

## **INFLUENCE OF THE EXPIRATORY PRESSURE LEVELS ON THE ALVEOLAR RECRUITMENT OF THE HEALTHY SUBJECTS**

### **INFLUENȚA NIVELULUI DE PRESIUNE EXPIRATORIE ASUPRA RECRUTĂRII ALVEOLARE ASUPRA SUBIECȚILOR SĂNĂTOȘI**

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#### **Abstract**

Few studies have analyzed the effect of different well-defined PEP levels on lung function since the majority of clinical trials use PEP mask and a pressure «fork». The objective of this study is to find out if there is a common level of PEP to be applied which allows optimization of alveolar recruitment, objectivity by tomography by electric impedance, for all subjects. The study was carried out on 14 healthy participants, 7 men and 7 women, aged 22 to 30. Participants had a exhale against four resistors of different values, determined by the tension of the spring, 5, 10, 15 and 20cmH<sub>2</sub>O. The measurement of alveolar recruitment during the experiment was carried out by an electrical impedance tomograph. Each participant reacted differently to the PEP levels, but by comparing the responses of the pulmonary function, it is noted that the individual characteristics can influence the alveolar recruitment, whatever the level of resistance applied. It would be interesting to investigate, on a larger sample and with several groups of participants with low inter-individual variability, whether there is a correlation between individual characteristics and the potential for alveolar recruitment. This would optimize care by adapting it to each subject.

**Keywords:** *positive expiratory pressure, pulmonary volume, expiratory impedance*

#### **Rezumat**

Există puține studii care au analizat efectul diferitelor niveluri de presiune expiratorie pozitivă (PEP) bine definite asupra funcției pulmonare, deoarece majoritatea studiilor clinice utilizează mască PEP și o „furcă” de presiune. Obiectivul acestui studiu este de a afla dacă există un nivel comun de PEP care trebuie aplicat, care permite optimizarea recrutării alveolare, relevate prin tomografie de impedanță electrică, pentru toți subiecții. Studiul a fost realizat pe 14 participanți sănătoși, 7 bărbați și 7 femei, cu vârste cuprinse între 22 și 30 de ani. Participanții au expirat împotriva a patru rezistențe de valori diferite, determinate de tensiunea arcului, 5, 10, 15 și 20cmH<sub>2</sub>O. Măsurarea recrutării alveolare în timpul experimentului a fost efectuată de un tomograf de impedanță electrică. Fiecare participant a reacționat diferit la nivelurile PEP, dar prin compararea răspunsurilor funcției pulmonare, se

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observă că recrutarea alveolară poate fi influențată de caracteristicile individuale, indiferent de nivelul de rezistență aplicat. Ar fi interesant de investigat, pe un eșantion mai mare și cu mai multe grupuri de participanți cu variabilitate interindividuală scăzută, dacă există o corelație între caracteristicile individuale și potențialul de recrutare alveolară. Acest lucru ar optimiza tratamentul prin individualizarea lui la fiecare subiect.

**Cuvinte cheie:** *presiune expiratorie pozitivă, volum pulmonar, impedanță expiratorie*

## **Introduction**

Alveolar recruitment (AR) is a dynamic phenomena and is defined as the re-expansion of previously collapsed lung areas by means of a brief and controlled increase in transpulmonary pressure [1].

The idea of AR is to create and maintain a collapse-free situation with the purpose of increasing the end-expiration volume and improve gas exchange. We more talk about alveolar recruitment and not pulmonary recruitment because the alveoli are located in the pulmonary lobules who constituted the functional element of the lung and responsible of the blood oxygenation. But the recruitment also appears in the bronchial level. The goals of alveolar recruitment are to stabilize unstable alveoli in order to limit closing-reopening phenomena but also to recruit collapsed areas in order to make ventilation more homogeneous.

Positive expiratory pressure consists of breathing against expiratory resistance, affixed to the nose or the mouth [2]. The subject must exhale against resistance, also called PEP, in order to successfully extract previously inspired air. In order to achieve this expiration, the oral pressure must therefore be lower than the alveolar pressure.

