



# Impact of continuous positive airway pressure on the pulmonary changes promoted by immersion in water

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## ABSTRACT

**Objective:** To determine whether different levels of CPAP improve the lung volumes and capacities of healthy subjects immersed in water. **Methods:** This was a randomized clinical trial, conducted between April and June of 2016, involving healthy female volunteers who were using oral contraceptives. Three 20-min immersion protocols were applied: control (no CPAP); CPAP5 (CPAP at 5 cmH<sub>2</sub>O); and CPAP10 (CPAP at 10 cmH<sub>2</sub>O). We evaluated HR, SpO<sub>2</sub>, FVC, FEV<sub>1</sub>, the FEV<sub>1</sub>/FVC ratio, peak expiratory flow rate (PEFR), and FEF<sub>25-75%</sub> at three time points: pre-immersion; 10 min after immersion; and 10 min after the end of each protocol. **Results:** We evaluated 13 healthy volunteers. The CPAP10 protocol reversed the restrictive pattern of lung function induced by immersion in water, maintaining pulmonary volumes and capacities for a longer period than did the CPAP5 protocol. **Conclusions:** When the hemodynamic change causing a persistent lung disorder, only the application of higher positive pressures is effective in maintaining long-term improvements in the pulmonary profile.

**Keywords:** Physical therapy modalities; Noninvasive ventilation; Continuous positive airway pressure.

## INTRODUCTION

Immersion in water results in physiological alterations to various systems, including the musculoskeletal, renal, respiratory, and cardiovascular systems.<sup>(1)</sup> The hydrostatic pressure compresses the thoracic cavity, reducing its circumference, which promotes cranial displacement of the diaphragm.<sup>(2)</sup> In healthy individuals, the cardiovascular effects, which include increases in venous return, blood volume, and central venous pressure, result in increased cardiac output, greater left atrial diameter, and higher cardiac volume.<sup>(3-5)</sup>

Cardiorespiratory changes induced by immersion in water reduce the end-expiratory volume and the length-tension ratio of the respiratory muscles, decreasing their capacity to generate and maintain adequate force, thus reducing MIP and MEP.<sup>(2)</sup> Such changes also increase pulmonary capillary pressure, which worsens lung function, reducing VC, FEV<sub>1</sub>, and functional residual capacity, thereby leading to the development of a restrictive pattern of lung function.<sup>(2,3,6)</sup> In fact, in clinical practice, many cardiopulmonary diseases induce a restrictive pattern as a consequence of pulmonary congestion, via mechanisms similar to those promoted by immersion in water.

The therapeutic arsenal used by physiotherapists in the treatment of pulmonary congestion and its respiratory complications includes respiratory exercises, incentive spirometry, and noninvasive positive-pressure ventilation

(NPPV).<sup>(7,8)</sup> In a study involving the induction of restrictive pulmonary characteristics by immersion in water, Vepo et al.<sup>(9)</sup> found that neither respiratory exercises nor incentive spirometry were effective in normalizing lung function during the immersion.

Applying NPPV in the continuous positive airway pressure (CPAP) mode has been shown to improve the hemodynamic status of patients with pulmonary congestion due to heart failure, reducing cardiac preload and afterload, thus increasing lung compliance and lung volumes, as well as reducing the work of breathing.<sup>(10)</sup> Other studies have shown that, in patients with heart disease, NPPV reduces venous return, pulmonary capillary pressure, and central venous pressure, consequently normalizing pulmonary function.<sup>(11,12)</sup>

Some therapeutic approaches do not reverse the restrictive pattern of lung function during the maintenance of hemodynamic changes in this model of pulmonary congestion induced by immersion in water, and there is evidence that NPPV, in CPAP mode, constitutes an important therapeutic tool for the treatment of this condition. It is therefore imperative to investigate the effects that NPPV has on the hemodynamic changes that induce the restrictive pattern characteristic of pulmonary congestion. Therefore, the objective of this study was to determine whether the use of NPPV in CPAP mode at various pressures improves lung volumes and capacities in healthy subjects immersed in water.

