



## Effects of non-invasive ventilatory support in tolerance to the effort of patients with hemodialysis

### *Suporte ventilatório não invasivo na tolerância ao esforço de pacientes hemodialisados*

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#### Abstract

**Introduction:** The kidney system is responsible for the maintenance of homeostasis and in patients with Chronic Kidney Disease the kidney functions changes, contributing for the development of various complications that will have adverse effects in tolerance to the physical exercise and in Quality of Life of this patients. **Objective:** To evaluate the Effects of non-invasive ventilatory support in tolerance to the patients' physical exercise in dialysis. **Methods:** The patients performed two 6-minute walk tests, following an adapted protocol for treadmill, one of them without the use of non-invasive ventilatory support and the other with non-invasive ventilatory support during the walk. Besides, the patients answered a questionnaire of quality of life and the KDQOL-SF™ specific for the population under study. **Results:** It was noticed that there was not statistical difference in the distance recorded during the 6-minute walk tests. Regarding the quality of life, the greater impact of the disease was in relation to "Professional Activity". **Conclusion:** In conclusion, a non-invasive ventilatory support did not cause significant effects in tolerance to the exercise of this population. However, we should take into consideration the limitations suffered during the research development.

**Keywords:** Chronic Kidney Failure. Quality of Life. Tolerance to the Exercise.

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## Resumo

**Introdução:** O sistema renal é responsável pela manutenção da homeostasia do corpo e, em pacientes com Doença Renal Crônica a função dos rins se altera, contribuindo para o desenvolvimento de várias complicações que influenciarão negativamente na tolerância ao exercício físico e na qualidade de vida destes pacientes. **Objetivo:** Avaliar os efeitos do uso da ventilação mecânica não invasiva na tolerância ao exercício físico de pacientes em tratamento dialítico. **Métodos:** Os pacientes realizaram dois testes de caminhada de seis minutos, seguindo um protocolo adaptado para esteira, sendo um teste sem o uso da ventilação não invasiva e outro teste com ventilação não invasiva durante a caminhada. Além disso, os pacientes responderam um questionário de qualidade de vida o KDQOL-SFTM específico para a população estudada. **Resultados:** Foi observado que não houve diferença estatística na distância percorrida durante os testes de caminhada em esteira. Em relação à qualidade de vida, o maior impacto da doença foi em relação à "Atividade Profissional". **Conclusão:** Em conclusão, a ventilação não invasiva, não causou efeitos significativos na tolerância ao exercício desta população, porém, devem-se levar em consideração as limitações sofridas durante o desenvolvimento da pesquisa.

**Palavras-Chave:** Falência Renal Crônica. Qualidade de Vida. Tolerância ao Exercício.

## Introduction

The Chronic Kidney Disease (CKD) is determined by the loss of glomerular, tubular and endocrine function of kidneys in a progressive and irreversible way (1, 2). With its progression, kidneys become unable to maintain the normal functioning of body systems (1), requiring the treatment of renal replacement (3).

The number of patients on dialysis and served by SUS in the country has grown in the past few years, contributing to characterize this disease as a public health problem (4). According to 2011 Census from Brazilian Society of Nephrology (BSN), currently there are 91.314 Brazilians on dialysis per year, considering that 84.9% of services are carried out by SUS (5).

The kidney system is responsible for the maintenance of homeostasis, removing toxic substances and wastes, and for the hormone production. With its function changed by CKD, patients are more prone to systemic arterial hypertension, water retention, anemia (2) and musculoskeletal disorders (6), including the respiratory musculature (1). Patients may develop a generalized muscle weakness, affecting negatively on the tolerance to physical exercise and on the quality of life (QL) of patients (1, 6).

The functional capacity of these individuals is precarious, damaging both the performance of physical activities and the development of their daily life activities (7). One way to measure the functional status of patients is to perform a 6-minute walk test (6WT), in addition to providing information regarding cardiorespiratory responses to the exercise (8). This test can

be performed on a treadmill (tread6WT) when there is no runner available or the necessity of a more specific monitoring of the patient (9).

