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# The Effect of a Single Hemodialysis Session on Pulmonary Functions in Patients with End-Stage Renal Disease

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## ABSTRACT

**Objective:** Changes in pulmonary functions have not been thoroughly investigated in patients undergoing hemodialysis (HD). The aim of this study was to determine the effect of a single HD session on pulmonary functions, measured by spirometry, in patients with end-stage renal disease (ESRD) undergoing chronic hemodialysis (CHD) treatment.
**Methods:** Thirty patients with ESRD who were on CHD treatment for at least 12 months between January 2018 and January 2020 were enrolled. The pre-dialysis and post-dialysis spirometric measurements were recorded by a portable spirometry device.
**Results:** The mean age and HD vintage of 30 patients (70% male, 20% diabetic, mean BMI: 26.0 ± 4.7 (kg/m$^2$)) were 55.6 ± 11.4 years and 117.6 ± 66.3 months, respectively. Half of the patients (50%) were smokers (mean 11.5 ± 13.59 packs/year). The spirometric measurements of most of the patients were abnormal (40% restrictive, 30% obstructive respiratory disorder, 30% normal). The $FEV_3$(L), predicted $FEV_1$(%), $FEF_{25}$(L), and predicted $FEF_{25}$(%) values were significantly increased after the HD session. A positive correlation between BMI and Delta $FEV_3$ (L) values ($r = 0.377$, $P = .04$) was observed. A significant improvement in $FEV_3$ values after a single HD session was recorded, which was independently related to higher BMI ($\beta = 0.501$, $P < .01$) and non-smoking ($\beta = 0.495$, $P < .05$).
**Conclusion:** Spirometric measurements are abnormal in most CHD patients, and a considerable improvement in pulmonary functions is possible with a single HD session. Having a high BMI and being a non-smoker appear to have significant positive effects on amelioration in $FEV_3$ (L). Larger trials are needed to evaluate pulmonary functions in CHD patients.
**Keywords:** End-stage renal disease, $FEF_{25}$, $FEV_1$, $FEV_3$, hemodialysis, lung functions, spirometry

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## INTRODUCTION

Patients with end-stage renal disease (ESRD) undergoing chronic hemodialysis (CHD) treatment are potentially prone to intravascular and extravascular volume overload and subsequent interstitial pulmonary edema, which is presented mostly with dyspnea, in clinical practice. Peripheral edema and arterial blood pressure are the parameters commonly used to assess the volume status of such patients. Monitoring the interdialytic weight gain (IDWG) and ensuring that the patient maintains dry weight, which is in an euvolemic state, are major considerations for volume management. Moreover, the biochemical parameters, the diameter of the inferior vena cava, continuous blood volume monitoring, bioimpedance measurements, and lung ultrasound are used to objectively assess the volume status of patients suffering from ESRD.[1] Nevertheless, the need for objective and practical ways of fluid overload and respiratory function measurement is still unmet. The other consequences of ESRD are varying degrees of left-sided heart failure causing arterial hypertension, anemia, metabolic acidosis, uremic cardiomyopathy, and vessel and tissue calcification. Moreover, the toxic effects of uremia on the endothelium of the pulmonary capillaries lead to increased permeability of the pulmonary capillary, leading to edema and increased resistance in the small airways and alveoli.[2] A single HD session may theoretically improve lung functions by correction of uremia and metabolic acidosis, and eliminate pulmonary edema by removing the fluid with ultrafiltration. However, there are few publications in the literature investigating the relationship between lung volumes and ESRD. As a cheap and practical way of measuring lung volumes, spirometry is becoming more and more popular. Its failure incidence is only 1.9%, and the rate of adverse events is as low as 0.44%.[3] The aim of this study was to investigate the changes in pulmonary functions after a single HD session in patients with ESRD, by using spirometry.