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## METHODS

### Study design and subject selection

This was a randomized clinical trial, conducted between April and June of 2016 at a federal university in the Brazilian state of Rio Grande do Sul. All procedures were performed in accordance with Brazilian National Health Council Resolution no. 466/12, and the study was approved by the research ethics committee of the institution (CAEE no. 56861216.7.0000.5323). All participating subjects gave written informed consent.

The sample, determined by sample size calculation for the analysis of quantitative variables of a proportion of a population of infinite size, considering a 95% confidence level, a 5% maximum error of estimation, and an estimated prevalence of 50%, was composed of volunteers who met the following criteria: being healthy; being female; being between 18 and 40 years of age; using oral contraceptives during the study period (to ensure homogeneity of the sample, considering that the use of oral contraceptives stabilizes the levels of female sex hormones, thus avoiding possible changes in lung function due to hormonal fluctuations occurring during the various phases of the menstrual cycle); and having given written informed consent. We excluded subjects who, for any reason, did not participate in all stages of the study; subjects who were unable to perform the maneuvers involved in the assessment and the NPPV; subjects who showed some alteration during spirometry; subjects who presented cardiovascular, respiratory, neurological, or musculoskeletal diseases; subjects who were on medication (except oral contraceptives); and subjects who were smokers or former smokers.

### Data collection

The volunteers were submitted to anamnesis (regarding general health status, associated diseases, and medication use) and physical examination (to determine weight, height, and body mass index), performed by a single evaluator according to the standardized criteria established by the International Society for the Advancement of Kinanthropometry.<sup>(13)</sup> The subjects also underwent cardiopulmonary evaluation, in which HR, SpO<sub>2</sub>, systolic blood pressure, and diastolic blood pressure were determined in accordance with the recommendations made in the Fourth Brazilian Guidelines for the Management of Hypertension.<sup>(14)</sup> We analyzed pulmonary function by spirometry (Koko Legend®; nSpire Health Inc., Hertford, UK), in accordance with the criteria established by the American Thoracic Society/European Respiratory Society<sup>(15)</sup> and the Brazilian Thoracic Association,<sup>(16)</sup> using the predicted values for FVC, FEV<sub>1</sub>, and the FEV<sub>1</sub>/FVC ratio, as well as for the peak expiratory flow rate (PEFR) and FEF<sub>25-75%</sub>, determined by Pereira et al.<sup>(17)</sup>

We measured slow vital capacity with a respirometer (Wright Mark 8; Ferraris Respiratory, Louisville, CO, USA). We also measured MIP and MEP, using a manometer (MV 120; Comercial Médica, São Paulo,

Brazil), as described by Neder et al.<sup>(18)</sup> These evaluations were performed while the subjects were seated, as recommended in the Brazilian Thoracic Association guidelines.<sup>(16)</sup>

### Intervention protocols

Each volunteer was immersed in water up to the level of the xiphoid process, after which NPPV, in CPAP mode (BiPAP®; Respironics, Murrysville, PA, USA), was applied via face mask. In this immersion model, the reduction in pulmonary function is mainly due to cardiovascular alterations, which, in healthy individuals, simulate a restrictive pattern of lung function, as is typically observed in certain cardiorespiratory complications, such as pulmonary congestion.<sup>(9)</sup> Vepo et al.<sup>(9)</sup> employed this model and reported that, by 10 min after immersion in water, subjects showed reductions in FVC and FEV<sub>1</sub> induced by hemodynamic changes, including increased blood volume and higher central venous pressure.

