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Upper Deflection Point Versus Lower Inflection Point on Pressure-Volume (P-V) Loop for Determination of Optimum Positive End Expiratory Pressure (PEEP) by Pressure-Volume (P-V) Loop in Acute Respiratory Distress Syndrome (ARDS) Patients: A Prospective Cohort Cross-Over Study

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Abstract

Background: Lung-protective ventilation has the best outcome in ARDS. Therefore, low tidal volume (6ml/kg of predicted body weight), limitation of plateau pressure (less than 30cmH_2O), and optimal PEEP are the key components of the lung protective ventilation. Pressure-Volume (P/V) loop is an important method to set PEEP, while the Lower Inflection Point (LIP) of the inflation limb is traditionally where PEEP is set; evidences suggest that the LIP does not correlate with the pressure at which recruited alveoli will begin to close. Setting PEEP slightly above the deflection point rather than the LIP may be more accurate in determining the optimum PEEP.

Aim: The aim is to compare two methods of optimum PEEP determination using Upper Deflection Point (UDP) versus Lower Inflection Point (LIP) on P-V loop in patients with ARDS, as regard lung mechanics, oxygenation and hemodynamics.

Patients and Methods: This study was carried out on 30 mechanically ventilated patients within 24 hours of fulfilling Berlin criteria for ARDS. All patients were ventilated with Low Tidal Volume Ventilation (LTVV). Pressure-Volume (P/V) loop was constructed using the quasistatic method with inspiratory flow rate of 3L/min and frequency 5 b/min. After (LIP) and (UDP) were determined on the (P/V) loop, the following parameters were measured before and 30 minutes after setting the optimum PEEP guided by (LIP) and (UDP): Peak airway pressure, mean airway pressure, plateau pressure, PaO_2/FIO_2 ratio, static compliance, Heart Rate (HR) and Mean Arterial Pressure (MAP).

Results: PEEP adjusted according to UDP showed significant increase in static compliance and PaO_2/FIO_2 ratio and significant decrease in peak airway pressure, plateau pressure and mean airway pressure values in comparison with PEEP adjusted according to LIP.

Conclusions: PEEP adjusted according to UDP results in better oxygenation, lung mechanics and hemodynamic stability. So, it is recommended to adjust PEEP according to UDP.

Key Words: *Optimum PEEP – Pressure-Volume (P/V) curve – Lower inflection point – Upper deflection point – Acute respiratory distress syndrome.*

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Introduction

ACUTE Respiratory Distress Syndrome (ARDS) is characterized by permeability pulmonary edema and refractory hypoxemia. Lung-protective ventilation is still the most important factor of better outcome in ARDS. So, low tidal volume (6ml/kg of predicted body weight), limitation of plateau pressure (less than 30cmH_2O), and optimal PEEP are the key components of the lung protective ventilation [1].

To select the optimum PEEP level to maintain the patency of airways and recruited alveoli together with the minimization of alveolar overdistension is not easy.

An important method to set PEEP is the Pressure-Volume (P/V) loop, while the Lower Inflection Point (LIP) of the inflation limb is traditionally where PEEP is set; evidences suggest that the LIP does not correlate with the pressure at which recruited alveoli will begin to close [2]. Setting PEEP slightly above the UDP rather than the LIP may be more valuable in determining the amount of PEEP required to prevent alveolar collapse, optimizing lung mechanics, improving oxygenation and reducing incidence of barotrauma [3].

Aim and objectives:

The aim of this study was to compare two methods of optimum PEEP determination using Upper Deflection Point (UDP) versus Lower Inflection Point (LIP) on (P/V) loop in patients with ARDS, as regard lung mechanics, oxygenation and hemodynamics.

Patients and Methods

This study was carried out in the Surgical Intensive Care Unit (SICU) in Tanta University Hospital during the period from June 2015 to June 2016, on 30 mechanically ventilated patients within 24 hours of fulfilling Berlin criteria for ARDS [4]:

1- $PaO_2/FiO_2 \leq 300$mmHg with PEEP $\geq 5cmH_2O$.

2- Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema detected by a chest radiograph or computed tomography scan. Not related to heart failure or fluid overload which is excluded by echocardiography. After approval from local and institutional ethical committees, informed consent was obtained from patient's close relative. All patients' data were confidential with secret code and private file for each patient and all data was used for the medical research only.

Patients younger than 18yrs and older than 70yrs old, pregnant patients, patients with neuromuscular disease, intracranial hypertension, left ventricular dysfunction (on echocardiography), hemodynamically unstable patients or on high dose vasopressors or inotropes, patients with obstructive lung disease, patients with organ failure and patients with barotrauma as interstitial emphysema, pneumothorax, pneumomediastinum, pneumoperitoneum or subcutaneous emphysema were excluded from the study.