This PEP allows an increase in intrabronchial and alveolar pressure, causing an increase in the size of the bronchi by increasing transpulmonary pressure. Resistance of the airways which depend on the diameter of the bronchi decrease.

The application of Positive Expiratory Pressure (PEP) is used when patients have excess secretions in their airways but also during the presence of alveolar collapse and finally as a prevention of respiratory complications [3]. Each physiotherapist applies these positive expiratory pressures in their own way.

Few studies have analyzed the effect of different well-defined PEP levels on lung function since the majority of clinical trials use PEP mask and a pressure «fork» [4, 5, 6, 7].

This research problem focused on the methods of using PEP: How a common PEP level would improve alveolar recruitment in healthy subjects with different individual characteristics?

The objective of this study is to find out if there is a common level of PEP to be applied which allows optimization of alveolar recruitment, objectivity by tomography by electric impedance, for all subjects.

The hypotheses of research are:

- PEP allows an objective alveolar recruitment by EIT, in all healthy subjects.
- There is a common PEP level where recruitment would be higher in all subjects.
- The level of PEP allowing the strongest recruitment is also the most durable during the five post PEP respiratory cycles.

### **Study population**

The experimental study was developed at Helfaut Hospital in the St Omer Region, France. Each participant was informed, before the experiment, of the modalities of this one. The study participants were selected according to several inclusion criteria:

- Age > 18
- Tidal Volume > or equal at 80% of its theoretical value
- MEVS > or equal at 80% of its theoretical value
- Vital Capacity > or equal at 80% of its theoretical value

Indeed, a tidal volume and vital capacity value equal to 80% of the theoretical value is considered normal.

The exclusion criteria were:

- Airway congestion at the time of the experiment
- Obstructive ventilatory disorder with a Tiffeneau ratio < 70%
- Misunderstanding of the instructions
- History of pneumothorax

The study was carried out on 14 healthy participants, 7 men and 7 women, all being members of the hospital medical teams, aged 22 to 30.

### **Protocol**

The subjects were seated in an armchair with a backrest. A belt of electrodes connected to the tomograph was located under the chest, at the level of the sixth intercostal space.

The subjects were asked beforehand to remain well seated at the bottom of the seat during the whole experiment so that the electrodes pick up correctly, and not to speak during the latter.

Participants had a exhale against four resistors of different values, determined by the tension of the spring, 5,10,15 and 20 cmH<sub>2</sub>O. The order of the applied PEP levels, set by the examiner via software and varied from subject to subject. This made it possible to limit the fatigability effect which could have been an experience bias, if PEP had been applied increasingly.

Following the launch of the recording, the subjects were asked to breathe calmly, on their rest ventilation (tidal volume), for one minute, objectified by a stopwatch. Then, they had to breathe in at most of their inspiratory reserve volume outside the PEP, and exhale in a slightly active way in the resistance imposed by the threshold PEP, until the end of their expiratory reserve volume. They were therefore asked to empty their lungs as much as possible.

They repeated this maximum inspiration and expiration against the resistive pressure 5 times. Then, the subjects ventilated spontaneously, in order to find a ventilation of rest, during one minute. Another resistive pressure was applied to their mouth, and 5 new repetitions of expiration against it, following maximum inspiration, were asked of them.

There was thus during the experiment, a minute of spontaneous ventilation of rest followed by 4 sets of 5 repetitions of maximum inspiration and total expiration against PEP, each interspersed with a minute of rest, and finally a minute of rest after the fourth series.

At the end of the experiment, participants were asked how they felt about PEP if they had been bothered by resistance-induced side effects.

Equipment used and measurements carried out:

- a) Spirometry

A forced and simple spirometry was carried out before the experiment to determine if the subjects fulfilled all the inclusion criteria, thanks to a portable USB spirometer connected to a computer. Spirometry was performed with a nose clip, which will be kept throughout the experiment.

b) EIT measurements

The measurement of alveolar recruitment during the experience was carried out by an electrical impedance tomograph, the Pulmo Vista 500. The belt comprising the 16 electrodes and connected to the tomograph was placed under the chest, around the thorax.

