

# Effects of PEEP-ZEEP technique on hemodynamics and ventilatory mechanics of neurological patients undergoing invasive mechanical ventilation

Efeitos da técnica PEEP-ZEEP sobre a hemodinâmica e a mecânica ventilatória de pacientes neurológicos submetidos à ventilação mecânica invasiva

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## Abstract

**Introduction:** The need for ventilatory support is one of the main reasons for the admission of neurological patients in an intensive care units (ICU). Respiratory therapy techniques are important to avoid or minimize pulmonary complications. However, there is limited number of studies describing hemodynamic and ventilatory changes following airway clearance techniques in neurological patients. **Objective:** To evaluate the effects of PEEP-ZEEP maneuver on hemodynamic and ventilatory mechanics of neurological patients undergoing invasive mechanical ventilation (IMV) admitted in a neurological ICU. **Methods:** The study had a randomized, crossover, prospective and quantitative approach. Neurological patients undergoing mechanical ventilation for more than 24 hours underwent PEEP-ZEEP and manual rib-cage compression (MRC) techniques. Data on hemodynamic (diastolic and systolic blood pressure), oxygenation (SpO<sub>2</sub>) and ventilatory mechanics (dynamic and static compliance and respiratory system resistance) were collected before and after the completion of each technique for analysis. **Results:** The study included 10 participants. No significant differences in hemodynamic, oxygenation and respiratory system resistance were found after both techniques. However, the application of PEEP-ZEEP maneuver improved static and dynamic compliance ( $p < 0.05$ ); these significant results were not demonstrated following MRC. **Conclusion:** Based on the improvement of static and dynamic compliance without hemodynamic changes, PEEP-ZEEP seems to be a safe technique in neurological patients undergoing mechanical ventilation.

**Keywords:** Physical Therapy Modalities; Neurology; Monitoring, Physiologic; Positive-Pressure Respiration; Intensive Care.

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## Resumo

**Introdução:** A necessidade de suporte ventilatório é uma das principais razões da admissão de pacientes neurológicos em unidades de terapia intensiva. Técnicas de fisioterapia respiratória são importantes para evitar ou minimizar complicações respiratórias. Porém, há um número limitado de estudos que descrevem alterações hemodinâmicas e na mecânica ventilatória com a realização de técnicas de remoção de secreção brônquica em pacientes neurológicos. **Objetivo:** Avaliar o efeito da técnica de PEEP-ZEEP sobre a hemodinâmica e a mecânica ventilatória de pacientes neurológicos submetidos à ventilação mecânica invasiva. **Métodos:** Tratou-se de um ensaio clínico randomizado, crossover e prospectivo, com abordagem quantitativa. Pacientes neurológicos submetidos à ventilação mecânica por mais de 24 horas receberam a intervenção das técnicas PEEP-ZEEP e de Compressão Torácica Manual (CTM), sendo coletados dados hemodinâmicos (pressão arterial), de oxigenação (SpO<sub>2</sub>) e da mecânica ventilatória (complacência estática e dinâmica e resistência de vias aéreas), antes e após a realização de cada técnica. **Resultados:** A amostra contou com 10 indivíduos. Não foram encontradas diferenças na hemodinâmica, na oxigenação e na resistência do sistema respiratório, após a aplicação das técnicas. Após a aplicação da PEEP-ZEEP, ainda, houve melhora nas complacências estática e dinâmica ( $p < 0,05$ ); o que não ocorreu após a Compressão Torácica Manual. **Conclusão:** Baseado na melhora da complacência dinâmica e estática do sistema respiratório sem alterações hemodinâmicas, a técnica de PEEP-ZEEP parece ser segura, para ser utilizada em pacientes neurológicos submetidos à ventilação mecânica invasiva.

**Palavras-chave:** Terapia Respiratória; Neurologia; Monitorização Fisiológica; Respiração com Pressão Positiva; Terapia Intensiva.