Patients meeting these criteria were monitored for Heart Rate (HR), invasive Arterial Blood Pressure (ABP) and oxygen saturation using (Nihon Khoden BSM-230 1K) monitor and arterial blood gases were done using (AVL-988). All patients were ventilated with Low Tidal Volume Ventilation (LTVV) using (eVent Medical Inspiration ^{LS}) ventilators as following [5]: I- Ventilator setup and adjustment: Predicted Body Weight (PBW) was calculated: Males = 50 + 0.91 [height (cm) - 152.4] and females = 45.5 + 0.91 [height (cm) - 152.4], volume assist/control mode was selected, ventilator was set to achieve initial tidal volume (V_T) = 8 ml/kg PBW, V_T was reduced by 1ml/kg at intervals ≤2 hours until V_T=6ml/kg PBW, initial rate was set to approximate baseline minute ventilation (not >35b/min) and V_T and Respiratory Rate (RR) were adjusted to achieve pH and plateau pressure goals. II- Plateau pressure goal: $\leq 30cmH_2O$: If plateau pressure (P_{plat}) $>30cmH_2O$: V_T was decreased by 1ml/kg steps (minimum=4ml/kg). If P_{plat} <25 cmH_2O and V_T <6ml/kg, VT was increased by 1ml/kg until P_{plat} $>25cmH_2O$ or V_T=6ml/kg. If P_{plat} $<30cmH_2O$ and breath stacking or dyssynchrony occurs, V_T was increased in 1ml/kg increments to 7 or 8ml/kg if P_{plat} remains <30 cmH_2O. III- pH goal: 7.30-7.45: Acidosis management (pH <7.30): If pH 7. 15-7.30: RR was increased until pH >7.30 (maximum set RR=35 b/min). If pH <7.15: RR was increased to 35b/min. If pH remains <7.15, V_T was increased in 1ml/kg steps until pH >7. 15 (P_{plat} target of 30 may be exceeded). If no improvement, $NaHCO_3$ was given. Alkalosis Management (pH >7.45): RR was decreased. IV-Oxygenation goal: PaO_2 55-80mmHg or SpO_2 88-95%.

Recruitment maneuver was done before determination of lower inflection point and upper deflection point on (P/V) loop using continuous positive airway pressure, $35cmH_2O$ for 45 seconds, followed by a return to the above settings [6].

Steps of determination of lower inflection point and upper deflection point on P/V loop [7-9]: Patient was deeply sedated (–5) by midazolam: Loading dose: 50mcg/kg slowly intravenous. Maintenance dose: 50-100mcg/kg/hr infusion according to level of sedation which was assessed by Richmond Agitation Sedation Scale (RASS). Muscle paralysis was done by a bolus dose (0. 15mg/kg) of cisatracurium followed by an infusion rate of 3mcg/kg/min. Ventilator was set to see pressure-volume loop (x=pressure, y=volume). Patient was placed in semi-sitting position on 100% FiO_2. High pressure alarm was set at $45cmH_2O$. PEEP turned to zero and V_T was increased to obtain PIP of 35-45 cmH_2O. Inspiratory flow rate was decreased to 3L/min and respiratory rate to 5/min, what is called the quasistatic method to have the pressure-volume curve. In which, we inflate the lung by a constant flow delivered by the ventilator without having to disconnect the patient from the ventilator. The flow of 3L/min was used to avoid the resistive factor generated by the high flow. That allows the analysis of the static mechanical properties of the lung including static compliance, Lower Inflection Point (LIP) and Upper Deflection Point (UDP). The LIP was determined as the point of change from initial slope, optimum PEEP was $2cmH_2O$ above LIP. Deflection point was determined by point of maximum curvature on expiratory limb. After determination of LIP and UDP, the ventilator was set to the previous settings. Recruitment maneuver (continuous positive airway pressure, $35 cmH_2O$ for 45 seconds) applied again and optimum PEEP was adjusted according to LIP and UDP each for 30 minutes, then measurements were taken at each point.

Measurements: The following parameters were measured before and 30 minutes after setting the optimum PEEP guided by (LIP) and (UDP): Peak airway pressure, mean airway pressure, plateau pressure, PaO_2/FIO_2 ratio, static compliance (Cstat), Heart Rate (HR) and Mean Arterial Pressure (MAP). After taking measurements, mechanical ventilation of patients continued with PEEP that gave the highest Static compliance (Cstat) and PaO_2/FIO_2 ratio.

Statistical presentation and analysis of this study was conducted using the, mean, standard deviation, and repeated measures analysis by SPSS V.24. *p*-value <0.05 was considered significant.

Results

Demographic data and patients characteristics are shown in (Table 1).