## METHODS

### Study Population



This cross-sectional study includes 30 patients with ESRD who were on CHD treatment for at least 12 months between January 2018 and January 2020. The criteria for exclusion from the study were the use of drugs that may affect lung functions, such as beta blockers or agonists, a recent history of surgery or trauma, a diagnosis of malignancy, glaucoma, intracranial pressure syndrome, myocardial infarction, unstable angina, or congestive heart failure, a known history of acute or chronic pulmonary disease (CPD) (i.e., hemoptysis, pneumothorax, asthma, chronic obstructive pulmonary disease (COPD), and interstitial lung disease), and an unwillingness to participate. Debilitated patients who could not cooperate with the spirometric maneuvers were also excluded. The study was approved by Recep Tayyip Erdoğan University Faculty of Medicine Human Research Ethics Committee (Approval Number: 2020/104), and a written informed consent was obtained from each patient before participation in the study.

Conventional HD was applied to all patients 3 times a week, with standard bicarbonate-containing dialysate and biocompatible low-flux HD membranes, for 4 hours. The dialysis adequacy parameters (urea reduction rate (URR), single-pool Kt/V (spKt/V) urea) were calculated using the method recommended by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guideline for HD Adequacy: 2015 Update.[4] All patients were anuric and none had residual renal function.

### Clinical and Laboratory Assessment

The initial assessment was made for all patients in January 2018, including demographics, (age, sex, body mass index (BMI), pre- and post-HD weight, smoking status, and the presence of diabetes mellitus), HD characteristics (HD vintage, vascular access type, ultrafiltration (UF) volume and dialysis adequacy (URR and spKt/V urea) parameters), and biochemical data (pre-and post-HD serum urea, creatinine, bicarbonate, albumin, electrolytes, ferritin, intact parathormone (PTH), and hemoglobin). Fasting peripheral blood samples were obtained on the same day and before the midweek HD sessions, and the standard biochemical analyses were done.

### Lung Function Measurement

A portable spirometer (MicroLab, Micro Medical Limited, England) was used for recording the spirometric parameters 30 minutes before and after the midweek HD session. We analyzed the data only from the subjects with 2 or more acceptable and reproducible forced expiratory vital capacity maneuvers after consecutive spirometry performances. The measurements were done in a sitting position while wearing a nose clip, using standard methodology, and by the same technician.[5] The forced vital capacity (FVC), forced expiratory volume in the first second ($FEV_1$), $FEV_1$/FVC ratio, forced expiratory volume in 3 seconds ($FEV_3$), forced expiratory volume in 6 seconds ($FEV_6$), peak expiratory flow rate (PEF), and forced expiratory flow at 25%, 50%, and 75% of the FVC ($FEF_{25,}$ $FEF_{50,}$ $FEF_{75}$) were measured and calculated as % predicted (% pred), using normal values determined on the basis of age, race, height, and sex.

### Statistical Analysis

The Number Cruncher Statistical System (NCSS) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. The descriptive statistical values (mean, median, standard deviation, ratio, frequency, minimum, maximum) and the data distribution were evaluated by the Shapiro–Wilk test. In the periodical comparisons of quantitative data, the Wilcoxon test was used. The relationship between the variables was determined using the Pearson correlation test. Multiple linear regression analysis was used to determine the effect of independent variables on dependent variables. Statistical significance was set at $P < .05$ and $P < .01$.

## RESULTS

The patients' mean age was 55.6 ± 11.4 years (range: 33-72 years). Seventy percent were male and the mean body mass index (BMI) was 26.0 ± 4.7 (kg/m$^2$). Half of the patients (50%) were smokers (mean 11.5 ± 13.59 packs/year). The mean dialysis vintage was 117.6 ± 66.3 months (range: 28-251 months). Six (20%) patients were diabetic. In accordance with the guideline recommendations, the majority of the patients (90%) were dialyzed via AV fistula. It was observed that the patients were in the target ranges in terms of dialysis adequacy (mean URR: 72.3 ± 6.7, spKt/V urea: 1.51 ± 0.31), serum electrolytes, nutritional parameters (mean serum albumin: 3.7 ± 0.3 g/dL), and anemia control (mean hemoglobin: 11.5 ± 1.6 g/dL, ferritin: 310.4 ± 413.5 ng/mL). Table 1 shows the demographic information, HD characteristics, and biochemical findings of the study population.

