

## **Minute ventilation stabilization during all pressure-control / support mechanical ventilation modes.**

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Short title: Minute ventilation stabilization in pressure support ventilation modes.

## Summary

**Goal:** To compare the effectiveness of ventilation control method „Automatic proportional minute ventilation (APMV) “versus manually set pressure control ventilation modes in relationship to lung mechanics and gas exchange.

**Type of the study:** prospective randomized

**Material and methods:** 80 patients undergoing coronary artery bypass grafting (CABG) were randomized into 2 groups. 40 patients in the first group No.1 (APMV group) were ventilated with pressure control (PCV) or pressure support ventilation (PSV) mode with APMV control. The other 40 patients (control group No.2) were ventilated with synchronized intermittent mandatory ventilation (SIMV-p) or pressure control modes (PCV) without APMV.

**Results:** Ventilation control with APMV was able to maintain minute ventilation more precisely in comparison with manual control ( $p < 0.01$ ), similarly deviations of  $\text{ETCO}_2$  were significantly lower ( $p < 0.01$ ). The number of manual corrections of ventilation settings was significantly lower when APMV was used ( $p < 0.01$ ). The differences in lung mechanics and hemodynamics were not statistically significant.

**Conclusion:** Ventilation using APMV is more precise in maintaining minute ventilation and gas exchange compared with manual settings. It required less staff intervention, while respiratory system mechanics and hemodynamics are comparable. APMV showed as effective and safe method applicable on top of all pressure control ventilation modes.

**Key words** Artefitial lung ventilation, Pressure controlled modes, Automatic proportional minute ventilation

## Introduction

Pressure-controlled mode represents the most prevalent method of artificial lung ventilation (ALV). Advantages of pressure-controlled ventilation are well known, e.g. patient safety, exponential flow curve ascent, peak-pressure stability etc. There are also a few disadvantages, e.g. gas exchange dependency from respiratory system mechanics (Campbell *et al.* 2002). Respiratory centre physiologically regulates components of respiratory system in a way to maintain adequate gas exchange with minimum energy expend, which was already demonstrated in clinical studies. Results confirm that the end parameter of regulation is minute ventilation (MV) or alveolar ventilation (VA) in order to maintain adequate gas exchange and thus acid-base balance (Török P *et al.* 2015, Török P *et al.* 2017).

Instability of alveolar ventilation in pressure-supported or controlled ventilation is mainly due to changes in respiratory system mechanics, patient's respiratory activity trigger and time constant of respiratory system (Török P *et al.* 2001) (Candik *et al.* 2018). Even at constant pressure, changes in lung and chest wall compliance, airway and endotracheal tube (ETT) resistance, lead to changes in respiratory volume (VT) as well as MV. This could lead to severe hypo/hyperventilation (Grasso *et al.* 2000). Magnitude of MV, or VA also consists of ventilatory drive of the patient and respiratory frequency, that can be influenced by sedatives, opiates, muscle relaxants, changes in chest wall compliance and intra - abdominal pressure (IAP) etc. (Chen *et al.* 2011). Considering the facts given, the use of pressure-controlled regimes is tightly connected with continuous gas exchange monitoring, mainly  $\text{ETCO}_2$ ,  $\text{SpO}_2$ , respiratory system mechanics measurement, eventually dead space to tidal volume ratio (VD/VT) measurement is also necessary.

There is substantial workload imposed on ICU staff regarding changes in ventilation parameters that require adjustment (Dojat *et al.* 1997). Modern ventilators have many servosystems that could be used in pressure-controlled mode, e.g. ASV (adaptive support

ventilation Bennet, USA) PRVC (pressure regulated volume control Maquet Gettinge) Germany, etc. (Manual\_Bennett\_840. 2015). All mentioned modes are representing only one specific ventilation regime and cannot be used on top of other pressure-controlled ventilation modes.

