values taken for analysis. Daily calibration verification was performed using a 3 L syringe, with accuracy maintained within $\pm 2.5\%$ error tolerance. Measured spirometric parameters included FVC, FEV₁, FEV₁/FVC ratio, FEF_{25–75%}, and PEF (when available).

Spirometry was performed at the beginning of the study and also in the case of the transplantation group, in the week before transplantation. Then, six months later, participants in both groups were called to the hospital once again and spirometry was repeated. Then, the changes in spirometry findings in the two groups were compared, as well as within group after follow-up.

Statistical analysis

Qualitative variables were reported with number and percentage, and quantitative variables were reported with mean and standard deviation (in cases where the data did not follow a normal distribution, the median and the interquartile range were reported). The normality of the data was assessed by the Shapiro–Wilk test. In order to determine the difference between the compared groups, Chi-2 test, T-test and paired t-test (Mann-Whitney U test and Wilcoxon signed ranks test in cases where the data did not follow a normal distribution) were used. Data were analyzed using SPSS version 26 software, with a significance level set at P -value $< .05$.

RESULTS

Demographic characteristics of patients

The distribution of demographic and clinical factors was assessed and compared between the hemodialysis and kidney transplantation groups. As shown in Table 1, the groups were comparable with respect to most baseline characteristics. Smoking history was identical between the groups. However, the prevalence of hypertension was significantly higher in the hemodialysis group ($P = .045$).

Comparison of Lung function between the two groups at baseline and six months follow-up

Lung function by spirometry indices of FEV₁, FVC, FEV₁/FVC, PEFR, FEF_{25–75%} before the initiation of hemodialysis or kidney transplantation was compared between the two groups. As shown in Table 2 and Figure 1, only PEFR was significantly higher in the hemodialysis group ($P = .01$). Lung function was also compared between the two groups six months after the initiation of hemodialysis and kidney transplantation; only PEFR was significantly higher in the hemodialysis group ($P \leq .001$).

Comparison of Lung function before and six months after six months of hemodialysis and kidney transplantation

Analysis of lung function parameters in the hemodialysis group before and six months after the initiation of hemodialysis showed that all parameters increased significantly in the six-month follow-up. In the study of these parameters in the group of patients undergoing kidney transplantation, it was observed that FEV₁, FVC and FEV₁/FVC

Table 1. Description of demographic and clinical factors of patients participating in the study

Parametera	Hemodialysis Patients n (%)	Kidney Transplant Patients n (%)	Total Patients n (%)	P
Age (years)	47.48 ± 7.10	42.68 ± 10.09	45.08 ± 8.97	.06 ^b
Duration of Dialysis (months)	7.80 ± 1.91	8.48 ± 1.50	8.14 ± 1.73	.20 ^c
Gender (male)	12 (48)	13 (52)	25 (50)	.77 ^d
Smoking History (yes)	10 (40)	10 (40)	20 (40)	1.00 ^d
Cause of Kidney Failure				
HTN	10 (40)	7 (28)	17 (34)	.209 ^d
Diabetic Nephropathy	9 (36)	6 (24)	15 (30)	
Reflux Nephropathy	6 (24)	12 (48)	18 (36)	
Previous Disease History				
Diabetes (yes)	10 (40)	7 (28)	17 (34)	.37 ^d
ADPKD (yes)	3 (12)	2 (8)	5 (10)	1.00 ^e
HTN (yes)	18 (72)	11 (44)	29 (58)	.045 ^d

^a Qualitative parameters are given as numbers (percentages) and quantitative parameters are given as mean ± standard deviation.

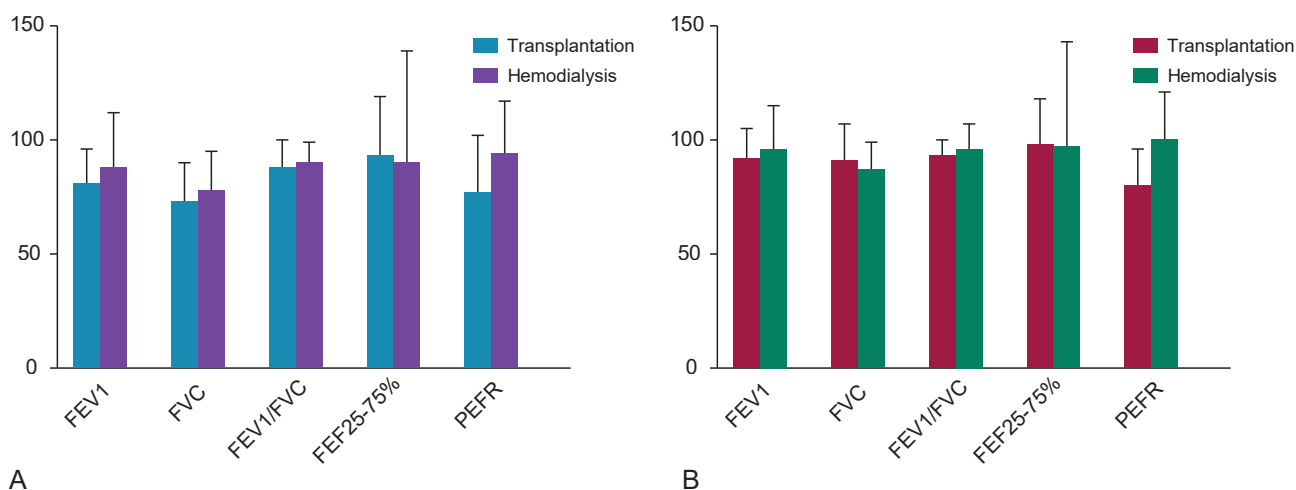
^b Independent T-test, ^c Mann-Whitney U test, ^d Chi-square test, ^e Fisher's Exact Test.

