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Original Article

Association between reduced lung function, hydration and nutritional status in patients on hemodialysis: An observational study using bioelectrical impedance vector analysis (BIVA)

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SUMMARY

Background & aims: This study aimed to determine the lung function and to investigate the association between pulmonary parameters, hydration, and nutritional status – assessed by bioelectrical impedance vector analysis (BIVA) – in patients on HD.
Methods: A cross-sectional study, including patients with CKD on HD, age >18 years. Laboratory data, lung function and body composition by bioimpedance were evaluated.
Results: The sample consisted of 42 participants, 23 (55%) male and age 54±14 years. Reduced lung function was prevalent in 30 (71%) participants, and compared to those with preserved lung function, they had higher dialysis vintage, lower body weight, body mass index, adipose tissue mass and fat tissue. Regarding hydration status and bioimpedance parameters, participants with reduced lung function had significant difference in the variable overhydration (OH) ($P = 0.034$). OH, phase angle (PhA) and reactance (Xc) correlated with forced vital capacity (FVC) and forced expiratory volume in 1st second (FEV_1). Regarding BIVA, the mean

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vector of patients with reduced lung function indicated hyperhydration and malnutrition and the mean vector of preserved lung function indicated normohydration and adequate nutritional status. The multivariate logistic regression analysis to determine predictors of reduced lung function showed that OH was significantly associated with this condition.

Conclusions: Participants with reduced lung function had lower weight, body mass index, fat tissue and hyperhydration, consequently, bioimpedance parameters (OH, PhA and Xc) were correlated with respiratory variables. Fluid status was a predictor of reduced lung function in patients on HD.

Introduction

In end-stage kidney disease (ESKD), the decline of glomerular filtration rate (GFR) and uremic myopathy lead to multiple organ dysfunction, particularly affecting the respiratory system [1]. The link between the kidney and lung involves the control of blood pressure, fluid dynamics, regulation of acid-base balance, mechanistic pathways including immune response, oxidative stress and phosphate metabolism [2].

Patients with chronic kidney disease (CKD) have lower pulmonary function, decreased respiratory muscle strength and diaphragmatic dysfunction compared to the healthy individuals. These conditions are associated with clinical symptoms such as fatigue, cough, hiccup and dyspnea and reflect negatively in the quality of life [3,4].

The previous study conducted by Mukai *et al.* [5] analyzed lung function using spirometry in 404 patients with CKD in GFR categories G1-5, and the restrictive lung disorder (RLD) was common in individuals receiving hemodialysis (HD). The study findings demonstrated that RLD related to protein-energy wasting (PEW), inflammation, cardiovascular disease and decrease of renal function [5]. Furthermore, the respiratory abnormalities often develop associated with chronic fluid overload in CKD [2]. Hypervolaemia is also a frequent condition in dialysis patients, leading to hypertension, cardiac dysfunction, increased mortality risk, and making its measurement is a challenge in clinical practice [6].

An available and surrogate method for assessment hydration status is the bioelectrical impedance analysis (BIA). It is a non-invasive technique that is easy to use and allows the assessment of fluid status and body composition in ESKD patients [7,8]. BIA is based on the principle that body tissues offer different opposition to the passage of electrical current [9]. Among the BIA parameters, the phase angle (PhA) has been used as a marker of water distribution, and cell integrity, and muscle mass [10–12].

In addition, the bioelectrical impedance vector analysis (BIVA) involves a graph method based on patterns of the resistance-reactance graph (RXc graph) that plotted the bioimpedance vectors normalized by height and allows to obtain information simultaneously about changes in hydration status and body composition assessment [13–15]. The distinctive feature of BIVA is that it is an autonomous procedure, independent of equations or predictive models, and allowing for the assessment of the patient through direct measurements of impedance vectors [16].

The study conducted by Yilmaz *et al.* [17] identified negative correlations between spirometry variables such as forced vital capacity (FVC), forced expiratory volume in the 1st second (FEV_1) and peak expiratory flow (PEF), with hydration status measured by BIA. These findings showed that volume overload was a predictor of respiratory capacity, and the improvement of lung functions occurs with the removal of fluids by HD.

Despite these findings, the association between lung function, hydration and nutritional status in CKD patients has not been thoroughly explored. Therefore, the aim of this study was to determine the lung function and to investigate the association between pulmonary parameters, hydration and nutritional status, assessed using BIVA, in patients with CKD undergoing HD, as well as to identify independent predictors of reduced lung function in this population.

Methods

Participants and design

This cross-sectional study was conducted in a single nephrology unit, located in a tertiary hospital, from April 2023 and April 2024, following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [18].

This study was approved by Presentation Certificate for Ethical Appreciation (CAAE) number 61277522.1.0000.8093, and informed written consent was obtained from all participants, according to the general recommendations of the Declaration of Helsinki.

