

# Negative effects of chronic kidney failure on lung function and functional capacity

Efeitos negativos da insuficiência renal crônica sobre a função pulmonar e a capacidade funcional

Juliana L. Cury<sup>1</sup>, Antonio F. Brunetto<sup>2†</sup>, Ricardo D. Aydos<sup>3</sup>

## Abstract

**Objective:** To evaluate lung function and functional capacity in patients with chronic kidney failure (CKF) undergoing dialysis and in patients after kidney transplant. **Methods:** Seventy-two participants were evaluated: 32 patients with CKF on dialysis (DG) for at least six months, ten patients who had kidney transplants (TG) at least six months earlier, and 30 healthy subjects as a control group (CG). All groups were evaluated using spirometry, with maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP), and using the six-minute walking test (6MWT). The SPSS 12.0 software was used for statistical analysis, with a minimum significance level of  $\alpha < 0.05$ . **Results:** There was a decreased lung function in the DG for FVC, FEV1, MVV, VC, MIP and MEP, and decreased FEV1 and MVV in the TG compared to the CG (one-way ANOVA/Fisher's post-hoc;  $p < 0.01$ ). There was also an association (chi-square) between decreased MIP and belonging to the DG ( $\lambda = 0.5$ ,  $p < 0.001$ ), between lower performance in the 6MWT for the DG and TG ( $p < 0.01$ ) compared to the CG (one-way ANOVA/Fisher's post-hoc), and between MIP and MEP (Pearson's coefficient;  $r = 0.752$ ;  $p < 0.01$ ). **Conclusions:** Patients with CKF undergoing dialysis showed impaired functional capacity and lung function that were not completely reverted in the kidney transplant patients.

**Key words:** dialysis; kidney transplant; spirometry; respiratory muscles; functional capacity.

## Resumo

**Objetivo:** Avaliar a função pulmonar e a capacidade funcional em pacientes com insuficiência renal crônica (IRC) em hemodiálise e em pacientes após transplante renal. **Métodos:** Foram avaliados 72 indivíduos, sendo 32 pacientes com IRC em hemodiálise (GD) há mais de 6 meses, 10 pacientes transplantados renais (GT) há, pelo menos, 6 meses e 30 sujeitos saudáveis para grupo controle (GC). Todos os grupos foram avaliados utilizando espirometria, pressões inspiratória (PImax) e expiratória (PEmax) máximas e teste da caminhada em seis minutos (TC6min). Para análise estatística, foi utilizado o programa SPSS 12.0, com nível mínimo de significância  $\alpha < 0,05$ . **Resultados:** Foram encontrados resultados estatisticamente significativos ( $p < 0,01$ ) para: diminuição da função pulmonar no GD para Capacidade vital forçada (CVF), Volume expirado forçado (VEF1), Ventilação voluntária máxima (VVM), Capacidade vital (CV), PImax, PEmax e, para o GT, diminuição do VEF1 e VVM, quando comparados ao GC (ANOVA uma via/post hoc Fischer); associação (qui-quadrado) entre diminuição da PImax e pertencer ao GD ( $\lambda = 0,5$ ,  $p < 0,001$ ); menor desempenho no TC6min no GD e GT ( $p < 0,01$ ) quando comparados ao GC (ANOVA uma via/post hoc Fischer). Encontrou-se correlação significativa (coeficiente de Pearson) entre PImax e PEmax ( $r = 0,752$ ,  $P < 0,01$ ). **Conclusões:** Pode-se concluir que existem alterações na capacidade funcional e na função pulmonar do paciente com IRC em hemodiálise, as quais são indicativas de prejuízos funcionais que não se apresentam completamente revertidos no paciente transplantado renal.

**Palavras-chave:** hemodiálise; transplante renal; espirometria; músculos respiratórios; capacidade funcional.

Received: 13/03/08 – Revised: 31/03/09 – Accepted: 18/08/09

<sup>1</sup>Department of Physical Therapy, Centro Universitário da Grande Dourados (UNIGRAN), Dourados (MS), Brazil

<sup>2</sup>Department of Physical Therapy, Universidade Estadual de Londrina (UEL), Londrina (PR), Brazil

<sup>3</sup>Faculty of Medicine, Universidade Federal do Mato Grosso do Sul (UFMS), Campo Grande (MS), Brazil

<sup>†</sup>In Memoriam

Correspondence to: Juliana Loprete Cury, Rua Antônio de Carvalho, 2.535, COHAFABA 3º Plano, CEP 79826-250, Dourados (MS), Brazil, email: julianalc@gmail.com

## Introduction

Chronic kidney failure (CKF) is an irreversible pathological condition characterized by loss of the kidneys' ability to maintain homeostasis. The kidneys regulate the body's vital functions such as water, acid-base and electrolyte balance, and participate in hormonal functions and blood pressure regulation. Patients with CKF require dialysis in the form of hemodialysis or peritoneal dialysis for survival, because these can partially replace the impaired kidney function while the patient awaits a definitive solution through kidney transplant, if possible<sup>1</sup>.

The number of patients with CKF has been growing over recent years. In 1994, Brazil had 24,000 patients maintained through dialysis programs<sup>2</sup>. In 2004, data from around the world showed that the United States, Japan and Brazil were the top three in numbers of patients with CKF, and Brazil had more than 58,000 cases. Worldwide, it is expected that the figure of 1,371,000 patients undergoing dialysis in 2004 will have jumped to more than 2,000,000 patients in 2010, thus showing an increase in the prevalence of this disease<sup>2,3</sup>.

