

## *The effect of PEEP on the right ventricle*

### *A transeosophageal echocardiography and tissue Doppler study*

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#### ABSTRACT

**The effect of PEEP on the right ventricle. A transeosophageal echocardiography and tissue Doppler study.**

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The aim of this study was to determine how low and moderate levels of PEEP affect right ventricular structure and function. The study involved 14 patients under mechanical ventilation (pressure controlled). To perform the study, we used transeosophageal echocardiography (M-mode, two-dimensional, tissue Doppler) and 10 parameters were recorded. Measurements were performed initially with PEEP 0 cmH<sub>2</sub>O, then 10 minutes after applying PEEP 5cmH<sub>2</sub>O and 10 minutes after applying PEEP 10cmH<sub>2</sub>O. After applying PEEP 5 cmH<sub>2</sub>O, there was no statistically significant change observed in any parameter. In contrast, after the application of PEEP 10cmH<sub>2</sub>O, significant changes in most parameters were recorded: St changed from 10,86±3,8 cm/sec (mean±SD) at PEEP 0 cmH<sub>2</sub>O to 8,7±2,9 at PEEP 10 cmH<sub>2</sub>O, TAPSE changed from 2,876±0,643cm to 2,385±0,556cm, IVA from 2,2692±0,93m/sec<sup>2</sup> to 2,8536±1,628m/sec<sup>2</sup>, ET from 259,27±17,47 msec to 229,34±31,22msec, EDA from 21,372±5,01cm<sup>2</sup> to 18,87±4,15cm<sup>2</sup>, left ventricular eccentricity index at end-diastole from 0,9±0,07 to 0,99±0,08. After applying PEEP 10cmH<sub>2</sub>O, a trend towards an increase in MPI index of right ventricle and a decline in ESA of the right ventricle were recorded.

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With respect to other parameters no statistically significant differences were recorded. After applying PEEP=5cmH<sub>2</sub>O there is no significant change noted in the overall structure and function of right heart. After applying PEEP=10cmH<sub>2</sub>O changes were recorded

in the structure and function of right ventricle caused mainly by the reduction of preload and less by the augmentation of afterload.

## INTRODUCTION

End-expiratory alveolar collapse is a common event in patients under mechanical ventilation, causing atelectasis which impair gas exchange and oxygenation. Positive end-expiratory pressure (PEEP) is an established method for mitigating this trend towards alveolar collapse in mechanically ventilated patients. Yet, in patients with respiratory disease, high values of PEEP, necessary for retaining oxygenation, may have negative effect on cardiac function<sup>1,2</sup>. RV function is the primary determinant of cardiac output in critically ill patients<sup>3</sup> and its dysfunction is associated with poor outcomes and can be induced by mechanical ventilation and PEEP therapy<sup>4</sup>.

In 1948, Cournand et al. studied the intermittent positive-pressure breathing, with or without continuous positive airway pressure (CPAP) and concluded that ventilation with positive pressure reduces venous return and right ventricular filling, with a result of cardiac output decrease<sup>5</sup>.

Later on, other researchers studied PEEP effects and presumed that the decrease in cardiac output during mechanical ventilation is partially attributed to the myocardial systolic impairment<sup>6-8</sup>, a theory not confirmed on subse-

quent studies<sup>9,10</sup>. On the contrary, some studies revealed that PEEP application in patients with congestive heart failure could increase cardiac output<sup>11,12</sup>. Moreover, it seems that PEEP application could reinforce right ventricle (RV) ejection either through increasing the functional residual capacity<sup>13</sup> or through reducing the pulmonary hypoxic vasoconstriction, after the opening of atelectatic alveoli<sup>14-16</sup>.

Therefore, the effects of PEEP on cardiac function vary and they are often unpredictable, either with a predominantly positive effect, or a negative one, depending on a patient's condition. The ideal value of PEEP is not easily defined and remains atopic of controversy.

The aim of this study was to perform a step-wise PEEP escalation in anesthetized, fully mechanically ventilated patients and to assess their RV function with tissue Doppler and conventional echocardiography.