PEEP values adjusted according to UDP ($8.46\pm1.71 cmH_2O$) showed significant decrease (*p*-value of 0.001) in comparison with PEEP values adjusted according to LIP ($15.56\pm2.76 cmH_2O$) as shown in Fig. (1).

There was significant decrease (*p*-value of 0.001) in peak airway pressure values at PEEP adjusted according to UDP ($31.23 \pm 3.78 cmH_2O$) in comparison with peak airway pressure values at PEEP adjusted according to LIP ($36.83\pm4.71 cmH_2O$) as shown in (Table 2).

Also, a significant decrease (*p*-value of 0.001) in plateau pressure values at PEEP adjusted according to UDP ($24.77\pm3.08 cmH_2O$) in comparison with plateau pressure values at PEEP adjusted according to LIP ($29.80\pm3.55 cmH_2O$) is shown in (Table 2).

Furthermore, a significant decrease (*p*-value of 0.001) in mean airway pressure values at PEEP adjusted according to UDP ($14.73\pm2.12 cmH_2O$) in comparison with mean airway pressure values at PEEP adjusted according to LIP ($19.30\pm2.58 cmH_2O$) is shown in (Table 2).

A significant increase (*p*-value of 0.001) in static compliance values at PEEP adjusted according to UDP ($61.10\pm7.16 ml/cmH_2O$) in comparison with static compliance values at PEEP adjusted according to LIP ($49.90\pm5.50 ml/cmH_2O$) was found as shown in (Table 2).

There was significant increase (*p*-value of 0.001) in PaO_2/FIO_2 ratio values at PEEP adjusted according to UDP (332.63±32.27) in comparison with PaO_2/FIO_2 ratio values at PEEP adjusted according to LIP (312.50±34.99) as shown in (Table 2).

An insignificant difference in mean arterial blood pressure values with *p*-value of 0.290 and heart rate values with *p*-value of 0.195 is shown in (Table 2).

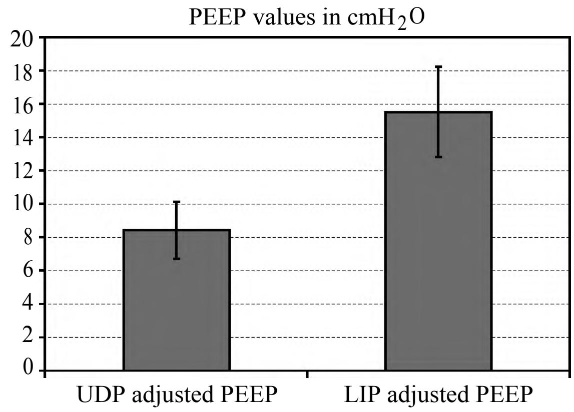

Fig. (1): PEEP values in cmH_2O adjusted according to UDP versus PEEP values adjusted according to LIP.

Table (1): Demographic data and patients characteristics.

Characteristics	Patients
Age (years)	Range: (18-70)
	Mean ± SD: (35.64±4.13)
Sex:	
Male	20
Female	10
Weight (Kg)	Range: (60-80)
	Mean ± SD: (70.84±6.06)
Diagnosis:	
Pneumonia	7
Sepsis	8
Major trauma	10
Drowning	1
Pancreatitis	2
Aspiration of gastric contents	2
ARDS grade:	
Mild	19
Moderate	11
Severe	0

Table (2): Measurements at PEEP adjusted according to UDP versus PEEP adjusted according to LIP.

Measurements	PEEP adjusted according to UDP	PEEP adjusted according to LIP
P/F ratio:		
Range	261-3 81	242-371
Mean ± SD	332.63±32.27	312.50±34.99
F-test		175.915
p-value	*p*1:0.001 * *p*2:0.008#	*p*1:0.001*
Static compliance in ml/cmH2O:		
Range	47-73	39-59
Mean ± SD	61.10±7.16	49.90±5.50
F-test		243.711
p-value	*p*1:0.001 * *p*2:0.001 #	*p*1:0.001 *
Plateau pressure in cmH2O:		
Range	18-31	22-35
Mean ± SD	24.77±3.08	29.80±3.55
F-test		99.265
p-value	*p*1:0.001 * *p*2:0.001 #	*p*1:0.001 *
Peak airway pressure in cmH2O:		
Range	22-39	26-45
Mean ± SD	31.23±3.78	36.83±4.71
F-test		62.731
p-value	*p*1:0.001 * *p*2:0.001 #	*p*1:0.001 *
Mean airway pressure in cmH2O:		
Range	10-19	13-25
Mean ± SD	14.73±2.12	19.30±2.58
F-test		120.886
p-value	*p*1:0.001 * *p*2:0.001 #	*p*1:0.001 *
Mean arterial blood pressure in mmHg:		
Range	79-117	77-115
Mean ± SD	93.80±10.07	91.93±10.05
F-test		1.691
p-value		0.290
Heart rate in bpm:		
Range	70-91	70-94
Mean ± SD	78.93±4.83	80.70±4.93
F-test		2.287
p-value		0.195