## Introduction

Neurological disorders predominate on critically ill patients admitted in Intensive Care Units (ICUs)<sup>1</sup>. One of the main reasons of admission of these patients in ICUs is the need for ventilatory support to assist or to replace spontaneous breathing, since patients usually have abrupt changes in their clinical condition<sup>1-4</sup>. Invasive Mechanical Ventilation (IMV) is defined as a ventilatory support method, and is associated with many risks, especially when prolonged<sup>1,2,5,6</sup>.

Neurological critically ill patients are at an increased risk of ventilator acquired pneumonia (VAP), leading to a worse neurological outcome<sup>7</sup>. In these patients, VAP is mainly characterized by atelectasis or consolidation of the lower lobes. Thus, strategies should be implemented to prevent lung collapse and/or consolidation and lung infections and to accelerate weaning from mechanical ventilation<sup>7</sup>.

Respiratory therapy is an important adjunct in the treatment of patients requiring ventilatory support as it improves airway clearance, bronchial mucus removal and expansion of collapsed lung regions. Hence, it improves oxygen saturation, lung compliance and airway resistance, restoring therefore, pulmonary function<sup>9-15</sup>. However, it is necessary to promote studies with respiratory therapy techniques that bring benefits without producing hemodynamic changes, since negative effects can result from some techniques, as increase in mean arterial pressure and heart rate<sup>9-11,13</sup>.

Some techniques have evidenced benefits, such as Manual Rib-Cage Compression (MRC) and tracheal suction, which are effective in improving mechanical ventilation and removal of bronchial mucus without causing negative effects<sup>11-16</sup>. However, some techniques need to be more studied to understand its safety and real benefits, as Positive End-Expiratory Pressure – Zero End-Expiratory Pressure (PEEP-ZEEP) maneuver<sup>10,11,13</sup>.

Theoretically, when PEEP rises during the PEEP-ZEEP technique, gas is redistributed through collateral ventilation, reaching adjacent alveoli previously collapsed by mucus. A small airway reopening is possible by the mucus removal. When ZEEP is applied the expiratory flow pattern is changed aiding transport of secretions from smaller airways to those more central<sup>10</sup>.

To study positive effects of PEEP-ZEEP technique it can be compared to MRC, since MRC has been proven to be a safe and effective technique by previous studies<sup>10</sup>. Both techniques aim for airway clearance by changing the airflow, the difference is that MRC requires physical effort from the therapist while the other makes use of changes in the ventilator parameters<sup>10</sup>.

The aim of this study was to evaluate the effect of PEEP-ZEEP maneuver on the hemodynamic and ventilatory mechanic of neurological patients undergoing IMV admitted in a neurological ICU. The initial hypothesis is that the maneuver may present benefits on respiratory mechanics (e.g. lung compliance and airway resistance) without changing hemodynamic variables on patients undergoing mechanical ventilation.

