Manual Therapy, Posturology & Rehabilitation Journal
ISSN: 2236-5435

RESEARCH ARTICLE

Muscle strength and pulmonary function in individuals with chronic kidney disease: a cross-sectional study

Lívia G. da Rocha[1], Júlio Henrique Policarpo[1], Beatriz Luiza M. Cunha[2], Juliana R. da Silva[1], Patrícia Érika de M. Marinho[2]

[1] Integrated Multidisciplinary Residency Program in Health at the Hospital das Clínicas of the Federal University of Pernambuco (UFPE), Recife-PE, Brazil.
[2] Postgraduate Program in Physiotherapy at the Federal University of Pernambuco (UFPE), Recife (PE), Brazil.

Abstract

Background: Respiratory muscle weakness in chronic kidney disease (CKD) is described by decline in lung function and respiratory pressures in patients who are still in the conservative stage of the treatment. **Objective:** To assess respiratory muscle strength and lung function in patients in stages 4 and 5 of CKD. **Methods:** It was a cross-sectional study developed between February and July 2015 at an university hospital, and approved by the Institutional Ethics Committee (Report No. 1.360.173). Patients of both sexes, aged between 18 and 59 years, and diagnosed with CKD stages 4 and 5 non-dialytic were included. There were collected information about gender, age, comorbidities, and length of treatment for kidney disease. Inspiratory and expiratory muscle strength (manovacuometry) and lung function [forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, and peak expiratory flow (PEF) (portable digital spirometer)] were assessed. **Results:** 22 patients in the CKD stages 4 and 5 participated of this study, they presented a prevalence of inspiratory muscle weakness of 70% and 75% and expiratory muscle weakness 90% and 83.3%, respectively. In terms of lung function, patients in the CKD stage 4 had lower spirometrics values. **Conclusion:** Patients in the stages 4 and 5 of CKD undergoing by the conservative treatment had reduced respiratory muscle strength and changes in the pulmonary function.

Keywords: Renal insufficiency; respiratory muscles; maximal respiratory pressures; spirometry; muscle weakness.

BACKGROUND

Uremic sarcopenia in chronic kidney disease (CKD) is a systemic process triggered by chronic anemia, increased muscle-protein catabolism, malnutrition, chronic inflammation, and metabolic acidosis. This process results in deterioration of muscle function[1–3] and weakness of the respiratory muscles. This weakness characterizes the decline in lung function and maximum inspiratory and expiratory pressures[4,5]. Although it is known that patients undergoing dialysis treatment present changes in the functions of the respiratory system resulting from the accumulation and extravasation of liquids, changes in the uptake, consumption, and transport of oxygen, and protein-muscle deficit[5–7] , the pulmonary function of patients in a conservative stage of CKD still needs to be investigated due to the scarcity of studies in the literature[4,5] .

Thus, considering the possible repercussions of CKD on respiratory muscle strength and lung function in these patients undergoing conservative treatment, the objective of the present study was to evaluate respiratory muscle strength and lung function in patients in stages 4 and 5 of non-dialysis CKD.

Corresponding author Patrícia Érika de Melo Marinho
Email: patricia.marinho@ufpe.br

Received: 20 Dec , 2023.
Accepted: 09 May, 2024.
Published: 30 May, 2024.

METHODS

A cross-sectional study was carried out in the nephrology outpatient clinic of a university (Hospital das Clínicas) from February to July 2015. The study was approved by the institutional ethics committee (Report No. 1,360,173) in accordance with Resolution 466/12 of the National Health Council and respects the Declaration of Helsinki (1964)[8,9]. The sample was selected by convenience, consisting of patients treated at the outpatient clinic during the study period. Patients of both sexes were included, with an established age between 18 and 59, a diagnosis of CKD confirmed in stages 4 and 5 without dialysis, and the ability to perform the evaluation procedures[10]. Patients with previous lung disease and spirometric changes, acute heart disease, using drugs that affected lung function and respiratory muscle strength (anticholinergics, bronchodilators, and corticosteroids), hemodynamically unstable (systolic blood pressure [SBP] > 160 mmHg and dyastolic blood pressure [DBP] > 100) were excluded—mmHg), undergoing physiotherapeutic monitoring, smokers and history of hospital admission in the last three months.

Initially, information was collected on sex and age, presence of comorbidities, CKD staging and treatment time, renal function, smoking, and alcohol consumption. Renal function was assessed based on the glomerular filtration rate (eGFR) estimate from the equation developed[11] and made available for calculation through an online tool[12]. Participants were grouped into stages 4 and 5 of CKD when they presented a GFR between 15-29 mL/min/1.73 m2 and less than or equal to 15 mL/mlin/1.73 m2, respectively[10].