## MATERIAL AND METHODS

The study (observational) was conducted after the approval of the scientific committee of bioethics and is part of the main writer's (of this article) PhD Thesis<sup>17</sup>.

The inclusion criteria were: intubated patients of intensive care unit, haemodynamic stability,

sinus rhythm, without oxygenation and ventilation problems during the study.

All patients were sedated with midazolam and cis-atracurium, under pressure control mechanical ventilation. Blood pressure was measured invasively through radial artery catheterization.

Exclusion criteria were: patients with atrial fibrillation or conduction disorders (inability to obtain tissue Doppler imaging at tricuspid annulus), patients with stomach or oesophagus pathologies (contraindication for transesophageal echocardiography) and patients with hypovolemic shock, pneumothorax and bronchial asthma (absolute and relative contraindications for PEEP insertion).

In many critically ill patients, low quality images are obtained with transthoracic echo, because the acoustic windows are suboptimal<sup>18</sup>. So, transesophageal echocardiography was selected as the method of choice.

All echo measurements were conducted at three different PEEP values: at first at 0 PEEP, ten minutes after insertion of 5cmH<sub>2</sub>O PEEP and ten minutes after insertion of 10cmH<sub>2</sub>O PEEP. Previous studies have demonstrated that all cardiorespiratory effects take place just a few seconds after PEEP insertion<sup>19</sup>.

The GE Vivid 7 cardiac ultrasound machine with a high frequency (6MHz) transesophageal

transducer for adults (6T) was used for acquisition of images. These images were stored in an external hard disk and all the measurements were done at second time using the manufacturing software (EchoPac GE Vingmed, Horten Norway).

The echocardiographic study was performed according to ASE/EAE guidelines for transesophageal echocardiography and for evaluation of right ventricle function<sup>20</sup>. The indexes that are measured during the study were the following:

- St (Tricuspid annular Systolic velocity): Peak systolic velocity of the tricuspid annulus (tissue doppler).
- TAPSE (Tricuspid Annular Peak Systolic Excursion): Distance of systolic excursion of the RV annular plane towards the apex (M-Mode).
- MPI of RV (Myocardial Performance Index): The ratio of total isovolumic time (isovolumic contraction time and isovolumic relaxation time) divided by RV ejection time.
- IVA (Myocardial Isovolumic Acceleration Time): The ratio of peak isovolumic RV myocardial velocity divided by time to peak velocity, measured at the level of the lateral tricuspid annulus during the isovolumic contraction.
- ET (Ejection Time): Time of ejection to the pulmonary artery, measured in the right ventricle outflow tract.

-Eccentricity index of left ventricle in end-systole (EccIndS) and end-diastole (EccIndD): The ratio of anterior-inferior and septal-posterolateral cavity dimensions, measured at end-systole and end-diastole.

-End diastolic (EDA) and end-systolic (ESA) right ventricle area.

-FAC (Fractional Area Change): The percentage change in right ventricle area between end-diastole and end-systole.

All the Doppler indexes mentioned above were measured for each patient and for every PEEP value several times (3 times) per respiratory circle, using eventually the mean value for statistical analysis. In that way each value was representative of the overall conditions during the respiration and could be reliably compared to each other, in the different PEEP values inserted.

A non-parametric statistical test (Friedman ANOVA) was used for the comparison between the three different results of each index. Non-parametric multiple comparisons using the Schaich- Hamerle test, were conducted for the cases there was statistical significance between the three different values of the indexes. The level of statistical significance was defined as  $p < 0.05$ . The datanalysis was completed using the statistical package SPSS v. 19.0.

## RESULTS

Patient's demographic data are presented in table 1.