Considering these, we developed an extension method, that could be applied on top of all pressure controlled and assisted ventilation modes, named “Automatic proportional minute ventilation (APMV)”

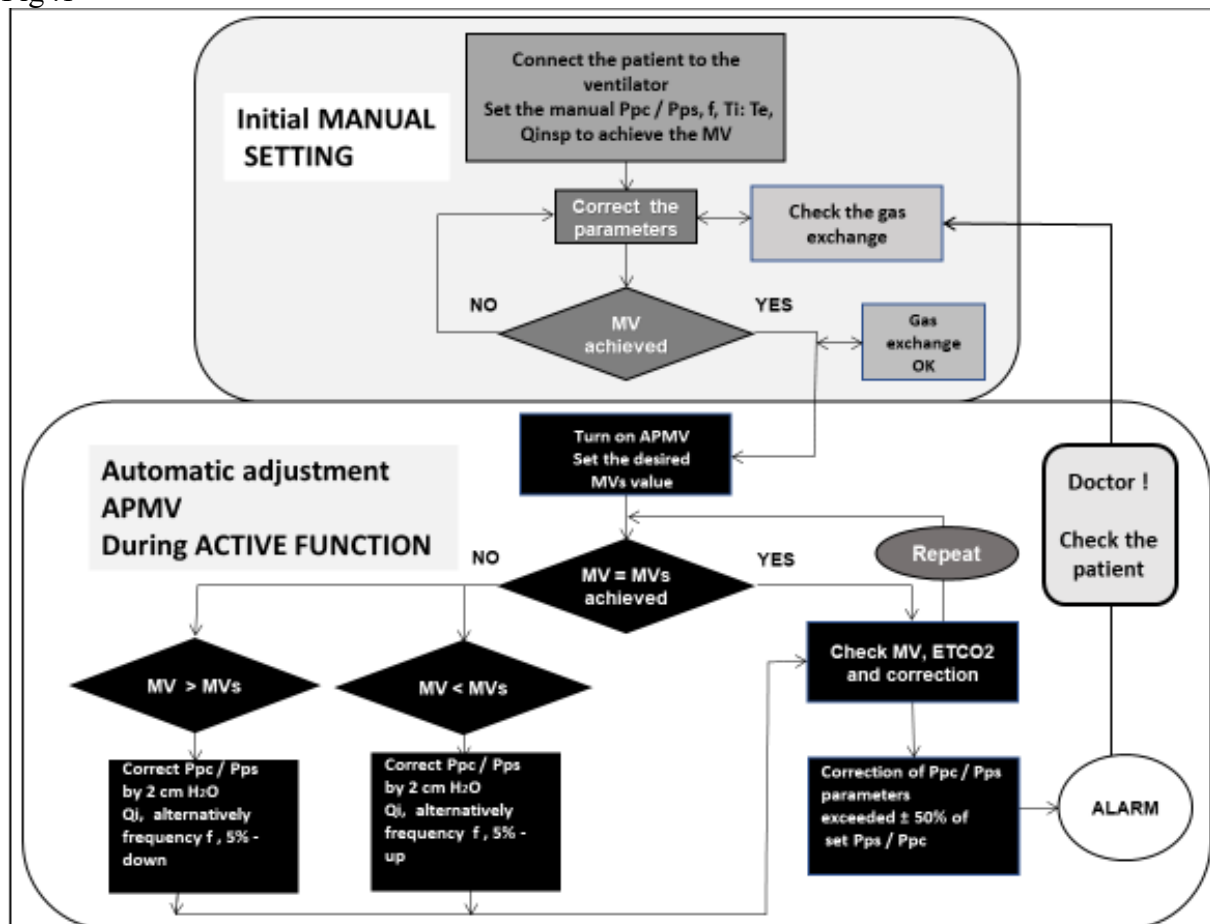
APMV is computer-assisted proportional auto-adaptive ventilation methods used over any pressure applied ventilation mode. Amount of ventilatory support that was set manually on the ventilator is adapting to the changes in respiratory system mechanics and ventilation drive in order to maintain an adequate minute ventilation and adequate gas exchange (Manual\_Servoventilator\_AURA\_V. 2017).

How does APMV work? The ventilator computer measures MV each 10-20 seconds and compares the value with MV set by the physician (minute ventilation servo (MV<sub>s</sub>)). In case of decrease or increase of measured MV compared to MV<sub>s</sub>, computer adjusts MV by increasing or decreasing the pressure of pressure support/control (Pps/pc)  $\pm$  1-2 cmH<sub>2</sub>O keeping MV and MV<sub>s</sub> equal. The regulation of changes of inspiratory pressure Pps/pc is based on comparison of measured MV and targeted MV<sub>s</sub>. In order to maintain stable ETCO<sub>2</sub> value throughout the postoperative weaning from the mechanical ventilation using APMV method, the ventilator can change MV up to a maximum of 1,5 times the MV<sub>s</sub>, which represent manually set MV by the physician.. Further increase or decrease in MV by APMV is blocked by the software in order to prevent barotrauma or severe hypo/hyperventilation (Dojat *et al.* 2000, Gruber *et al.* 2008) and (Roubik *et al.* 2011).