The eligible participants enrolled if they met the following criteria: age $\geq$ 18 years, including elderly, with GFR of less than 15 mL/minute/1.73 m^2, calculated using the Chronic Kidney Disease Epidemiology Collaboration equation [19], undergoing HD 4-h dialysis 3 times per week for the previous 3 months. Exclusion criteria included patients with ESKD who were hospitalized during the data collection, those with acute myocardial infarction at last three months, individuals with decompensated coronary artery disease, those with active infectious or inflammatory process, and pregnant women.

Baseline demographic and clinical data

Age, dialysis vintage in months, presence of comorbidities and smoking history were collected through interviews or electronic medical record, registered in a previously prepared questionnaire.

Malnutrition Inflammation Score (MIS)

MIS consists an integrated method that providing information about the nutritional status, specific to CKD, that contains seven original Subjective Global Assessment components and three new items (body mass index, serum concentrations of albumin and total iron binding capacity) [20]. Each MIS component has four levels of severity from 0 (normal) to 3 (very severe). The sum of all components ranges from 0 to 30; a higher total score represents a more severe degree of PEW.

Laboratory data

Fasting blood samples (~5 ml) were collected before dialysis and the results of laboratory data were obtained from the electronic medical records. The biochemical parameters considered were urea (mg/dL); creatinine (mg/dL); albumin (g/dL); hemoglobin (g/dL); serum calcium (mg/dL); serum phosphate (mg/dL); serum potassium (mg/dL), parathyroid hormone (PTH-pg/mL) and C-reactive protein (CRP-mg/dL). Kt/V (K-dialyzer clearance of urea, t-dialysis time, V-volume of distribution of urea) was measured using the Daugirdas formula and evaluated the dialysis efficacy [21]. Daily protein intake was estimated as the normalized protein nitrogen appearance rate (nPNA) [22].

Pulmonary function and inspiratory muscle strength

The respiratory assessment was obtained after the dialysis, during the same day as bioimpedance evaluation. Spirometry was carried out to assess pulmonary volumes and airflows using a portable spirometer Microlab ML3500® (CareFusion, Yorba Linda, United States). Three forced expiration manoeuvres were performed for validity and reproducibility purposes according to American Thoracic Society/European Respiratory Society criteria, with patients sitting in a room with controlled

temperature, ambient pressure, and relative humidity [23]. The following variables were analysed: FVC (L), FEV_1 (L), FEV_1/FVC ratio (percentage) and PEF (L/min). Obtained values were recorded and compared with the predicted values for the Brazilian population [24]. The obstructive pattern was determined as FEV1/FVC ratio < 0.70 and restrictive pattern as FEV1/FVC ratio ≥ 0.70 and predicted FVC < 80%, that determined reduced lung function, and the severity of lung function impairment was based on % of predicted FVC: mild < 80%, moderate 50–59%, and severe < 50% [25].

Manovacuometry was carried out to evaluate static inspiratory muscle strength using a digital manovacuometer (MVD300®, Globalmed, Porto Alegre, Brazil). The maximal inspiratory pressure (MIP, cmH_2O) was obtained, according to American Thoracic Society (ATS), with individuals seated and wearing a nose clip to avoid air escape [26]. Three to 5 reproducible (≤10% of variation between values) manoeuvres were performed and the inspiratory effort were sustained for at least 1 second each. The highest value was considered for the study [27]. The results are expressed as absolute values and as a percentage of predicted values by sex and age, according to Pessoa *et al.* [28]. Dynamic inspiratory muscle strength was measured based on the S-Index (cmH_2O) obtained using the POWERbreathe KH2® device (International Ltd., Warwickshire, United Kingdom), employing the same technique used to measure MIP described above [29]. Eight manoeuvrers were performed with a 30-second rest between each, the maximum value obtained between manoeuvrers considered [30].

Bioelectrical impedance analysis (BIA)

Body composition was evaluated using a tetrapolar, multifrequency, bioimpedance spectroscopy (BIS), Body Composition Monitor (Fresenius Medical Care®, Bad Homburg, Germany), performed 30 minutes after the second HD session of the week.

The participants were instructed not to exercise eight hours before, not to consume alcohol in the previous 12 hours, not to consume any type of food or drink for at least four hours before, not to use any kind of moisturizer lotion on the body and remove metal objects (cell phone, keys, belts), including those attached to the body such as earrings, rings, and watches. Participants remained in a supine position, the electrodes were positioned on the side against the arteriovenous fistula, in the dorsal region in the hand (one between the head of the ulna and the radius, and the other in the proximal phalanx of the third finger) and in the foot (an electrode between the medial and lateral malleoli and another in the third metatarsal region).

