

## Evaluation of maximum respiratory pressures in chronic renal patients at the pre and post hemodialysis moment

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### ABSTRACT

**Introduction and Objective:** Maximal inspiratory and expiratory pressures ( $PI_{max}$  and  $PE_{max}$ ) are used to assess the integrity of respiratory muscles by measuring their strength. The aim of this study was to assess the immediate influence of hemodialysis (HD) on respiratory muscle strength by measuring  $PI_{max}$  and  $PE_{max}$ , investigating the integrity of that musculature and/or the presence of muscular weakness. **Method:** A prospective, cross-sectional study was carried out on a convenience sample of 35 patients with chronic kidney disease (26 men and 9 women; mean age,  $51.7 \pm 14.7$  years) at the Nephrology Division of the Hospital Universitário Alzira Vellano, in the city of Alfenas, in the state of Minas Gerais, Brazil. Patients had their  $PI_{max}$  and  $PE_{max}$  taken in the seated position (at  $90^\circ$ ) by using a digital manovacuometer (MVD 300®) attached to a notebook for reading and recording data obtained before and after the HD session. **Results:** Both  $PI_{max}$  and  $PE_{max}$  were lower than the values predicted for pre- and post-HD ( $p < 0.0001$ ). Comparing the values obtained pre-HD and post-HD,  $PI_{max}$  showed a slight improvement ( $p = 0.0420$ ), evidenced only in patients with pre-HD values below  $60 \text{ cmH}_2\text{O}$  (Wilcoxon;  $p = 0.0480$ ). Post-HD  $PE_{max}$  did not differ from the pre-HD measure ( $p = 0.4987$ ). **Conclusion:** The CKD patients showed a serious impairment of their respiratory muscle function, and only one isolated HD session could not significantly improve their maximum respiratory pressures. A slight improvement in the inspiratory strength was observed in patients whose  $PI_{max}$  was lower than  $60 \text{ cmH}_2\text{O}$  before the procedure.

**Keyword:** muscular strength, chronic kidney failure, renal dialysis.

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### INTRODUCTION

Chronic kidney disease (CKD) is currently a problem of public health. Its incidence has increased and results mainly from the longer life expectancy and increased prevalence of diabetes mellitus and hypertension. The estimates for the year 2010 in the United States are of 520,000 dialysis patients and 178,000 renal transplants, with a projected increase in the population of patients with CKD of 4.1% per year.<sup>1</sup>

Among CKD patients undergoing dialysis, hemodialysis (HD) is the most frequently used modality (90.7%).<sup>2</sup> Such intervention is usually performed three times a week, three to four hours per session. Although advances in HD have improved the survival of those patients, significant changes in their quality of life have been shown.<sup>3,4</sup> The physical functioning of such patients has been shown to be decreased, including a reduction in physical activity, muscle weakness, anemia, ventricular dysfunction, and several metabolic and hormonal alterations.<sup>4</sup> Some studies have reported that HD patients are deeply physically unfit.<sup>3</sup>

Muscle performance can be assessed through muscle strength, endurance, and resistance to fatigue. The measurement of those characteristics provides significant indices for the functional evaluation of the respiratory musculature.<sup>5</sup>

Chronic kidney disease and all its metabolic alterations can result in a variety of physiopathological conditions that favor the development of respiratory muscle weakness. However, little is known about the performance of respiratory muscles and the acute effects of HD on them.

In addition, patients with CKD receiving dialysis treatment are subject to fast

changes in the volume and biochemical composition of body fluids, which may adversely affect respiratory muscle function.<sup>6,7</sup>

Maximum inspiratory (PI<sub>max</sub>) and expiratory (PE<sub>max</sub>) mouth pressures produced during static efforts are considered a reflex of the strength of the respiratory muscles. The relations of those maximum static pressures to age, sex, and general muscle development have been described by some authors<sup>8,9</sup>, as has been the influence of the lung volume in which the measurements were taken.<sup>10,11,12,13</sup> The most widely used test for assessing the overall strength of inspiratory and expiratory muscles consists in measuring maximum static mouth pressures.<sup>14</sup> Those tests have the advantage of being non invasive, and normal values have been well established in adults.<sup>8,15,16,17</sup>

