

The Effect of Different Values of Positive End Expiratory Pressure on Ventilation Parameters among Critically Ill Patients

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Abstract

Background: The application of mechanical ventilation for critically ill patients is a life-support system that can maintain their adequate lung function. Positive end-expiratory pressure is a significant adjunct mode for mechanically ventilated patients. Historically, it is ordinarily applied for mechanically ventilated patients to improve oxygenation and alveolar ventilation and reduce alveolar atelectasis and ventilation/perfusion mismatch. Although several international studies revealed the extensive positive effects of high positive end-expiratory pressure (≥ 10 cmH₂O) for critically ill patients with or without lung disorders, low levels of positive end-expiratory pressure (3 to 5 cmH₂O) are regularly used for mechanically ventilated patients. **Aim:** The current study aimed to investigate the effect of different values of positive end-expiratory pressure on ventilation parameters among critically ill patients. **Method:** A quasi-experimental research design was utilized in the current study involving a convenience sample of 164 adult mechanically ventilated patients. Data were collected using a critically ill patient's ventilation parameters assessment tool. **Results:** The current study revealed that the modification of positive end-expiratory pressure values from moderate (6-8 cmH₂O) to high (8-10 cmH₂O) improved patients' ventilatory parameters. More investigations are required to support the evidence of using this approach when caring for mechanically ventilated patients.

Key Words : Positive End-Expiratory Pressure, Ventilation Parameters, Critically Ill Patients

Introduction

Respiratory insufficiency is the common cause for admission to intensive care units (ICUs) among hospitalized patients. Besides, most ICU patients may need mechanical ventilatory support (Dumanlidağ, Yuzkat, Soyalp, & Gülhas, 2019). The application of mechanical ventilation for critically ill patients is a life-support system that can maintain their adequate lung function (Samary, Silva, Gamade Abreu, Pelosi, & Rocco, 2016). Moreover, it is a life-saving procedure for patients with acute respiratory distress syndrome (ARDS) as it may improve gas exchange and lung recruitment (Grübler, Wigger, Berger, & Blöchlinger, 2017). Despite the several benefits of mechanical ventilation, it also has many risks that depend on the modification of ventilator settings and analysis of ventilator output data which directs the ventilation strategy (Samary, et al., 2016). One of these settings or parameters is the positive end-expiratory pressure (PEEP) which is a significant adjunct mode for mechanically ventilated patients (Dumanlidağ et al, 2019).

Positive end-expiratory pressure is the pressure that exists in the alveoli at the end of expiration which is above the atmospheric pressure. PEEP has two main types including the extrinsic PEEP that is delivered by the ventilator and the intrinsic PEEP that is caused by air trapping (Samary et al., 2016). The extrinsic PEEP is commonly one of the first ventilator parameters adjusted with the initiation of mechanical ventilation (Determann, et al., 2010). Historically, PEEP is used for mechanically ventilated patients to improve their oxygenation and alveolar ventilation and reduce alveolar atelectasis and ventilation/perfusion mismatch (Waly,

2021). Additionally, the application of PEEP raises the respiratory system pressure during mechanical ventilation and opens the adhered or fluid-filled alveoli (Dumanlidağ et al., 2019).

Some studies examined the effect of modification of PEEP ranged between low (3-5 cm H₂O) and high (≥ 10 cm H₂O). Most of these studies reported the positive effect of a high PEEP value over a low value (Neto, et al., 2016; Waly, 2021). Some investigators examined the bi-level of PEEP (5 and 15 cm H₂O) among mechanically ventilated patients with healthy and diseased lungs (Di Marco, et al., 2010). They reported that high PEEP significantly increased the pulmonary capillary blood flow and partial arterial oxygen tension (PaO₂)/fraction of inspired oxygen (PaO₂/FiO₂) among the ARDS patients. Waly (2021) assessed the different levels of ascending and descending PEEP (5, 7 and 10 cm H₂O) for under anesthesia obese patients and reported that PEEP at level 10 cm H₂O significantly increased the driving pressure, peak airway pressure, and plateau pressure.