If it is necessary to increase or decrease the pressure more than  $\pm$ 50% to maintain MV, the alarm is sound and physician's presence is required for parameters setting (Manual\_Servoventilator\_AURA\_V. 2017, Török P *et al.* 2015).

Basic algorithm of APMV is explained on Fig. 1

Fig.1



## Material and Methods

Study was performed at Intensive Care Unit, East Slovakian Institute of Cardiovascular Diseases in Košice, Slovakia, between June 1. 2015 to December 31. 2016 and it was backed up by ethics committee approval by VÚSCH a. s. /EK No. VZ/7/KardO/2011/. All patients had their informed consents signed before they were enrolled in the study.

We created two groups of patients after CABG (coronary artery bypass grafting) that were ventilated with two different pressure-operated ventilation modes. The group 1 (APMV group, n=40) consisted of patients who were ventilated using PCV/PS controlled using APMV method. The second group of patients (n=40) were ventilated by using pressure-controlled ventilation (PCV), and pressure supported ventilation (PS), manually set by the physician without APMV method.

Patients in both groups were selected from operating chart as follows: even patient numbers were enrolled in group 2 and odd patient number in group 1 e.g. APMV group. Exclusion criteria were LVEF less than 30%, Chronic obstructive pulmonary disease ( COPD) Gold stage III and IV, bronchial asthma, Chronic renal failure (CHRF) patients requiring haemodialysis. We were monitoring ventilation parameters, hemodynamics and gas exchange in the lung by monitor (CARESCAPE™, B850, GE Healthcare USA). In group 1 we used PCV/PS with APMV method using servo-ventilator Chirolog Aura V (Chirana Medical a.s. Slovakia), and in group 2 we used PCV/PS mode using servo-ventilator Servo-I (Maquet group, Germany). Ventilation parameters were monitoring every 15 minutes during the first 2

hours since admission to ICU. Patients were not relaxed, only lightly sedated using 1% Propofol titration Richmond agitation and sedation score (RASS -2-0). After connecting patient to the ventilator, the MV has been set to 80 – 100 ml/kg IBV/min, PEEP to 0.8 – 1.1 cmH<sub>2</sub>O for each 10 kg ideal boey weight (IBV), but no less than 5 and no more than 10 cm H<sub>2</sub>O. PEEP was decreased only before weaning procedure at the end of ALV in both groups.

MV has been corrected to maintain ETCO<sub>2</sub> in a range between 35-42 mmHg for the first 10 minutes. The stability of MV was defined as the deviation of  $\pm 5\%$  in ETCO<sub>2</sub> value. Then APMV method was implemented with MVs equal to patient's MV. Average Imnspiratory fraction of oxygen (FiO<sub>2</sub>) was between  $0.45 \pm 0.05$  in both groups in order to obtain SpO<sub>2</sub> at least 94%. There was no need to change FiO<sub>2</sub> during measurement. Ventilation frequency has been set to  $16.5 \pm 2$  breaths/min calculated according to the pattern:  $f = \text{INT} (21 - \text{IBW (kg)}) / 17$ ). Specific tidal volume (VTs) ranged from 4.9 – 5.9 ml/kg IBV. Demographic data of both groups are showed in Table 1 and 2.

Statistical evaluation compared group 1 and 2 in demographic data, ventilation parameters describing the changes in ventilation, ventilator parameters settings, respiratory system mechanics, hemodynamic parameters and nurse and doctor time spent with ventilator were performed by the two-tail dependent Student's t-test and linear correlation.

Table 1.

<b>Demographic data in group 1 (APMV) mean and <math>\pm</math>SD</b>	
<b>Number of patients</b>	<b>40</b>
<b>Average body weight <math>\pm</math> SD (kg)</b>	<b>87 <math>\pm</math> 9.5</b>
<b>Age (year)</b>	<b>62 <math>\pm</math> 7.9</b>
<b>Height (cm)</b>	<b>171 <math>\pm</math> 13</b>
<b>BSA body surface area (m2)</b>	<b>2.0 <math>\pm</math> 0.19</b>

Table 2.