Respiratory Muscle Strength

Maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) were assessed using a digital manometer (MVD-300, Globalmed, Brazil). To determine MIP, individuals were instructed to perform a maximum inspiratory effort based on the residual volume and, for MEP, a maximum expiratory effort based on total lung capacity[13]. Maximum respiratory pressures were evaluated according to the American Standard Thoracic Society (ATS)[14]. At least three reproducible maneuvers were performed with a difference of up to 10% between each measurement, with the highest value being considered. The predicted values of MIP and MEP were estimated based on the normality equations proposed by Neder et al.[15], and the reference values expected for the Brazilian population were adopted[16]. Muscle strength was classified as "muscle weakness" (MIP < 60cmH2O and MEP < 120 cmH2O for women and MIP < 80 cmH2O and MEP < 150 cmH2O for men) and "no weakness" when the values were equal to or higher than the predicted values.

Lung Function

The pulmonary function test was performed using a portable digital spirometer (MicroLoop, Viasys Healthcare®, England). The forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio was measured and peak expiratory flow (PEF) in predicted, absolute and percentage values, according to the standards described by ATS[16,17]. Three reproducible measurements were taken, with a maximum variation of 10% between them, with the highest value being considered. Lung

involvement was classified according to the guidelines established by the Brazilian Society of Pneumology and Phthisiology[18].

Statistical analysis

The results of continuous variables were expressed as means and 95% confidence intervals. Categorical variables were expressed in relative and absolute values. Initially, normality distribution and homogeneity of variances were verified using the Shapiro-Wilk and Levene tests, respectively. Patients with stages 4 and 5 of CKD were compared regarding the continuous variables of interest using the Student's t-test for independent samples. The prevalence of respiratory muscle weakness was verified, and the comparison between groups in stages 4 and 5 was analyzed using Fisher's exact test to consider the categorical variables. Statistical analysis was performed using the SPSS program (IBM, Chicago, IL, USA) version 25.0, and $p < 0.05$ was adopted as significant.

RESULTS

The characteristics of the 22 patients are described in Table 1. Patients with CKD in stage 4 had a longer smoking period of 127.20 months (7.42 - 246.98; p=0.040).

Table 1. Characterization of patients with chronic kidney disease stages 4 and 5

Variables	mean (95% CI)	mean (95% CI)
Idade (years)	42,50 (33,23 - 51,77)	42,83 (35,93 - 49,74)
Sex n (%)		
Feminine	4 (40)	7 (58,3)
Masculine	6 (60)	5 (41,7)
Weight (Kg)	64,18 (55,31 - 73,04)	72,86 (60,59 - 85,14)
Height (cm)	162,10 (155,19 - 169,01)	162,17 (155,61 - 168,72)
BMI (Kg/m²)	24,23 (22,36 - 26,10)	27,44 (23,79 - 31,09)
Clinics		
Staging n (%)	10 (45,45)	12 (54,55)
Treament time (months)	56,40 (5,81 - 106,99)	51,33 (18,52 - 84,15)
Comorbidities n (%)		
0 to 1	8 (80)	6 (50)
2 or more	2 (20)	6 (50)
Lifestyle n (%)		
Alcoholism	2 (20)	0 (0)
Active smoking	1 (10)	0 (0)
Ex smorker	3 (30)	4 (33,3)

Notes*: CKD = chronic kidney disease; CI = confidence interval; BMI = body mass index.

Table 2 presents the characteristics of the patients regarding th performance of respiratory muscle strength and lung function.

Table 2. Respiratory muscle strength and lung function of patients with chronic kidney disease stages 4 and 5.

Variables	CKD Stage 4	CKD Stage 5	p-value
	Mean (95% CI)	Mean (95% CI)	
RMF			
IPmáx (cmH_2O)	63,90 (46,54 - 81,26)	65,75 (50,89 - 80,61)	0,858
EPmáx (cmH_2O)	83,80 (56,45 - 111,15)	94,33 (70,93 - 117,73)	0,519
Predicted FMR			
IPmáx (cmH_2O)	107,92 (96,70 - 119,14)	102,05 (92,49 - 111,61)	0,382
EPmáx (cmH_2O)	113,95 (99,65 – 128,25)	106,26 (93,74 – 118,78)	0,376
FMR Predicted Performance			
IPmáx (%)	58,84 (46,15 - 71,52)	63,74 (52,13 - 75,34)	0,533
EPmáx (%)	71,95 (54,53 - 89,37)	87,98 (71,16 - 104,80)	0,158
Lung Function			
FEV_1 (% prev.)	69,70 (55,14 - 84,26)	86,50 (76,14 - 96,86)	0,044
CVF (% prev.)	75,80 (64,22 - 87,38)	87,42 (76,18 - 98,65)	0,127
PEF (% prev.)	50,60 (38,55 - 62,65)	69,58 (56,30 - 82,87)	0,032
FEV_1/FVC	75,10 (69,22 - 80,98)	82,33 (72,21 - 87,45)	0,051

Notes*: CKD: chronic kidney disease; CI: confidence interval; RMF: respiratory muscle strength; MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure; FEV1 % predicted: forced expiratory volume in the first second, percentage of predicted; FVC % predicted: forced vital capacity, percentage of predicted; PEF % predicted: peak expiratory flow, percentage of predicted; FEV1/FVC ratio. Student's t test, $p < 0.05$.