Other studies assessed high against low PEEP levels combined with low tidal volume among ARDS patients. They reported that high PEEP values enhanced oxygenation (Meade, et al., 2008) and reduced the duration of mechanical ventilation (Mercat, et al., 2008). Also, the use of high PEEP values in the emergency department was associated with reduction of ventilation and hospitalization periods among mechanically ventilated patients with or without ARDS (Fuller, et al., 2017).

On the other hand, Hemmes, Gamade Abreu, Pelosi, and Schultz (2014) examined the effect of a high versus low level of PEEP with

recruitment maneuvers on postoperative respiratory complications for patients undergoing open abdominal surgery. The investigators found that high PEEP and recruitment maneuvers are least beneficial postoperatively, and low PEEP without recruitment maneuvers are recommended intra-operatively. **Neto, et al., (2016)** conducted a systematic review and meta-analysis for investigating the association between PEEP and the outcomes of patients without ARDS. They reported that high PEEP reduced the incidence of ARDS and hypoxemia.

Delivery of PEEP is used to prevent distal small airway and lung alveoli from collapsing (**Slutsky, Villar & Pesenti, 2016**). Hence, any level of PEEP is important to keep lungs open after expiration and enhance the alveolar recruitment (**Albert, 2012**). Thereby, several approaches have been utilized to identify the perfect PEEP value for mechanically ventilated patients. The first approach is the evaluation of lung compliance shifting from low to high due to the low inflection point of the pressure-volume curve with 2 cmH₂O PEEP above this point. The other approaches are the use of procedures related to PEEP and FiO₂, and transpulmonary pressure measurement through an esophageal catheter (**Talmor, et al., 2008**). The optimal PEEP approach is individualized for each patient.

Although several international studies revealed the extensive positive effects of high PEEP (≥ 10 cmH₂O) for critically ill patients with or without lung disorders, low levels of PEEP (3 to 5 cmH₂O) are regularly used in ICUs. Most of these studies investigated the effect of PEEP on hemodynamic (**Grübler et al., 2017**), and oxygenation (**Algera, et al., 2020; Laffey, et al.,**

2016) parameters, and the central venous pressure (**Al-Sayaghi, et al., 2019**). However, to the best of our knowledge, studies which examined the effect of PEEP on ventilation parameters are scarce particularly in Egypt (**Waly, 2021**). Thus, the current study was conducted to address this topic.

Aim of the study

This study aimed to investigate the effect of different values of PEEP on ventilation parameters among critically ill patients.

Research hypothesis

To fulfill the aim of the current study, we hypothesized that increasing PEEP more than 6 cmH₂O for mechanically ventilated patients will improve their ventilation status.

Method

Research Design

A quasi-experimental design was utilized in this study. This design is used to evaluate the effectiveness of an intervention on a certain outcome in the absence of randomization (**Polit & Beck, 2018**). It is the most appropriate design for the current study as it aims to investigate the effect of PEEP on ventilation parameters.

Setting

This study was carried out in two ICUs affiliated with Mansoura University Hospital including the Anesthesia ICU and the Neurosurgery ICU. The two units are well equipped with advanced technology required for the management of mechanically ventilated patients. These units are located on the first floor in the main building of the hospital. The capacity of the Anesthesia ICU is eight beds, and it receives critically ill patients with different diagnoses from the hospital's different units. The most common diagnoses in this ICU are diabetic

ketoacidosis, diabetic coma, hepatic coma, hysterectomy, and critically ill postoperative patients. The capacity of Neurosurgery ICU is five beds and it receives preoperative and postoperative neurosurgical patients that require ICU. The most common diagnoses in this unit are aneurysm, meningioma, glioma, glioblastoma multiform posterior fossa tumor, and an arterio-venous malformation. The nurse-patient ratio in these units is nearly 1:2.

Subjects

A convenience sample of 164 patients was enrolled in this study according to the following criteria; adults ≥ 18 years old, males and females, mechanically ventilated in the study settings, and hemodynamically stable.