Patients with CKF undergoing dialysis can develop dysfunction in multiple systems such as the musculoskeletal, cardiovascular, metabolic and respiratory systems. The musculoskeletal system is seriously affected, and there are several interrelated causal factors in the development of muscle problems in patients with CKF. Among them are decreased protein-calorie intake, muscle atrophy through disuse and muscle protein imbalance, which mostly affect type II muscle fibers; reduction of the vascular and capillary bed; presence of intravascular calcification and decreased local blood flow. These results are part of the pathogenesis of uremic myopathy and are commonly described in the literature in relation to skeletal muscles such as the deltoid, quadriceps and abdominal muscles<sup>4-9</sup>.

The muscles responsible for respiratory function, such as the diaphragm and intercostals, among others, are classified as skeletal muscles and may show decreases in muscle strength and endurance properties resulting from uremic myopathy. Some authors<sup>10</sup> who have studied the involvement of uremia in the diaphragm have concluded that loss of strength occurs through severe uremia. The ventilatory deficit due to this impairment in respiratory muscles, combined with other lung tissue impairments, compromises the functioning of this system, thereby contributing towards decreased lung capacity<sup>11,12</sup>.

Other complications in lung tissue are found in patients with CKF, such as pulmonary edema, pleural effusion (mainly in terminal patients with CKF), pulmonary and pleural fibrosis and calcification, pulmonary hypertension, decreased pulmonary capillary blood flow and hypoxemia<sup>13,14</sup>. There are also deficits in oxygen supply to the muscles as a result of decreased

peripheral microcirculation, decreased muscle ATP synthesis due to deficiencies in the use of carbohydrates, signs of insulin resistance and changes to glycolytic enzymes, and decreased oxidation of fatty acids<sup>15-17</sup>.

Some changes found in patients with CKF undergoing dialysis are also observed in transplant patients, even after restoration of kidney function. These changes can be partially attributed to immunosuppressive therapy, which commonly uses corticosteroids. This medication is associated with decreased synthesis and increased protein catabolism, which could hamper full return of the functions of kidney transplant patients<sup>18-20</sup>.

From the above, it can be seen that the changes to the musculoskeletal, metabolic, circulatory and respiratory systems may be directly involved in the decreased lung function and functional capacity of patients with CKF and would appear not to be fully reversed after kidney transplantation. It is unknown which factor most affects the functional capacity of these patients.

The aim of this study was to evaluate pulmonary function and functional capacity among patients with CKF undergoing dialysis and among kidney transplant patients. Hence, the hypotheses for the present study were that the muscle complications due to CKF significantly affect the respiratory muscles, thereby impairing the lung function and functional capacity of patients undergoing dialysis, and that such lung and functional capacity changes are present in patients even after kidney transplantation. Methods for evaluating lung function using spirometry and maximum respiratory pressure and for evaluating functional capacity using the 6MWT enable precise analysis and easy clinical assessment of the parenchymal, airway, respiratory muscle pump components and the circulatory and metabolic functional performance of these patients.

## Methods

This study was approved by the Ethics Committee for Human Research (CEP/UNIGRAN) of the University Center of Grande Dourados, under the number 010/2006. A cross-sectional observational study was conducted between July and November 2006, in which all the 72 subjects between 24 and 71 years of age who underwent dialysis and those on the list of kidney transplant patients during this period, in a town in the interior of Mato Grosso do Sul (MS), were evaluated. All the subjects participated voluntarily in the study and signed a consent form that was prepared in accordance with resolution 196/96 of the National Health Council of the Ministry of Health.

Twenty-eight subjects who had previous history of smoking or had quit smoking less than five years earlier, or exhibited

uncontrolled hypertension, recent ischemic heart disease (no more than three months ago), unstable angina, severe cardiac arrhythmias, skeletal disease limiting physical activity and respiratory and neurological diseases were not included.

The subjects were divided into three groups: dialysis group (DG), transplant group (TG) and control group (CG). For the DG, all 32 patients with CKF were included (27 men and five women). These individuals had been undergoing dialysis regularly for at least six months; they were clinically stable, without anemia, and were under clinical follow-up. This group included two former smokers who had quit more than 10 years earlier. The TG was composed of 10 individuals (9 men and 1 woman) who had undergone kidney transplant at least six months earlier. These patients were stable from a clinical and surgical point of view and were also under regularly clinical follow-up. To form the CG, 30 healthy subjects chosen for convenience were evaluated: these were of the same age and gender as the other two groups and fulfilled the same criteria for non-inclusion.

All the subjects underwent functional evaluation for the following parameters: pulmonary function (spirometry and respiratory muscle strength) and functional capacity. All tests were performed by a trained evaluator. For DG, the evaluations were conducted on the second and third day of dialysis in the week (Wednesday and Friday or Thursday and Saturday)<sup>21</sup>.