<b>Demographic data in group 2 (PCV/PS) mean and <math>\pm</math>SD</b>	
<b>Number of patients</b>	<b>40</b>
<b>Average body weight <math>\pm</math> SD (kg)</b>	<b>89 <math>\pm</math> 9.1</b>
<b>Age (year)</b>	<b>61 <math>\pm</math> 7.2</b>
<b>Height (cm)</b>	<b>169 <math>\pm</math> 15</b>
<b>BSA body surface area (m2)</b>	<b>2.0 <math>\pm</math> 0.12</b>

No statistical difference between groups 1 and 2 in demographic data was observed.

## Results

Average ventilation parameters used in groups 1 and 2 respectively are showed in Table 3 and 4. Results are presented as a mean value  $\pm$  standard deviation (SD). The statistical significance of the differences or changes in results was calculated using the two-tail dependent Student's t-test and linear correlation.

Table 3. Change of average ventilatory parameters in group 1 in 0, 45, 60, 90, 120 minutes from the onset of ALV

Average ventilation parameters (mean $\pm$ SD) (n =40) in group No.1 - PS - APMV						
Parameters	Time (min)	0	45	60	90	120
Measured MV (l*min <sup>-1</sup> )		7,12 $\pm$ 1,8	7,2 $\pm$ 1,5	7,5 $\pm$ 1,5	7,2 $\pm$ 1,9	7,7 $\pm$ 1,4
Breathing frequency f (c*min <sup>-1</sup> )		15,5 $\pm$ 0,5	15,5 $\pm$ 0,5	15,5 $\pm$ 0,5	18 $\pm$ 2,8	17 $\pm$ 2,2
PEEP (cm H <sub>2</sub> O)		8 $\pm$ 1	8 $\pm$ 1	8 $\pm$ 1	4 $\pm$ 1	4 $\pm$ 0,5
FiO <sub>2</sub>		0,43 $\pm$ 0,03	0,43 $\pm$ 0,03	0,43 $\pm$ 0,03	0,43 $\pm$ 0,03	0,43 $\pm$ 0,03
Pps/Ppc driving pressure (cm H <sub>2</sub> O)		11 $\pm$ 1,3	12 $\pm$ 1,5	12 $\pm$ 1,5	10 $\pm$ 2	8 $\pm$ 1
Trigger activity		No	No	No/Yes	Yes	Yes

Table 4. Change of average ventilatory parameters in group 2 in 0, 45, 60, 90, 120 minutes from the onset of ALV

Average ventilation parameters (mean $\pm$ SD) (n =40) in group No.2 - PCV/PS						
Parameters	Time (min)	0	45	60	90	120
Measured MV (l*min <sup>-1</sup> )		7 $\pm$ 1,4	6,4 $\pm$ 1,1	7,4 $\pm$ 1,7	7,4 $\pm$ 1,6	8 $\pm$ 1,2
Breathing frequency f (c*min <sup>-1</sup> )		14,5 $\pm$ 0,5	15,5 $\pm$ 0,5	14,5 $\pm$ 0,5	18 $\pm$ 2,2	18 $\pm$ 2,0
PEEP (cm H <sub>2</sub> O)		8 $\pm$ 1	8 $\pm$ 1	8 $\pm$ 1	6 $\pm$ 1	4 $\pm$ 0,5
FiO <sub>2</sub>		0,45 $\pm$ 0,05	0,45 $\pm$ 0,05	0,45 $\pm$ 0,05	0,45 $\pm$ 0,05	0,45 $\pm$ 0,05
Pps/Ppc driving pressure (cm H <sub>2</sub> O)		10 $\pm$ 1	13 $\pm$ 2,1	13 $\pm$ 1,9	10 $\pm$ 0,8	9 $\pm$ 2
Trigger activity		No	No	No/Yes	Yes	Yes

The average duration of postoperative artificial ventilation including using T-piece was 3.1  $\pm$  1.3 hours in group 1 vs. 3.3  $\pm$  1.4 hours in the group 2 (p=NS). After 1.4  $\pm$  0.5 hours when patient's start breath, trigger was the main control element of ventilation. Because after activation of spontaneous ventilation trigger is regarding to ventilation volume usually irregular. The APMV method regulated each separate ventilation volumes by changes of Pps/Ppc, that requested minute ventilation to be achieved.