A high PI<sub>max</sub> (> 80 cmH<sub>2</sub>O) or high PE<sub>max</sub> (> 90 cmH<sub>2</sub>O) exclude clinically significant inspiratory or expiratory weakness.<sup>18</sup>

A PI<sub>max</sub> value is considered to be low when below 60% of the predicted value, the latter being established based on variables, such as sex and age<sup>16</sup>, body weight<sup>19</sup>, and height.<sup>20</sup>

Values greater than 60 cmH<sub>2</sub>O clinically exclude respiratory muscle weakness<sup>18</sup> and there is consensus that patients with PI<sub>max</sub> £ @[sinal de menor??]@ 60 cmH<sub>2</sub>O need specific training of the respiratory muscles.<sup>21</sup>

Conventionally, PI<sub>max</sub> has been measured based on residual volume (RV) and PE<sub>max</sub> has been measured based on total lung capacity (TLC), by using a nasal clip. The highest pressure registered and sustained over a second represents PI<sub>max</sub> or PE<sub>max</sub>.<sup>22</sup>

Thus, the measurement of maximum respiratory pressures (PI<sub>max</sub> and PE<sub>max</sub>), routinely performed at the bedside with the aid of a portable vacuumeter, is a simple and useful procedure for assessing severely ill patients, which can be applied in a wide range of clinical situations, such as CKD patients on dialysis.<sup>23</sup>

This study aimed at measuring maximum respiratory pressures in patients with CKD undergoing routine HD, and to compare the results obtained with the predicted values in distinct moments (pre-HD and post-HD), assessing the immediate influence of the procedure on those values.

## PATIENTS AND METHODS

### PATIENTS

This was a prospective, descriptive, cross-sectional study in a convenience sample comprising 35 patients [9 smokers and 26 nonsmokers; 26 men (74.3%) and

9 women] with CKD secondary to several underlying diseases, routinely undergoing HD sessions at the HUAV. The study included patients aged ≥ 18 years with CKD of any etiology, undergoing HD for more than one month, aware, cooperative, who agreed to provide written informed consent. The following patients were excluded: age < 18 years; pregnant or lactating women; HD time shorter than one month; noncooperative; patients refusing to provide written informed consent.

All volunteers received information about their participations in the project and provided written informed consent, agreeing to take part in the study in accordance with Resolution 196/96 of the National Health Council. This study was approved by the Committee on Ethics and Research involving human beings of the Universidade de Alfenas – UNIFENAS, protocol n0 106/2005.

Data were collected from August to September 2005, at the HD unit of the hospital, in the city of Alfenas, Minas Gerais State.

A microprocessing equipment (digital vacuumeter, model MVD300®, MDI Produtos e Sistemas Ltda., series number 00000043) was used. It has a calibration certificate (number 0016/2005) and the following characteristics: measurement unit, cmH<sub>2</sub>O; resolution of 1 cmH<sub>2</sub>O; measuring capacity up to 500 cmH<sub>2</sub>O. The pattern used for calibration was codified as MVD300® n/s 14, calibrated on 07/27/2005, valid until 11/26/2005, and DIMCI 1984/2004 certification issued by INMETRO.

In addition to checking the pressures, the device provides, by use of a specific program, graphs and predicted values for each patient according to sex, age, weight, and height, based on a scientific article that evaluated and established values for the Brazilian population.<sup>16</sup> Such data were visualized on line, entered into the program of the device (software, version 1.4; hardware, version 1.27), and later analyzed.

The computer to which the MVD300® was coupled to was a Toshiba notebook, Pentium 1.6 GHz, of Intel-Centrino technology.

### METHODOLOGY

First, the volunteers received instructions on the study procedures, with a careful explanation about the technique to be used and an emphasis on its noninvasive character and virtual absence of contraindications.

All subjects, while still fasting, underwent weight and height measurements, and had their vital data checked. Then, their maximum respiratory pressures were taken, a procedure that, depending on their

understanding and cooperation, lasted, on average, approximately 15 minutes. After that, the patients were fed, and, then connected to the HD machine. The total time between weighing and beginning HD was estimated in 30 minutes. At the end of the HD session, right after disconnection from the HD machine, the patients were immediately weighed, had their vital data assessed and their maximum respiratory pressures measured again, being then sent to the cafeteria right after.