The pulmonary function evaluation was performed using spirometry, and followed the criteria established by the American Thoracic Society<sup>22</sup>, with reference values as reported by Knudson et al.<sup>23</sup>. The interpretation of the tests followed the guidelines for pulmonary function tests published by the Brazilian Society of Pulmonology and Phthysiology<sup>24</sup>. The Pony MicroQuark spirometer (Cosmed; Pavona di Albano, Rome, Italy) was used in the tests, and the following parameters were obtained: forced vital capacity (FVC), forced expiratory volume in one second (FEV1), Tüffenaar index (FEV1/%FVC), forced expiratory flow 25%-75% (FEF25%-75%), peak expiratory flow (PEF), maximal voluntary ventilation (MVV) held directly, vital capacity (VC), tidal volume (VT) and minute volume (MV). Only reproducible evidence with variation of less than 5% was taken into consideration, and the largest value was selected for the study.

Respiratory muscle strength was evaluated through the maximal respiratory pressure test, following the protocol of Black and Hyatt<sup>25</sup>. The subjects' MIP and MEP were evaluated, using an analog manovacuometer (Commercial Médica M120; São Paulo, SP, Brazil). The measurements were performed three times or until the value became reproducible, and the largest value obtained was used for this study. The reference values for normal populations followed those described by Neder et al.<sup>26</sup> for the Brazilian population. MIP values were classified according to the risk values for postoperative complications proposed

by Bellinetti and Thomson<sup>27</sup>, as less than or equal to 75% of predicted and greater than 75% of predicted.

To evaluate functional capacity, the 6MWT was performed, as validated by Guyatt et al.<sup>28</sup> for patients with heart failure, with reference values as described by Troosters et al.<sup>29</sup>. The test was performed in a wide ventilated corridor of 30 meters in length, and the patients were encouraged with standardized phrases every minute. Along with the test, measurements of vital signs were made to monitor the patients' performance: heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR) and the dyspnea value reported by the individual through viewing the Borg scale at the beginning (b) and at the end (e) of the test<sup>30</sup>.

The results were shown as means (and standard deviations) with the significance level established at  $\alpha < 0.05$ . To compare the groups in relation to parameters with normal distribution, one-way ANOVA with post-hoc Fisher's LSD (least significant difference) was used. For parameters without normal distribution, Kruskal-Wallis with post-hoc Mann-Whitney (only for the weight parameter) was used. For correlations, Pearson's correlation coefficient was used, since the correlated variables were normally distributed. The chi-square test was used for associations of groups and variables. For statistical analysis, the SPSS 12.0 software was used.

## Results

It can be seen in Table 1 that the groups were homogeneous, showing a difference only in the weight parameter, in which the DG was lower than the other groups.

From the spirometry results (Table 2), it can be seen that there were differences between the groups in relation to the parameters evaluated. The DG had lower values for FVC, FEV1, MVV, MIP and MEP, while the TG had lower values for FEV1 and MVV, in comparison with CG. Interestingly, the FVC and MVV parameters showed values within the normal range (mean > 80% of predicted) in all three groups.

In classifying the spirometry results from the subjects in the three groups, into normal ventilatory function or obstructive, restrictive and mixed disorders, there was only one case of

**Table 1.** Characteristics of the study subjects.

	Dialysis (n=32)	Transplantation (n=10)	Control (n=30)	p-value
Age (years)	43.91 (2.32)	50.4 (2.79)	48.4 (2.6)	0.26
Weight (kg)	65.93 (2.2)	75.27 (5.18)	71.78 (2.23)	0.05 *
Height (m)	1.67 (0.01)	1.71 (0.02)	1.67 (0.01)	0.4
Bmi (kg/m <sup>2</sup> )	23.67 (0.69)	25.87 (1.61)	25.68 (0.78)	0.15
Time (years)	2.77 (0.32)	4.0 (0.58)		

\* Kruskal-Wallis  $p < 0.05$  between groups:  $\chi^2=6.215$ ,  $gl=2$ ,  $p=0.045$ . CG>DG ( $p=0.031$ ; Mann-Whitney).

**Table 2.** Pulmonary function of the study subjects.

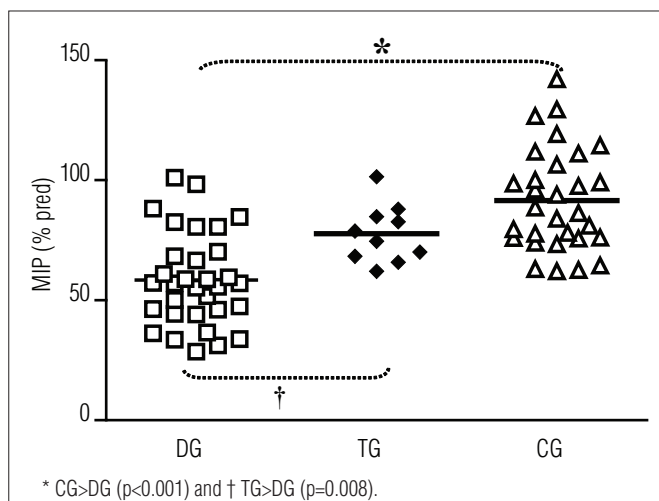
	Dialysis (n=32)	Transplantation (n=10)	Control (n=30)	p-value
FVC (%pred)	91.17 (2.88)	94.81 (4.33)	104.33 (2.17)	<0.01 *
FEV1 (%pred)	91.13 (3.17)	97.98 (4.54)	110.03 (2.69)	<0.01 *
FEV1/FVC% (%pred)	100.06 (1.65)	101.57 (2.34)	104.43 (2.2)	0.26
FEF25-75% (%pred)	95.43 (5.5)	104.19 (7.02)	109.86 (6.23)	0.2
Peak Flow (L/s)	7.47 (0.32)	8.25 (0.44)	6.69 (0.44)	0.09
MVV (%pred)	82.05 (3.52)	93.17 (5.46)	118.37 (4.39)	<0.01 *
MIP (cmH <sub>2</sub> O)	67.19 (4.1)	87.0 (5.1)	94.13 (3.5)	<0.01 *
MEP (cmH <sub>2</sub> O)	76.25 (5.06)	89.2 (6.1)	107.6 (4.59)	<0.01 *