A patient has been shifted to PS mode in both groups. We compared the deviations in minute ventilation (MV) from target value (MV<sub>t</sub>), which was not statistically significant (p=NS) between group 1 and 2. We observed statistically significant difference between MV and MV<sub>t</sub> in group 2 in 30, 45 and 120 minutes from the onset of artificial lung ventilation (p<0.01). Therefore, manually adjustment of Ppc/Pps was necessary to maintain targeted MV. Stability of MV was statistically significantly better in group 1 (p<0.01), no manual

adjustment was necessary see Fig.2 and Fig.3. We considered MV to be adequate if deviation in  $\text{ETCO}_2$  value was  $\pm 5\%$  (mmHg) continuously measured by capnometer.

Fig. 2. Present measured and target average values in group 1 and 2 of parameters MV and MVs. Measured MV in group 2 showed far higher differences compared with group 1.

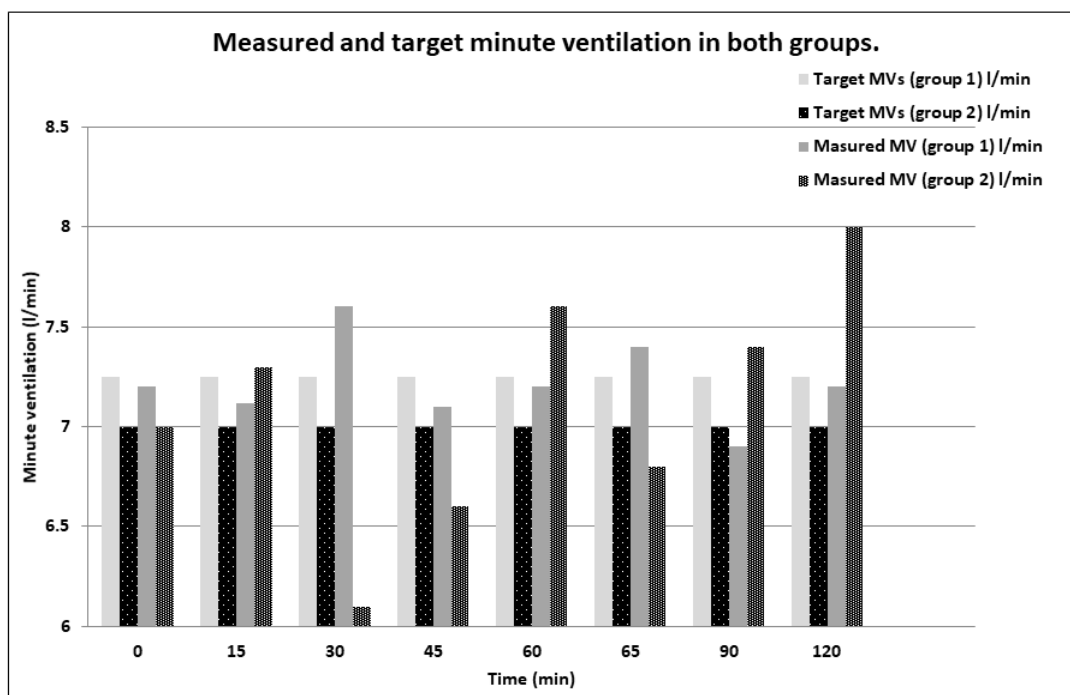


Fig. 3. Showed deviation of MV in percentage (%). We can see that MV in group 1 is more stable (+3.6 to 4.1%) compared with group 2. (-14.8 to 12.5%), ( $p < 0.01$ ).