The subjects received instructions to breath connected to the MVD300® through a pressure line and individual mouth piece. In addition to being individualized, all material underwent sterilization with ethylene oxide at the HUAV.

No previous contact of the examiner with the patients occurred, the technique was non-invasive, and only the respiratory patterns necessary for each specific measure were explained to the subjects. The subjects underwent a short practice session before the valid measures were recorded aiming at getting them acquainted with the technique.

For measuring  $PI_{max}$ , a nasal clip was placed and the subject instructed to connect the mouth piece to the vacuumeter. Then, the subject was asked to empty his/her lungs by blowing as hard as possible, until RV level, and then to breath in maximally up to the TLC level, holding it in for one second. This maneuver was repeated three times, and its values were recorded by the equipment. The highest value recorded was used for analysis.

For measuring  $PE_{max}$ , the subject was asked to fill his/her lungs with air as much as possible, up to the TLC level, by breathing in deeply. Then, with the nasal clip on and the mouth piece correctly connected to the vacuumeter, the subject was asked to breath out maximally until RV level, and hold it out for one second. This maneuver was also repeated three times and the values were recorded by the equipment. The highest value recorded was used for analysis.

Then, the patient's records with the values obtained in the tests and the reference values predicted for each patient were analyzed.

## STATISTICS

The normality of data distribution was assessed by use of the Shapiro-Wilk test. For comparing the predicted inspiratory and expiratory pressures before and after HD, the paired Student *t* test and Wilcoxon test were used. Spearman coefficient was used to assess the existence of a correlation between the differences of the inspiratory and expiratory pressures and

the differences of weight before and after HD. The results were considered statistically significant when  $p < 0.05$ .

## RESULTS

The following descriptive characteristics of the population studied were observed: mean age, 51.7 years; mean pre-HD weight, 62.0 kg; mean post-HD weight, 60.0 kg; and mean HD time up to the date of examination, 654.0 days.

Of the patients, 74.3% were men, and considering the underlying diseases leading to CKD, diabetes mellitus was the major cause, being present in 40.0% of the patients.

Regarding  $PI_{max}$  and  $PE_{max}$  values, both the predicted values and those recorded before and after HD, as well as their differences in the two measuring occasions, and the pre- and post-HD weight, followed approximately a normal distribution (Shapiro-Wilk;  $p > 0.1000$ ). The following variables did not have a normal distribution (Shapiro-Wilk;  $p < 0.1000$ ): difference in weight (post-HD *versus* pre-HD); systolic and diastolic blood pressure; pre- and post-HD heart and respiratory rates. The maximum respiratory pressure values are shown in Table 1.

Using the paired *t* test for comparing maximum respiratory pressures before and after HD (Figures 1 and 2), both  $PI_{max}$  and  $PE_{max}$  in both occasions were significantly lower than those predicted for a normal population with similar demographic characteristics ( $p < 0.0001$ ). When comparing the pre-HD and post-HD values of each maximum respiratory pressure,  $PI_{max}$  showed a slight, but significant, improvement after the procedure ( $p = 0.0420$ ), but  $PE_{max}$  did not ( $p = 0.4987$ ).

The  $PI_{max}$  values before and after HD had an approximately normal distribution (Shapiro-Wilk;  $p > 0.1787$ ) for patients with values higher than 60 cmH<sub>2</sub>O. However, for patients with  $PI_{max}$  values lower than 60 cmH<sub>2</sub>O, the post-HD  $PI_{max}$  values did not follow that distribution (Shapiro-Wilk;  $p = 0.0082$ ).

Applying the paired *t* test for comparing  $PI_{max}$  before and after HD, no differences were found ( $p = 0.4669$ ) in patients with  $PI_{max}$  values higher than 60 cmH<sub>2</sub>O. However, applying the Wilcoxon test, a slight, but significant ( $p = 0.0480$ ), increase was observed in  $PI_{max}$  after HD for patients with values lower than 60 cmH<sub>2</sub>O before the procedure (Figure 3).