\* ANOVA  $p < 0.01$  between groups; post-hoc Fisher's LSD (least significant difference); FVC ( $F_{2,69} = 6.777$ ,  $p = 0.002$ ; LSD CG>DG,  $p = 0.001$ ); FEV1 ( $F_{2,69} = 10.592$ ,  $p < 0.001$ ; LSD CG>DG,  $p < 0.001$ ; CG>TG,  $p = 0.046$ ); MVV ( $F_{2,69} = 22.613$ ,  $p < 0.001$ ; LSD CG>DG,  $p < 0.001$ ; CG>TG,  $p = 0.002$ ); MIP (cmH<sub>2</sub>O): ( $F_{2,69} = 13.527$ ,  $p < 0.001$ ; LSD TG>DG,  $p = 0.010$ ; CG>DG,  $p < 0.001$ ); MEP (cmH<sub>2</sub>O): ( $F_{2,69} = 11.182$ ,  $p < 0.001$ ; LSD CG>DG,  $p < 0.001$ ).

**Table 3.** Six-minute walking distance test on the study subjects.

	Dialysis (n=32)	Transplantation (n=10)	Control (n=30)	p-value
6MWT (m)	434.69 (13.25)	456.9 (18.06)	502.53 (8.01)	<0.01 **
HRI (ppm)	81.88 (2.21)	76.9 (4.54)	74.77 (2.25)	0.09
HRe (ppm)	99.0 (3.67)	88.9 (5.1)	95.1 (2.24)	0.25
RFi (bpm)	18.44 (0.49)	17.30 (0.79)	16.4 (0.59)	0.03 *
RFe (bpm)	22.5 (0.71)	24.1 (0.82)	21.43 (0.73)	0.16
SAPi (mmHg)	144.38 (3.2)	132.5 (5.54)	116.5 (2.29)	<0.01 **
SAPe (mmHg)	152.66 (4.15)	145.0 (5.22)	131.83 (2.94)	<0.01 **
DAPI (mmHg)	92.81 (2.74)	84.5 (2.83)	75.0 (1.9)	<0.01 **
DAPE (mmHg)	92.5 (2.91)	82.0 (3.27)	77.5 (1.71)	<0.01 **
Borgi	1.06 (0.04)	1.1 (0.1)	1.0 (0.0)	0.3
Borge	1.88 (0.26)	2.2 (0.36)	1.33 (0.15)	0.09

\* ANOVA  $p < 0.05$ ; \*\* ANOVA  $p < 0.01$  between groups; post-hoc Fisher's LSD (least significant difference): 6MWT: ( $F_{2,69} = 9.612$ ,  $p < 0.001$ ; LSD CG>DG,  $p < 0.001$ ; CG>TG,  $p = 0.045$ ); HRI: ( $F_{2,69} = 2.492$ ,  $p = 0.09$ ); HRe: ( $F_{2,69} = 1.402$ ,  $p = 0.253$ ); RFi: ( $F_{2,69} = 3.738$ ,  $p = 0.029$ ; LSD DG>CG,  $p = 0.008$ ); RFe: ( $F_{2,69} = 1.892$ ,  $p = 0.158$ ); SAPi: ( $F_{2,69} = 23.753$ ,  $p < 0.001$ ; LSD DG>TG,  $p = 0.043$ ; DG>CG,  $p < 0.001$ ); SAPe: ( $F_{2,69} = 8.620$ ,  $p < 0.001$ ; LSD DG>CG,  $p < 0.001$ ); DAPI: ( $F_{2,69} = 14.976$ ,  $p < 0.001$ ; LSD DG>CG,  $p < 0.001$ ; TG>CG,  $p = 0.046$ ); DAPE: ( $F_{2,69} = 10.365$ ,  $p < 0.001$ ; LSD DG>TG,  $p = 0.031$ ; DG>CG,  $p < 0.001$ ); Borgi: ( $F_{2,69} = 1.243$ ,  $p = 0.295$ ); Borge: ( $F_{2,69} = 2.546$ ,  $p = 0.086$ ).

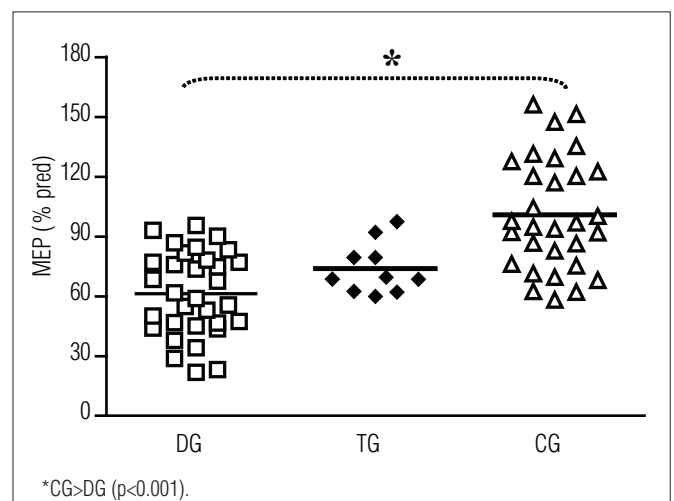
**Figure 1.** MIP variation between three groups.

mixed disorder in the DG (a former smoker who quit 11 years earlier), seven cases of restrictive disorder in the DG and one case of restrictive disorder in the TG. The remaining subjects had normal ventilatory function.