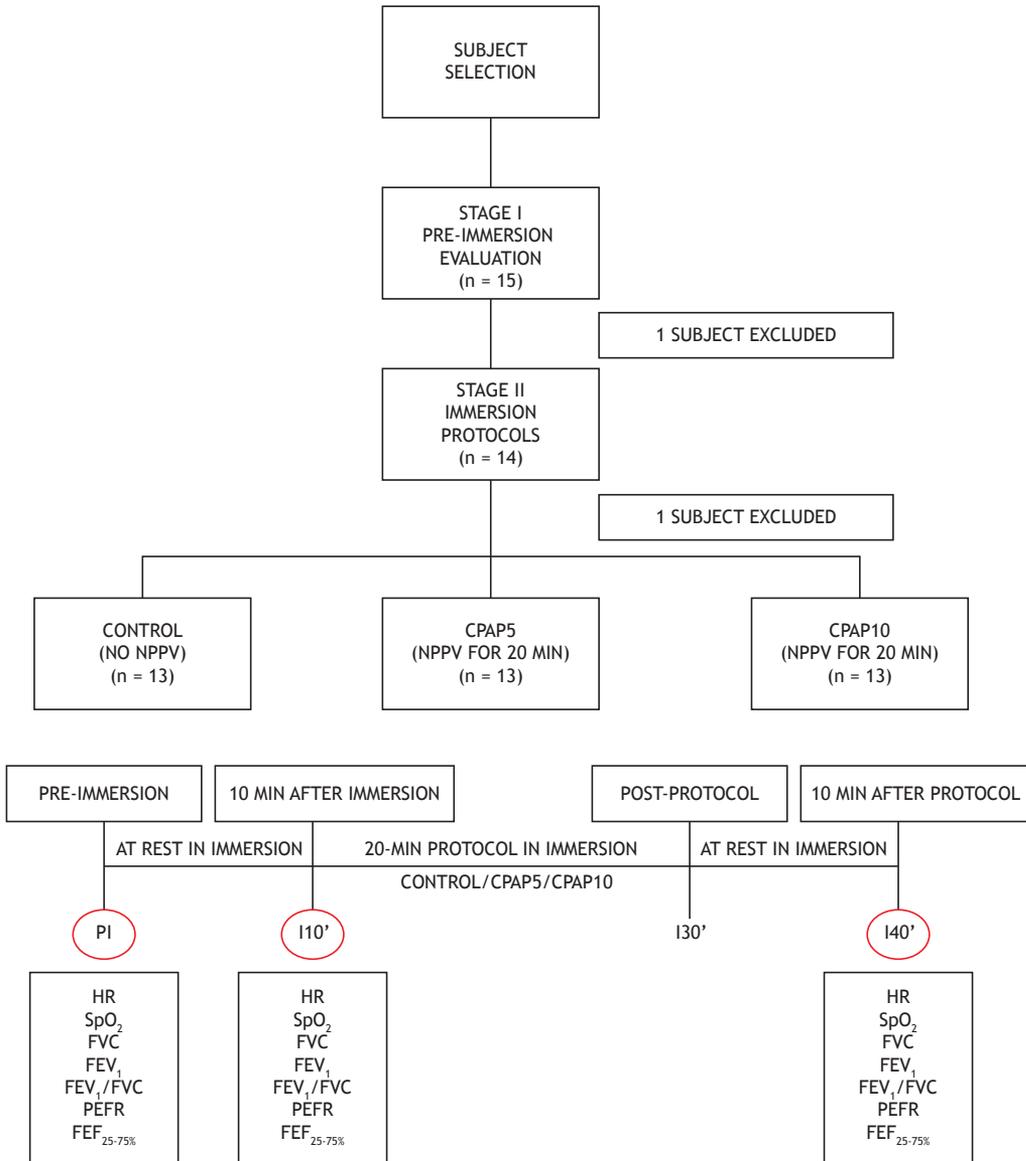
All subjects participated in three NPPV immersion protocols, with an interval of at least 24 h between each application, in a sequence defined by block randomization, as shown in Figure 1. The protocols lasted for 20 min each and were given the following designations: control—during spontaneous breathing, at rest and without ventilatory support; CPAP5—CPAP of 5 cmH<sub>2</sub>O, according to Reis et al.<sup>(19)</sup>; and CPAP10—CPAP of 10 cmH<sub>2</sub>O, according to Bellone et al.<sup>(20)</sup> During the application of each protocol, the variables FC, SpO<sub>2</sub>, FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC ratio, PEFR, and FEF<sub>25-75%</sub> were evaluated at the following time points (Figure 1): before immersion in water (pre-immersion); at 10 min after immersion in water; and at 10 min after the end of the protocol (i.e., 40 min after the initiation of the protocol).

### Statistical analysis

The results are expressed as means and standard deviations. The Shapiro-Wilk test was used in order to determine the distribution of the data, which was found to be normal for all of the variables analyzed. The data were analyzed by one-way repeated-measures ANOVA and Fisher's post-hoc test, as appropriate. Values of  $p < 0.05$  were considered significant. The program GraphPad Prism, version 6.01 (GraphPad Inc., San Diego, CA, USA) was used for the statistical analyses and for the creation of the graphics.