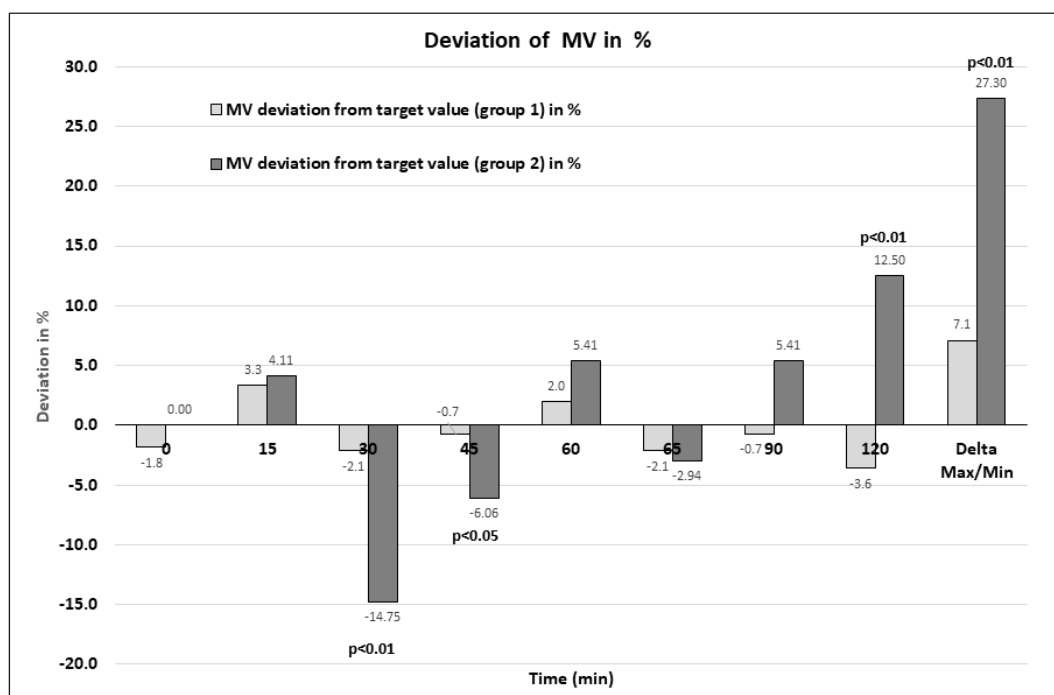


Fig. 4. Shows differences in average of ETCO<sub>2</sub> value between groups 1 and 2. The difference up to 30 minutes of ventilatory onset was not statistically significant ( $38 \pm 4$  mmHg vs  $39 \pm 7.5$ ). After 45 minutes from onset of ventilation, difference was up to 8 mmHg between both groups ( $p < 0.01$ ) t-test. This mean, that gas exchange in group 1 was more stable compare with group 2. . Group 1 linear regression showed increasing trend of ETCO<sub>2</sub> and in group 2 decreasing trend of ETCO<sub>2</sub>, while both are in acceptable range.