Information about age, weight, height, diastolic and systolic blood pressure were included in the machine. All results were recorded in software (Fluid Management Tool v.3, Fresenius Medical Care) for further analysis. Total body water (TBW, L), extracellular water (ECW, L), intracellular water (ICW, L), overhydration (OH, L), adipose tissue mass (ATM, kg) and body cell mass (BCM, kg) were obtained. Lean tissue index (LTI, kg/m^2) and fat tissue index (FTI, kg/m^2) were calculated using lean tissue mass (LTM, kg) and fat tissue mass (FTM, kg) divided by height squared (m^2), respectively.

The value of the PhA obtained, through the BIA, was found at the frequency of 50 kHz. BIA parameters resistance (R, ohm) and reactance (Xc, ohm) were used to obtain the impedance (Z, ohm), according to the following formula: $Z = \sqrt{(R^2 + Xc^2)}$ [31]. R, Xc, and Z were standardized by height (H) in meters: R/H, Xc/H, Z/H (ohm/m).

BIVA 2002 software was employed (developed by Piccoli A, Pastori G, Department of Medical and Surgical Sciences, University of Padova, Padova, Italy; available at email: apiccoli@unipd.it) with the creation of 50%, 75%, and 95% tolerance ellipses (Figure 1A), as well as confidence ellipses. The normalization of R and Xc by H was expressed as *z*-scores (*z*-R/H and *z*-Xc/H) with the reference population described by Piccoli, Pillon & Dumler [32]. Patients with vectors outside the 75% ellipse in the upper quadrant (underweight) and lower quadrant (cachexia) on the right side of the graph were classified as malnourished, according to the visualization in the tolerance ellipses (Figure 1A). Patients with vectors outside the 75% ellipses in the major axis in the direction of hyperhydration (lower quadrant) were classified as hyperhydrated and outside the 75% ellipse in the upper quadrant as dehydrated. Variations along the minor axis indicate changes in BCM (increase or decrease in membranes and soft tissue interfaces), with vectors located to the left or right of the axis respectively, indicating more or less BCM [14,33,34]. Group vectors (preserved and reduced lung function) were plotted as the mean and 95% confidence intervals on the Z score.

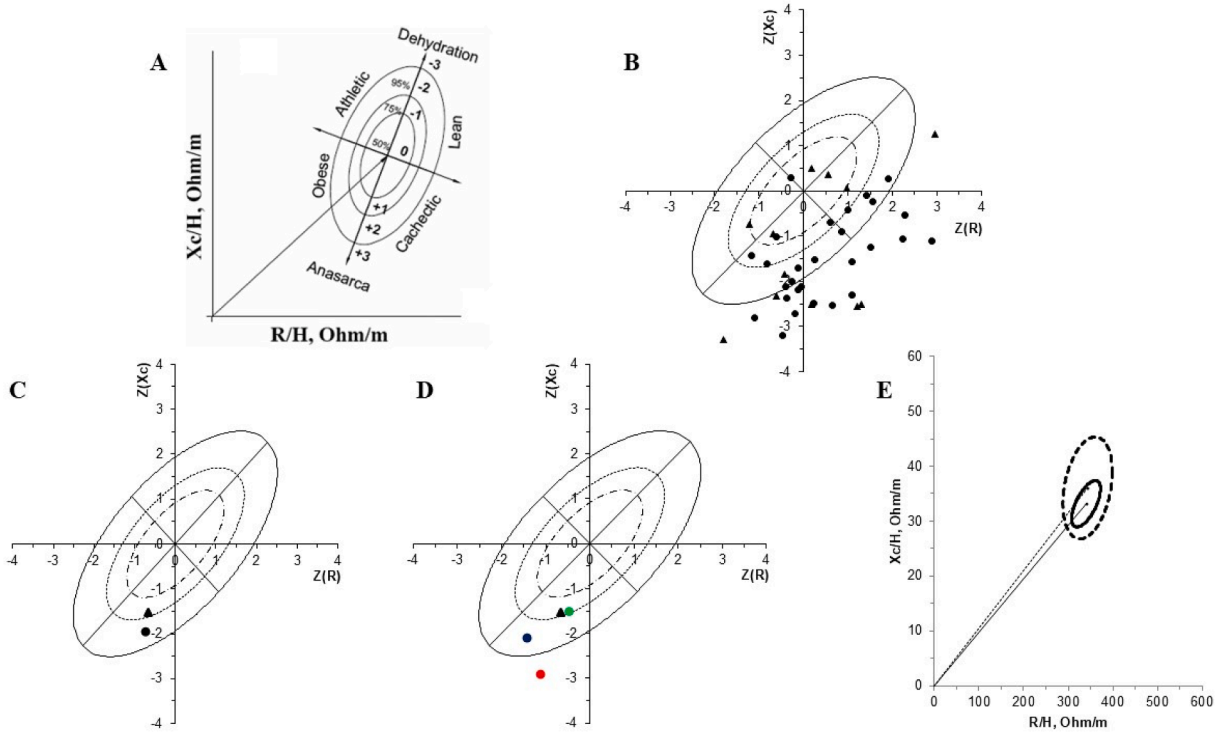

Figure 1. **(A)** Graph with regions of elliptic probability on RXc plane normalized by height (R/H and Xc/H, in Ω/m). **(B)** Distribution of individual vectors on resistance-reactance graph for preserved lung function (▲) and reduced lung function ((●). **(C)** Position of vector mean for preserved lung function (▲) and reduced lung function (●). **(D)** Position of vector mean for preserved lung function (▲) and reduced lung function ((●) according to severity of function impairment in mild (**green**), moderate (**blue**) and severe (**red**). **(E**) Confidence ellipses for preserved lung function (dashed line) and reduced lung function (black line) at the end of the study.