## RESULTS

Of the 15 volunteers evaluated, 2 were excluded: for presenting with spirometric changes at the initial evaluation ( $n = 1$ ); and for not participating in all of the stages of data collection ( $n = 1$ ). The final sample therefore comprised 13 volunteers, with a mean age of  $23.6 \pm 5.5$  years. As can be seen in Table 1, the anthropometric characteristics of the volunteers were within the limits of normality for age and gender, as were the cardiovascular and respiratory parameters evaluated before the application of the protocols.



**Figure 1.** Study design and outline of the application of non-invasive positive pressure ventilation protocols (VNIPP). CPAP: continuous positive airway pressure; and PEFR: peak expiratory flow rate.

At 10 min after immersion in water, all of the subjects showed reductions in FVC and FEV<sub>1</sub>, suggesting a restrictive alteration to the pulmonary pattern, as previously observed by Vepo et al.<sup>(9)</sup> Those reductions persisted at 10 min after the end of the control protocol and at 10 min after the end of the CPAP5 protocol. However, the pulmonary changes induced by immersion were normalized after application of the CPAP10 protocol (Figure 2).

The FEV<sub>1</sub>/FVC ratio also showed a reduction at 10 min after immersion, in all subjects and in all three protocols. In accordance with the reductions in FVC and FEV<sub>1</sub>, the reduction in the FEV<sub>1</sub>/FVC ratio persisted at 10 min after the application of the control and CPAP5 protocols, as well as being reversed after the application of the CPAP10 protocol (Figure 3). The

PEFR and FEF<sub>25-75%</sub> values were also decreased at 10 min after immersion in water. At 10 min after the end of the CPAP5 and CPAP10 protocols, the PEFR values were normalized, although neither protocol was able to normalize the FEF<sub>25-75%</sub> values (Table 2).

In the cardiorespiratory evaluation, a reduction in HR was observed at 10 min after immersion in water, and that reduction persisted at all of the evaluation time points, for all of the protocols. However, no changes were observed for SpO<sub>2</sub>, which remained at basal values after immersion and at all other evaluation time points, for all of the protocols (Table 2).

## DISCUSSION

In the present study, we demonstrated that the application of CPAP at 10 cmH<sub>2</sub>O can restore the

**Table 1.** Initial physical, respiratory and cardiovascular evaluation of the subjects evaluated (n = 13).<sup>a</sup>

Parameter	Value
Age, years	23.6 ± 5.5
Height, m	1.60 ± 0.02
Weight, kg	63.7 ± 11.6
BMI, kg/m <sup>2</sup>	23.6 ± 3.5
HR, bpm	76.2 ± 6.4
SBP, mmHg	120.5 ± 8.6
DBP, mmHg	71.9 ± 7.7
SpO <sub>2</sub> , %	98.4 ± 0.8
MIP, cmH <sub>2</sub> O	98.5 ± 26.3
MEP, cmH <sub>2</sub> O	103.1 ± 26.5
SVC, L	3.3 ± 0.3
SVC, % of predicted	82.2 ± 3.0
FVC, L	3.9 ± 0.6
FVC, % of predicted	98.9 ± 11.4
FEV <sub>1</sub> , l	3.5 ± 0.5
FEV <sub>1</sub> , % of predicted	99.9 ± 10.7
FEV <sub>1</sub> /FVC	0.9 ± 0.1
FEV <sub>1</sub> /FVC, %	98.0 ± 7.0
PEFR, L/min	8.4 ± 1.7
PEFR, % of predicted	106.2 ± 16.3
FEF <sub>25-75%</sub> , L/min	4.4 ± 1.1
FEF <sub>25-75%</sub> , % of predicted	95.2 ± 19.9

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; SVC: slow vital capacity; PEFR: peak expiratory flow rate. <sup>a</sup>Values expressed as mean ± SD.

restrictive pattern of lung function induced by immersion in water in healthy individuals, maintaining pulmonary volumes and capacities at normal levels for a longer period when compared with CPAP at 5 cmH<sub>2</sub>O. To our knowledge, this is the first study suggesting that, in situations in which a hemodynamic change that causes a restrictive pattern of lung function persists, the application of higher positive pressures is an effective means of maintaining improvements in the pulmonary profile.