**Table 1:** Demographic data of patient's study

<b>Patients, n (number)</b>	<b>14</b>
Male-female, n (number)	12-2
Age, years	70,36 ± 13,19
APACHE II	18 ± 5,7
<b>Comorbidities, n (number)</b>	
Stroke	4
Trauma	3
Status epilepticus	3
Ileus	2
Coma	2
<b>MV characteristics</b>	
PCV, cmH <sub>2</sub> O	18
MV, days before	2 (1 - 3)
Vt, ml/Kg	7,2 (6,8 - 7,6)
Vt, lt	0,48 (0,44 - 0,52)
PaCO <sub>2</sub> , mmHg	39 (37 - 41)
FiO <sub>2</sub>	0,4 (0,35 - 0,45)

*Values are mean (min-max). Age, APACHE II are presented as mean ± SD, APACHE II: acute physiology and chronic health evaluation II, PCV: pressure control ventilation, Vt: tidal volume, MV days before: duration of controlled mechanical ventilation (MV) in days before recording, PaCO<sub>2</sub>: partial pressure of carbon dioxide in the arterial blood, FiO<sub>2</sub>: fraction of inspired oxygen.*

The results of all the indexes measured are presented in table 2. Application of 5cmH<sub>2</sub>O PEEP did not affect significantly any of the parameters measured. On the other hand, application of 10cmH<sub>2</sub>O PEEP induced significant changes in the following indexes: St was reduced from 10,86±3,8 cm/sec to 8,7±2,9cm/sec (Image 1), TAPSE was reduced from 2,876 ± 0,643 to 2,385±0,556cm, IVA of the RV increased from 2,2692±0,93m/sec<sup>2</sup> to

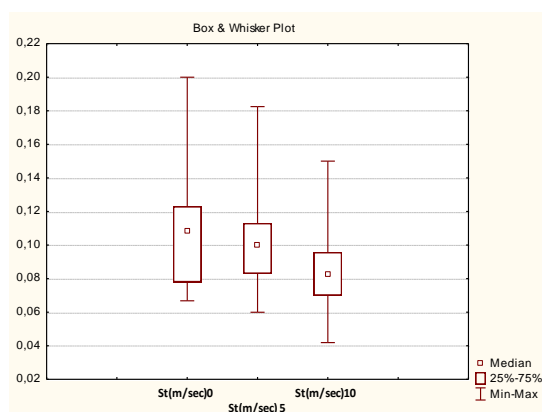
2,8536±1,628 m/sec<sup>2</sup>, ET in RV outflow tract was reduced from 259,27±17,47msec to 229,34 ±31,22msec, Left ventricle eccentricity index in end-dias-tole increased from 0,9±0,07

to 0,99±0,08 (Image 2,3), EDA of the RV decreased from 21,372±5,01 cm<sup>2</sup> to 18,87±4,15cm<sup>2</sup>.

**Table 2:** Results of measurements of echocardiographic parameters (mean±SD) in different PEEP degrees.

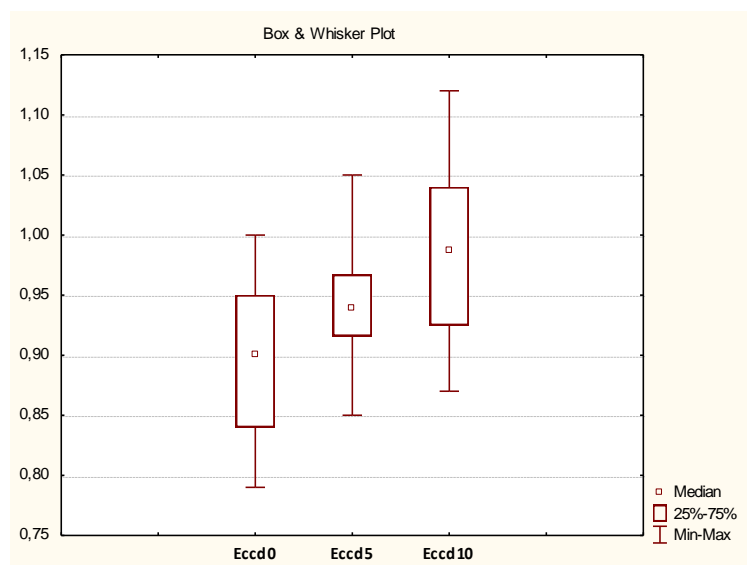
	PEEP 0 (cmH <sub>2</sub> O)	PEEP 5 (cmH <sub>2</sub> O)	PEEP 10 (cmH <sub>2</sub> O)	PEEP 0-5 (cmH <sub>2</sub> O)	PEEP 0-10 (cmH <sub>2</sub> O)
St (cm/sec)	10,86±3,8	10,72±3,54	8,7±2,9	0,558	0,0005
TAPSE (cm)	2,876±0,643	2,621±0,506	2,385±0,556	0,142	0,0063
MPI	0,4974±0,266	0,6886±0,4	0,7321±0,7	0,558	0,1350
IVA (m/sec <sup>2</sup> )	2,2692±0,93	2,5586±1,007	2,8536±1,628	0,392	0,0460
ET (msec)	259,27±17,47	238,713±20,29	229,34±31,22	0,070	0,0020
EccInd S	0,8858±0,126	0,8975±0,096	0,9074±0,124	0,392	0,1912
EccInd D	0,9±0,07	0,94±0,06	0,99±0,08	0,142	0,0460
EDA (cm <sup>2</sup> )	21,372±5,01	20,107±3,79	18,87±4,15	0,558	0,0054
ESA (cm <sup>2</sup> )	10,792±3,87	10,185±2,93	9,88±3,03	0,331	0,0617
FAC	0,504±0,073	0,495±0,095	0,48±0,082	0,771	0,3298