Statistical analysis

Continuous variables were described using mean±standard deviation or median and interquartile range. Absolute numbers and percentages were used to describe categorical variables. The normality of the continuous variables was tested using the Shapiro-Wilk test.

Based on the presence of lung impairment, patients were separated into two groups and T Student's, Mann Whitney (for quantitative variables) or Chi-square (for qualitative variables) tests were used for comparisons between these groups. Pearson and Spearman correlation coefficients were used to verify the correlation between bioimpedance and respiratory measurements, considering an absolute magnitude for the correlation coefficient of 00–0.10 to be negligible; 0.10–0.39 weak; 0.40–0.69 moderate; 0.70–0.89 strong and 0.90–1.00 very strong [35].

Multiple binary logistic regression analysis was performed to identify the main variables related to the reduced lung function. For better adjustments and predictive power, the likelihood ratio was used, and the regression variables was analysed by the Wald test. The Omnibus and Homer & Lemeshow tests evaluated the quality of the model.

The vector means of the resistance-reactance graph were analysed using the Hotelling's T^2 test and univariate analysis (F test). Statistical analyses were performed using IBM SPSS (Statistical Package for Social Science) software for Windows (version 26.0; IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered statistically significant for all analyses.

The G*Power 3.1 software was used to calculate the sample size, in which a significance level of 5%, with a statistical power of 90%, according to the difference the variable FVC between groups with and without fluid overload (1.81±0.90 and 3.17±0.96) in the previous study conducted by Yilmaz *et al.* [17]. Considering a sample loss of 20%, the study population calculated consisted of 24 patients.

Results

Initially, 134 patients undergoing HD during the data collection, in the nephrology unit, and 76 were excluded. Of 58 eligible participants, 16 did not complete the assessments, so the final sample consisted of 42 available participants for this study (Supplementary Figure 1).

Of the remaining 42 participants, the average age was 54±14 years, 23 (55%) were male and median of dialysis vintage 20 (8–41) months (Table 1). Among them, 15 (36%) had diabetes, 33 (79%) had hypertension, 3 (7%) current smokers and 30 (71%) participants had reduced lung function, and these individuals showed higher significant dialysis vintage.

The respiratory data and body composition of all participants are presented in Table 2. The levels of FVC, % predicted FVC, FEV_1 and % predicted FEV_1, PEF and % predicted PEF were lowest for reduced lung function patients. No differences were found for variables of respiratory muscle strength comparing both groups. Participants with reduced lung function had lower variables such weight, BMI, ATM, FTM and FTI, compared to the individuals with preserved lung function. Regarding hydration status, the participants with reduced lung function had significant difference in the variable OH (P= 0.034). According to severity of function impairment, 19 (63%) had mild, 8 (27%) moderate, 3 (10%) severe. The patients enrolled in the study did not have obstructive pattern.

The BIVA results are shown as explained according to the schedule in Figure 1A. The vector of each individual according to lung function after the transformations of the impedance measures into z-score is indicated in Figure 1B. Based on the resistance-reactance graph, the malnutrition rate was 25 (83.3%) in the participants with reduced lung function and 7 (58.3%) in the preserved lung function group. Regarding hydration, the reduced lung function group contained 4 (13.3%) hyperhydrated patients and 26 (86.7%) normally hydrated. In relation to the preserved lung function, 2 (16.7%) were hyperhydrated, 1 (8.3%) dehydrated and 9 (75%) normally hydrated. The mean of the preserved lung function group vector is in the 75% tolerance ellipse, in the lower right quadrant (Figure 1C). The mean vector of the reduced lung function group is located in the 95% ellipse in the lower right quadrant, indicating malnutrition and a worse nutritional status when compared with preserved lung function group (Figure 1C). Regarding hydration status, the mean vector of the group with reduced lung function indicated hyperhydration and the mean vector of the group with preserved lung function indicated normohydration. The means vectors of the groups according to severity of function