Hemodynamic changes during immersion in water occur in part by hemodilution due to the transfer of fluid—from the interstitial spaces to the intravascular spaces—within the lower limbs.<sup>(5,21)</sup> In the respiratory system, those changes promote reductions in pulmonary volumes and capacities, characteristic of a restrictive pattern.<sup>(22)</sup>

In clinical practice, pulmonary complications due to cardiovascular changes lead to a restrictive pulmonary pattern, mainly due to the increase in intrathoracic blood volume. In patients with heart disease, pulmonary congestion, which is characterized by elevated pulmonary and systemic venous pressures, is usually related to ventricular dysfunction and a reduction in cardiac output.<sup>(23,24)</sup> Left untreated, pulmonary congestion can progress to pulmonary edema, which constitutes a medical emergency.<sup>(23-25)</sup>

The model of a restrictive pattern of lung function used in the present study, as previously described by

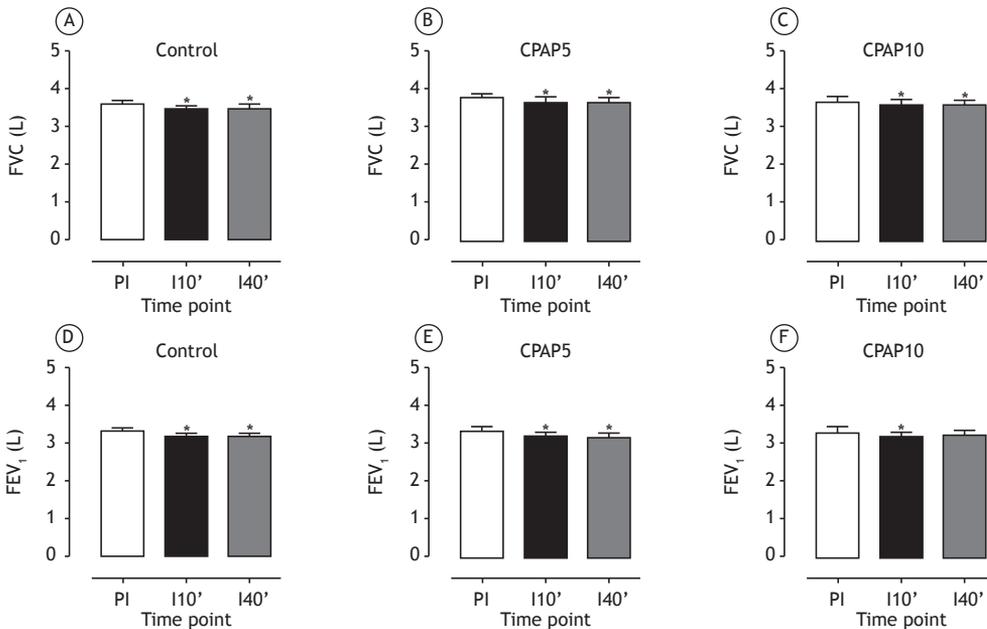
Vepo et al.,<sup>(9)</sup> uses immersion in water to promote increased central blood volume in healthy subjects and, consequently, hemodynamic changes similar to those developed in patients with pulmonary congestion. Thus, this model allows the analysis and clarification of the effects of CPAP exclusively on changes in lung volumes and capacities promoted by isolated hemodynamic factors, avoiding the risk that associated diseases will influence the findings.

After applying CPAP to subjects immersed in water, we found that only the use of a CPAP level of 10 cmH<sub>2</sub>O provided sustained improvements in lung volumes and capacities. This suggests that when the hemodynamic changes that contribute to congestive pulmonary disease are not controlled, higher positive pressures are required in order to maintain improvements in lung function. Likewise, Vepo et al.<sup>(9)</sup> observed no improvements in lung volumes and capacities when respiratory exercises and incentive spirometry were applied in subjects immersed in water, suggesting that these techniques do not provide the expected benefits when the primary hemodynamic change is not controlled or reversed.