## DISCUSSION

Muscle weakness is a complication of CKD<sup>7,24,25</sup> and muscle mass loss is the most significant predictor of mortality in HD patients.<sup>26</sup> The cause is unknown, but has been related to carnitine deficiency<sup>25</sup>, vitamin D deficiency<sup>27</sup>, excessive amount of parathyroid hormone<sup>28</sup>, aluminum toxicity<sup>29</sup>, and other uremic toxins.<sup>30,31</sup> Uremia causes atrophy of type II muscle fibers<sup>29</sup> and alterations in myofibrillar ATPase, with an important reduction in energy use by the muscle, in creatine phosphorylation, and its contractility.<sup>32</sup>

Studies assessing the respiratory muscle function in patients with CKD are scarce.<sup>33</sup> Several studies<sup>34</sup> have shown a reduction in expiratory and inspiratory muscle strength, and even a greater reduction after HD.

All those alterations known in uremia cause a reduction in the respiratory pressures ( $PI_{max}$  and  $PE_{max}$ ) as already reported by the previously cited authors.

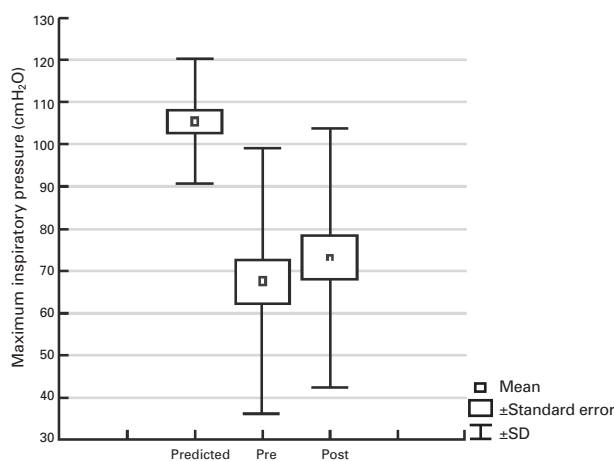
The results of this study have shown that patients with CKD on HD treatment have reductions in  $PI_{max}$  and  $PE_{max}$  as compared with the values predicted for a healthy Brazilian population with similar demographic characteristics (sex and age).<sup>16</sup> Patients showed a decrease in mean  $PI_{max}$  and  $PE_{max}$  in relation to the values predicted before and after HD. Both  $PI_{max}$  and  $PE_{max}$  before and after HD had mean values significantly lower than the predicted ones ( $p < 0.0001$ ), showing an important impairment of respiratory muscle strength in that group of patients.

Regarding  $PI_{max}$  measurements before and after HD, an approximately normal distribution was observed for patients with baseline values greater than 60 cmH<sub>2</sub>O, which is considered the lower limit of normality. However, post-HD  $PI_{max}$  did not follow that distribution for patients with baseline values lower than 60 cmH<sub>2</sub>O, which reflects the heterogeneity of that subgroup of patients in regard to the degree of CKD-induced impairment of respiratory function.

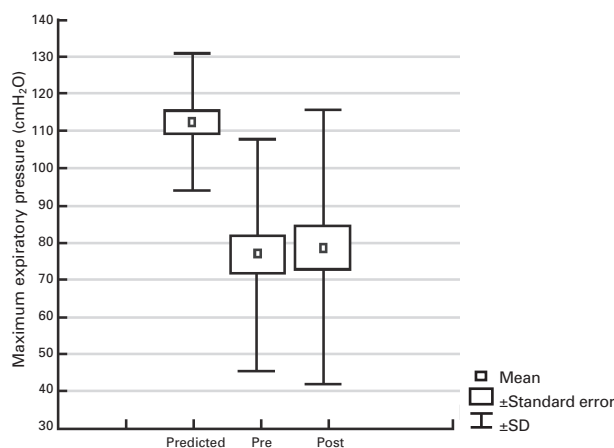
When comparing the pre-HD and post-HD  $PI_{max}$  values by using the paired t test, no differences were observed in patients with baseline values greater than 60 cmH<sub>2</sub>O ( $p = 0.4669$ ). However, by using the

Wilcoxon test, a slight increase in post-HD  $PI_{max}$  was observed as compared with the baseline period (pre-HD), which was statistically significant ( $p = 0.0480$ ).

**Figure 1.** Values of maximum inspiratory pressure: predicted, pre-hemodialysis and post-hemodialysis (n = 35). Pre-hemodialysis and post-hemodialysis  $PI_{max} <$  predicted value ( $p < 0.0001$ ); post-hemodialysis  $PI_{max} >$  pre-hemodialysis  $PI_{max}$  ( $p = 0.0420$ ).