Exclusion criteria

- Chest diseases (acute respiratory distress syndrome & chronic obstructive pulmonary disease).
- Neuromuscular diseases (Gilliam Barre syndrome, Myasthenia gravis & cerebral palsy).
- Cardiac diseases (heart failure & dysthymia).
- Hepatic diseases.
- Traumatic patients.

Data Collection Tool

One tool was utilized to collect data for the current study namely 'Critically Ill Patient's Ventilation Parameters Assessment Tool'. It was developed by the principal investigator (PI) after reviewing relevant literature (Kim, Shin, Kim, Jung, & Kwak, 2010; Retamal, Buggedo, Larsson, & Bruhn, 2015; Shojaee et al, 2017; Zhou & Han, 2016). It involved two parts as follows:

Part 1: Critically ill patient's socio-demographic characteristics and health-relevant data

This part includes items related to patients' socio-demographic characteristics such as age, gender, marital status, and educational level. It also covers patients' health-relevant data including the diagnosis, date and type of admission, and referral, present history, length of ICU stay, and respiratory assessment. It also involves patients' past medical and surgical history.

Part II: Critically ill patient's ventilation parameters record

This part was used to collect data about the ventilator parameters including the tidal volume, respiratory rate, inspiratory: expiratory (I:E) ratio, PSV, pressure and FiO_2 .

Validity of the tool

The data collection tool was tested for its content-related validity by a panel of 5 faculty staff members from the Critical Care and Emergency Nursing Department, Faculty of Nursing, and one from the Anesthesia and Intensive Care, Faculty of Medicine, Mansoura University. Recommended modifications were made accordingly.

Pilot study

A pilot study was carried out on 16 critically ill patients to test the feasibility, objectivity, and applicability of the tool, and estimate the time needed to complete the data collection sheet for each patient. Based on the results of the pilot study, necessary modifications were made before commencing the process of data collection. Patients who participated in the pilot study were excluded from the main sample.

Ethical Considerations

Ethical approval was secured from the Research Ethical Committee (REC), Faculty of Nursing, Mansoura University. Official approval to carry out the study was granted from the hospital's administrative authority.

Informed consent was obtained from the eligible patients' next of kin. It was emphasized to them that participation in this study was entirely voluntary and that refusal to take part in the study would not affect the treatment or care the patient receives. They were also assured that they had the right to withdraw from the study at any stage without any responsibility. Anonymity and confidentiality of the participants' personal information were maintained through using codes on datasheets instead of names.

Data Collection

This study was conducted between January and June 2018 throughout three phases including preparation, implementation, and evaluation.

Preparation Phase:

- Ethical approval was secured from the REC of the Faculty of Nursing, Mansoura University.
- Official approval to initiate the study was granted from the authority of the study's settings.
- The PI daily screened the study settings for identifying eligible patients, then contacted the next of kin, explained the aim, nature, and procedure of the study, and invited them to allow their patients to take part in this investigation.
- Eligible patients were randomly assigned into two groups: a study group and a control group.
- **The study group** involved critically ill patients who were on mechanical ventilation with PEEP of 6-10 cm H₂O.
- **The control group** involved critically ill patients who were on mechanical ventilation with PEEP of 3-5 cm H₂O.

Implementation Phase

For the study and control groups

- Participant patients were assessed, and the socio-demographic characteristics and health-relevant data were collected from their records using part I of the tool.
- The PI performed a respiratory assessment for all enrolled patients and the data were recorded in their datasheet using part I of the tool.
- The past medical and surgical history was collected from the patient's records using part I of the tool.

For the study group

- The ventilator parameters were observed and recorded three times: in the morning shift before the intervention (first time), then in the afternoon shift after increasing the PEEP (second time), and at the night shift (third time).
- Any changes in the ventilator parameters induced by the physician in the afternoon or night shifts according to the ABG readings were recorded using part II of the tool.

For the control group

- The ventilator's PEEP was fixed on 5 cm H₂O.

Evaluation Phase

- The ventilator parameters were compared within each group throughout the three shifts (morning, afternoon, and night) and between the two groups.