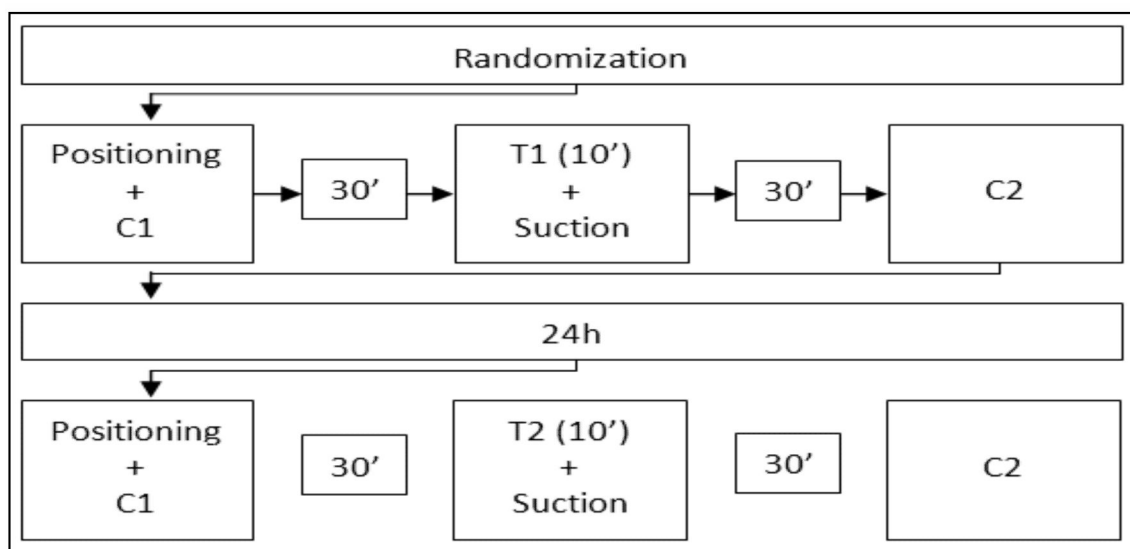
## Methods

The study has a randomized, crossover, prospective and quantitative approach. The data was collected in 2013, between February and May, at a neurological ICU at Hospital Universitário São Francisco de Paula, Pelotas/RS, Brazil, after the institution Ethics Committee approval (certificate number for ethics appreciation 09912412.4.0000.5339) as well as the family and legal responsible approval through an Informed Consent Form.

Adults with neurological injury and submitted to IMV for longer than 24 hours were included. Exclusion criteria were: hemodynamically unstable patients (mean arterial pressure < 60mmHg or > 110mmHg, heart rate < 40bpm or > 130bpm, SpO<sub>2</sub> < 88%, absence of vasopressor increase in the last 2 hours), rib-cage fracture, undrained pneumothorax, presence of chest tube, severe bronchospasm and high levels of PEEP (> 8 cmH<sub>2</sub>O). Airway clearance protocols, PEEP-ZEEP and MRC, were applied just once, with application order defined by randomization with sealed and opaque envelopes with sequential numbering.

After selecting patients according to the eligibility criteria and acceptance, the techniques were randomized and the patients were positioned in supine with head elevation of 30 degrees and with a neutral neck position. Thereafter, first data were collected (C1). After 30 minutes of C1 the patient underwent the first airway clearance technique (T1), for about ten minutes. 30 minutes after the intervention data were again collected (C2). 24 hours after, the same patient underwent the second technique (T2) obeying the randomization and the standard of data collection sequence, as shown in Figure 1. IMV mode was maintained as previously set by the patient's physician and physiotherapist. During the application of both techniques there was no external interference, except for the continuous infusion of medications pre-established on prescription. There was not a blinded evaluator to collect data, only one physiotherapist conducted the techniques. At the end of the study all the participants received daily physical therapy, with no change in the routine of service due to the study.

**Figure 1** | Application and data collect protocol.



MRC – Manual rib-cage compression; PEEP-ZEEP – Positive End Expiratory Pressure – Zero End Expiratory Pressure; IMV – Invasive Mechanical Ventilation; ICU – Intensive Care Unit; HUSFP/RS – Hospital São Francisco de Paula/RS; C1 – data collect 30 minutes before intervention; T1 – first technique applied according to randomization; C2 – data collect 30 minutes after intervention; T2 – second technique applied according to randomization.

## PEEP-ZEEP

At the inspiration phase of ventilatory cycle PEEP was raised to 15 cmH<sub>2</sub>O, with a limited peak inspiratory pressure (PIP) up to 40 cmH<sub>2</sub>O. After the patient performed five ventilatory cycles PEEP was suddenly reduced to zero pressure at expiration phase (ZEEP), and at the next inspiration phase PEEP was returned to the previously adjusted values. The maneuver was repeated for 10 minutes with a two ventilatory cycle pause between each repetition<sup>2,10,13</sup>.