**Figure 2.** Values of maximum expiratory pressure: predicted, pre-hemodialysis and post-hemodialysis (n = 35). Pre-hemodialysis and post-hemodialysis  $PE_{max} <$  predicted value ( $p < 0.0001$ ); post-hemodialysis  $PE_{max}$  similar to pre-hemodialysis  $PE_{max}$  ( $p = 0.4987$ ).

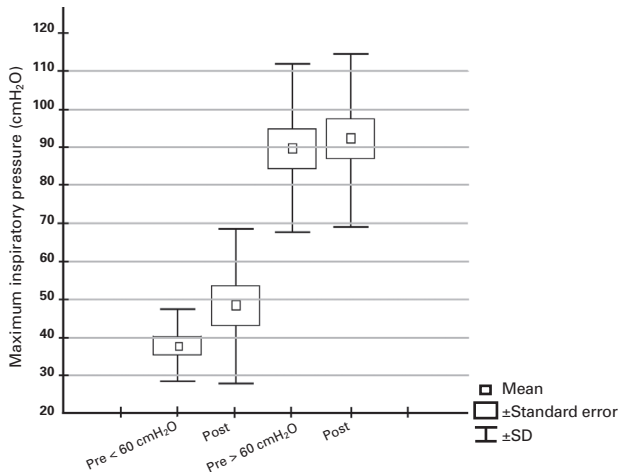


**Table 1**

PREDICTED, PRE- AND POST-HEMODIALYSIS VALUES OF MAXIMUM RESPIRATORY PRESSURES ( $PI_{MAX}$  AND  $PE_{MAX}$ ; CMH<sub>2</sub>O) (N = 35) ( $p > 0.1000$ )

| Pressure  | $PI_{max}$ |      |         |         | $PE_{max}$ |      |         |         |
|-----------|------------|------|---------|---------|------------|------|---------|---------|
|           | Mean       | SD   | Minimum | Maximum | Mean       | SD   | Minimum | Maximum |
| Predicted | 105.5      | 15.0 | 78.0    | 131.0   | 112.5      | 18.4 | 75.0    | 141.0   |
| Pre-      | 67.5       | 31.4 | 20.0    | 145.0   | 76.9       | 31.1 | 30.0    | 162.0   |
| Post-     | 73.2       | 30.7 | 30.0    | 143.0   | 79.0       | 36.7 | 24.0    | 158.0   |

**Figure 3.** Behavior of post-hemodialysis  $PI_{max}$  in subgroups of patients with pre-hemodialysis values lower or higher than  $60\text{ cmH}_2\text{O}$ . A statistically significant increase (post-hemodialysis versus pre-hemodialysis) was observed in the group with pre-hemodialysis values lower than  $60\text{ cmH}_2\text{O}$  ( $p = 0.0480$ ).



However, when comparing pre-HD and post-HD values of maximum inspiratory and expiratory pressures, post-HD  $PI_{max}$  slightly and significantly improved in relation to the baseline period ( $p = 0.0420$ ), but  $PE_{max}$  did not behave in the same way ( $p = 0.4987$ ). In addition, as already reported, when subgrouping the patients, HD sessions were observed to influence the  $PI_{max}$  increase only in patients with baseline values lower than  $60\text{ cmH}_2\text{O}$ , indicating that more severely ill patients seem to benefit more intensely from HD.

Some studies<sup>33,35</sup> have reported that patients with CKD showed significantly reduced  $PI_{max}$ , but a significant improvement of that pressure was observed after HD. Those results are partially in accordance with those obtained in the present investigation, in which a significant impairment in  $PI_{max}$  values was observed in patients with CKD as compared with those in a normal population. However, in our study, the isolated effect of a HD session on  $PI_{max}$  was not significant, except for a mild improvement in the subgroup of patients with a more severely impaired  $PI_{max}$ .

Still in regard to that aspect, some researchers have reported patients with CKD and significantly reduced pressures as compared with the normal population, which is in accordance with our data.<sup>34</sup> But unlike our findings and those of other authors,<sup>33,35</sup> many have reported worsening of those measures after HD.<sup>34</sup> Such reports were based on the rapid changes induced by dialysis in calcium concentration in the intra- and extracellular spaces to explain alterations in muscle function.