Regarding the prevalence of respiratory muscle weakness in stages 4 and 5 of CKD, 70% and 75% presented inspiratory muscle weakness, respectively, while expiratory muscle weakness was observed in 90% and 83.3% for the respective stages. Women had a higher prevalence of muscle weakness in both stages, with 81.8% (n=3) for inspiratory muscle weakness and 100% for expiratory muscle weakness (n=7), respectively. Regarding lung function, patients in CKD stage 4 had lower numerical spirometric values than those in stage 5 (Table 2).

DISCUSSION

The present study found a high prevalence of inspiratory and expiratory muscle weakness in patients with both stages of CKD undergoing conservative treatment. A reduction in spirometric values was also observed in patients in stage 4 of CKD. Respiratory changes are frequent in patients with advanced degrees of CKD due to circulatory and interstitial volume overload, and changes in respiratory mechanics are developed, predisposing to weakness of the respiratory muscles[19]. In this study, respiratory muscle weakness compromised patients' inspiratory and expiratory muscles in the conservative stage of CKD treatment. Faria et al. (2013) investigated the respiratory muscle function of pre-dialysis patients with a 33.3% reduction in inspiratory and expiratory muscle strength[20]. In a previous study, these authors found the presence of respiratory muscle weakness since stage 3 of CKD and attributed this finding to a possible multicausal origin[21].

A relevant finding was found in patients with CKD in stage 4 regarding the spirometric reduction in relation to those in stage 5; however, it can be seen that the former had a longer exposure time to smoke. Exposure to harmful particles and gases can damage the structures of the lung parenchyma and vasculature, releasing inflammatory substances[22].

The results of this study are similar to those described by Navaneethan et al. (2016), who observed both obstructive and restrictive changes in patients with CKD and found that the reduction in FEV1 was associated with smoking, female gender, and albuminuria[23].

Hypoxemia, by activating inflammatory mechanisms and oxidative stress, can be a possible explanation for our study's findings in relation to the reduction in lung function. Still, in agreement with the findings of the study by Navaneethan et al. (2016), hypoxemia worsens albuminuria, in addition to the presence of vasculitis and increased extracellular volume in CKD, compromising the restrictive component of lung function[23].

This study detected changes in respiratory muscle strength and lung function in patients with stages 4 and 5 of CKD in a conservative stage. The impairment of lung function in stage 4 patients who had a more prolonged exposure to smoke is noteworthy.

Assessing respiratory muscle strength and lung function in patients in the conservative stage of CKD is necessary in clinical practice[23]. Although the present study did not evaluate lung function after using a bronchodilator, the results drew attention because they detected a reduction in lung function and respiratory muscle strength in a pre-dialysis phase. This finding may be a one-off, not representing the reality of patients with CKD in these stages. Therefore, studies with a more significant number of patients could be developed to verify which obstructive and restrictive components represent the most frequently expected changes for this patient population.

CONCLUSION

Patients in stages 4 and 5 of CKD undergoing conservative treatment showed reduced respiratory muscle strength and changes in lung function. Although this finding may represent a particularity of the sample in this study, respiratory functional assessment is necessary in clinical practice, especially when taking into account that CKD is a chronic, progressive disease with multiple clinical-functional manifestations.

Author Contributions: L.G.R.: literature search, data collection; L.G.R., J.H.P., B.L.M.C., J.R. da S., and P.E. de M.M.: manuscript preparation; P.E. de M.M.: study design, and analysis of data. All the authors have read and approved the final version of the manuscript.

Financial Support: None

Conflict of Interest: The authors have not conflict of interest.

REFERENCES

1. Chatzipetrou V, Bégin MJ, Hars M, Trombetti A. Sarcopenia in Chronic Kidney Disease: A Scoping Review of Prevalence, Risk Factors, Association with Outcomes, and Treatment. Calcif Tissue Int. 2022;110(1):1–31.
2. Nishi H, Takemura K, Higashihara T, Inagi R. Uremic Sarcopenia: Clinical Evidence and Basic Experimental Approach. Nutrients. 2020;12(6):1814.