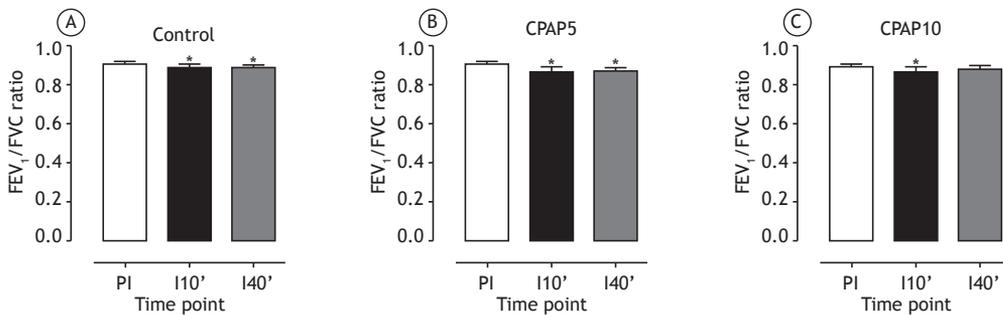
Although pharmacotherapy, with diuretics and vasodilators, is an essential tool in combating fluid retention and relieving the respiratory symptoms of pulmonary congestion,<sup>(24,26,27)</sup> the use of pharmacotherapy in combination with positive pressure has become increasingly more widespread as a means of normalizing the hemodynamic status of patients with pulmonary congestion and of preventing its recurrence. Therefore, CPAP is a mode of ventilation applied in a wide spectrum of clinical situations<sup>(28)</sup> and is often indicated for patients in critical condition, such as those with acute cardiogenic pulmonary edema (ACPE). In such cases, the Brazilian Guidelines on Mechanical Ventilation<sup>(28)</sup> recommend the use of CPAP at 5-10 cmH<sub>2</sub>O, which justifies the choice of pressures employed in the present study.

The pulmonary benefits derived from CPAP are due, in large part, to the elevation of intrathoracic pressure and consequent reduction of left ventricular afterload promoted by the pressurization of the airways. That pressurization consequently increases cardiac output, promoting improvements in lung volumes and capacities, thus reducing respiratory distress.<sup>(11,12)</sup> The hemodynamic effects of CPAP have been fully elucidated for the population of patients with pulmonary hypertension due to left ventricular dysfunction. However, our study demonstrated that, when the cause of the hemodynamic imbalance persists, the improvement in pulmonary function is maintained only when higher CPAP is applied to the airways, regardless of the pulmonary improvements observed immediately after application of the technique.

Although numerous studies have involved the application of CPAP for the treatment of cardiogenic pulmonary edema, using the same range of positive pressures employed in the present study, those studies have varied in terms of the effects that such pressures



**Figure 2.** FVC and FEV<sub>1</sub> in the control protocol (in A and D, respectively), the CPAP5 (5 cmH<sub>2</sub>O) protocol (in B and E, respectively), and the CPAP10 (10 cmH<sub>2</sub>O) protocol (in C and F, respectively), at the time points evaluated (data expressed as mean ± SD). CPAP: continuous positive airway pressure; PI: pre-immersion; I10': 10 min after immersion; I40': 10 min after the end of the (20-min) protocol. \*p < 0.05 vs. PI (one-way repeated-measures ANOVA and Fisher's post-hoc test).



**Figure 3.** FEV<sub>1</sub>/FVC ratio in the control protocol (in A), the CPAP5 (5 cmH<sub>2</sub>O) protocol (in B), and the CPAP10 (10 cmH<sub>2</sub>O) protocol (in C), at the time points evaluated (data expressed as mean ± SD). CPAP: continuous positive airway pressure; PI: pre-immersion; I10': 10 min after immersion; I40': 10 min after the end of the (20-min) protocol. \*p < 0.05 vs. PI (one-way repeated-measures ANOVA and Fisher's post-hoc test).