Data Analysis

The collected data were analyzed using the Statistically Package for Social Sciences (SPSS) version 25.0 Armonk, NY: IBM Corp. Qualitative data were expressed as frequencies and percentages. The Chi-square test (or Fisher's exact test) was used to compare

the qualitative data of the two groups. Quantitative data were initially tested for normality using Kolmogorov-Smirnov and were described as mean \pm standard deviation (SD) if normally distributed or median and interquartile range (IQR) if not. For quantitative data with two related readings: paired-samples t-test was used for normally distributed data and the non-parametric alternative; Wilcoxon's signed ranks test was used if not. Moreover, the repeated-measures ANOVA test was used if data

were normally distributed in all readings, and the non-parametric alternative Friedman's test was used if not. The statistical significance was set at a *P*-value of ≤ 0.050 .

Results

Table 1 showed that there were no statistically significant differences between the two groups regarding their socio-demographic characteristics. This reflects the homogeneity of the study and control groups.

Table 1 Differences in socio-demographic characteristics between the studied groups

Variable	P value
Age	0.635
Gender	0.637
Marital status	0.072
Employment status	0.685
Education	0.443

Data are presented as frequency. *P*-value ≤ 0.05

Table 2 depicts the past and present medical history of the studied groups. The current findings noted that hypertension (56.1% & 32.9% respectively) and seizure (45.1% & 42.7% respectively) were evident

diagnoses in the past medical history of the study group and control groups, while tuberculosis (35.4%) was only evident among patients of the control group. Statistically significant differences were found between the two groups regarding the past medical history (*p* ≤ 0.050).

Table 2 Past medical history of the studied groups

Past medical history	Study group n=82		Control group n=82		Significant test	
	N	%	N	%	²	<i>P</i> value
• Hypertension	46	56.1	27	32.9	8.912	0.003
• Diabetes mellitus	2	2.4	8	9.8	3.834	0.050
• Stroke	0	0	1	1.2	1.006	1.000
• Tuberculosis	0	0	29	35.4	35.230	<0.0005
• Heart disease	0	0	1	1.2	1.006	1.000
• Kidney disease	3	3.7	3	3.7	0.000	1.000
• Seizure	37	45.1	35	42.7	0.099	0.753
• Cancer	0	0	2	2.4	2.025	0.497
• History of surgery	0	0	6	7.3	5.855	0.029

Data are presented as frequency (percentage). ²: Chi-Square *P* value ≤ 0.05

According to table 3, dyspnea was the mutual chief complaint in the study and control groups (79.3% and 67.1% respectively). Likewise, the evident diagnosis among patients of the study group was glioblastoma (30.5%), but aneurysm (36.6%) was the highest in the control group. Neurosurgery was the most common cause of admission for patients in both groups (63.4% and 59.8% respectively). Most patients (74.4%) of the study group and 46.3% of

the control group were referred to the ICU from the hospital's wards. Additionally, 43.9% of the control group were referred from the outpatient. Statistically significant differences were found between the two groups regarding their medical diagnosis and admission referral ($P < 0.05$). The length of ICU stay for patients in the two groups was between 6 and 10 days (65.9% and 73.2% respectively).

Table 3 Current medical history of the studied groups

Variable	Category	Study group n=82		Control group n=82		Significant test	
		N	%	N	%	χ^2	P
Chief complain	• Dyspnea	65	79.3	55	67.1	3.106	0.078
	• Desaturated	17	20.7	27	32.9		
Diagnosis	• Glioblastoma	25	30.5	21	25.6	16.420	0.003
	• Meningioma	20	24.2	21	25.6		
	• Aneurysm	12	14.6	30	36.6		
	• Tracheostomy	8	9.8	6	7.3		
	• Hysterectomy	17	20.7	4	4.9		
Bodyweight	• 50Kg-65Kg	20	24.2	32	39	4.068	0.131
	• >65Kg-80Kg	55	67	44	53.6		
	• >80Kg	7	8.5	6	7.3		
Admission type	• Medical	7	8.5	16	19.5	5.125	0.163
	• Surgical	12	14.6	11	13.4		
	• Neurosurgical	52	63.4	49	59.8		
	• Others	11	13.4	6	7.3		
Admission referral	• Outpatient	19	23.2	36	43.9	14.198	<0.001
	• ER	2	2.4	8	9.8		
	• Ward	61	74.4	38	46.3		
ICU length of stay	• 1-5 days	28	34.1	22	26.8	1.036	0.309
	• 6-10 days	54	65.9	60	73.2		