A previously cited study<sup>33</sup> investigated the inspiratory muscle strength of 21 patients (13 men and 8 women; age range, 27 to 78 years) with CKD undergoing chronic HD. The authors have reported that  $PI_{max}$  was significantly reduced in all patients, except one, before the HD session, as compared with the predicted reference values. After HD, a significant increase in  $PI_{max}$  (from  $52.9 \pm 3.5\%$  to  $60.7 \pm 3.7\%$  of the predicted value;  $p < 0.0001$ ) was observed. However, when analyzing individual data, the results showed no significant correlation between inspiratory muscle strength before HD and the duration of HD treatment.

Studies assessing the performance of respiratory muscles in patients with CKD undergoing continuous dialysis treatment are scarce, but almost all of them postulate that dialysis, although vital for those patients, seems to have no effect, or even adverse effects, on the performance of different muscle groups.<sup>34</sup> In short, the results obtained in the present investigation, added to those available in the literature, show that isolated HD seems to have varied effects on the respiratory muscle function, from an evident improvement to no significant influence, or even worsening.<sup>34</sup> Such conflicting results indicate that more studies with comparable populations and methods are still required to clarify that issue.

One limitation of the present study relates to the non standardization of the technique for measuring maximum respiratory pressures. This has hindered the comparison between the several reports in the literature.

The  $PI_{max}$  and  $PE_{max}$  tests are volitive, because they rely on the understanding and collaboration of the participants. Thus, learning the technique has a positive or negative determinant effect on the results, characterizing a limitation of the technique.

For the tests, the subjects are required to learn the technique through previous training, a method that favors the obtainment of more authentic values of maximum respiratory pressures. This is achieved as the subject performs successive efforts, obtaining an increase in the mean value of the measures.

Thus, in this study, three measurements were taken, and the highest values obtained, for both inspiratory and expiratory measures, were considered the best pressures. When added to the assays preceding the maneuvers, approximately five measures were taken for each patient, and it is difficult to state with certainty that such number of measurements was ideal.

Other limiting factors of this study include some particular characteristics of the population investigated. Most patients were at an advanced age, had a low educational and cooperation level, were on an extremely impaired general condition, and tired. Many of them lived in neighboring cities, had to travel on public transportation in an uncomfortable way, in addition to having to wake up much earlier than usually, observing longer fasting periods, and waiting longer, which certainly ended in aggravating their fatigue and feelings of sickness.

Considering those characteristics and the fact that intense and sometimes fast changes occur in the clinical condition of those patients, in order to obtain more reliable respiratory pressure values in that population, this measuring method should be applied not only in one single day. It should be applied in more than one occasion, such as every other day, and for a longer period (two to four weeks), aiming at obtaining a more significant number of values so as to more clearly assess the existence of other influencing factors besides the HD procedure itself.

The results of our study have shown a statistically significant, although slight, improvement in  $PI_{max}$ , but not in  $PE_{max}$ , post-HD *versus* pre-HD. This supports the findings of some researchers that one single HD session does not seem to be enough to positively influence those variables from the clinical view point.

However, during the study, the intense clinical and emotional impairment of those patients was evident, as was the certainty of its progression. Several organs, especially the lungs, are impaired due to CKD.

Measuring and monitoring respiratory muscle function through  $PI_{max}$  and  $PE_{max}$  measures in CKD patients, in addition to other tests for lung function assessment, is a simple and important way to plan interventions that can benefit them, reducing morbidity and mortality, and improving their quality of life. In conditions of respiratory muscle weakness, mainly inspiratory ( $PI_{max} < 60 \text{ cmH}_2\text{O}$ ), a protocol for early muscle strengthening can be initiated in an attempt to avoid greater problems, such as respiratory failure due to ventilation deficit.

## CONCLUSION

The results of our study have shown that patients with CKD on HD have significant alterations in maximum respiratory pressures, both inspiratory and expiratory, which are significantly reduced in relation to normal reference values. One single HD session in isolation slightly, positively, and significantly influenced  $PI_{max}$ ,

but not  $PE_{max}$ , as compared with baseline values (pre-dialysis). This positive influence on  $PI_{max}$  was more evident in patients with a more marked impairment of that variable before dialysis. Those data indicate that more adequate monitoring of the respiratory muscle function of CKD patients is required to prevent greater risks of deterioration and impairment.

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