**Image 1:** Results of peak systolic velocity of the tricuspid annulus (St) on Box & Whisker Plot diagram.



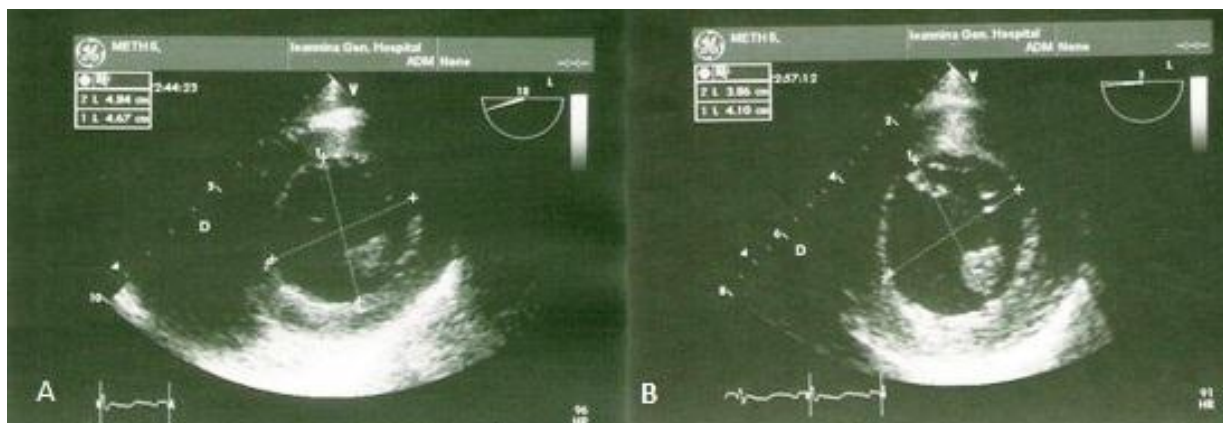
After applying PEEP the St decreases and the change becomes statistical significant between 0 and 10cmH<sub>2</sub>O PEEP.

**Image 2:** Results of Eccentricity index of LV in diastole on Box & Whisker Plot diagram.



*The values increase after applying PEEP.*

**Image 3:** An echo image of Eccentricity index of left ventricle in end-diastole without PEEP (A) and after applying 10cmH<sub>2</sub>O PEEP (B).



*Values 0,96/1,06 respectively. A case of a patient in our study whose index increased >1 after applying 10cmH<sub>2</sub>O PEEP. The linear trend of the interventricular septum is evident in image B.*

In MPI of the RV, did not reveal a statistically significant change, though a trend towards an increase was recorded when 10cmH<sub>2</sub>O was used. ESA of the RV displayed a trend towards

reduction when 10cmH<sub>2</sub>O was used (borderline non statistical significant, p=0,06). FAC of the RV and eccentricity index of the left ven-



tricle in end-systole do not change after PEEP application.

No changes of blood pressure and cardiac rhythm were noted after PEEP application.