Data are presented as frequency (percentage). χ^2 : Chi-square test (Monte Carlo significance). P-value ≤ 0.05 . ER: emergency & ICU: intensive care unit.

Table 4 compares the ventilator parameters between the studied groups. The results illustrated highly statistically significant differences between the study and control groups regarding FiO_2 , Vt , P values, $RR1_v$, $RR3_v+p$, pressure, PSV, and I:E ratio ($p = < 0.0005$ for all).

With the application of high PEEP for the study group, a notable reduction was observed over time (morning, afternoon, and night shifts) in the FiO_2 (56.34±13.65 & 40.24±1.55 respectively), $RR1_v$ (14±3.35, 11.39±2.43 & 10.63±2.82 respectively), $RR3_v+p$ (23.5±3.48, 19.58±1.53 & 18.62±1.44 respectively), pressure (19.64±0.89, 16.27±3.3 & 12.54±3.66 respectively) and PSV (17.51±11.56, 11.65±1.82 & 10.65±2.63 respectively).

Moreover, highly statistically significant differences were noted among patients in the study group concerning ventilator parameters (FiO₂, RR1_v, RR3_v+p, pressure, & PSV) with a p-value <0.0005 for all.

With high PEEP values, a slight reduction was observed in the study group in RR2_p readings (9.26±4.062, 8.219±2.53 & 8.97±4.177 respectively) with no statistically significant differences. Conversely, a generous rising in I:E ratio and Vt2-p values were found overtime (1.81±0.326, 2.13±0.266, & 2.32±0.36 respectively) and (451.18±65.67, 502.219±55.82 & 537.54±48.52 respectively) with highly statistically significant differences (p = <0.0005 for both).

For the control group, the FiO₂ values depicted a slight increase over the three shifts (66.06±12.7, 66.77±10.99, & 67.01±10.82 respectively) with no statistically significant

differences (p =0.362). Nevertheless, a marked increase in Vt2-p values (418.32±85.42, 429.7 ±84.1 & 448.35±90.7 respectively) and I:E ratio (1.83±0.41, 1.91±0.3 & 2.09±0.31 respectively) was noticed throughout the three shifts with statistically significant differences (p=0.038 0.0005 respectively).

No statistically significant differences were noted over the three shifts in the control group regarding the RR1_v (15.71±2.12, 15.69±2.13 & 15.69±2.13 respectively), RR2_p (7.76±4.75, 7.75±4.39 & 7.25±4.41 respectively), RR3_v+p (21.22±5.32, 21.32±5.029, & 20.77±4.55 respectively), and PSV (14.52±1.88, 14.59±1.99 & 14.59±1.99 respectively).

In summary, the findings of the current study showed no improvement in ventilator parameters among patients in the control group who received a fixed PEEP value (3-5 cm H₂O).

Table 4 :Comparing the ventilator parameters between the studied groups with different PEEP Values