The utilization of non-invasive ventilatory support (NIV) can improve tolerance to the exercise, as it improves the cardiorespiratory response during the exercise (10). The usage of this therapeutic modality is indicated in acute respiratory failure, chronic obstructive pulmonary disease (COPD), acute pulmonary edema, congestive heart failure (CHF) (11), among other situations. However, there are no studies regarding the usage of NIV in patients with CKD. In this sense, this study aims to estimate the usage effects of non-invasive ventilatory support in the tolerance to the effort in the treadmill 6-minute walk test of patients in dialysis. Furthermore, this study proposes an evaluation of pulmonary function and the quality of life in patients with CKD in dialysis.

## Methods

### Study description, population and sample

An almost experimental study was made at the Clinical School of Physiotherapy from College of Health Sciences of Trairi of the Federal University of Rio Grande do Norte (FACISA/UFRN), with initial sample of 21 individuals with CKD in dialysis, registered at the Health Department of the city of Santa Cruz/RN and residents. This was a non-probability sampling, defined by the accessibility to the individual. This almost experimental protocol was submitted and approved by Ethics

Committee in Research from the Federal University of Rio Grande do Norte, under the number 249.874/2013, following the guidelines of the Resolution 196/96, from the National Health Council.

Inclusion criteria were established: individuals of both sexes, with diagnosis of CKD, in dialysis and with medical permission for executing the research protocol provided by the cardiologist participant in the research. Patients with cognitive impairment, presenting any kind of limitation (orthopedic, musculoskeletal, rheumatologic, cardiopulmonary or neurological) that could prevent tests accomplishment, and other clinical conditions that could be exacerbated by physical effort were excluded from the sample.

#### Procedure for data collection

Initially, all patients signed an Informed Consent Document (ICD), attesting to be aware and in agreement of procedures performed during the study. Moreover, individuals underwent a cardiac evaluation, so that they could be released to perform tests suggested in the protocol.

The research occurred in three distinct phases, performed every other day. The first phase is the execution of an assessment (anamnesis and physical exam) and pulmonary function tests (spirometry and manovacuometry). The other two phases consisted in the execution of a tread6WT in two distinct situations, following the protocol suggested by Camargo et al. (9). The initial speed was 2km/h, and may be increased by 1km/h every 30 seconds, depending on the patient tolerance, reaching a maximum of 8km/h, or if requested to be reduced, this would be done in 0,5km/h in every request. Tests in a treadmill was performed without inclination. In order to obtain the value of the forecasted traveled distance for each patient, a formula proposed by Iwama et al. (12) was used. Phases were executed always at the same time and the room temperature was kept always in 26°C.

Pulmonary function tests were obtained through the device Koko Legend Spirometer 314000 — Nspire, following the recommendations of Pereira (13) and Silva et al. (14). Predicted values were calculated according to the reference of normality established by Pereira et al. (15).

Maximum inspiratory and expiratory pressures (maxIP and maxEP) were measured through the digital manovacuometer Globalmed® MVD300, adopting the protocol suggested by Souza (16). References of normality, measurement of values and the choice of the

best curves respected the description of the method proposed by Neder et al. (17).

#### Experimental protocol

After performed the initial evaluation, patients underwent two tread6WT. Tests occurred in every other day and their order was drawn for each patient. Each test occurred as follows:

Test 1 (tread6WT without NIV): Initially, the following were measured: systemic arterial pressure (AP) at rest, peripheral heart rate (HR) at rest, respiratory rate (R) at rest, oxygen peripheral saturation (O2Ps) at rest and the sensation of effort through the noticed effort scale of BORG (18). Afterwards, a tread6WT was accomplished. During the test, parameters AP, HR, R and O2Ps and Borg were monitored. In the second, fourth and sixth minutes. After five minutes from the end of the tread6WT, the same variables were measured again, in order to verify the return of vital signs to pre-test values.