In the evaluation of respiratory muscle strength (Table 2 and Figures 1 and 2), lower values for MIP and MEP were observed in the DG group than in the CG. The DG also showed a lower value for MIP than seen in the TG, but the latter group showed a tendency for the MIP to be lower than the MIP of the CG. The MEP had lower value only in the DG, compared with the CG, but with a tendency for the TG also to be lower than the CG.

The classification of inspiratory muscle strength in relation to the percentage of predicted values showed that 78.1% of DG subjects, 50% of TG subjects and 20% of CG subject showed values less than or equal to 75% of predicted values. This result showed statistical significance in the chi-square test ( $X^2 = 20.93$ ,  $gl = 2$ ,  $p < 0.001$ ) and strength of association of 50% ( $\lambda = 0.5$ ,  $p < 0.001$ ), when analyzing the MIP as a dependent variable. Therefore, individuals in the DG had a higher chance of showing inspiratory muscle strength lower than the general population.

Functional capacity was lower for both DG and TG, compared with CG (Table 3). In analyzing the values of total traveled distance in each group, it was observed that in the DG, only three individuals (15.63%) walked more than 500 meters, whereas 56.67% of the CG walked more than 500 meters (which is the expected minimum normal value, according to authors who mention this test)<sup>31</sup>. These results did not show significant associations in the chi-square test, but there was a tendency for individuals with CKF to walk shorter distances than would be expected for the general population. This can be shown best through comparing the result from the 6MWT with the reference values<sup>30</sup>. ANOVA showed significant differences between

**Figure 2.** MEP variation between three groups.

the groups ( $p < 0.0001$ ): CG>DG (LSD  $p < 0.001$ ); CG>TG (LSD  $p < 0.05$ ); mean 6MWT in the DG, 56.9% of predicted; in the TG, 62.3% of predicted; and in the CG, 70.2% of predicted.

There were positive correlations between FVC and MIP ( $r = 0.310$ ;  $p < 0.05$ ), FVC and MEP ( $r = 0.332$ ;  $p < 0.05$ ), MVV and MIP ( $r = 0.463$ ;  $p < 0.001$ ), MVV and MEP ( $r = 0.430$ ;  $p < 0.001$ ) and MIP and MEP ( $r = 0.752$ ;  $p < 0.001$ ) (Figure 3).

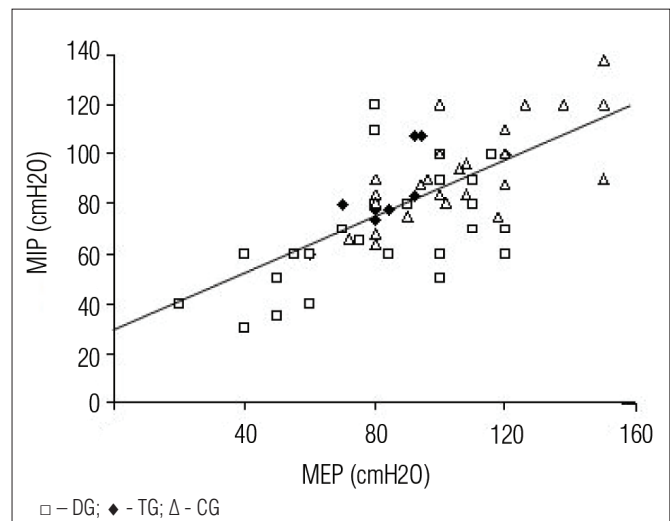
There were correlations between FVC and 6MWT ( $r = 0.355$ ,  $p = 0.046$ ) and between FVC and MVV ( $r = 0.469$ ,  $p = 0.007$ ) only in the DG.

## Discussion

In this study, it was seen that the DG showed the worst results for lung function (FVC, FEV1, MVV, MIP and MEP) and functional capacity (6MWT), in comparison with the CG. It is noteworthy that the worst result found for the DG was the significant decrease in inspiratory muscle strength and its correlation with proportional loss of expiratory muscle strength. The TG also showed lower results for lung function (MVV and MIP) and functional capacity (6MWT), compared with the CG. Attention is drawn to the positive correlation results between respiratory muscle strength (MIP and MEP) and the volumetric parameters (FVC) and overall functioning of the respiratory system (MVV) in the study groups, thus suggesting that the muscle strength parameter was the main component with the greatest influence on impairment of lung function in patients undergoing dialysis and in kidney transplant patients.