The impedance measurements will be expressed as a percentage of a reference impedance in order to be able to compare the subjects with each other.

Following a transposition of the Pulmo Vista files on Microsoft Excel, we obtain an impedance curve over time. The tomography provides a large number of recorded measurements per second. For the analysis of these measurements, we retained only the points corresponding to the lower vertices of the curve which represent the impedance at the expiratory tele volume (minimum impedance) and the upper of the curve (+1) which represent the impedance at the end of inspiration volume.

The measured variables are:

- Minimum impedance during PEP and post PEP over over 5 respiratory cycles

It's possible to objectify alveolar recruitment when an increase in functional residual capacity is observed, so an increase in the expiratory reserve volume and the residual volume. In addition, the study participants didn't have respiratory, and therefore theoretically no bronchial congestion or pulmonary hyperinflation. The alveolar recruitment induced by PEP will then be clearly objectible by the increase in the pulmonary volume, that is to say the increase in the functional residual capacity and in the tidal volume. Thus, thanks to the points -1 of the curve (end of expiration point) of the impedance with respect to time, it's possible to observe an alveolar recruitment during an increase in their value.

The average of the points -1 during the first minute of the experiment was calculated so that it serves as the minimum reference impedance ( $I_{ref}$ ). The comparison of the minimum impedance between the different PEP levels is expressed as a percentage of the  $I_{ref}$  for each subject. The minimum post PEP impedance was measured over 5 respiratory cycles following PEP. It's expressed as a percentage of  $I_{ref}$ .

- Variations in overall impedance to objectify impedance during inspiration

Recruitment can also be objectified during an increase in tidal volume, so we measured the variations in impedance during inspiration (corresponding to the difference between points +1 and -1). These variations are expressed as a percentage of the variations in impedance during the inspiration of rest.

- The number of respiratory cycles where alveolar recruitment would occur

According to the method based on increasing or decreasing the minimum impedance, whether or not representing alveolar recruitment, it's possible to objectify the number of respiratory cycles where effective recruitment takes place. We can speak of recruitment during PEP when we observe an increase in the minimum impedance compared to the  $P_{ref}$ . Which would represent an increase in the residual volume at the respiratory level.

The evolution of the impedance during PEP was measured by calculating the difference between the minimum impedance values after expiration and the point -1 following the first expiration against

PEP. The difference can be positive or negative, and the increase or decrease with respect to Pref is expressed in % of Pref. When this difference is positive, there is a recruitment that can be objectified directly by the Tomograph by Electrical Impedance. In post-PEP, recruitment is carried out when the value of the minimum impedance is greater than that of rest Iref, which means that the functional residual capacity has increased.

- Respiratory rate

It was calculated during the minute of rest following each PEP. The summary of respiratory frequencies after each level of PEP will be presented later.

Results are expressed as means and standard deviations. The comparison of the means was carried out using an analysis of variance for repeated measurements when the results followed a normal distribution, otherwise a non-parametric test (Friedman's test) was used. Indeed we are in the framework of an experiment where the same quantity was measured several times on the same subjects, in order to follow its evolution during different situations, in particular during the different PEP levels.

### Results

Due to electrode belt capture defects during maximum expirations, a subject's data could not be analyzed. The data of thirteen participants were therefore analyzed, the table of their individual characteristics is presented in Table 1. Among these thirteen participants, some outliers, related to the electrode belt, were excluded; this is indicated when the n (number of participants) is decreased.

Table 1. Results obtained during respiratory cycles performed with PEP

	PEP 5cmH <sub>2</sub> O	PEP 10cmH <sub>2</sub> O	PEP 15cmH <sub>2</sub> O	PEP 20cmH <sub>2</sub> O	P
n	12	12	12	12	
Minimum impedance (% Iref) average; SD	71,1; 56,6	72,2; 55,3	63,9; 50,0	68,4; 55,0	NS
n	10	10	10	10	
Variation in impedance (%) average; SD	620,6; 232,2	630,5; 255,1	621,3; 263,4	627,7; 224,9	NS