Test 2 (NIV during the tread6WT): This phase was similar to phase 1 — the only modification was the use of NIV by positive pressure of two levels (bilevel) during the tread6WT.

The AP at rest, during and at the end of tests was measured indirectly through the aneroid sphygmomanometer and Premium® stethoscope. The HR and O2Ps at rest, during and after the test, were measured using a digital pulse oximeter Solmedica® MD300C1. An evaluator measured the R during the Test 1, with the hand placed next to the nose of the individual and, during the Test 2 that was obtained through the device of NIV.

The device used to generate the non-invasive ventilatory support was the BIPAP® Synchrony II — Respironics. The inspiratory positive airway pressure (IPAP) was the minimum that guaranteed the patient a tidal volume of 8-10ml/Kg; the expiratory positive airway pressure (EPAP) was the minimum that guaranteed an O2Ps of 90-92%.

#### Analysis of Quality of Life

In order to evaluate the QL of patients, the Kidney Disease and Quality-of-Life Short-Form (KDQOL-SF™1.3) was used, which is a specific tool that evaluates individuals with CKD, applicable to patients undergoing some kind of dialysis program. By including issues related to generic and specific aspects of the kidney disease, it can be considered the most complete questionnaire available nowadays to evaluate the QL of patients with

CKD. The KDQOL-SF™ consists of 80 items, divided into 19 dimensions and includes the SF-36 more 45 items related to CKD (19).

The score of each item of this tool varies from zero to 100, with the higher values as a reflection of a better QL (20).

#### Statistical Analysis

Obtained data were analyzed through descriptive and inferential statistics, using the SPSS v. 20 for Windows as a program. The statistical significance will be considered for  $p$ -value with a value of less than or equal to 0,05. A generalized estimating equation (GEE) was performed.

## Results

Six patients with CKD in dialysis composed the final sample of this study. The majority were women (66.67%) and the age average was 47.2 years-old ( $\pm 14.9$ ). Fifteen individuals did not participate in the research because they were framed in some of the exclusion criteria, refusal or death (Table 1). All patients were treated by hemodialysis and the average time of dialysis, in months, was 44.5 ( $\pm 51.3$ ).

**Table 1** - General Characteristics of the Sample Studied

Characteristics	n	%
<b>Sample</b>		
<b>Initial Sample</b>	21	100
<b>Final Sample</b>	6	28.57
<b>Sex</b>		
Men	2	33.33
Women	4	66.67
<b>Reasons of the sample loss</b>		
<b>Death</b>	1	6.67
<b>Refusal</b>	8	53.34
<b>Physical Limitation</b>	5	33.34
<b>Other (Severe Anemia)</b>	1	6.67

The variables of spirometry, maxIP and maxEP were analyzed using descriptive statistics in order to characterize the pulmonary function of the sample and the results are shown in Table 2.

**Table 2** - Sample Characterization according to Pulmonary Function

Pulmonary Function	n	%
<b>Spirometry</b>		
Restrictive Ventilatory Disorder	3	60
Normal Spirometry	2	40
<b>Respiratory Muscle Strength</b>		
maxIP		
Normal	2	33.33
Reduced	4	66.67
maxEP		
Normal	4	66.67
Reduced	2	33.33

Note: maxIP (Maximum Inspiratory Pressure); maxEP (Maximum Expiratory Pressure).

The distance traveled in the tread6WT had an average of 407.5m ( $\pm 115.68$ m), however, but none of the patients in this study were able to reach the individual expected distance for the tread6WT. There was no significant statistical difference between distances traveled and in the tread6WT without NIV and with NIV, as described in Table 3.