## DISCUSSION

One of the main results of this study is that application of a 5cmH<sub>2</sub>O PEEP in patients under mechanical ventilation does not affect neither the structure nor the function of the right ventricle. On the other hand, the effect of application of a 10cmH<sub>2</sub>O PEEP is complex and provokes changes in the preload and the afterload<sup>21</sup>.

Previous research has proven that PEEP causes dilation of lungs and increase in intrathoracic pressure, inducing restriction of the diastolic filling of the right ventricle<sup>22</sup> and an increase in pulmonary vascular resistance<sup>23</sup>. The elevated intrathoracic pressure impedes the venous flow into the thorax, and compresses cardiac chambers, resulting in a reduction of the diastolic filling and the preload of the right ventricle<sup>1,24</sup>. The increase in PEEP values causes increase in elasticity of the right ventricle<sup>25,26</sup>. The increase of pulmonary vascular resistance is a result of lung dilatation, which impairs perfusion in some small pulmonary vessels and changes the diameter of pulmonary vessels<sup>27</sup>. The above mentioned mechanisms result in a reduction of the preload of the right

ventricle (due to the restriction of the diastolic filling of the right ventricle) and in an increase in the afterload of the right ventricle (due to the increase of pulmonary vascular resistance). In our study, a significant reduction of St and of TAPSE was found, indicating right ventricle systolic dysfunction. St values <11.5cm/sec are related with systolic dysfunction of the right ventricle (RV EF<50%), with a sensitivity of 90% and a specificity of 85% respectively<sup>28,29</sup>. However, recent guidelines for right ventricle assessment correlate St values<10cm/sec with right ventricle's systolic dysfunction<sup>20</sup>. Moreover, TAPSE (with normal values>15mm) is well correlated with ejection fraction (EF) of the right ventricle and reflects also the function of the free wall of the right ventricle along the longitudinal axis<sup>30,31</sup>; though it is preload dependent<sup>19</sup>. In our study, there was a significant reduction of St below the normal cutoff (when PEEP of 10cmH<sub>2</sub>O was applied) and a significant reduction of TAPSE, though without falling below the lower normal cutoff.

On the other hand, FAC of the right ventricle did not change after PEEP increase. This index is well correlated with RV EF<sup>30</sup>, though it is also preload and afterload dependent. Moreover, a borderline statistically significant increase of time of IVA (p=0,046) was found

(normal values  $1.4-3\text{m/sec}^2$ )<sup>20</sup>. It seems that IVA reflects the systolic function of the right ventricle and is less load dependent<sup>28,32</sup>; IVA values of  $>1.1\text{m/sec}^2$  are well correlated with  $\text{RV EF} > 45\%$  measured with MRI, with a 90% sensitivity and specificity<sup>30</sup>. IVA is proportionally correlated with RV systolic function<sup>31-33</sup>. The results of FAC and IVA in our study indicate that application of  $10\text{cmH}_2\text{O}$  PEEP does not affect the systolic function of the right ventricle. It is widely accepted that RV EF and the parameters that are related with it, can be influenced by preload and therefore do not illustrate accurately the systolic function of the right ventricle<sup>20</sup>. Therefore, St and TAPSE reduction may reflect a reduction in the systolic function of the right ventricle, not because of a dysfunction of its contractility, but because of a distention inability of myocardial fiber of the right ventricle and a consequent reduction of its contraction, according to the Frank-Starling law.

In our study, it was found a reduction of ET in the right ventricular outflow tract and a trend towards an increase of MPI (normal values with tissue Doppler  $<0.55$ )<sup>20</sup>. It is known from previous studies that the reduction in ET is conversely related with pulmonary artery pressure<sup>35</sup>; while MPI index is usually increased in patients with systolic or diastolic dysfunction

of the right ventricle<sup>35,36</sup>, and in cases with high pulmonary artery pressures<sup>35</sup>. MPI values have prognostic significance in patients with pulmonary hypertension<sup>35,36</sup>. Therefore, the reduction of ET and the trend for an increase of MPI, which were found in this study, show an increase in pulmonary vascular pressures after application of  $10\text{cmH}_2\text{O}$  PEEP.