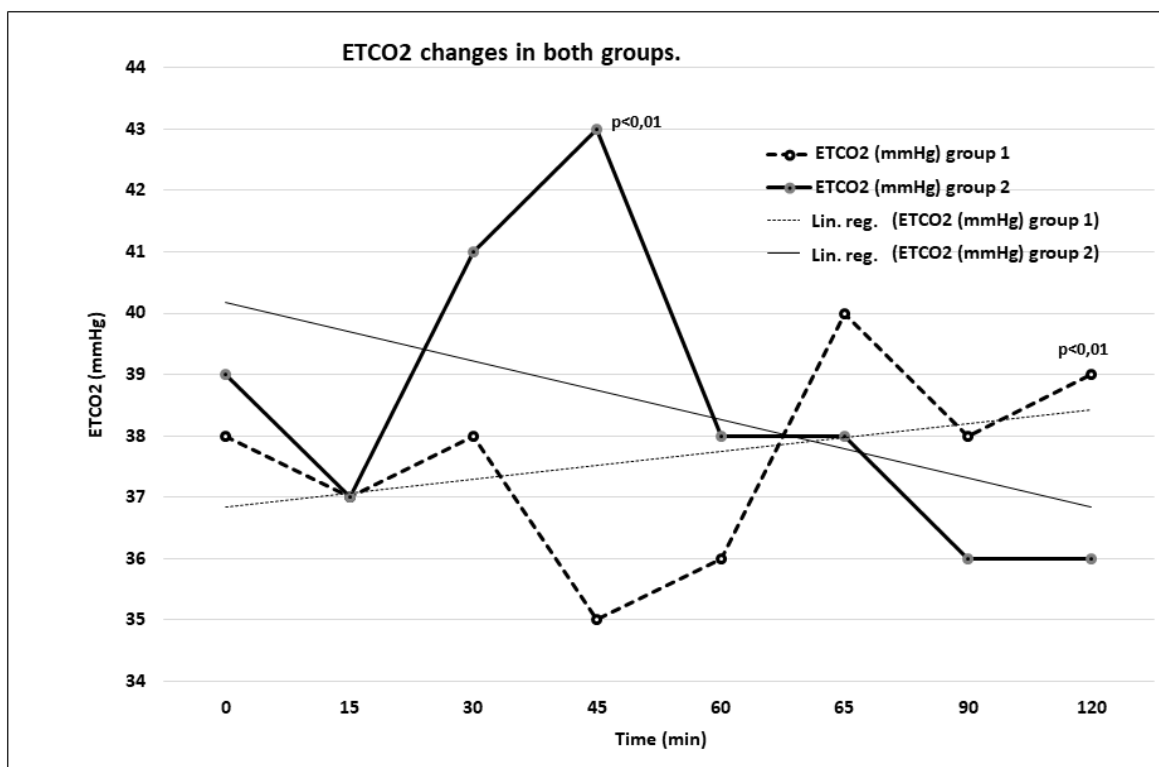
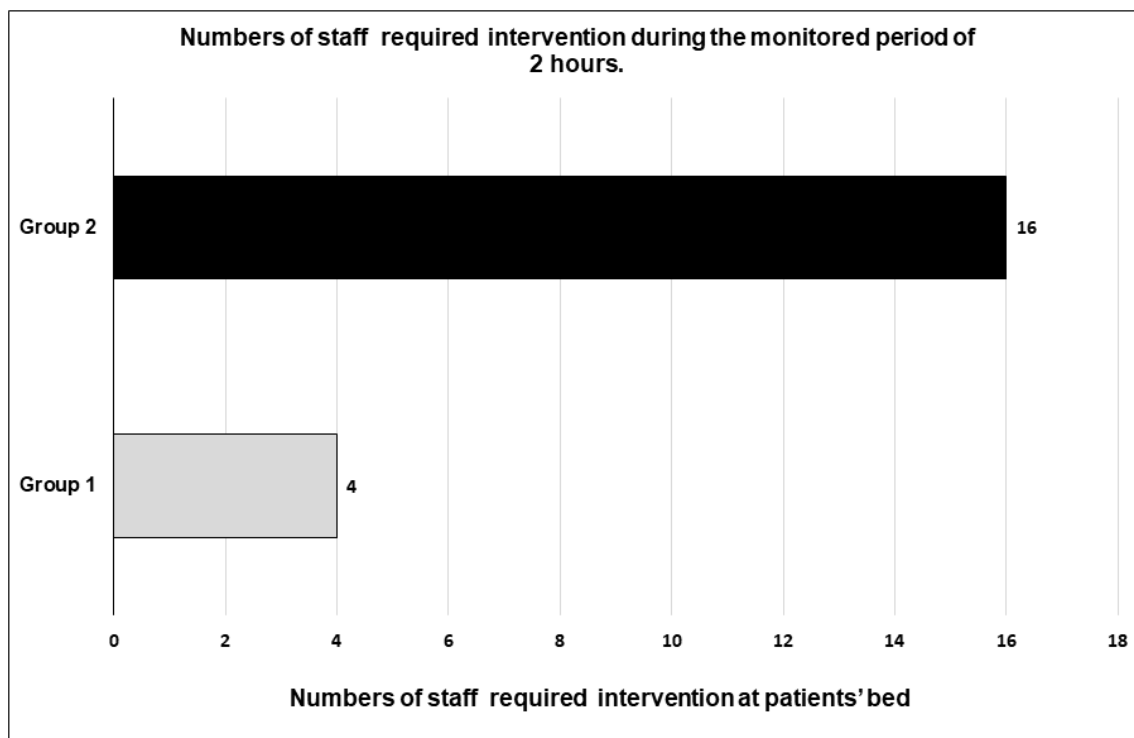




Fig. 5. Showed the number of events, ( with artificial ventilation related intervention ), which required staff to come to patients in whole group 1 and 2. 4 times often intervention of nurses and doctors was needed in group 2 compare with group 1 In group 1 no one of 4 interventions was related to ventilation parameters changes (the reason was alarm range setting, trigger sensitivity setting, and patients' physiological requirements).