The mechanisms proposed to explain the worse results from the volumetric component found in the present study, as defined by decreased FVC but FEV1/FVC% index within the normal range<sup>24</sup>, with a tendency for subjects to show restrictive disorders, are not entirely clear in the literature. However, the present authors propose that the main disorders associated with these results are the following: chronic and often subclinical pulmonary edema; decreased serum albumin with consequent water and protein imbalance in the microcirculation; interstitial fibrosis and calcification of the lung parenchyma and bronchial tree; recurrent infections; and alveolitis and fibrosis due to corticosteroid therapy in immunosuppressed patients. Studies that evaluate lung function in patients with CKF undergoing dialysis and after kidney transplantation have described results similar to those found in the present study and help to explain the lesion mechanisms<sup>14,31-33</sup>.

One of the first studies to demonstrate the behavior of lung function in patients with CKF at different stages of the disease was carried out by Bush and Gabriel<sup>34</sup>. These authors studied 80 patients: 20 patients with CKF under medical treatment only (pre-dialysis), 20 patients undergoing continuous ambulatory



**Figure 3.** Correlation between MIP and MEP ( $r = 0.752$ ;  $p < 0.01$ ).

peritoneal dialysis (CAPD), 20 patients undergoing dialysis and 20 kidney transplantation patients. They evaluated the FVC, FEV1, FEV1/FVC%, PEF, TLC (total lung capacity) and RV (residual volume) parameters as spirometry parameters, along with CO (carbon monoxide) diffusion. They found values within normal range for the pre-dialysis group; a small reduction in spirometric parameters and large reduction in CO diffusion in patients undergoing CAPD; a small reduction in spirometric parameters but increased RV in the dialysis group; and normal spirometric values for the post-transplantation group, but with decreased TLC and CO diffusion and the lowest RV value. They did not find any correlation between the lung function parameters and the biochemical tests and duration and severity of CKF.

Another component that was lower in the DG and TG, in the spirometric evaluation, was the MVV. The three groups were within the normal range (>80% of predicted), but with lower values than in the CG, thus showing that patients with CKF undergoing dialysis and kidney transplant patients have limitations to their ventilatory capacity. There has only been one report of this parameter in evaluating lung function<sup>35</sup> in patients with CKF. However, that author did not compare the value obtained with normal values. A correlation between MVV and FVC was also found in the DG, thus suggesting that the reduction in MVV appears in individuals who have lower FVC. This may be another factor indicative of the negative effect of decreased lung volume, even if still within normal limits, which may cause a functional impairment for individuals with CKF.

The decrease in both inspiratory and expiratory muscle strength found in the DG and TG groups demonstrates that CKF significantly affects both the inspiratory and the expiratory respiratory muscles. This can be interpreted through the positive correlation found between MIP and MEP, thereby showing that respiratory muscle strength is decreased overall,

and that patients have a linear decrease in the two components (inspiratory and expiratory). Even after kidney transplant, patients do not seem to fully recover respiratory muscle strength, thus showing that factors other than uremia maintain the muscle deficit in this population.

The causal factors relating to the decrease in the respiratory muscle strength component have been described in the literature as due to the causal mechanisms of uremic myopathy. They include decreases in muscle mass (cross-sectional area, mainly of type II fibers) found in studies on mice and humans, decreases in oxidative metabolism, decreases in muscle protein synthesis and decreases in calcium plasmatic concentration<sup>6-10</sup>.

For transplantation patients, it is believed that the use of corticosteroid immunosuppressant therapy impedes the recovery of muscle fibers after kidney transplantation by causing a decrease in muscle protein synthesis and impairment of oxidative metabolism<sup>18-20</sup>. Other factors such as the age of the population, sedentary lifestyle and lack of systematic rehabilitation programs for kidney transplantation patients in Brazil, may lead these individuals to maintain deficits that may have negative influences on their functional outcome.

Some authors have reported on evaluations of respiratory muscles among patients with CKF. Gómez-Fernández et al.<sup>36</sup> were among the first authors to report on evaluations of maximal respiratory pressures in this population. They evaluated CKF patients who underwent CAPD and found decreased MIP in patients with CKF (59.6% of predicted values), compared with controls (82.7% of predicted values). Other authors<sup>14,33,35</sup> have also found results similar to those found in the present study. There is a consensus that respiratory muscle strength is decreased, and the pathogenesis of this condition is similar to what is observed in peripheral muscles.

The results from the 6MWT in this study demonstrated that individuals in the DG and TG had worse results than did those in the CG. Oh-Park et al.<sup>37</sup> evaluated the 6MWT and reported that the CKF patients walked distances that were shorter than what is considered to be normal, with a mean of 405 meters for dialysis patients, i.e. a value slightly lower than what was found in the present study. Becker-Cohen et al.<sup>38</sup> evaluated the 6MWT in children and young adults with CKF and with kidney transplants who were still undergoing dialysis. They found values within normality and, although there were no specific predictive values for children, they found that on average, the distance that they were able to walk was only 100 meters less than what the adults who were evaluated could achieve. Those authors therefore considered this result to be normal.

Decreased functional capacity is caused by multiple factors, including cardiovascular, respiratory and muscle problems, in which the capability to capture, transport and use O<sub>2</sub> might

be harmed. In this study, it was found that the component that showed further injury and was thus a negative influence on functional capacity was lung function, with a positive correlation between FVC and functional capacity in the DG. This suggests that even a small reduction in FVC may influence these individuals' performance in the functional capacity test, although the FVC values were within normal ranges.