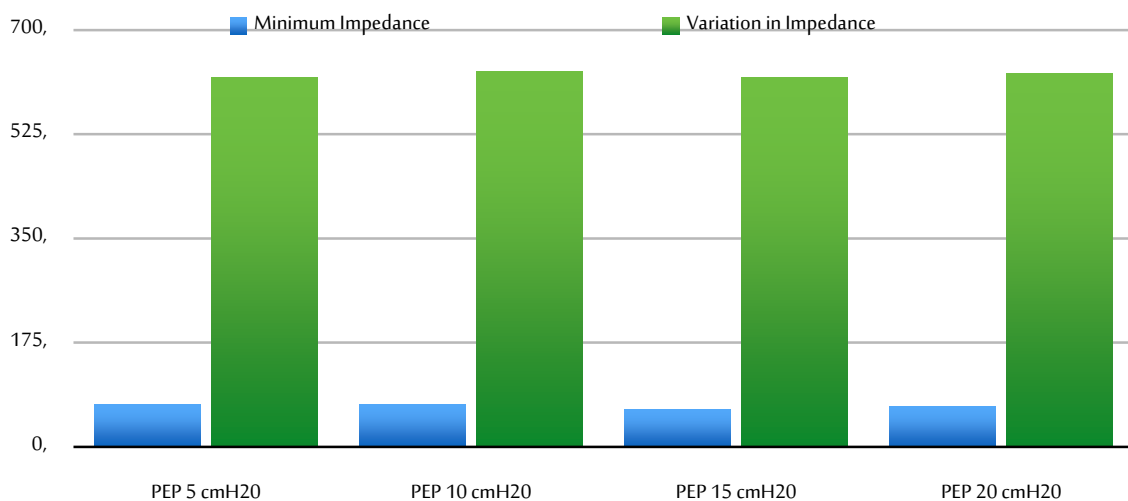


Figure 1. Comparison of the influence of the different PEEP levels on the minimum impedance and the variations in impedance on inspiration

No significant difference between the different PEEP levels was shown on the minimum impedance and on the variation of impedance during inspiration.

Table 2. Comparison of the increase in the minimum impedance compared to the Pref impedance and the number of cycles in which a recruitment can be objectified, according to the different pep levels

	PEP 5cmH20	PEP 10cmH20	PEP 15cmH20	PEP 20cmH20	P
n	8	8	8	8	
Increase in impedance (% Pref) average; SD	41,8; 59,3	0,1; 22,2	-8,6; 17,8	-0,8; 30,5	0,036
n	10	10	10	10	
Number of recruitment cycles (%) average; SD	78; 30	55; 39	60; 36	55; 40	NS