$\text{PaO}_2/\text{FiO}_2$  was  $309 \pm 18$  mmHg in group 1 and  $305 \pm 10$  mmHg in group 2 ( $p=\text{NS}$ ). Static pulmonary compliance ( $C_{st}$ ) in first and last hour of ventilation was  $41 \pm 10$  to  $49 \pm 13$  ml.cm  $\text{H}_2\text{O}^{-1}$  in group 1 vs.  $42 \pm 7$  to  $48 \pm 15$  ml.cm  $\text{H}_2\text{O}^{-1}$  in group 2 ( $p=\text{NS}$ ). We didn't find any statistically significant difference in airway resistance ( $R_{aw}$ ), that was  $3.1 \pm 0.44$  cm $\text{H}_2\text{O} \cdot \text{l}^{-1} \cdot \text{s}^{-1}$  ( $P=\text{NS}$ ). After resuming of spontaneous ventilation in PSV mode, the respiratory frequency was  $15.5 \pm 2.9$  breaths/min and  $16 \pm 3.1$  breaths/min in group 1 and 2 respectively ( $p=\text{NS}$ ).

## Discussion

We used PCV/PS ventilation mode with new APMV method and compared with manually set ventilator parameters in PCV/PS ventilation mode. To our best knowledge this is a first work with this approach in ventilation area. There are changes in MV and VT caused by change in respiratory system mechanics and because of resuming of spontaneous ventilation activity. APMV automatically corrects problems with instability in mechanical ventilation (changes in respiratory system mechanics, changing respiratory drive of the patient). Ventilation parameters in non-APMV (PCV/PS) group must be corrected manually by the staff, whereas in AMPV group, MV is corrected itself by APMV algorithm. APMV algorithm maintained MV very close to physicians demanded MVs. We applied intelligent system regarding APMV that changes pressure support in each extent, thus amount of flow, mainly peak flow ( $Q$ ), as well as ventilation frequency.

Comparison of APMV method and manually set parameters by staff showed a greater stability in gas exchange in patients ventilated with APMV. This can be also seen in variation of  $\text{ETCO}_2$ . Changes in respiratory system mechanics occur very frequently in mechanically

ventilated patients. This could lead to hypoventilation, hyperventilation or ventilation asynchrony during either pressure support (PS) ventilation or pressure-controlled ventilation (PCV) modes (Arnal *et al.* 2013, Clavieras *et al.* 2013, Grasso *et al.* 2000, Tonetti *et al.* 2017, Török P *et al.* 2017). With constant pressure support, changes in respiratory system mechanics in terms of decrease in compliance or increase in resistance require change of ventilation frequency in order to maintain the MV (Török P *et al.* 2015, Török P *et al.* 2001). Changes in respiratory system mechanics also present with changes in time constants of different lung compartments that can lead to worsening in lung gas distribution homogeneity (Gruber *et al.* 2008) (Candik *et al.* 2018). Changes in PaCO<sub>2</sub> (EtCO<sub>2</sub>) were, using APMV method, much lower due to better stability in minute ventilation (Manual\_Servoventilator\_AURA\_V. 2017). Experimental studies (Campbell *et al.* 2002, Török P *et al.* 2017) show that respiratory frequency is compensatory increased whenever there is decrease in compliance. The same relationship has been showed in experiment work (Arnal *et al.* 2013, Dojat *et al.* 2000) where changes in VT were compared regarding to respiratory system mechanics by using PS vs ASV (adaptive supporting ventilation) ventilation mode. In PS mode it has been shown a decrease in both VT and MV, while the same substantial decrease of VT and MV was present in ASV ventilation mode. The ASV mode is compensating MV by the ventilator. In comparison with APMV method which is not ventilation mode per se. APMV method could be used as a universal extension for all pressure-based ventilator modes. Other ventilator modes operate similarly however, they represent individual ventilatory modes and do not allow the advantages of proportional regulation in these pressure-based ventilatory modes (Manual\_Bennett\_840. 2015).

We used two types of ventilators (Aura V and Servo I Maquet) which in pressure controlled regimes are identical according to ISO standard. In group 1 we used only ventilator Aura V with APMV method because only this one machine was equipped with APMV regulation method.

## **Conclusion**

Presented results suggest that MV regulation by automatic proportional minute ventilation (APMV) method is more precise regarding to deviation of MV and EtCO<sub>2</sub>. The staff time spent with ventilator in APMV was 4 times shorter than in group 2. APMV seems feasible idea for achieving better stabilization of controlled or supported ventilation. APMV method could be used as an extension on top of all pressure-based ventilation modes (pressure-controlled ventilation – PCV, pressure support – PS, synchronized intermittent mandatory ventilation – SIMV-p, bilevel ventilation - BiPAP, etc.

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