ADPKD, Autosomal Dominant Polycystic Kidney Disease; HTN, hypertension; PPIs, Proton-pump inhibitors

Table 2. Comparison of Lung function between the two groups at the baseline and after six month follow-up

Parameter	At the baseline			At six month follow-up		
	Kidney Transplant Patients	Hemodialysis Patients	P	Kidney Transplant Patients	Hemodialysis Patients	P
FEV1 (%)	80.95 ± 14.84	88.13 ± 23.52	.21 ^a	92.47 ± 12.67	96.71 ± 18.25	.34 ^b
FVC (%)	73.73 ± 15.86	77.81 ± 17.15	.38 ^b	90.97 ± 15.74	87.56 ± 11.88	.39 ^b
FEV1/FVC	88.44 ± 11.04	90.25 ± 8.55	.16 ^a	93.39 ± 11.04	96.85 ± 10.71	.21 ^a
FEF25-75%	93.99 ± 24.89	90.17 ± 48.9	.20 ^a	98.52 ± 19.39	97.86 ± 44.79	.30 ^a
PEFR (L/min)	77.07 ± 25.42	94.64 ± 22.79	.01 ^b	79.69 ± 16.68	100.4 ± 20.25	< .001 ^b

^a Mann-Whitney U test, ^b Independent T-test.

**Figure 1.** Comparison of respiratory function factors between the two groups, (A) at the baseline and, (B) after six month follow up.

increased significantly in the six-month follow-up (Table 3 and Figure 2). Changes in lung function parameters were calculated and compared between the two groups using Mann-Whitney U test. Only the change in the FVC parameter demonstrated a statistically significant difference between the

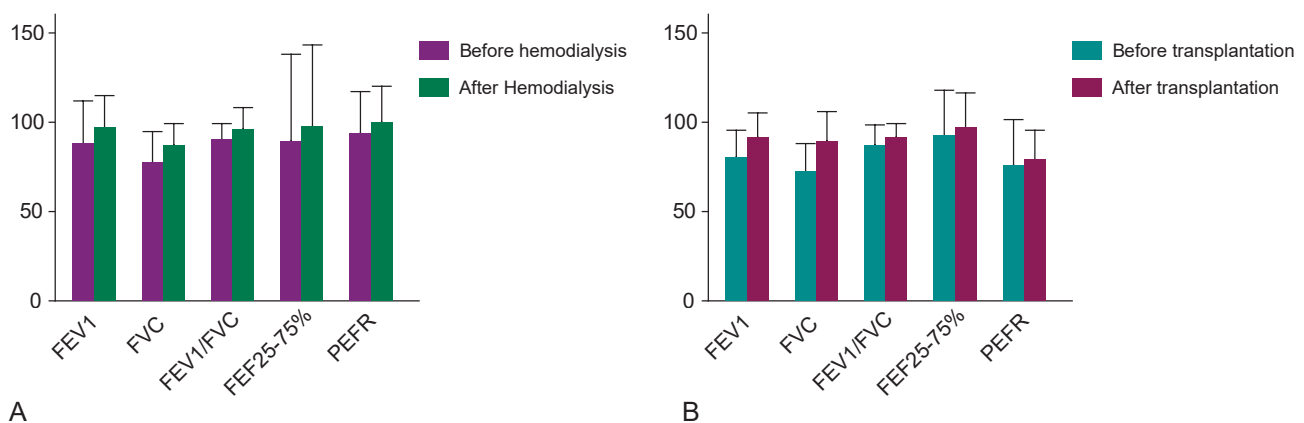
groups ($P < .05$).