Parameter	Study group (n=82)			Control group (n= 82)			Significant tests		
	PEEP(6-8 cmH ₂ O)			PEEP(3-5 cmH ₂ O)			F	P2	2
	Morning	Afternoon	Night	Morning	Afternoon	Night			
FiO ₂	56.341±13.65	40.24±1.55	40.24±1.55	66.06±12.69	66.76±10.98	67.01±10.82	90.269	<0.0005	0.358
	P1-<0.0005			P1=0.362					
Vt2-p	451.18±65.67	502.21±55.82	537.54±48.52	418.32±85.42	429.68±84.1	448.35±90.69	9.80	<0.0005	0.057
	P1-<0.0005			P1=0.038					
RR1_v	14±3.35	11.39±2.43	10.63±2.82	15.71±2.12	15.69±2.13	15.69±2.13	48.035	<0.0005	0.237
	P1-<0.0005			P1=0.320					
RR2_p	9.26±4.062	8.219±2.53	8.97±4.177	7.76±4.75	7.75±4.39	7.25±4.41	1.718	0.186	0.012
	P1=0.154			P1=0.354					
RR3v+p	23.5±3.48	19.58±1.53	18.62±1.44	21.22±5.32	21.32±5.029	20.77±4.55	39.302	<0.0005	0.196
	P1-<0.0005			P1=0.386					
I:E-ratio	1.81±0.326	2.13±0.266	2.32±0.36	1.83±0.41	1.91±0.3	2.09±0.31	10.794	<0.0005	0.063
	P1-<0.0005			P1-<0.0005					
Pressure	19.64±0.89	16.27±3.3	12.54±3.66	20.57±2.43	20.57±2.43	20.57±2.43	17.98	<0.0005	0.246
	P1-<0.0005			---					
PSV	17.51±11.56	11.65±1.82	10.65±2.63	14.52±1.88	14.59±1.99	14.59±1.99	76.726	<0.0005	0.351
	P1-<0.0005			P1=0.38					

Data are presented as mean ± SD. P values by repeated-measures ANOVA, Which P1: significant difference between

times in intervention and control group, P2: significant changes between times and groups on parameter. FiO₂: Fraction

of inspired oxygen, V_t - p: Tidal volume-patient, RR- V: Respiratory rate-ventilator, RR-P: Respiratory rate-patient, I:E-ratio: Inspiratory: Expiratory ratio and PSV:Pressure support ventilation

Discussion

The findings of the current study revealed no statistically significant differences between the study group and the control group concerning their socio-demographic characteristics. Similarly, **Setak-Berenjestanaki, et al. (2018)** investigated the prophylactic effect of different PEEP values on the incidence rate of atelectasis post-cardiac surgery and reported no significant differences in age or gender of the studied groups. These findings are also supported by other similar studies (**Al-Sayaghi et al., 2019; Atashkoei, Yavari, Zarrintan, Bilejani, & Zarrintan, 2020; Shojaee et al., 2017**).

The findings of the present study illustrated that hypertension and seizure were evident in the past medical history of the two groups. However, tuberculosis was also an evident diagnosis in the medical history of the control group. Statistically significant differences were noted between the two groups regarding their medical and surgical history. These findings are congruent with the results of another study that examined the PEEP elevation recruitment maneuver among mechanically ventilated patients to predict their fluid responsiveness (**Vallier et al. 2020**). The researchers of the same study reported that almost one-quarter of the studied patients had a history of arterial hypertension, however, few patients had diabetes.

These results are contradicting with the study of **Beitler et al.**

(2019) which investigated the effect of PEEP titration with an esophageal pressure-guided strategy on mortality rate among ARDS patients. They noted that the risk factors for ARDS were mainly due to the history of sepsis followed by any other pulmonary problems. In the same sense, **Shojaee et al. (2017)** studied the effect of PEEP on CVP among mechanically ventilated patients and reported that most patients in their investigation had a history of pneumo-sepsis. This discrepancy may be due to the nature of the sample in these two studies. In **Shojaee et al.'s (2017)** study, most patients were in the age group between 60-79 years old. In **Beitler et al.'s (2019)** study, all patients had ARDS.

The current study found that glioblastoma was the common diagnosis among the study group compared with the aneurysm (neurological disorder) among the control group. An investigation conducted by **Al-Sayaghi et al. (2019)** reported that the studied sample had intrapulmonary and extrapulmonary disorders with an equal percentage. This discrepancy could be attributed to the nature of the study setting as **Al-Sayaghi et al.'s** study was conducted in the casualty and the general ICUs.