The change in pulmonary function test values of all patients' before and after a single HD session is shown in Table 2 and Figure 1. When the pre-dialysis pulmonary function test results of the patients were examined; 40% normal, 30% obstructive

**Table 1.** Demographic, Clinical, and Laboratory Characteristics of All Patients

| | All Patients ($n$ = 30) | |
|---|---|---|
| **Parameters** | **Mean ± SD** | **Min-Max (Median)** |
| Demographic characteristics | | |
| Age (years) | 55.6 ± 11.4 | 33-72 (55.5) |
| Gender (M/F), $n$ (%) | 21 (70%)/9 (30%) | |
| Height (cm) | 166.8 ± 11.6 | 145-185 (165.5) |
| Weight (kg) (pre-dialysis) | 72.4 ± 14.5 | 39-103 (72) |
| Weight (kg) (post-dialysis) | 70.0 ± 14.5 | 38-100 (70) |
| BMI (kg/m$^2$) | 26.0 ± 4.7 | 15-35.5 (25.8) |
| Smoking status | 15 (50%) | |
| Smoking history (pack/years), $n$ (%) | 11.5 ± 13.5 | 0-50 (2.5) |
| DM, $n$ (%) | 6 (20%) | |
| Hemodialysis characteristics | | |
| HD vintage (months) | 117.6 ± 66.3 | 28-251 (98) |
| Vascular access (AVF/catheters), $n$ (%) | 27 (90%)/3 (10%) | |
| Ultrafiltration (mL) | 2.7 ± 1.3 | 0-7 (2.0) |
| URR (%) | 72.3 ± 6.7 | 57.5-81.3 (73.7) |
| spKt/V urea | 1.51 ± 0.31 | 1.0-2.4 (1.5) |
| Laboratory findings (serum) | | |
| Pre-HD urea (mg/dL) | 167.8 ± 29.9 | 96-212 (164) |
| Pre-HD creatinine (mg/dL) | 10.0 ± 2.9 | 4-16 (10.1) |
| Post-HD urea (mg/dL) | 46.4 ± 13.5 | 25-70 (44.5) |
| Post-HD creatinine (mg/dL) | 3.8 ± 1.7 | 1.4-7.7 (3.2) |
| Pre-HD bicarbonate (meq/L) | 20.3 ± 2.2 | 14.1-26.5 (20.7) |
| Post-HD bicarbonate (meq/L) | 26.5 ± 2.7 | 17.9-30.3 (27.1) |
| Albumin (g/dL) | 3.7 ± 0.3 | 3.0-4.4 (3.8) |
| Sodium (mmol/L) | 138.2 ± 3.2 | 133-144 (138.5) |
| Potassium (mmol/L) | 5.4 ± 0.7 | 3.8-7.4 (5.5) |
| Uric acid (mmol/L) | 5.7 ± 1.2 | 3.4-8.3 (5.7) |
| Calcium (mmol/L) | 9.2 ± 0.6 | 8-10.4 (9.3) |
| Phosphorus (mmol/L) | 5.3 ± 1.8 | 2.1-8.9 (4.7) |
| PTH (pg/mL) | 670.4 ± 663.4 | 1.8-2950 (556) |
| Ferritin (ng/mL) | 310.4 ± 413.5 | 5-1850 (214) |
| Hb (gr/dL) | 11.5 ± 1.6 | 8.3-15 (11.7) |
| Htc (%) | 37.1 ± 5.7 | 27.4-50.5 (36.6) |

n, number; Mean ± SD, mean ± standard deviation; Min-Max, minimum-maximum; (M/F), male/female; BMI, body mass index; DM, diabetes mellitus; HD, hemodialysis; AVF, arteriovenous fistula; URR, urea reduction rate; spKt/V, single-pool Kt/V; PTH, parathormone; Hb, hemoglobin; Htc, hematocrit.



($FEV_1$/FVC ratio < 70%) and 40% restrictive ($FEV_1$/FVC ratio >70% and FVC <80% predicted) patterns were detected. However, because most of the patients with obstructive pattern also had low FVC, they could be included in the category of mixed respiratory disorder. The percentages of the predicted spirometric parameters (% pred) and the changes in spirometric measurements among patients after a single HD session can be summarized as follows:

**Table 2.** The Change in Pulmonary Function Test Values of All Patients Before and After a Single Dialysis Session

| Parameters | Pre-dialysis ($n$ = 30) | | Post-dialysis ($n$ = 30) | | $P$ |
|---|---|---|---|---|---|
| | Mean ± SD | Range (Median) | Mean ± SD | Range (Median) | |
| FVC (L) | 2.76 ± 0.8 | 1.28-4.24 (2.72) | 2.88 ± 0.88 | 1.24-4.7 (2.87) | .066 |
| Predicted FVC (%) | 77.47 ± 18.2 | 38-116 (76.5) | 80.03 ± 17.84 | 46-127 (79.5) | .073 |
| $FEV_1$ (L) | 2.05 ± 0.74 | 1.03-3.31 (2.05) | 2.08 ± 0.82 | 0.56-3.59 (1.94) | .104 |
| Predicted $FEV_1$ (%) | 70 ± 18.89 | 33-110 (72.5) | 73.87 ± 21.98 | 34-113 (73) | .037* |
| $FEV_1$/FVC | 74.09 ± 14.04 | 31.1-96.5 (78.35) | 75.05 ± 15.37 | 36.8-100 (78.9) | .750 |
| Predicted $FEV_1$/FVC | 95.1 ± 18.07 | 38-123 (101.5) | 96.43 ± 20.23 | 46-129 (102.5) | .697 |
| $FEV_3$ (L) | 2.63 ± 0.8 | 1.26-4.18 (2.5) | 2.76 ± 0.86 | 1.24-4.7 (2.77) | .028* |
| $FEV_6$ (L) | 2.74 ± 0.8 | 1.28-4.24 (2.71) | 2.77 ± 0.85 | 1.24-4.7 (2.77) | .188 |
| PEF (L/min) | 3.17 ± 1.33 | 1.22-5.77 (3.1) | 3.26 ± 1.59 | 1.11-6.98 (3.18) | .537 |
| Predicted PEF (%) | 40.83 ± 14.31 | 18-79 (39) | 42.07 ± 18.19 | 13-91 (37.5) | .673 |
| $FEF_{75}$ (L/min) | 3.01 ± 1.36 | 0.95-5.65 (2.78) | 3.01 ± 1.73 | 0.59-7.01 (2.88) | .440 |
| Predicted $FEF_{75}$ (%) | 43.83 ± 17.06 | 15-88 (42.5) | 43.43 ± 23 | 12-101 (38) | .446 |
| $FEF_{50}$ (L/min) | 2.31 ± 1.14 | 0.64-4.17 (2.38) | 2.48 ± 1.2 | 0.8-4.49 (2.29) | .213 |
| Predicted $FEF_{50}$ (%) | 53.97 ± 24.01 | 14-104 (60) | 58.33 ± 26.44 | 19-103 (56.5) | .226 |
| $FEF_{25}$ (L/min) | 1 ± 0.58 | 0.21-2.9 (0.9) | 1.16 ± 0.6 | 0.36-2.36 (1.03) | .014* |
| Predicted $FEF_{25}$ (%) | 61.43 ± 26.05 | 15-107 (64) | 74.53 ± 37.86 | 17-182 (68.5) | .008** |

*$P$ <.05.
**$P$ < .01.
Wilcoxon Rank test is the test used for statistical analysis.
$n$, number; Mean ± SD, mean ± standard deviation.



### Forced Vital Capacity (FVC)

The mean FVC of the patients was 77.47 ± 18.2% predicted, which increased to 80.03 ± 17.84% pred after HD, although this improvement was not statistically significant ($P$ > .05).

### Forced Expiratory Volume ($FEV_1$)

The mean $FEV_1$ of the patients was 70 ± 18.89% pred which increased to 73.87 ± 21.98% pred after HD, and this increase was statistically significant ($P$ = .037*).