DISCUSSION

Chronic kidney disease (CKD), mostly caused by diabetes, hypertension, obesity, and aging is a global health problem and can lead to ESKD,

Table 3. Comparison of Lung function before and six months after six months of hemodialysis and kidney transplantation

Parameter	Hemodialysis group			kidney transplantation		
	At the baseline	At six month follow-up	P	At the baseline	At six month follow-up	P
FEV1 (%)	88.13 ± 23.52	96.71 ± 18.25	< .001 ^a	80.95 ± 14.84	92.47 ± 12.67	< .001 ^b
FVC (%)	77.81 ± 17.15	87.56 ± 11.88	< .001 ^b	73.73 ± 15.86	90.97 ± 15.74	< .001 ^b
FEV1/FVC	90.25 ± 8.55	96.85 ± 10.71	.001 ^b	88.44 ± 11.04	93.39 ± 11.04	.01 ^a
FEF25-75%	90.17 ± 48.9	97.86 ± 44.79	.001 ^a	93.99 ± 24.89	98.52 ± 19.39	.12 ^a
PEFR (L/min)	94.64 ± 22.79	100.4 ± 20.25	.006 ^b	77.07 ± 25.42	79.69 ± 16.68	.57 ^b

^a Wilcoxon Signed Ranks Test, ^b Paired t-test.**Figure 2.** Comparison of respiratory function before and six months after, (A) hemodialysis and, (B) kidney transplantation.

increased mortality, and decreased quality of life. ESKD affects multiple organ systems, including the respiratory, cardiovascular, and metabolic disorders.¹⁹ Hemodialysis and kidney transplantation have long been used to improve quality of life and reduce mortality in these patients, but evidence regarding the superiority of one method over the other remains inconsistent. Therefore, this study was conducted to compare these two approaches regarding the improvement spirometric parameters in ESKD patients.

In this study, among FEV1, FVC, FEV1/FVC, PEFR, FEF_{25-75%} parameters, only PEFR was significantly higher in the hemodialysis group both at the baseline and after six months of follow-up. This may be explained by the better baseline condition of this parameter prior to hemodialysis initiation, as the mean change in PEFR over six months was not significantly different between the two groups. Within-group analysis showed that in the hemodialysis group, all spirometric parameters improved significantly at six months, whereas in the transplant group, only FEV1, FVC, and FEV1/FVC demonstrated significant improvement.

Previous studies have reported different findings.

In a study by Abdalla *et al.*, it was shown that there were significant differences between the hemodialysis, kidney transplantation, and control groups regarding FVC, FEV1, FEF_{25-75%}, PEFR, and MVV. Although FVC and FEV1 were within normal limits in the three study groups, the values of these spirometric parameters in the hemodialysis group were lower than the other groups. FEF_{25-75%} was below normal in the hemodialysis group and within normal limits in the transplant and control groups.²⁰

Similarly to our results, a study comparing transplant and dialysis patients showed that the difference between the groups regarding pulmonary function was not statistically significant. The slightly lower than normal FEF_{25-75%} values in hemodialysis group suggested that hyperinflation due to airway obstruction occurs mainly at the bronchiole level, which appears to resolve after six months following transplantation.²¹

Long-term use of immunosuppressive drugs, including corticosteroids in all of our kidney transplant recipients, may have contributed to the lower baseline values of FEV1/FVC, PEFR, and FEF25-75% observed in the transplant group.

Immunosuppressive drugs and steroids used after transplantation have been associated with myopathy and muscle wasting,²² and decreased respiratory muscle strength has been reported after transplantation.²³

In line with our results, a study by Sharma *et al.* reported that patients undergoing hemodialysis showed statistically significant increases in the mean of FVC, FEV1, FEV1/FVC, FEF_{25-75%}, and PEFR after six months of hemodialysis.²⁵ Our findings also showed an increase in FVC in the hemodialysis group, which are consistent with other studies.^{19,21,26-28} Although a decrease in FVC and decreased airflow by spirometry have been observed previously, Kovacevic *et al.* found that patients undergoing long-term hemodialysis showed a significant decrease in FVC.²⁷ Chronic subclinical pulmonary edema due to increased capillary permeability and hypoalbuminemia has been proposed as a cause of decreased FVC.^{26,29}

The improvement in FEF_{25-75%} after six months of hemodialysis may reflect improved small-airway function associated with correction of fluid overload. However, persistent small-airway abnormalities may also result from chronic peribronchial changes.^{26,29}

Plesner *et al.* (2016) examined changes in spirometric parameters in COPD patients undergoing dialysis and found that improvements in FEV1/FVC and FEV1 were significantly associated with the patients' ultrafiltered volume. When this volume was greater than 0.3 body weight, significant improvements in FEV1/FVC and FEV1 were observed.³¹

Interestingly, some studies have pointed out the role of sex in improving respiratory function in hemodialysis patients. The results of Momeni *et al.* study showed that hemodialysis did not significantly change spirometric parameters in women, while it significantly increased FEV1 and FVC and decreased FEV1/FVC in men. The differences in VC, PEF, and FEF parameters were not significant for all patients (both men and women) after dialysis compared to before.⁹

Lang *et al.* examined the initial effects of hemodialysis on pulmonary function in 14 patients with ESKD, and in contrast to our study, they concluded that hemodialysis had no initial effect on them.³² Rahgoushai *et al.* similarly examined the short-term effects of dialysis on lung function

in 26 patients and found that FVC increased significantly immediately after dialysis, while no obvious improvements occurred for VC, FEV1/FVC, and FEV1.²⁶ Our study considered long-term effects, reflecting the fact that clinically meaningful changes require a sufficient amount of time.