Our findings illustrated that neurosurgery was the most common cause of ICU admission for the study and control groups. Significant differences were found between the two groups regarding the medical diagnosis and the admission referral. This can be attributed to the nature of the current study setting as patients were recruited from the neurosurgery and anesthesia ICUs. Another reason could be related to patients' diagnosis (glioblastoma and aneurysm) which is characterized by

quick deterioration that requires mechanical ventilation. These findings are supported by other investigations which recruited patients with neurological problems (**Backhaus et al. 2017; Boone et al. 2017**).

On the contrary, **Algera et al. (2020)** who investigated the effect of ranged PEEP from lower to higher on ventilator-free days among ICU patients without ARDS, reported that most of the studied patients were admitted to the ICU for medical reasons. Another study found that the most frequent cause of ICU admission was nonrespiratory disorders followed by pneumosepsis (**Shojaee et al., 2017**). This contradiction may be due to the nature of the study setting and population as the first study involved patients without ARDS and the other one enrolled nontraumatic patients.

The present study showed that the length of the ICU stay for the highest proportions of patients in the two groups was from six to ten days with no statistically significant differences between the two groups. These findings are matching with the report of some similar investigations (**Algera et al. 2020; Beitler et al. 2019; Neto, 2014**). However, this is inconsistent with the results of other studies which delineated that the ICU length of stay was more than ten days among their studied patients (**Boone et al. 2017; Luo et al. 2020**). On the other hand, **Hansen et al. (2015)** recorded a lower length of stay than nearly two days only after coronary artery bypass grafting with moderate PEEP (5-8 cmH₂O).

The current findings portrayed highly statistically significant differences between the study and control groups regarding the ventilator parameters including the FiO₂, Vt_{2-p}, RR1_v,

RR3_{v+p}, pressure, PSV, and I: E ratio. Supporting our findings, **Spadaro, et al., (2018)** evaluate the ventilation-perfusion mismatch and respiratory mechanics at different PEEP values among patients undergoing protective one-lung ventilation. They found that a relatively high PEEP level (10 cmH₂O) enhanced gas exchange and ventilatory mechanics. These findings are also consistent with **Rauseo et al., (2018)** who found that PEEP levels from 5 to 8 cmH₂O can improve oxygenation and lung mechanics post thoracic surgery. **Karbing et al's., (2020)** study findings showed that PEEP modification at 5, then 15 or 20 cmH₂O can improve the total lung ventilation for ARDS patients.

Furthermore, a very recent study revealed that the higher PaO₂/FiO₂ ratio was recorded at PEEP 10. The author also reported that the oxygenation of mechanically ventilated obese patients was significantly improved with decremental PEEP (10, 7, and 5) rather than the incremental PEEP approach (**Waly, 2021**). In the same context, **Algera et al. (2020)** reported that during the first 5 days of ventilation, the FiO₂ and PaO₂/FiO₂ differed significantly between the two studied groups. In the same study, the investigators revealed that the driving pressure was significantly higher in the higher PEEP group. Similarly, **Gernoth, Wagner, Pelosi, and Luecke (2009)** reported that the application of high PEEP resulted in PaO₂/FiO₂ ratio improvement by one-fifth (22%).

On the contrary to the current findings, **Bikker, Bommel, Miranda, Bakker, and Gommers (2008)** applied the stepwise PEEP reduction approach for patients with different respiratory disorders. They found that the declined PEEP levels were non significantly

associated with PaO₂/FiO₂ ratio changes. Similar findings were also noted among cardiac surgery patients postoperatively (**Karsten, Grusnick, Paarmann, Heringlake, and Heinze, 2015**). Our findings are also contradicting the report of **Zhou, et al., (2019)** which highlighted that high PEEP did not influence the ventilatory indices of both groups including the tidal volume, minute volume, and oxygenation.

The current study depicted highly statistically significant differences in the ventilator parameters in the study group throughout the three shifts except for the RR_{2_p}. However, no significant differences were detected in the control group except for the Vt_{2-p} and I: E ratio. This can be attributed to the use of a fixed PEEP value (3-5 cm H₂O) for the control group, unlike the study group in which patients received different levels of PEEP.