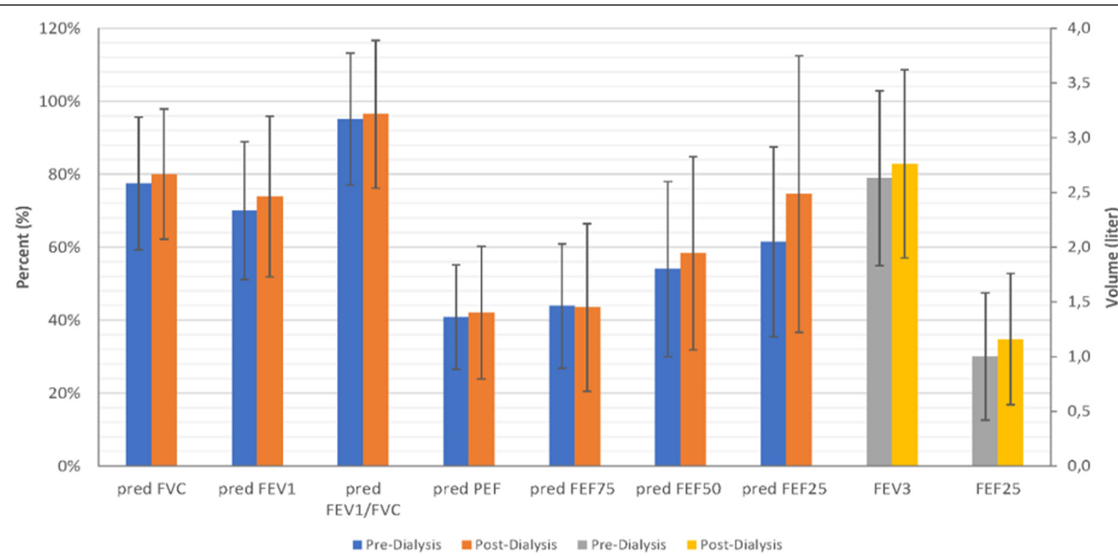


**Figure 1.** The change in lung volumes before and after a single hemodialysis session.

**Table 3.** Analysis of Correlation Between Clinical-Laboratory Features and Changes in Lung Volumes After a HD Session

| Parameters | Delta Pred FEV1 (%) | Delta $FEF_{25}$ (L) | Delta $FEV_3$ (L) |
|---|---|---|---|
| Age | | | |
| *r* | 0.009 | 0.121 | 0.14 |
| *P* | .961 | .524 | .461 |
| HD vintage | | | |
| *r* | −0.022 | −0.155 | 0.068 |
| *P* | .907 | .413 | .721 |
| Dry weight | | | |
| *r* | 0.041 | −0.02 | 0.301 |
| *P* | .828 | .916 | .106 |
| BMI | | | |
| *r* | 0.148 | −0.171 | 0.377 |
| *p* | .435 | .365 | .04* |
| URR | | | |
| *r* | 0.189 | 0.152 | −0.119 |
| *P* | .318 | .423 | .531 |
| spKt/V urea | | | |
| *r* | 0.144 | 0.093 | −0.138 |
| *P* | .449 | .625 | .467 |
| Albumin | | | |
| *r* | 0.022 | 0.306 | 0.01 |
| *P* | .909 | .1 | .958 |
| Hemoglobin | | | |
| *r* | −0.159 | −0.266 | −0.079 |
| *P* | .4 | .156 | .677 |
| Ultrafiltration | | | |
| *r* | 0.024 | −0.322 | 0.085 |
| *P* | .902 | .088 | .662 |

Pred, predicted; HD, hemodialysis; BMI, body mass index; URR, urea reduction rate; spKt/V, single-pool Kt/V.

**Table 4.** Findings of Multiple Regression Analysis Related to the İnterpretation of $FEV_3$ Change with Some Variables

| Variables | B | S. error | β | *t* | *P* |
|---|---|---|---|---|---|
| Constant | −1.084 | 0.645 | | −1.680 | .106 |
| Gender | −0.115 | 0.112 | −0.193 | −1.030 | .313 |
| Hemodialysis vintage | 0.001 | 0.001 | 0.177 | 0.973 | .340 |
| BMI | 0.028 | 0.010 | 0.495 | 2.888 | *.008*** |
| Non-smoking | 0.266 | 0.098 | 0.501 | 2.720 | *.012** |
| Albumin | 0.076 | 0.149 | 0.088 | 0.509 | .615 |

S. error, standard error; BMI, body mass index. $^*P < .05$, $^{**}P < .01$
Italics denote statistically significant values.

### Forced Expiratory Volume$_1$/Forced Vital Capacity ($FEV_1$/FVC)

The patients' mean $FEV_1$/FVC was 95.1 ± 18.07% pred. After HD, it increased to 96.43 ± 20.23% pred, but this increase did not reach statistical significance ($P > .05$).