**Table 3** - Distance traveled in tread6WT and comparative analysis of both tests

Treatment	Average	Estimative	Standard Error	$p$ -value	CI 95%
<b>Without NIV x With NIV</b>	-	-28.0608	14.86753	0.118	-
<b>Tread6WT</b>					
<b>Without NIV</b>	390.5125	-	6.45413	-	378.0653 :
<b>With NIV</b>	362.4517	-	8.46944	-	403.3694 :
					346.2263 :
					379.4375

Note:  $p$ -value = 0,05; CI (Confidence Interval).

Regarding the evaluation of the QL, all the patients answered the KDQOL-SF™ questionnaire. The highest scores were obtained for dimensions related to the "Quality of Social Interaction", "Social Support" and "Social Function", while the lowest scores were "Professional Activity". All the patients' results are shown in Table 4.

The IPAP of each patient was the minimum to guarantee a tidal volume (TV) of 8-10ml/kg, the average of pressures used in this sample was 8cmH<sub>2</sub>O. The EPAP of each individual was to guarantee a SpO<sub>2</sub> of 90-92%, the average of pressures used in this study was 4cmH<sub>2</sub>O.

**Tabela 4** - Descriptive Evaluation of Quality of Life of the sample studied

Dimensions	Minimum	Maximum	Average	Variation
<b>ESRD</b>				
Symptoms/ Problems	64.6	100	87.5	0 – 100
Effects of Kidney Disease in Daily Life	31	81.25	64	0 – 100
Weight of Kidney Disease	31	68.75	49.9375	0 – 100
Professional Activity	0	0	0	0 – 100
Cognitive Function	73.30	100	86.6575	0 – 100
Quality of Social Interaction	86.66	100	94.9975	0 – 100
Sexual Function	0	100	59.375	0 – 100
Sleep	58	73	67.07	0 – 100
Social Support	66.66	100	91.665	0 – 100
Encouraging of Dialysis Staff	75	100	87.5	0 – 100
Patient Satisfaction	33.2	83	44.27	0 – 100
<b>SF-36</b>				
Physical Function	20	90	55	0 – 100
Physical Performance	0	100	56.25	0 – 100
Pain	50	100	76.875	0 – 100
Health	45	65	51.25	0 – 100
Emotional Function	40	96	69	0 – 100
Emotional Performance	66.66	100	74.995	0 – 100
Social Function	75	100	93.75	0 – 100
Vitality	50	90	72.5	0 – 100

Note: ESRD (Scales Related to Kidney Disease); SF-36 (Short Form Health Survey).

## Discussion

During this study, a treadmill walk test protocol was adopted, proposed by Camargo et al. (9). An ergometer was used to perform the test because the NIV device available was not portable, making impossible to perform a conventional walk test.

Patients with CKD develop changes in several body systems, characterizing the uremic syndrome. Among these changes, we can find atrophy and weakness of skeletal muscles, which are clinical manifestations of uremic myopathy. The muscles responsible for breathing may have their strength and resistance decreased during the myopathy, once these muscles are classified as skeletal (1, 20 - 23).

In this study, it was verified that maxIP was reduced in most of the sample (66.67%). It was also observed that maxEP was reduced in a part of the sample (33.33%). These results are similar to those found by Cury et al. (1), which compared the maxIP and maxEP among dialyzed patients (DG), transplanted (TG) and one control group (CG). When the DG was compared with the CG, it was observed a reduction in both maxIP and maxEP. When comparing the DG with the CG, it was observed a reduction in both maxIP and maxEP. When comparing DG with the TG, the maxIP of the DG also presented a reduction, and compared with the CG, the TG presented a disposition for low maxIP and maxEP. Dipp et al. (23), evaluated 30 individuals and found a reduction in maxEP of 14.2% in relation to predicted values. However, the maxIP presented no statistical difference. In the study of Kovelis (24), it was analyzed 17 patients with CKD and authors observed no significant alteration in maxIP and maxEP, which is different from the findings of this study.