Table 1
Baseline characteristics and laboratory data of all participants

Variables	All patients (n=42)	Preserved lung function (n=12)	Reduced lung function (n=30)	*P* value
Demographics and clinical characteristics				
Age, years	54±14	55±14	52±12	0.915
Male, n (%)	23 (55)	5 (42)	18 (60)	0.231
Dialysis vintage, months	20 [8–41]	24 [8–59]	42 [25–117]	**0.042**
Diabetes, n (%)	15 (36)	5 (42)	10 (33)	0.434
Hypertension, n (%)	33 (79)	8 (67)	25 (83)	0.216
History of smoking				
Current smokers, n (%)	3 (7)	1 (8)	2 (7)	0.646
Ex-somokers, n (%)	14 (33)	4 (33)	10 (33)	0.647
MIS (points)	4±3	3±2	6±4	0.188
Laboratory data				
Serum urea, mg/dL	129.81±33.51	143.00±43.31	133.25±28.73	0.064
Serum creatinine, mg/dL	10.04±3.89	9.57±2.22	11.98±4.44	0.536
Albumin, g/dL	3.92±0.38	3.82±0.22	3.88±0.50	0.653
Hemoglobin, g/dL	9.96±1.55	9.15±1.35	10.36±1.20	0.907
Serum calcium, mg/dL	8.27±0.98	7.75±1.03	8.48±1.18	0.677
Serum phosphate, mg/dL	4.75±1.16	5.40±0.79	5.13±1.45	0.103
Serum potassium, mg/dL	5.11±0.92	5.72±0.48	5.68±0.90	0.343
PTH, pg/mL	754.69±697.22	699.15±623.60	1130±801.18	0.254
CRP, mg/dL	0.93 [0.45–1.76]	0.40 [0.40–2.18]	1.04 [0.62–1.50]	0.229
Kt/V	1.37±0.50	1.81±0.98	1.48±0.64	0.642
nPNA, g/kg/day[a]	1.15±0.34	1.28±0.38	1.19±0.38	0.316

MIS: Malnutrition Inflammation Score; PTH: parathyroid hormone; CRP: C-reactive protein; Kt/V: K-dialyzer clearance of urea, t-dialysis time, V-volume of distribution of urea; nPNA: normalized protein nitrogen appearance rate.
Data are expressed as the mean± standard deviation, median (interquartile range), or percentage.
Bold indicates $P < 0.050$.
[a] 26 participants were evaluated.

impairment are illustrated in Figure 1D. The means vectors of the group with preserved lung function and mild impairment were between the 50th and 75th tolerance ellipse in the lower right quadrant, indicating normohydration. The subgroups with moderate and severe impairment were in and outside the 75% ellipse in the lower right quadrant, indicating malnutrition. The means vectors of the moderate and severe groups indicate hyperhydration, and the severe group is more hyperhydrated than others, because it is outside of 95% ellipse. The confidence ellipses between the R/H and Xc/H vectors are illustrated in Figure 1E, according to lung function at the end of the study. The Hotelling's test ($T^2 = 1$) and the F test ($F = 0.5$) also showed no significant difference ($P = 0.624$) between groups at the end of the study.

Negative correlations were found between OH and FVC (rho = - 0.330; $P = 0.032$), FEV_1 (rho = -0.400; $P = 0.009$) and S-Index (rho = -0.400; $P = 0.020$), bioimpedance vector such Xc was positively correlated with pulmonary function tests: FVC (rho = 0.310; $P = 0.043$) and FEV_1 (rho = 0.430; $P = 0.005$) (Supplementary Figure 2). Additionally, PhA was positively and moderately correlated with the parameters: FEV_1 (rho = 0.430; $P = 0.004$) and MIP (rho = 0.400; $P = 0.009$). The multivariate logistic regression analysis to determine predictors of reduced lung function showed that this condition was significantly associated with fluid status (OH) (Table 3).

Discussion

To the best of our knowledge, this is the first study to evaluate the association of the respiratory and BIA parameters through the BIVA in patients undergoing HD. The reduced lung function was a prevalent condition in the sample and our results showed the associations of hydration and nutritional status in this condition (Figure 2). Participants with reduced lung function had lower weight, BMI, fat tissue and hyperhydration as compared to those with preserved lung function. In addition, BIA parameters (OH, PhA and Xc) were correlated with pulmonary variables such FVC and FEV_1.