### Forced expiratory flow ($FEF_{25}$)

The mean $FEF_{25}$ % of the patients was measured as 61.43 ± 26.05% pred and 1 ± 0.58 L. After HD, it increased to 74.53 ± 37% pred and 1.16 ± 0.6 L, respectively. This increase was statistically significant for both measurements, with *P* values < .05.

### Peak expiratory flow (PEF)

The mean PEF of the patients was 40.83 ± 14.31% pred, far below the normal range, which is more than 80% of the predicted values. After HD, the mean PEF increased to 42.07 ± 18.19% pred, but the change was not significant ($P > .05$).



### Forced Expiratory Volume ($FEV_3$)

In the last measurement (post-HD), the increase in $FEV_3$ value compared to the first measurement was found to be statistically significant ($P = .028$).

The analysis of correlation between the patients' clinical features and the change in lung volumes is shown in Table 3. No significant correlation was found between age, HD vintage, dry weight, dialysis adequacy (URR and spKt/V urea), serum albumin, hemoglobin, and ultrafiltration, and the change in delta pred $FEV_1$ (%), $FEF_{25}$ (L), and $FEV_3$ (L) values. There was a positive correlation between BMI and the delta $FEV_3$ (L) value ($r = 0.377$, $P = .04$).

The multiple linear regression analysis performed to determine the effect of some variables on the change in $FEV_3$ showed statistical significance ($F_{(5,24)} = 2.873$, $P < .05$) (Table 4), and explains 37.4% of the variance in the dependent variable, which is the $FEV_3$ change of some independent variables in the model ($R_2 = 0.374$, $P < .05$). The results of multiple regression analysis showed that improvement in the $FEV_3$ values after a single HD session was statistically significantly and independently related with higher BMI (β = 0.495, $P < 0.008$) and non-smoking (β = 0.501, $P < 0.012$). No significant differences in any of the spirometric measurements after the HD session were seen when compared on the basis of sex, HD vintage, and serum albumin levels.

## DISCUSSION

The $FEV_3$ and $FEF_{25}$ values and the percentage of the predicted $FEV_1$ and $FEF_{25}$ (%) values were found to be significantly increased after a single session of HD in our study population.

These changes indicate an improvement in the function of both large and small airways. The improvement in $FEV_3$ values was significantly related with higher BMI and non-smoking.

Patients with ESRD undergoing CHD treatment are potentially prone to intravascular and extravascular volume overload (hypervolemia) and subsequent interstitial pulmonary edema, which is presented mostly with dyspnea in clinical practice. Except for hypervolemia, various complications such as uremia, chronic metabolic acidosis, inflammation, malnutrition, hypoalbuminemia, anemia, vessel and tissue calcifications, and comorbidities (e.g., heart failure) contribute to the lung damage. A single HD session may theoretically improve lung functions by correcting some of these pathologies.



The frequency of CPD at dialysis initiation is 12%, most of which may be recognized by spirometry. Various conditions, including obesity and smoking, are associated with reduced lung functions in patients with ESRD. After adjustment for these comorbidities, CPD was shown to be associated with a poor prognosis. The chances of undergoing transplantation are 30% lower for patients with CPD, than for patients without CPD. ESRD patients with CPD have a higher risk of hospitalization and respiratory infections. The morbidity and mortality risks are also increased.[6] Plesner et al.[7] assessed the rate of COPD in CHD patients using spirometry, and found that 46% of the patients had an obstructive ventilatory defect, indicative of COPD according to the GOLD criteria. They concluded that COPD is a frequent and underdiagnosed comorbidity in patients on CHD, and all patients undergoing dialysis should be screened with spirometry in order to assess and manage dyspnea appropriately.[7] Spirometry is a cheap and practical way of measuring lung volumes. Therefore, this study was designed to investigate the effects of a single HD session on pulmonary function tests measured by spirometry in ESRD patients. In this study, we found that the results of pulmonary function test for most of our patients were abnormal (the percentages of restrictive and obstructive ventilatory defects were 40% and 30%, respectively) in accordance with the literature described above. The rate of pulmonary functions recorded within the normal limits was only 30%. Kovacevic et al.[8] investigated the pulmonary function improvement in patients undergoing regular HD, and they found that ventilatory functions (especially vital capacity (VC) and $FEV_1$) in male chronic HD patients were significantly improved, whereas there was no statistical significance in female patients. In our study, the change in $FEV_1$, $FEV_3$, and $FEF_{25}$ were found to be significantly ameliorated after a single HD session. These findings may be interpreted as showing an improvement in all degrees of airflow limitation from the large to the small airways. However, we could not demonstrate a significant change in FVC value, nor a difference by gender.