This change of strength regarding musculature affects the function of the respiratory system and contributes to the reduction of pulmonary capacity (1). Besides, the deficient pulmonary function of these patients can be a direct result of the increase of uremic toxins circulation, or can be indirectly affected by the volume overload, anemia, immunosuppression, heterotopic calcification, malnutrition, electrolytic disorders and acid-basic unbalance (25).

Regarding the pulmonary function, it was found that 60% of the sample presented a degree of restrictive ventilatory disorder (RVD). Corroborating with these findings, Faria et al. (21), as performing a forced spirometry, observed that 2 patients presented a mild RVD and 4 patients presented a mixed ventilatory disorder

(MVD). Cury et al. (1) showed that in the group of individuals undergoing dialysis, 1 individual presented a MVD and 7 were classified as presenting a RVD, in the group of transplanted only 1 individual presented a RVD and the sample remaining presented no alteration in the spirometry.

The dialysis routine of patients with CKD has impact in the QL, mainly harming physical capacity and performance of daily activities, increasing sedentary habits and thus increasing the risk of mortality (23, 25).

In this study, best results in the QL questionnaire were observed in the field of "Quality of Social Interaction", "Social Support" and "Social Function". Similar to the findings of this research, the results found by Coutinho et al. (26) and Fahur et al. (27). Schardong et al. (20), through the analysis of QL from patients with CKD, found that the worst scores in the KDQOL-SF™ questionnaire were seen in the field of "Overload of Kidney Disease" and "Professional Role", which supports the findings of this research that, in his evaluation, found that the field with lower score in the same questionnaire was to "Professional Role". Some studies describe this same result regarding "Professional Role" (26 - 28).

The reduction of functional capacity is related to a number of factors such as cardiopulmonary and musculoskeletal changes, among others. These factors characterized the uremic syndrome and leads to dyspnea, fatigue, anemia, muscular weakness among other alterations (23, 25).

When evaluated the functional capacity of patients with CKD through the tread6WT, it was observed that none of them reached the expected value of the individual distance traveled. Lima et al. (29), evaluated patients with CKD before and after the program during the tread6WT. Regarding their functional capacity, it was observed that values obtained in the 6WT were significantly lower than the predicted values for this population. Cury et al. (1) observed that there is a tendency for individuals with CKD to obtain lower results in comparing the expected with the general population. Faria et al (21) noticed that only one individual from the sample, after the 6WT, presented a lower result than the expected in the walk test, and the other patients achieved the expected values.

When evaluated the effect of the use of NIV in the tolerance to the effort in the tread6WT, it was observed no significant difference in the tolerance to the effort of patients during the tread6WT with or without NIV. However, studies with other populations that performed the 6WT, showed that the use of this therapeutic

modality improves the performance of patients, as shown by Lima et al. (29), in a sample of patients with CHF, the use of NIV through the CPAP increased the distance traveled in the 6WT when compared to the control group that made no use of NIV. Costa et al. (30) studied the use of NIV through the do Bipap® in patients with COPD and observed an increase in the distance traveled in the 6WT after the use of this therapeutic modality.

## Conclusion

It can be observed that patients with CKD present pulmonary disorders and reduction of their QL. Alterations in the pulmonary system of patients in this sample were discreet, but contribute directly for the reduction of their functional capacity, as well as the low QL presented by them.

The use of NIV through the Bipap® during the tread6WT cased no significant effects in the tolerance to the physical exercise of patients with CKD. Some study limitations may have contributed to these results: reduced sample size, patients' familiarity with the ergometer used and clinical profile (insignificant cardiorespiratory limitations). Furthermore, this was the first study regarding effects of NIV in tolerance to the exercise in patients with CKD.

In this sense, it is suggested to perform other studies with larger samples, and composed by patients with different compromising levels of functional capacity, in order to investigate the effects of NIV in patients with CKD, and to observe there is any impact in pulmonary function and QL of individuals.

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