Table 2
Respiratory data and body composition of all participants

Variables	All patients (n=42)	Preserved lung function (n=12)	Reduced lung function (n=30)	*P* value
Pulmonary function				
FVC, L	2.63±0.75	2.45±0.42	2.26±0.65	**<0.001**
Percent predicted FVC, %	70.48±15.87	87.50±6.81	61.33±10.85	**<0.001**
FEV_1, L	2.25±0.68	2.15±0.50	1.92±0.71	**0.002**
Percent predicted FEV_1, %	74.38±19.84	93.00±8.91	63.42±17.55	**<0.001**
FEV_1/FVC	86 [82–92]	86 [82–93]	89 [76–96]	0.690
Percent predicted FEV_1/FVC, %	106 [99–113]	106 [102–111]	108 [92–116]	0.880
PEF, L/min	5.47 [3.40–6.64]	9.36 [5.04–17.44]	4.37 [2.43–6.30]	**<0.001**
Percent predicted PEF, %	59.29±23.48	74.50±29.95	47.67±18.90	**<0.001**
Inspiratory muscle strength				
MIP, cmH_2O	83.07±30.70	73.12±27.45	79.88±41.26	0.960
Percent predicted MIP, %	88.02±33.25	91.25±34.21	87.50±44.11	0.998
S-Index, cmH_2O	55.39±19.14	52.48±16.94	50.69±21.46	0.120
Examination and BIA parameters				
Weight, kg	69.38±12.99	68.41±9.56	62.42±13.51	**0.040**
Height, m	1.61±0.07	1.52±0.59	1.60±0.68	0.849
BMI, kg/m^2	26.78±4.98	29.89±6.20	24.34±5.06	**0.047**
TBW, L	33.67±5.59	28.95±2.42	32.72±5.13	0.717
ECW, L	14.90±2.18	13.62±1.70	14.54±2.29	0.878
ICW, L	18.77±3.75	15.32±0.85	18.18±3.09	0.658
OH, L	- 0.55±1.79	- 0.62±1.34	0.22±1.74	**0.034**
ATM, kg	31.16±13.61	39.45±9.62	23.32±14.36	**0.018**
BCM, kg	20.70 [17.37–25.70]	15.55 [15.25–16.38]	23.45 [16.55–25.92]	0.229
LTM, kg	36.90 [32.38–44.22]	28.75 [28.32–29.25]	41.55 [31.30–44.48]	0.263
LTI, kg/m^2	14.73±2.92	12.50±0.95	14.90±2.42	0.578
FTM, kg	22.90±10.00	29.00±7.07	17.12±10.54	**0.018**
FTI, kg/m^2	12.09±5.63	18.10±6.25	9.52±5.88	**0.020**
PhA, °	5.72±1.24	5.08±0.89	5.28±0.97	0.360
R/H, ohm/m	336.45 [293.04–367.32]	363.66 [306.63–472.48]	318.98 [283.25–364.03]	0.472
Xc/H, ohm/m	33.18 [26.22–40.24]	29.70 [24.85–49.46]	30.09 [24.80–37.79]	0.380
Z/H, ohm/m	338.60 [294.14–368.80]	364.88 [307.67–475.08]	320.36 [284.44–365.38]	0.472

FVC: forced vital capacity; FEV_1: forced expiratory volume in the 1^{st} second; PEF: peak expiratory flow; MIP: maximal inspiratory pressure; BIA: bioelectrical impedance analysis; BMI: body mass index; TBW, total body water, ECW, extracellular water; ICW, intracellular water; OH: overhydration; ATM: adipose tissue mass; BCM: body cell mass; LTM: lean tissue mass; LTI, lean tissue index; FTM: fat tissue mass; FTI, fat tissue index; PhA, phase angle; R/H: resistance for height; Xc/H: reactance for height; Z/H: impedance for height.
Bold indicates $P < 0.050$.
Data are expressed as the mean± standard deviation and median (interquartile range).

Table 3
Multivariate logistic regression analysis of factors associated with reduced lung function

Model	Independent variable	β	Odds ratio	95% CI	*P* value
1	OH, L	0.46	1.59	1.00–2.52	**0.046**
	Sex, male	0.78	2.18	0.51–9.27	0.293
2	OH, L	0.50	1.64	1.03–2.62	**0.037**
	Sex, male	1.25	3.50	0.56–21.83	0.179
	Age, years	- 0.03	0.97	0.91–1.04	0.377

95% CI: 95% interval confiance; OH: overhydration.
Bold indicates $P < 0.050$.

Reactance is related to properties of cell membrane capacitance and refers to the capacity to store electrons across tissue interfaces and cell membranes, therefore, according to our results, directly related to better lung capacity [9]. According to BIVA, the malnutrition rate was 83.3% in the group of patients with reduced lung function and 58.3% in the group with preserved lung function. The vector mean of the reduced lung function group was located in the 95% ellipse in the lower right quadrant,