There may be many reasons for changes in lung function in CHD patients. Interstitial edema due to increased volume load in the lung is among the most important causes of this condition. In a study by Plesner et al.,[7] which examines the effects of excess fluid removal (ultrafiltration) by HD on pulmonary functions, HD was found to cause a slight decrease in mean $FEV_1$ and FVC, which was more prominent in patients who had a smaller amount of extra fluid removed by HD, than the $FEV_1$/FVC ratio, and there was no change in the number of subjects with obstructive defect indicative of COPD after HD.[7] In our study, there was no relationship between the rate of ultrafiltration (UF) and HD adequacy parameters (*URR,* spKt/V*)* and the changes in lung volumes (delta $FEV_1$, $FEV_3$ and $FEF_{25}$) after the HD session. The variability in lung volume changes before and after HD may be explained by the changing characteristics of lung dynamics, which cannot be explained solely by the simple lung volumes measured by spirometry and the volume of fluid removed in the HD session. Expiratory and inspiratory muscle strength, malnutrition, electrolyte and blood pressure changes, and patient and technician efforts may play a role in this situation.

Respiratory muscle weakness is another issue that should be evaluated in ESRD. This is related to several factors such as anemia, malnutrition, decreased serum calcium levels, increased oxidative stress, etc. Uremia exerts its detrimental effects on muscles via intravascular calcification and a consequent decrease in the blood flow. The respiratory muscles are affected, as are other striated muscles in different parts of the body. In a study by Tavana et al.[9] the PImax and PEmax values, which are used to measure respiratory muscle strength, were found to increase after transplantation compared to the pre-transplantation period. Authors concluded that the final values are still lower than the normal limits. This supports the idea that mechanisms other than uremic myopathy might play a role in the respiratory muscle weakness in patients with ESRD.[9] The volume of air exhaled in the first 3 seconds of the expiration maneuver of spirometry is called the $FEV_3$ value. Both FVC and $FEV_3$ are good parameters for reflecting lung functions, and may have a relationship with muscle strength.[10] In this study, we found that improvement in $FEV_3$ values after a single HD session was statistically significantly and independently related with a higher BMI and non-smoking. These results were consistent with the literature information above; and may indicate the relationship between nutrition and muscle strength with pulmonary functions.

An increase in plasma concentration of endothelin-1 (ET-1) in HD and peritoneal dialysis patients compared with healthy controls has been demonstrated in several studies.[11] ET-1 can have a broncho-constrictive and vasoconstrictive effect on one side and a proinflammatory effect on the other, creating a vicious circle of pathophysiologic events in patients with ESRD. Kovacevic et al.[12] compared 3 groups of patients for their ET-1 levels and lung volumes: HD patients, continuous ambulatory peritoneal dialysis (CAPD) patients without any cardiovascular or respiratory diseases, and healthy volunteers. The results showed that patients undergoing HD or CAPD had significant difference in values of most lung function parameters between subjects, with ET-1 levels less than 6.6 pg/mL and subjects with ET-1 levels higher than 6.6 pg/mL. There was no difference in lung volumes in correlation with ET-1 levels in the control group. The ET-1 levels in both the dialysis groups were substantially higher compared to the healthy subjects. The authors concluded that the higher levels of ET-1 in dialysis patients are associated with lower values of lung volumes.[12] The findings of this study emphasize the effect of inflammation and its consequences on lung functions.