Another factor not evaluated in this study but of functional interest is that patients with CKF may show decreased O<sub>2</sub> consumption (VO<sub>2</sub>)<sup>4</sup>, as reported by Sietsema et al.<sup>39</sup>. They demonstrated in their study that maximum O<sub>2</sub> consumption values greater than 17.5 ml/min/kg are strong and important predictors of survival among patients with CKF, thereby indicating that functional capacity evaluation is essential within the follow-up for patients with CKF.

The 6MWT provides important measurements for following up patients' evolution during the disease and also for evaluating the benefits of rehabilitation programs developed among these individuals. Although this test is still infrequently used for evaluating patients with CKF, and this disease does not appear as an indication for 6MWT, as described by the American Thoracic Society<sup>30</sup>, the results from the 6MWT can be of practical use for physical therapists working in dialysis units and care centers for kidney transplantation patients. This idea is reinforced in the study by Reboredo et al.<sup>40</sup>, who evaluated functional capacity by means of the 6MWT and correlated the results with cardiopulmonary tests. They concluded that the 6MWT can be used as a means of evaluating patients with CKF.

Regarding the anthropometric characteristics of the study population, it was observed that the sample was homogeneous in relation to the parameters of age, height and BMI. There was a significant difference regarding weight. Although this study did not include the aim of evaluating nutritional status, it was found that the means of the groups were within the normal range for BMI. This result is positive, since low weight is a factor of negative prognosis for chronic diseases, and overweight is a risk factor for cardiovascular disease<sup>41</sup>.

Some difficulties were found in carrying out the tests, since the subjects with CKF (DG) showed limitations and complications after dialysis sessions, which hampered their performance in all the functional tests. It was impossible to match the number of subjects in the TG with the numbers in the other groups, since many of these individuals did not join in the project, thus impairing the homogeneity among the groups.

## Conclusions : : : .

From analysis on the results, we can conclude that respiratory muscle strength, lung function and functional capacity

in patients with CKF undergoing dialysis and in kidney transplantation patients show lower values than those of the general population, and that patients undergoing dialysis have greater impairment of muscle and lung function than do kidney

transplant patients. Based on the correlations found between respiratory muscle strength and FVC and MVV parameters, it appears that muscle strength is the respiratory component that is most affected in individuals with CKF.

## References

- Parmar MS. Chronic renal disease: early identification and active management of patients with renal impairment in primary care can improve outcomes. *BMJ*. 2002;325(7355):85-90.
- Romão Jr JE. Doença renal crônica: definição, epidemiologia e classificação. *J Bras Nefrol*. 2004;26(3 Supl 1):S1-3.
- Grassmann A, Gioberge S, Moeller S, Brown G. ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. *Nephrol Dial Transplant*. 2005;20(12):2587-93.
- Violan MA, Pomes T, Maldonado S, Roura G, De la Fuente I, Verdaguer T, et al. Exercise capacity in hemodialysis and renal transplant patients. *Transplant Proc*. 2002;34(1):417-8.
- McIntyre CW, Selby NM, Sigrist M, Pearce LE, Mercer TH, Nais PF. Patients receiving maintenance dialysis have more severe functionally significant skeletal muscle wasting than patients with dialysis-independent chronic kidney disease. *Nephrol Dial Transplant*. 2006;21(8):2210-6.
- Quintanilla AP, Sahgal V. Uremic myopathy. *Inter J Artif Org*. 1984;7(5):239-42.
- Fahal IH, Bell GM, Bone JM, Edwards RH. Physiological abnormalities of skeletal muscle in dialysis patients. *Nephrol Dial Transplant*. 1997;12(1):119-27.
- Adey D, Kumar R, McCarthy JT, Nair KS. Reduced synthesis of muscle proteins in chronic renal failure. *Am J Physiol Endocrinol Metab*. 2000;278(2):E219-25.
- Cupisti A, Licitra R, Chisari C, Stampacchia G, D'Alessandro C, Galetta F, et al. Skeletal muscle and nutritional assessment in chronic renal failure patients on a protein-restricted diet. *J Inter Med*. 2004;255(1):115-24.
- Tarasuik A, Heimer D, Bark H. Effect of chronic renal failure on skeletal and diaphragmatic muscle contraction. *Am Rev Respir Dis*. 1992;146(6):1383-8.
- Kemp GJ, Crowe AV, Anijeet HK, Gong QY, Bimson WE, Frostick SP, et al. Abnormal mitochondrial function and muscle wasting, but normal contractile efficiency, in haemodialysed patients studied non-invasively in vivo. *Nephrol Dial Transplant*. 2004;19(6):1520-7.
- Sakkas GK, Sargean AJ, Mercer TH, Baal D, Koufaki P, Karatzaferi C, et al. Changes in muscle morphology in dialysis patients after 6 months of aerobic exercise training. *Nephrol Dial Transplant*. 2003;18(9):1854-61.
- Marrades RM, Roca J, Campistol JM, Diaz O, Barberá JÁ, Torregosa JV, et al. Effects of erythropoietin on muscle O<sub>2</sub> transport during exercise in patients with chronic renal failure. *J Clin Invest*. 1996;97(9):2092-100.
- Karacan O, Tatal E, Colak T, Sezer S, Eyüboğlu FO, Haberal M. Pulmonary function in renal transplant recipients and end-stage renal disease patients undergoing maintenance dialysis. *Transplant Proc*. 2006;38(2):396-400.
- Moreira PR, Barros E. Atualização em fisiologia e fisiopatologia renal: bases fisiopatológicas da miopatia na insuficiência renal crônica. *J Bras Nefrol*. 2000;22(1):34-8.
- Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Hypertension*. 2003;42(5):1050-65.
- Bardin T. Musculoskeletal manifestations of chronic renal failure. *Curr Opin Rheumatol*. 2003;15(1):48-54.
- Van Balkom RH, Zhan WZ, Prakash YS, Dekhuijzen PN, Sieck GC. Corticosteroid effects on isotonic contractile properties of rat diaphragm muscle. *J Appl Physiol*. 1997;83(4):1062-7.
- Koerts-de Lang E, Schols AM, Rooyackers OE, Gayan-Ramirez G, Decramer M, Wouters EF. Different effects of corticosteroid-induced muscle wasting compared with undernutrition on rat diaphragm energy metabolism. *Eur J Appl Physiol*. 2000;85(5-6):493-8.
- Mitsui T, Azuma H, Nagasawa M, Iuchi T, Akaike M, Odomi M, et al. Chronic corticosteroid administration causes mitochondrial dysfunction in skeletal muscle. *J Neurol*. 2002;249(8):1004-9.
- Kovelis D, Pitta FO, Probst VS, Peres CPA, Delfino VDA, Mocelin AJ, et al. Função pulmonar e força muscular respiratória em pacientes com doença renal crônica submetidos à hemodiálise. *J Bras Pneumol*. 2008;34(11):907-12.
- Standardization of spirometry, 1994 Update. American Thoracic Society. *Am J Respir Crit Care Med*. 1995;152(3):1107-36.
- Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. Changes in the normal maximal expiratory flow-volume curve with growth and aging. *Am Rev Respir Dis*. 1983;127(6):725-34.
- Sociedade brasileira de pneumologia e fisiologia. Diretrizes para testes de função pulmonar. *J Bras Pneumol*. 2002;28(Supl 3):S1-238.
- Black LF, Hyatt RE. Maximal respiratory pressures: normal values and relationship to age and sex. *Am Rev Respir Dis*. 1969;99(5):969-74.
- 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):719-27.
- Bellinetti LM, Thomson JC. Avaliação muscular respiratória nas toracotomias e laparotomias superiores eletivas. *J Bras Pneumol*. 2006;32(2):99-105.