## Manual Rib-Cage Compression

Manual compression at expiratory phase of the ventilatory cycle on the anterolateral region of the chest at the level of the six last ribs was carried out. Each compression was interrupted at the end of each expiratory stage to release inspiration. The maneuver was performed for 10 minutes<sup>12,15,16</sup>.

At the end of each technique the patient underwent tracheal suction following the recommendations of the American Association of Respiratory Care<sup>17</sup>.

## Data collection

All patients had their vital signs monitored by the multiparameter monitor Infinity Delta XL (Drager, USA) and were ventilated by Servo (Maquet, Germany) or Inter 5 (Intermed, Brazil), as previously set by the patient's physician and physiotherapist. Data collected included the following variables and parameters: patients characteristics (age, gender, neurological injury, acute respiratory failure – ARF cause), days of hospitalization, days with IMV, static compliance (Cst) and dynamic compliance (Cdyn) of the respiratory system, flow, respiratory rate (RR), diastolic blood pressure (DBP) and systolic blood pressure (SBP), peak inspiratory pressure (PIP), plateau pressure (Ppt),

positive end expiratory pressure (PEEP), respiratory system resistance (Rsr), peripheral oxygen saturation ( $SpO_2$ ) and tidal volume ( $V_t$ ).

Variables were collected from the data presented in the vital signs monitor and ventilator. Blood pressure was measured noninvasively and peripheral oxygen saturation by pulse oximeter. Cst is calculated by  $V_t/(P_{pt}-PEEP)$ , Cdyn by  $V_t/(PIP-PEEP)$  and Rsr is calculated by  $(PIP-P_{pt})/flow^6$ . In order to calculate airways resistance the ventilation mode to measure plateau pressure was set on volume controlled with squared wave flow.

### Statistical Analysis

Data were statistically analyzed using Statistical Package for Social Sciences (SPSS) 20.0. Normality was verified using Kolmogorov-Smirnov test. Student's t-test was used for inter-group comparisons, with significance set as  $p < 0.05$ . Data are described as mean  $\pm$  standard deviation (SD) or absolute frequency (n) and percentage (%).

### Results

Among all patients admitted in the ICU during the study, 13 were eligible to participate. There were two refusals and one exclusion due to high PEEP (12  $cmH_2O$ ) and hemodynamic instability (use of norepinephrine infused at 18 ml/h and increasing), therefore, 10 patients completed the study. No subjects were under neuromuscular blocking effect, however, all participants were receiving continuous infusion of sedatives (midazolam and fentanyl, individually dosed by the physician) to maintain a Richmond Agitation-Sedation Scale (RASS.) of -3 to -1; this target is a routine in the ICU where the study was conducted, and not a purpose of the study.

The main diagnosis was traumatic brain injury (40%), followed by stroke (30%). Respiratory failure and need for ventilatory support was caused by nosocomial pneumonia in 70% of the cases. Sample characterization is shown in Table 1. The sample is equally distributed in relation to IMV mode, as 50% was on pressure-controlled ventilation and 50% on volume-controlled ventilation; parameters are shown in Table 1.

On intra-group analysis, for both interventions, hemodynamic variables (SBP and DBP) had no significant differences, which also happened with peripheral oxygen saturation ( $SpO_2$ ), as described in Tables 2 and 3.

**Table 1** | Characterization of the study sample.

<b>Characteristic</b>	<b>N</b>
Age (years)	48.8±23.5
Gender	
Female	4 (40)
Male	6 (60)
Hospitalization (days)	2.3±1.3
IMV (days)	3.6±3.3
Neurologic injury	
Stroke	3 (30)
Cancer	1 (10)
SH	1 (10)
Parkinson	1 (10)
TBI	4 (40)
ARF cause	
Atelectasis	1 (10)
Non described	2 (20)
PNn	7 (70)
IMV parameters	
Vt (ml)	399±66.8
Flow (L/min)	44.8±17.7
PIP (cmH <sub>2</sub> O)	23.3±3.5
PEEP (cmH <sub>2</sub> O)	5±0
RR	14.6±2.2
FiO <sub>2</sub>	39.7±11.6