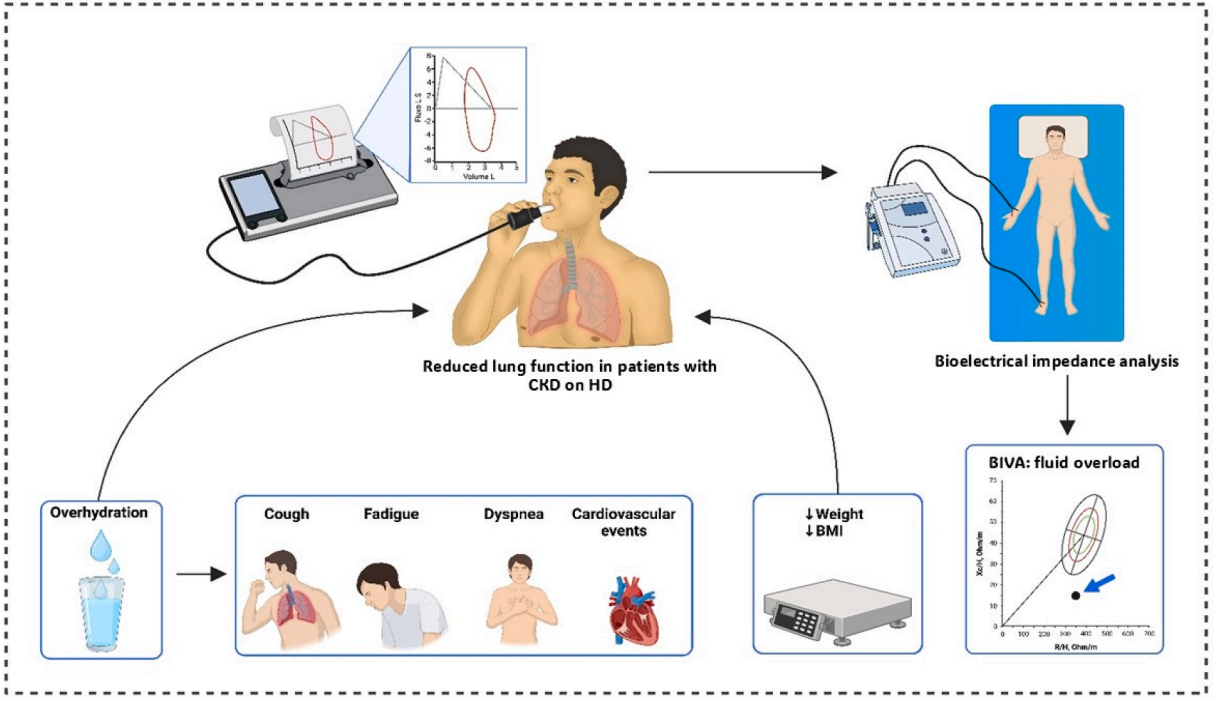

Figure 2. Factors involved in reduced lung function in patients with CKD on HD, association with bioelectrical impedance analysis (the position in lower right quadrant by BIVA) and consequences of overhydration (cough, fatigue, dyspnea, cardiovascular events). CKD: chronic kidney disease; HD: hemodialysis; BMI: body mass index; BIVA: bioelectrical impedance vector analysis. BioRender® was used to create the figure.

indicating a worse nutritional status when compared with group of patients with preserved lung function. The vector mean position of the groups with moderate and severe impairment indicates hyperhydration.

Several studies observed, through spirometry, decreased FVC, reduced airflows and RLD in this population [5,36–38]. The prospective study conducted by Sharma *et al.* [36] with 50 patients undergoing HD, the spirometry tests were performed before and after 4-h HD sessions, and the authors reported 12% of participants with preserved lung function. They found the mean FEV_1/FVC ratio was similar before and after HD sessions (97.8±20.8% and 99.3±20.1% of predicted, respectively, $P > 0.05$). The authors suggest that chronic subclinical pulmonary edema leads to increased capillary permeability, and with the hypoalbuminemia were reported as causes of lower FVC, consequently, pulmonary abnormalities. Hypoalbuminemia contributes to reduction of colloid osmotic pressure in plasma, in addition, the accumulation of proinflammatory cytokines and the fluid overload are conditions to development of respiratory dysfunction [39].

The pulmonary function was explored in an observational study with 102 patients on HD by Anees *et al.* [37], in which spirometry was performed before and after HD. According to the authors, 75.5% of patients had RLD and the factor associated with this condition was the presence of diabetes. These authors related many potential reasons for the occurrence of RDL in patients with CKD such as left ventricular hypertrophy, iron deposition, increased extra-vascular lung volume, pleural effusion, pulmonary hypertension and severe uremia. These factors affect overall respiratory function, especially, muscle strength, causing ventilatory defect. Regarding diabetes, possibly, the higher levels of systemic inflammatory mediators, microangiopathy and persistent inadequate blood glucose control were involved in pulmonary function impairment. In contrast, we did not find an association between diabetes and reduced lung function, possibly because we involved a relatively small sample with 36% prevalence of diabetes.

CKD requires special attention to fluid overload related to poor outcomes such as cardiovascular events. Hydration status is traditionally assessed non quantitatively by clinical examination, and bedside medical methods used to standardize and more precisely quantify volemic status in patients with CKD [8]. The accurate methodologies to assess hydration status such as isotope dilution, plasma osmolarity, urinary indices, point-of-care ultrasound are costly, relatively invasive and used for research settings [40]. However, the bioimpedance devices are generally portable and could be used in CKD clinic assessments and even in patients' homes, may be an alternative to assessment hydration status [7].