Becher et al., (2014) found that the increased PEEP raises the mean and peak airway pressures that enhanced respiratory system compliance and recruitment. Besides, **Fredes, et al's., (2019)** study illustrated that the increased resistance level was noted at the lowest PEEP levels, whilst, the highest respiratory system elastance was observed at the highest PEEP values (≥ 15 cmH₂O) without significant association.

Walkey, et al., (2017) conducted a meta-analysis and a systematic review to examine higher PEEP versus lower PEEP among ARDS patients. The authors found that a high PEEP also did not significantly reduce the incidence of barotrauma, or ventilator-free days when compared with a low PEEP approach. They went further by concluding that a higher PEEP strategy is unlikely to

enhance ARDS patients' clinical outcomes.

Concerning the RR, the present data showed a significant reduction over the three shifts in the intervention group RR_{1_v} and RR_{3_v+p}. The RR should be adjusted during MV to maintain a minute volume appropriate to the patient's metabolic demands. Clinically the increased respiratory rates may damage lung tissues (**Vieillard-Baron et al. 2002**). On the contrary, other investigations reported no changes in RR with PEEP modification. This may be because the patients received an intermittent dose of sedation (**Beitler et al., 2019; Karbing et al., 2020**). Another study conducted by **Boone et al., (2017)** to compare different PEEP values with different degrees of lung injury showed an increased RR at PEEP 5 - 10. This may be due to the increased risk of sepsis.

Haberthür and Guttman, (2005) found that high PEEP was significantly associated with increased expiratory time and declined RR. On the other hand, **Shojaee, et al., (2017)** recorded equal RR among the intervention and control groups in their study with no significant relationship between both groups. This disagreement could be due to the nature of the study population including patients with sepsis and ARDS.

The current study found a statistically significant difference in the PSV between the two groups and within the intervention group. The pressure ventilation improves the patients' respiratory characteristics and ABG parameters. A study conducted by **Aydin et al., (2016)** revealed that volume control ventilation (VCV) was associated with greater Vt and less dead-space ventilation. Another observational study

documented that the risk of postoperative pulmonary complications was higher in patients who received pressure control ventilation (PCV) compared with those who received VCV particularly with PEEP <5 cmH₂O (Bagchi et al., 2017). Moreover, two other studies found that the PCV was superior to the VCV based on lower peak inspiratory pressure (PIP) with improved ABG parameters (Choi et al., 2011; Tyagi, Kumar, Sethi, & Mohta, 2011). Yet, no specific mode of controlled mechanical ventilation is recommended (Young, et al., 2019).

Two meta-analysis studies suggested that patients with uninjured lungs could benefit from ventilation with low Vt (Neto et al., 2014; Neto et al., 2015). In the same line, Spadaro, et al., (2018) suggested that high PEEP (10 cmH₂O) with low tidal volume (4 to 5 ml/kg) should be applied intra-operatively to maintain respiratory pressure and reduce intrapulmonary shunt. On the contrary, a prospective study reported no association between the tidal volume and the patients' outcomes (Neto et al., 2016). The same study found no reduction in in-hospital mortality rate or shorter duration of ventilation with high PEEP. However, hypoxemia was less frequently seen with the use of higher PEEP and ARDS developed less frequently. Hence, proper PEEP value should be applied for pulmonary protection and not only for improving oxygenation (Hess, 2015).

The findings of the current study highlighted the significant positive effect of high PEEP on patients' ventilatory parameters which supports the proposed research hypothesis.

Limitations

The study was conducted on a small sample of patients in two ICUs in one university hospital which restricts

the generalizability of the research findings.

Conclusion and Recommendations

The findings of the current study contribute to the body of knowledge related to mechanically ventilated patient care. Our investigation concludes that the elevation of PEEP up to 10 cmH₂O can improve the ventilation parameters of critically ill patients. Further large-scale studies in different ICUs on the same focus are needed to strengthen the evidence that supports the use of this approach.

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