3. Gomez-Fernádez P, Sanchez A. L, Miguel JL, Almarez M, Vila PM. Effect of parathyroidectomy on respiratory muscle strenght in uremic myopathy. Am J Nephrol. 1987;466–9.
4. Fassbinder TRC, Winkelmann ER, Schneider J, Wendland J, Oliveira OB de. Functional Capacity and Quality of Life in Patients with Chronic Kidney Disease In Pre-Dialytic Treatment and on Hemodialysis - A Cross sectional study. Jornal Brasileiro de Nefrologia. 2015;37(1).
5. Lamberti N, Piva G, Battaglia Y, Franchi M, Pizzolato M, Argentoni A, et al. Inspiratory–Expiratory Muscle Training Improved Respiratory Muscle Strength in Dialysis Patients: A Pilot Randomised Trial. Adv Respir Med. 2023;91(1):93–102.
6. Yuenyongchaiwat K, Vasinsarunkul P, Phongsukree P, Chaturattanachaiyaporn K, Tritanon O. Duration of hemodialysis associated with cardio-respiratory dysfunction and breathlessness: a multicenter study. PeerJ. 2020;8:e10333.
7. Gómez-Fernández P, Sánchez Agudo L, Calatrava JM, Escuin F, Selgas R, Martínez ME, et al. Respiratory Muscle Weakness in Uremic Patients under Continuous Ambulatory Peritoneal Dialysis. Nephron. 1984;36(4):219–23.
8. Ministério da Saúde Brasil. Resolução no 510, de 7 de abril de 2016. Trata sobre as diretrizes e normas regulamentadoras de pesquisa em ciências humanas e sociais. 2016.
9. WMA. World Medical Association (WMA). Declaration of Helsinki. JAMA. 1997;277(11):925.
10. Kidney Disease: Improving Global Outcomes (KDIGO). Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int. 2012;3:1–150.
11. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race. New England Journal of Medicine. 4 de novembro de 2021;385(19):1737–49.
12. The CKD Epidemiology collaboration (CKD-EPI). Equations for glomerular filtration rate (GFR). Estimates GFR based on serum creatinine. The 2021 CKD-EPI equation. 2021.
13. Black LF, Hyatt RE. Maximal respiratory pressures: normal values and relationship to age and sex. J Respir Dis. 1969;99(5):696–702.
14. ATS/ERS Statement on Respiratory Muscle Testing. Am J Respir Crit Care Med. 15 de agosto de 2002;166(4):518–624.
15. Neder JA, Andreoni S, Lerario MC, Nery LE. Reference values for lung function tests. II. Maximal respiratory pressures and voluntary ventilation. Braz J Med Biol Res. 1999; 32(6):719-727.
16. Caruso P, Albuquerque ALP de, Santana PV, Cardenas LZ, Ferreira JG, Prina E, et al. Diagnostic methods to assess inspiratory and expiratory muscle strength. Jornal Brasileiro de Pneumologia. abril de 2015;41(2):110–23.
17. Pereira CA de C, Sato T, Rodrigues SC. Novos valores de referência para espirometria forçada em brasileiros adultos de raça branca. Jornal Brasileiro de Pneumologia. agosto de 2007;33(4):397–406.
18. Lung Function Testing: Selection of Reference Values and Interpretative Strategies. American Review of Respiratory Disease. novembro de 1991;144(5):1202–18.
19. Sociedade Brasileira de Pneumologia e Tisiologia (SBPT). Diretrizes para Testes de Função Pulmonar. J Pneumol. 2002;28(3):1–238.
20. Faria R de S, Fernandes N, Lovisi JCM, Reboredo M de M, Marta MS de M, Pinheiro B do V, *et al*. Pulmonary function and exercise tolerance are related to disease severity in pre-dialytic patients with chronic kidney disease: a cross-sectional study. BMC Nephrol. 4 de dezembro de 2013;14(1):184.
21. Faria R de S, Silva VSA, Reboredo M de M, Fernandes NM da S, Bastos MG, Cabral LF. Avaliação da função pulmonar, capacidade física e qualidade de vida de pacientes com doença renal crônica pré-dialítica. J Bras Nefrol. 2008;30(4):267–71.

22. Romain AP, Buist SA, Calverley PMA, Jenkins CR, HURD SS. GOLD Scientific Committee. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop Summary. Am J Respir Crit Care Med 2001;163:1256-76.
23. Navaneethan SD, Mandayam S, Arrigain S, Rahman M, Winkelmayer WC, Schold JD. Obstructive and restrictive lung function measures and CKD: National Health and Nutrition Examination Survey (NHANES) 2007-2012. American Journal of Kidney Diseases. setembro de 2016;68(3):414–21.