Another factor that is likely to be effective on respiratory functions in CHD patients is pulmonary hypertension (PH). In a study searching for the association of PH with inflammation and fluid overload, Yoo et al.[13] hypothesized that the volume overload induces a postcapillary PH in HD patients. Additionally, the chronic volume excess associated with ESRD patients' micro-inflammatory state might trigger some inflammatory mechanisms in the pulmonary vascular bed, causing vasoconstriction, remodeling, and microthrombotic events with consequent precapillary PH.[13] However, the effect of volume change on PH before and after HD was not evaluated in this study. The expected changes in the pulmonary function tests of ESRD patients with PH are as follows: vital capacity (VC), FVC, $FEV_1$, $FEV_1$/FVC and $FEF_{50}$ are lower, while total lung capacity and residual volume do not differ from the control group. Obstruction in the small airways is common in patients with pulmonary arterial hypertension (PAH). This study, by Jing et al.,[14] demonstrated that small-airway obstruction is the most notable characteristic of pulmonary function tests in idiopathic PAH, PAH related to congenital heart disease and PAH related to connective tissue disease patients; and $FEF_{50}$ may be the best indicator that describes the degree of obstruction.[14] In our study, the change in $FEF_{25}$ was significantly improved as another indicator of airflow limitation in the small airways. As a limitation, we did not evaluate the pulmonary arterial pressure values of the participants before and after the HD session, which might have an additive influence on the pulmonary function test results and oxygenation.

Hypoxemia during HD is another clinical problem in patients with ESRD. During HD, pulmonary edema around the small airways is decreased by the removal of excess fluid, and this may cause dilation of the small airways, resulting in decreased closing capacity. This improves the basal ventilation and perfusion.[15] In a study by Mukai et al.[16] there was restrictive lung dysfunction (RLD) (defined as $FEV_1$/FVC $\geq$ 0.70 and FVC% $<$ 80) in 36% of patients with glomerular filtration rate (GFR) <15 mL/min/1.73 $m^2$ (G5) and 14% of individuals with GFR >15 mL/min/1.73 $m^2$ (G1-4), and the degree of restriction was correlated with the GFR. The obstructive ventilatory defect ($FEV_1$/FVC $<$ 0.70) was less common, and there was a similar prevalence of obstruction between G1-4 (9%) and G5 (11%) patients. Importantly, 64% of those with coexisting protein-energy wasting (PEW), clinical signs of cardiovascular disease (CVD) and inflammation had restriction, while 79% of those without these complications had lung functions within normal range. In multivariate logistic regression analysis, there was an association between RLD and CVD, PEW and inflammation, after adjusting for Framingham's CVD risk score, the GFR category, and serum albumin.[16] In our study, the distribution of patients according to lung dysfunction was as follows: RLD: 40%, obstructive lung dysfunction: 30%, and normal lung functions: 30%. The obstructive lung dysfunction may be associated with smoking and undiagnosed obstructive lung diseases like asthma, COPD, or bronchiectasis. However, symptoms like dyspnea in such patients are often attributed to consequences of ESRD, and the request for spirometry by clinicians is therefore delayed. Scanning ESRD patients with spirometry may also be a beneficial way of selecting potential candidates for bronchodilators.[7]



There are some limitations of our study. To begin with, our sample size was small and the study was cross-sectional. In addition, we did not investigate some parameters known to affect lung functions, such as malnutrition, inflammation, and respiratory muscle strength, and the effects of these parameters on lung volumes. Furthermore, the effects of hemodiafiltration on lung functions could not be assessed, since complications such as intradialytic hypotension may develop during hemodiafiltration, and the fluid required for patients to reach their dry weight may not be provided in a single session. Lastly, we did not measure the diffusion capacity of the lung for carbon monoxide (DLCO), which may contribute to a better assessment of lung functions.

## CONCLUSION

Pulmonary function test results are abnormal in most CHD patients, and a considerable improvement in pulmonary functions is possible with a single HD session. Having a high BMI and being a non-smoker appear to have a significantly positive effect on amelioration in $FEV_3$ (L). Consequently, large-scale randomized controlled studies designed to address the factors contributing to ventilatory disorders, and attempts to improve lung functions in patients with ESRD, are needed.

**Ethics Committee Approval:** Ethics committee approval was received from the Recep Tayyip Erdoğan University Faculty of Medicine Human Research Ethics Committee (Approval Number: 2020/104).

**Informed Consent:** Written informed consent was obtained from all participants who participated in this study or from a legal guardian.

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