IMV – Invasive Mechanical Ventilation; SH – Subarachnoid Hemorrhage; TBI – Traumatic Brain Injury; ARF – Acute Respiratory Failure; PNn – nosocomial pneumonia; Vt – Tidal Volume; PIP – Peak Inspiratory Pressure; PEEP – positive end expiratory pressure; RR – Respiratory Rate; FiO<sub>2</sub> – fraction of inspired oxygen. Results expressed in mean ± standard deviation or absolute frequency (percentage).

**Table 2** | Hemodynamic changes before and after the interventions.

Technique	SBP		DBP	
	30' before	30' after	30' before	30' after
PEEP-ZEEP	127.2±24.9	130.5±20.1	72,7±16,1	72,3±13,1
	<i>p</i> = 0.177		<i>p</i> = 0.717	
MRC	123.8±24.5	124.8±18.6	72,6±18,5	72,1±12,7
	<i>p</i> = 0.635		<i>p</i> = 0.953	

MRC – Manual rib-cage compression; PEEP-ZEEP – Positive End Expiratory Pressure – Zero End Expiratory Pressure; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure. Results expressed in mean ± standard deviation.

**Table 3** | SpO<sub>2</sub> before and after the interventions.

Technique	SpO <sub>2</sub>	
	30' before	30' after
PEEP-ZEEP	96.8±2.1	96.7±2.5
	<i>p</i> = 0.582	
MRC	96.8±2.2	96.7±2.8
	<i>p</i> = 0.739	

MRC – Manual rib-cage compression; PEEP-ZEEP – Positive End Expiratory Pressure – Zero End Expiratory Pressure; SpO<sub>2</sub> - Peripheral Oxygen Saturation. Results expressed in mean ± standard deviation.

Table 4 shows respiratory mechanics before and after both interventions, PEEP-ZEEP and MRC. Cst, Cdyn and Rsr values were similar between the groups before techniques application. After the maneuvers, significant changes were not observed on Cst, Cdyn and Rsr with MRC, as well as Rsr with PEEP-ZEEP. However, significant changes in Cst (*p*=0.007) and Cdyn (*p*=0.030) were seen after PEEP-ZEEP technique application in intra-group analysis.

**Table 4** | Ventilatory mechanic variation before and after the interventions.

Technique	Cst		Cdyn		Rrs	
	30' before	30' after	30' before	30' after	30' before	30' after
PEEP-ZEEP	33.1±8.4	38.6±8.2	20.7±6.2	21.7±5.3	11.7±8.2	12.8±7
	<i>p</i> = 0.007		<i>p</i> = 0.030		<i>p</i> = 0.492	
MRC	34.7±8.9	36.4±8.5	20.6±5.7	21.1±3.8	12.8±7.1	13±6.3
	<i>p</i> = 0.161		<i>p</i> = 0.138		<i>p</i> = 0.574	

MRC – Manual tib-cage compression; PEEP-ZEEP – Positive End Expiratory Pressure – Zero End Expiratory Pressure; Cst – Static Compliance; Cdyn – Dynamic Compliance; Rrs – Respiratory System Resistance. Results expressed in mean ± standard deviation.

## Discussion

Patients on invasive mechanical ventilation support require specific care to prevent atelectasis and mucus accumulation, thus reducing the complications induced by IMV. MRC and PEEP-ZEEP maneuvers are used by physiotherapists for airway clearance, however, there is still no significant number of studies that describe the effects of both techniques on respiratory mechanics and hemodynamic, especially in a homogeneous sample, such as individuals with neurological disorders<sup>13</sup>.

In this study there was a higher prevalence of pneumonia as a cause of submission to IMV. Similar results are found in a previous study in which pneumonia was the main reason for IMV, reaching 33.3% of a sample of 12 patients, although conducted with a sample with different pathologies from our study<sup>8</sup>.