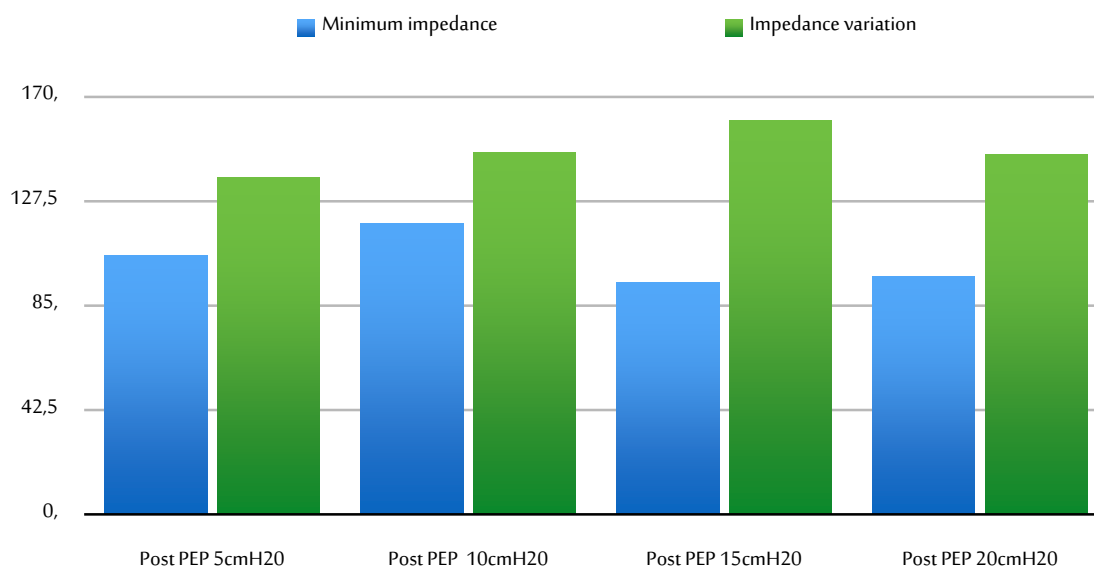


Figure 2. The minimum impedance and the inspiration impedance variation during the 5 Post-PEP respiratory cycles

We obtain significant differences concerning the increase in impedance during respiration against the four levels of pressure.

There is no significant difference between the PEP levels in the number of respiratory cycles in which a directly objectifiable alveolar recruitment takes place.

Table 3. Comparison of the minimum impedance and he variation of impedance during inspiration during the 5 post PEP cycles, after each level of PEEP

	PEP 5cmH20	PEP 10cmH20	PEP 15cmH20	PEP 20cmH20	P
n	12	12	12	12	
Minimum impedance (% Iref) average; SD	105; 45,2	118,6; 62,4	94,6; 22,2	96,9; 28,9	NS
n	13	13	13	13	
Impedance variation (%) average; SD	137,1; 66,3	147,5; 55,4	160,6; 92,4	146,4; 60,8	NS

Table 4. Comparison of the number of respiratory cycles in which recruitment takes place during the Post-PEP respiratory cycles

	Post PEP 5cmH <sub>2</sub> O	Post PEP 10cmH <sub>2</sub> O	Post PEP 15cmH <sub>2</sub> O	Post PEP 20cmH <sub>2</sub> O	P
n	12	12	12	12	
Number of recruitment (%) average; SD	33; 39	35; 41	22; 27	28; 39	NS

## Discussion

No level of PEP shows a significantly greater effect than the others. Indeed, in view of our results, we cannot conclude on a level of PEP which would increase the RFC or the volume inspired for all subjects, in a way superior to the others.

Subjects were asked to breathe out against the threshold PEP until the end of their expiratory reserve volume, so it's normal for the expiratory impedance to be lower than the I<sub>ref</sub> where subjects were breathing at their tidal volume. It's noted however that the PEP at 5cmH<sub>2</sub>O and at 10cmH<sub>2</sub>O give a minimum impedance greater than the other two and therefore induce a residual volume greater than the other PEP, but this insignificantly.

No conclusion is possible regarding the evolution of recruitment during PEP. Indeed, some subjects show a linear increase in the minimum impedance over the repetitions of expirations, and therefore increase their RV. While others tend to hire, by decreasing their RV. This varies according to each subject and each level of PEP. The alveolar recruitment cannot therefore be directly objectified by EIT in all subjects, during a complete expiration. One of our hypotheses isn't verified.

It should be noted, however, that PEP at 5cmH<sub>2</sub>O shows a very disparate increase in recruitment of up to more than 100% of the value of P<sub>ref</sub>. In addition, it's with this level that we observe the greatest number of cycles in which an alveolar recruitment is affected by a minimum impedance greater than that of P<sub>ref</sub> (Table 2).

Over the 5 post-PEP respiratory cycles, the comparisons of the means (Tables 3 and 4) don't reveal a more beneficial level of pressure. While the minimum impedance means are higher for pressures of 5 and 10cmH<sub>2</sub>O, the standard deviations are also higher. The objective of this work is to find a common level of PEP which would optimize recruitment by increasing it in its value and duration, for all subjects. The standard deviations, representing the dispersion of the values around their mean and therefore the difference in response of subjects to each level of PEP, therefore play an important role in the interpretation of the results.