In a cross-sectional study with 54 patients on HD, Yilmaz *et al.* [17] investigated the effects of the fluid overload in pulmonary function and reported similar results to ours. They performed the spirometric and bioimpedance tests before and after 30 min the midweek HD session and found negative correlation between FVC, % FVC, FEV_1, % FEV_1 and PEF, with volume status, higher levels these respiratory parameters after HD, and in the multiple regression analysis, the fluid overload was an independent factor associated with lower FVC and the presence of reduced respiratory abnormalities. These authors suggested that correction of volume overload after HD leads to improved lung function.

Although this study was conducted after HD, it showed that patients with reduced lung function presented hyperhydration according to BIVA and possibly this finding suggests insufficient fluid removal during HD. Regarding hydration status based on the severity of function impairment, the means vectors of moderate and severe groups indicate hyperhydration in the RXc graphs, with the severe group being more hyperhydrated than others. Through BIA analysis, ECW is composed of the interstitial water, the plasma volume, the transcellular water, and TBW is obtained by the sum of ECW and ICW [7]. In addition, OH correlated with spirometry parameters in our study, and being defined as the difference between an individual's weight with normal ECW (normally hydrated weight) and actual weight, it can be positive (fluid overload) or negative (fluid deficit), directly measuring altered fluid status [6–8].

The fluid overload increases the permeability of pulmonary capillaries and the transfer of fluid to interstitium, leading to interstitial edema and, consequently, restrictive ventilation dysfunction [37]. Excessive inter dialysis weight gain, prolonged exposure to uremic toxins and inadequate dialysis with low flux dialysers can exacerbate RLD in these patients [1,2]. When renal failure occurs, the compensatory role of kidney in respiratory acidosis may be less effective, resulting in prolonged blood

acidity with consequent limited rise of serum bicarbonate and retention hydrogen ions, consequently in the lungs, hyperventilation is responsible for weakness of respiratory muscles and low pulmonary capacity [41]. Among the measures of inspiratory muscle strength, S-Index negatively correlated with OH, and this finding demonstrated the impact of the fluid status in inspiratory muscle output throughout the total lung volume, related with respiratory muscle fatigue [29].

Previous studies reported inflammation and malnutrition related with RLD in patients with CKD [5,38,42]. In the cohort study carried out by Yoon *et al.* [42], 106 patients were enrolled, performed spirometry tests, evaluated nutritional status, cardiac function, biochemical data, and followed these participants for 26 months. These authors found the malnourished group was significantly older, had higher levels of CRP, lowers values of % FEV_1 and % FVC, and by cox regression analysis of factors associated with mortality, presence of malnutrition and ejection fraction were independent predictors for outcome. The muscle wasting, common in CKD, may influence the loss of strength and endurance in respiratory muscles, contributing to reduction in pulmonary capacity, consequently, functional impairment adversely impacts to perform daily activities and quality of life in this population [1,3]. In our findings, we found worse nutritional status and reduced body compartments (weight, BMI and fat tissue) associated with reduced lung function, possibly by compromisse of the elastic properties of the chest wall, small airway dysfunction and alterations in respiratory mechanics, that lead expiratory flow limitation, decrease in expansion pulmonary, lung capacity and a consequent respiratory weakness [43].

The present study has certain limitations. First, it was conducted on a small sample selection of patients on HD at one center, limiting the generalizability of our findings. Second, we did not evaluate the ultrafiltration during the dialysis session and the interdialytic weight gain that can interfere in fluid removal prescription. Third, the assessments were performed after HD, despite that, we found influence of volemic status on lung function. Among the strengths of our study, this is the first study in patients undergoing HD that evaluates the association of BIVA parameters and pulmonary assessment.

Conclusions

Patients with CKD and reduced lung function had hyperhydration, lower body weight, BMI and fat tissue. BIA parameters (OH, PhA, Xc) were correlated with pulmonary variables such as FVC and FEV_1. The mean vector of the group with reduced lung function was located in the 95% ellipse, in the lower right quadrant, and indicated malnutrition and hyperhydration as compared to the group with preserved lung function. Fluid status was a predictor of reduced lung function in patients undergoing HD.

Author contributions

S. Borges: Conceptualization; Investigation; Methodology; Data curation; Formal analysis; Supervision; Validation; Visualization; Writing - original draft; Writing - review & editing. A. T. Silva: Formal analysis; Supervision; Validation; Investigation; Writing - review & editing. T. F. Martins: Data curation; Investigation. L. A. Morais: Validation; Writing - review & editing. F. V. C. Machado: Validation; Writing - review & editing. G. C. Júnior: Supervision; Validation. G. F. B. Cipriano: Conceptualization; Investigation; Methodology; Supervision; Validation; Visualization; Writing - original draft; Writing - review & editing.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nutos.2025.05.012.

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