A reduction of end-diastolic surface area and a trend towards a reduction of end-systolic surface area of the right ventricle is recorded in this study, as reflected in FAC of the right ventricle, which did not change after PEEP application. A recent study showed that the FAC changes significantly after applying  $20\text{cmH}_2\text{O}$  PEEP<sup>4</sup>.

Application of  $10\text{cmH}_2\text{O}$  of PEEP did not change Eccentricity Index of the left ventricle in end-systole, while in end-diastole there was a statistically significant increase of this index, but values did not exceed 1. The major impact of RV function is usually considered to be a decrease in LV diastolic compliance if RV overdistention occurs, through the process of ventricular interdependence (changes of the right ventricle affect the structure of the left ventricle through interventricular septum)<sup>37</sup>. This index is based on ventricular interdependence, meaning that. Normal values of Eccentricity index are equal to 1 both in systole



and in diastole. Values  $>1$  in end-diastole indicate volume overload of the right ventricle, while values  $>1$  both in systole and in diastole indicate pressure overload of the right ventricle<sup>30,38</sup> (Image 3).

Values  $<1$  are not taken into account. In our study, the increase of Eccentricity index in end-diastole after applying 10cmH<sub>2</sub>O does not exceed 1 and so it cannot be taken into account. This finding is not opposed to the recorded reduction of end-diastolic surface area of the right ventricle. We could hypothesize that in PEEP values  $>10$  cmH<sub>2</sub>O the Eccentricity index would increase  $>1$ , with a consequent leftward movement of the interventricular septum.

Since the application of PEEP may have opposing effects, we think that our results are not against to the results of other studies<sup>4,25,39-42</sup>. The increase in pulmonary vascular resistance (increase of afterload), tend to lower the ejection of the right ventricle and increase its end-diastolic volume. On the other hand, the increase in elasticity of right ventricle tends to reduce its end-diastolic volume (reduction of preload). Hence, depending on which effect (on preload or on afterload) predominates after the increase of airway pressures, there will be a relative effect on end-diastolic volume of the

right ventricle which is partially reflected through its end-diastolic surface area.

In conclusion, in our study it seems that in PEEP values of 10cmH<sub>2</sub>O there is predominantly a reduction in the right ventricle preload, while an increase in the right ventricle afterload is also recorded. The gradual increase of Eccentricity Index in end diastole and the reduction of ET after PEEP increase, may indicate a possible significant increase in pulmonary vascular resistance after application of PEEP  $>10$ cmH<sub>2</sub>O, having as a predominant consequence an increase of the right ventricle afterload, an increase in right ventricle diameter and a leftward shift of the interventricular septum.

In the study most of the indexes were derived through tissue Doppler. This method, as any doppler method, depends on the angle between ultrasound beam and the tissue. The movement of free wall of the right ventricle is not always parallel to the ultrasound beam, having as a consequence the underestimation of St and IVA absolute values. However, in each patient the alignment was the same for all three values of PEEP, making the results comparable and reliable. Measurements of MPI do not have these limitations, as MPI is calculated using specific time and is independent of velocities absolute values.

Tricuspid annular peak systolic velocity is a validated method for the estimation of right ventricle's systolic function. However, it is dependent on the movement of the basis of the heart to the apex. New echocardiographic methods for the evaluation of systolic function of the right ventricle, like strain (myocardial deformation) could be used more accurately and reliably for the evaluation of biventricular systolic function on different PEEP values, as it is angle independent method.

The last limitation of the study is the small number of patients included. Consequently, the results cannot be definite and cannot be generated. However, they create a hypothesis which can be tested with larger studies.

In conclusion, from above, it appears that applying PEEP 5 cm H<sub>2</sub>O has no effect in the structure and the function of the right heart. In contrast, applying PEEP 10 cmH<sub>2</sub>O effects the structure and the function of the right ventricle; this is mainly attributed to reduced filling of the heart (reduced preload) and to a lesser extent to increased pulmonary vascular resistance (increased afterload). Further studies in the ICU population, using TEE imaging and tissue Doppler are warranted.

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