When we compare all of the study participants together, we can see that no meaningful results can be drawn. The study carried out does not allow the assumptions made to be validated. The PEP levels of 5 and 10cmH<sub>2</sub>O seem to be the pressures where the majority of subjects is recruiting, but we can't speak of clinical relevance because some subjects will shift their ventilation in their ERV for these same levels, which would be contrary to the clinical objective of opening airway.

However, in view of the curves of the subjects during their ventilation with PEP, it's possible to group them into two groups: one where the minimum impedance remains very high even during total expiration (> 90% I<sub>ref</sub>), and one where the impedance remains significantly lower.

When looking for a relationship between the individual characteristics of the subjects and the measured impedance testifying to alveolar recruitment, we note that in subjects whose BMI is

less than 22, the minimum impedance is much higher at the end of expiration than that of other topics for any level of PEP.

BMI is said to influence the potential for individual recruitment. But to confirm this new hypothesis, it would be necessary to conduct a study with more participants to draw any conclusion from these observations.

Concerning the methodology, we realized that it would have been more judicious to carry out inspirations and expirations at tidal volume while the PEP was applied. Indeed, the curves obtained would have immediately assessed recruitment during PEP by whether or not the minimum impedance was greater than the  $I_{ref}$ . We would have directly seen the evolution of the RFC, and not only that of the RV that can be observed in my experience when applying the PEP. We would also have directly seen the increase in inspired volume, compared to that of rest, if the subjects ventilated at tidal volume.

The instructions for maximum inspiration and expiration until the end of their ERV were clear instructions, which enabled participants to perform respiratory cycles against PEP in a repeatable manner. However, when calculating the variations in impedance between the end of expiration and the end of inspiration, we realize that some subjects repeated almost similar expirations but that others expired up to 31,6% less. That the expirations carried out against the first PEP put in place. This may be due to the increased difficulty when the level of PEP is high but can also be considered as a follow-up bias.

Attrition biases are also present in our study. The electrodes didn't always pick up correctly when exhaling against PEP. This forced me to sometimes exclude certain subjects and is responsible for missing data.

The EIT is recognized as a validated measurement tool and constitutes a strong point of the experiment. However, it does not distinguish recruitment from pulmonary hyperinflation.

The randomization of the order of applied PEP levels allowed my study to position participants blind opposite the treatment received, and the choice of threshold PEP allowed subjects to expire against the same level of PEP, not dependent on their expiratory flow [8].

This study is limited because the subjects included aren't representative of the population affected by the use of PEP. But it constitutes a study preliminary to a next study which would include subjects suffering from respiratory pathologies.

As mentioned earlier, there are few studies that have accurately compared multiple pressure levels using a threshold resistor. And when they show a more beneficial level than the others, one realizes their methodological weaknesses [9]. During clinical application, the pressure to be applied should be higher in affected patients because the pressure to open the alveoli is higher when they are collapsed, as described by [10].

## **Conclusions**

Studying the literature made we realize that there was no consensus on how PEP should be used. In order to show the effects of different levels of PEP on respiratory function, an experimental protocol where 4 different levels were tested was implemented. The EIT made it possible to analyze the alveolar recruitment by increasing the RFC or RV as well as tidal volume. Analysis of the results does not show a level of PEP common to all subjects which would induce a higher alveolar recruitment than the others.



This study constitutes a preliminary study which makes it possible to observe the adaptations of the respiratory function, according to the pressure levels applied, in each participant. The interest of this study was to determine a level of beneficial PEP in all healthy participants, which would then have been implemented in subjects suffering from respiratory pathology. The clinical objective would be to optimize the use of this instrumental technique by knowing the level of PEP adapted to the patient.

Each participant reacted differently to the PEP levels, but by comparing the responses of the pulmonary function, it is noted that the individual characteristics can influence the alveolar recruitment, whatever the level of resistance applied. It would be interesting to investigate, on a larger sample and with several groups of participants with low inter-individual variability, whether there is a correlation between individual characteristics and the potential for alveolar recruitment. This would optimize care by adapting it to the subject in front of us.

This work allowed us to take a critical look at what is done in professional practice. By studying the literature, and taking into account the methodological quality of the studies, we were able to take a step back from the conclusions that emanate from clinical trials.

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