**Table 2.** Cardiovascular and respiratory parameters evaluated in the immersion protocols.<sup>a</sup>

Parameter	Control			CPAP5			CPAP10		
	PI	I10'	I40'	PI	I10'	I40'	PI	I10'	I40'
HR, bpm	93.5 ± 15.1	78.8 ± 11.2*	79.8 ± 10.5*	101.3 ± 13.9	84.2 ± 10.4*	80.4 ± 13.5*	98.5 ± 14.4	82.2 ± 8.7*	78.4 ± 12.1*
SpO <sub>2</sub> , %	98.8 ± 1.0	98.5 ± 1.1	98.8 ± 0.9	98.3 ± 0.6	98.6 ± 0.9	98.8 ± 0.7	98.5 ± 1.7	98.5 ± 1.2	98.3 ± 1.9
PEFR, L/min	7.06 ± 1.3	7.0 ± 1.3*	6.9 ± 1.2	7.5 ± 1.1	7.2 ± 1.2*	7.3 ± 1.1	7.1 ± 1.0	6.6 ± 1.3*	6.9 ± 1.2
FEF <sub>25-75%</sub> , L/min	4.1 ± 0.7	3.9 ± 0.8*	3.8 ± 0.7*	4.3 ± 0.7	3.9 ± 0.6*	3.8 ± 0.6*	3.9 ± 0.8	3.9 ± 0.8	3.8 ± 0.7

CPAP5: CPAP of 5 cmH<sub>2</sub>O; CPAP10: CPAP of 10 cmH<sub>2</sub>O; PI: pre-immersion; I10': 10 min after immersion; I40': 10 min after the end of the (20-min) protocol; and PEFR: peak expiratory flow rate. <sup>a</sup>Values expressed as mean ± SD. \*p < 0.05 vs. PI (one-way repeated-measures ANOVA and Fisher's post-hoc test).

were found to have on mortality, ICU admission, and length of hospital stay, as well as in terms of the reported advantages of CPAP over conventional therapy.<sup>(20,29,30)</sup> It is known that CPAP increases survival and precludes the need for endotracheal intubation in patients with

ACPE.<sup>(29-31)</sup> However, in a randomized controlled study involving patients with ACPE, no differences were found between the patients receiving conventional oxygen therapy and those receiving CPAP in terms of the short- or long-term mortality rates.<sup>(32)</sup> The

divergences across studies are probably attributable to differences among the patient samples in terms of the associated clinical factors and the pharmacological interventions administered in combination with the CPAP. Both situations prevent the isolated analysis of the effects of CPAP on respiratory changes resulting from hemodynamic disturbances.

The reductions we observed in the other spirometric parameters, such as  $FEF_{25-75\%}$  and PEF, after immersion in water, were also reported by Vepo et al.<sup>(9)</sup> Those authors reported that  $FEF_{25-75\%}$  is directly dependent on the FVC values, its reduction therefore being expected during immersion. In addition, this parameter is known to be related to the distal airway permeability,<sup>(33)</sup> and it is reduced in proportion with the increase in intrathoracic blood volume and pulmonary capillary pressure observed in this model.

Regarding the cardiorespiratory parameters investigated, we demonstrated a reduction in HR in all of the protocols applied, which corroborates the findings of Kaneko et al.,<sup>(34)</sup> who employed a combination of CPAP and drug therapy in patients with ACPE. However, in our study, we were unable to associate that change with the application of positive airway pressure, because the same HR behavior was also observed in the control protocol. It has been suggested that the change observed results exclusively from immersion

in water.<sup>(35,36)</sup> The application of CPAP at 10 cmH<sub>2</sub>O has been shown to be superior to the conventional treatment for improving hypoxemia in patients with ACPE.<sup>(37)</sup> However, our study did not find significant differences between the CPAP protocols or the time points evaluated in terms of the SpO<sub>2</sub>, which could be related to the fact that our subjects were healthy and presented with normal SpO<sub>2</sub> values. It should be noted that our subjects reported fatigue after the application of the CPAP10 protocol, which might be attributable to the fact that they had normal pulmonary function and therefore had a lower tolerance to higher positive airway pressures. That might have limited the performance of the study participants during the spirometric evaluation performed immediately after the application of CPAP.

In summary, the findings of the present study suggest that the use of higher CPAP pressures is effective in maintaining improvements in lung volumes and capacities in situations in which the hemodynamic change causing the restrictive lung pattern persists. Our findings underscore the importance of adequately controlling the primary hemodynamic cause of pulmonary congestion, so that the combination of physiotherapeutic techniques and clinical practice will provide the maximum possible improvement of the respiratory changes present in this condition, for a longer period of time.

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