On the other hand, the association between physical activity and comorbidities that may alter lung function has been previously reported.³³ Higher levels of physical activity have been shown to be associated with better clinical outcomes in patients with chronic diseases, including transplant patients.³⁴ In our study, the diseases were matched between the two groups, but the physical activity of the patients was not considered.

Although the prevalence of hypertension differed significantly between the two groups, this difference should be considered when interpreting the pulmonary function findings. However, the study was not designed to assess the independent effect of hypertension on spirometric indices.

Our results are consistent with the findings of some studies and contradictory to others. Furthermore, the results of some studies were not exactly similar to our results. Differences in hemodialysis methods, dialysis duration, membrane type, disease severity, underlying diseases, and even inclusion criteria may be the reasons for this discrepancy. Small sample sizes in many studies limit the generalizability of the results. Lack of access to more patients for long-term follow-up and lack of patient cooperation were important limitations of this study. Also, we did not have access to a plethysmography device, which made it impossible to examine more precise parameters such as RV, TLC, RV/TLC, FRC and provide results with higher accuracy.

Limitation and strengths of the study

This study has some notable strengths. First, the prospective design allowed for the direct observation of temporal changes in pulmonary function, offering more reliable insight compared with the predominantly retrospective literature available in this field. Second, the application of standardized 2019 ATS/ERS spirometry protocols and the use of GLI reference equations ensured high methodological rigor and enhanced the validity and comparability of the respiratory measurements. Third, both patient groups were

well matched with respect to demographic and clinical characteristics, including major confounders such as smoking status and comorbidities, thereby reducing the likelihood that baseline imbalances influenced the observed outcomes. Additionally, the inclusion of a uniform hemodialysis protocol (consistent membrane, $Kt/V \geq 1.2$) and standardized immunosuppressive regimen in the transplant group further strengthened internal validity by minimizing treatment-related heterogeneity across participants. It should be noted that all enrolled patients in Hemodialysis Group had adequate dialysis ($Kt/V \geq 1.2$), and therefore patients with lower dialysis adequacy were not enrolled. In addition, as the primary objective of this study was strictly to compare spirometric parameters between hemodialysis and kidney transplant groups; accordingly, the data collected were aligned with this objective.

Despite these strengths, several limitations warrant consideration. The most significant limitation is the relatively small sample size—particularly in the transplant group, where the number of eligible candidates was inherently restricted and some patients did not return for follow-up spirometry—potentially reducing the statistical power to detect modest between-group differences and limiting the generalizability of the findings. Furthermore, all transplant recipients had undergone a period of hemodialysis prior to transplantation, an unavoidable limitation given organ availability, which could have contributed to baseline pulmonary impairments and partially confounded comparisons between modalities. Another limitation is the absence of plethysmographic measurements, which prevented a more comprehensive evaluation of lung mechanics, particularly parameters such as TLC, RV, RV/TLC, and FRC that may better capture subtle restrictive or obstructive changes. Additionally, objective assessment of physical activity—which is known to influence pulmonary recovery—was not incorporated into the study design. Finally, the single-center design of the study may limit external validity, as dialysis practices, transplant protocols, and patient characteristics may differ across institutions or geographic regions. Future multicenter studies with larger sample sizes, inclusion of advanced pulmonary function testing, and consideration of post-transplant physical

activity and rehabilitation are warranted to validate these findings and further elucidate the differential respiratory trajectories of ESKD patients undergoing hemodialysis. In addition, ultrafiltration volume was not available for all hemodialysis patients and therefore could not be analyzed. This factor may influence pulmonary function and should be considered in future studies.

CONCLUSION

Based on the results of the present study, in patients with ESKD, FEV1, FVC, FEV1/FVC, PEFR, and FEF25-75% improved significantly after six months of maintenance hemodialysis, whereas FEV1, FVC, and FEV1/FVC improved significantly six months following kidney transplantation. These findings indicate improvement in several spirometric measures with both treatment modalities, while the magnitude and pattern of change differed between groups. Further multicenter studies with larger sample sizes and more comprehensive pulmonary function testing are warranted.

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