28. Guyatt GH, Sullivan MJ, Thompson PJ, Fallen EL, Pugsley SO, Taylor DW, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. *Can Med Assoc J.* 1985;132(8):919-23.
29. Troosters T, Gosselink R, Decramer M. Six minute walking in healthy elderly subjects. *Eur Respir J.* 1999;14(2):270-4.
30. ATS Committee standards for clinical pulmonary function laboratories. ATS Statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med.* 2002;166(1):111-7.
31. Kalender B, Erk M, Pekpak MA, Apaydin S, Ataman R, Serdengeçti K, et al. The effect of renal transplantation on pulmonary function. *Nephron.* 2002;90(1):72-7.
32. Guleria S, Agarwal RK, Guleria R, Bhowmik D, Agarwal SK, Tiwari SC. The effect of renal transplantation on pulmonary function and respiratory muscle strength in patients with end-stage renal disease. *Transplant Proc.* 2005;37(2):664-5.
33. Karacan O, Tural E, Uyar M, Eyüboğlu FO, Sezar S, Özdemir FN. Pulmonary function in uremic patients on long-term hemodialysis. *Ren Fail.* 2004;26(3):273-8.
34. Bush A, Gabriel R. Pulmonary function in chronic renal failure: effects of dialysis and transplantation. *Thorax.* 1991;46(6):424-8.
35. Ulubay G, Akman B, Sezer S, Calik K, Eyuboglu Oner F, Ozdemir N, et al. Factors affecting exercise capacity in renal transplantation candidates on continuous ambulatory peritoneal dialysis therapy. *Transplant Proc.* 2006;38(2):401-5.
36. 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.
37. Oh-Park M, Fast A, Gopal S, Lynn R, Frei G, Drenth R, et al. Exercise for the dialyzed: aerobic and strength training during hemodialysis. *Am J Phys Med Rehabil.* 2002;81(11):814-21.
38. Becker-Cohen R, Nir A, Rinat C, Feinstein S, Algur N, Farber B, et al. Risk factors for cardiovascular disease in children and young adults after renal transplantation. *Clin J Am Soc Nephrol.* 2006;1(6):1284-92.
39. Sietsema KE, Amato A, Adler SG, Brass EE. Exercise capacity as a predictor of survival among ambulatory patients with end-stage renal disease. *Kidney Int.* 2004;65(2):719-24.
40. Reboredo MM, Henrique DMN, Faria RS, Bergamini BC, Bastos MG, Paula RB. Correlação entre a distância obtida no teste de caminhada de seis minutos e o pico de consumo de oxigênio em pacientes portadores de doença renal crônica em hemodiálise. *J Bras Nefrol.* 2007;29(2):85-9.
41. Leavey SF, McCullough KM, Hecking E, Goodkin D, Port FK, Young EW. Body mass index and mortality in 'healthier' as compared with 'sicker' haemodialysis patients: results from the dialysis outcomes and practice patterns study (DOPPS). *Nephrol Dial Transplant.* 2001;16(12):2386-94.