SpO<sub>2</sub> remained unchanged by application of MRC and PEEP-ZEEP. This result is similar to other studies in which PEEP-ZEEP was applied on patients undergoing coronary artery bypass surgery<sup>13</sup> and airway mucus hypersecretion<sup>11</sup>. In another research, when comparing MRC technique versus PEEP-ZEEP technique, it was observed significant increase of SpO<sub>2</sub> after the MRC but not after PEEP-ZEEP<sup>10</sup>; however, the underlying diseases were varied and may have affected the results, and also pulse oximetry was used, which can vary up to 4% for parameters above 94% of SpO<sub>2</sub>.

No differences were observed in hemodynamics (SBP and DBP) before and after application of both techniques used on this study. In contrast, the study of Rosa et al. found a not sustained increase in SBP of 22.72% immediately after isolated tracheal suction, which may have occurred by the collapse of airway zones caused by application of negative pressure during the technique<sup>8</sup>. However, in accordance with our study, Lobo and Rodrigues et al showed no significant changes in hemodynamics in patients undergoing similar techniques<sup>2,13</sup>. The reason for the hemodynamic stability may be explained by reduced venous return caused by the increase of intrathoracic pressure, reducing thus the cardiac output, which is minimized by optimizing left ventricular pumping<sup>4</sup>.

The application of MRC resulted in satisfactory clinical results on Cst and Cdyn, as the variables increased indicating a better lung compliance. This was, however without statistical significance. Rosa et al, using MRC, found no significant improvement in Cst and Cdyn. However, authors achieved a significant improvement in Rsr (*p*<0.02)<sup>8</sup>. In turn, in a study where the authors used MCC and PEEP-ZEEP, significant increase in Cst and Cdyn was obtained with both techniques (*p*=0.002 for both)<sup>10</sup>.



In our study a significant improvement in Cst and Cdyn ( $p=0.007$  and  $p=0.030$ , respectively) was observed only with PEEP-ZEEP application but Rsr remained unchanged. According to Guimarães et al., transitory bronchial constriction, variable secretion distribution patterns in patients' airways, mucociliary activity and individualized response to the applied intervention could explain the unchanged respiratory resistance observed after the use of airway clearance techniques. Moreover, because of the greatest contribution of the central and intermediate airways to respiratory system resistance, if the secretions displace from the periphery to more proximal airways (but are not completely removed by suctioning), there will be an increase in these resistance parameters<sup>18</sup>.

The positive result of PEEP-ZEEP technique can be explained by the redistribution of gases through collateral ventilation and mobilization of bronchial mucus, with consequent reopening of small airways and transport of secretions from smaller airways to those more central<sup>10</sup>.

Although the study has been enlightening about the safety and benefit of the techniques employed, it had some limitations. The study does not consider the possible influence caused by medications administered to each patient individually and patient's comorbidities, what could influence the results; no medication was altered or administered during the intervention, although patients received continuous infusions. There was not a blinded evaluator to collect data, however, only one physiotherapist conducted the techniques. The small sample size, while being homogeneous and characterized by patients with neurological injury, was also a limitation for the observed results because it compromises the statistical power of some analyses as well as the generalizability of the results. Also, there was no control group. It is understood by the authors that the lack of intracranial pressure control featured a limitation because it is essential for neurological patients since the hemodynamic changes can lead to an increase of this variable and, as a consequence, decrease in cerebral perfusion pressure. Yet, it was not possible to analyze the amount of secretion removed after each technique. New research involving the effects of the techniques on hemodynamic and ventilatory mechanics of patients with neurological injury are required for a consensus of the benefits of its applications.

## Conclusion

PEEP-ZEEP technique may have positive effects on ventilatory mechanics of mechanical ventilated patients, as its application resulted in significant positive changes in Cst and Cdyn. Regarding hemodynamics and oxygen saturation, both techniques, PEEP-ZEEP and MRC showed to be safe.

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