Discussion

Management of patients with Acute Respiratory Distress Syndrome (ARDS) has been focused on lung protective ventilation [1]. However, ventilation at low tidal volumes can result in collapse of the alveoli and has the potential to induce lung injury as a result of cyclic opening and closing of lung units (atelectrauma). This has led to widespread studies of optimal PEEP application to maintain the patency of airways and recruited alveoli, prevents end expiratory collapse, keeps the lung open and shifts the tidal ventilation towards the deflation limb of the pressure-volume curve, maximizes gas exchange and minimizes over-distention [10].

The current focus has shifted to find the proper method for setting the optimal (PEEP).

In this study, PEEP adjusted according to UDP showed significant increase in static compliance and PaO_2/FIO_2 ratio and significant decrease in peak airway pressure, plateau pressure and mean airway pressure values in comparison with PEEP adjusted according to LIP. This indicates better oxygenation and lung mechanics with the UDP guided PEEP.

In agreement with our study: Harris et al., who analyzed twenty four P/V curves obtained from patients with ARDS, they concluded that LIP rarely correlated with the point of maximum compliance increase. Also, LIP was always higher than UDP which is consistent with the expected hysteresis in patients with ARDS. This suggests that pressure required to prevent derecruitment may be substantially lower than that required to recruit and that ideally the deflation limb of the P/V loop should be used to identify the optimum PEEP to prevent derecruitment [11].

Also a study done by Hickling KG, in which, he used a mathematical model of the Acute Respiratory Distress Syndrome (ARDS) lung, incorporating simulated gravitational superimposed pressure and alveolar opening and closing pressures, to study the Pressure-Volume (P/V) loop during incremental and decremental Positive end-expiratory pressure (PEEP) trials with constant low tidal volume ventilation and its correlation with the "open lung PEEP" which is defined as the minimum PEEP preventing end expiratory collapse (derecruitment) of 97.5% of alveoli inflated at end-inspiration. The main result of this study was that during the incremental PEEP trial, there was no consistent relationship between the PEEP level giving maximum compliance and open-lung PEEP. In contrast, during the decremental PEEP trial, the lung has already been fully recruited (or nearly so). As PEEP is reduced from its highest level, the compliance initially increased because the alveolar compliance increased at lower alveolar volumes and the tidal ventilation shifted on the deflation limb. Only when the PEEP level fallen below that point on the deflation limb, end-expiratory collapse began to occur, this point was correlated to the UDP on the deflation limb and considered to be the open-lung PEEP [12].

In a similar study by Suh et al., on 17 patients with ARDS who underwent "optimal" PEEP titration by applying a recruitment maneuver and PEEP decrement. They attempted to recruit collapsed lung as much as possible and displace the lung mechanics of the patients towards the deflation limp of the PV curve. They then decreased PEEP by 2cmH_2O decrements to determine the optimal PEEP which defined as the lowest PEEP attainable without causing a significant drop (>10%) in PaO_2. Their results showed improvement in oxygenation and static compliance and no significant hemodynamic changes [13].

As regard to, a study done by Albaiceta et al., on 12 mechanically ventilated patients with early ARDS in which patients were transferred to the CT scanner. P/V loops were constructed using the continuous positive airway pressure technique where the ventilator was switched to CPAP mode, and airway pressure was raised from 0 to 35cmH_2O in 5cmH_2O steps. Ventilation was restored for 5 minutes, and then the maneuver was repeated, this time decreasing pressure from 35 to 0cmH_2O. At each step, transpulmonary pressures (calculated as airway pressure minus esophageal pressure) and volume were recorded, and a single CT scan slice was acquired at a fixed position. Data pairs of transpulmonary pressure and volume were fitted to a sigmoid model. Using this model, they calculated (LIP) on the inspiratory limb, and (UDP) on the expiratory limb. Their results showed that aeration and recruitment are parallel phenomena along inflation with higher level at the UDP than the LIP and loss of aeration and derecruitment have a threshold at the UDP on the deflation limb [14].

Also a study done by Albaiceta et al., on eight patients with early ARDS and both limbs of the static pressure-volume curve were obtained and inflection points calculated using a sigmoid model. During ventilation with the low tidal volume strategy, they applied a PEEP 2cmH_2O above the LIP and a PEEP equal to the UDP. Oxygenation, lung compliance and resistance and changes in lung aeration (measured on three computed tomography slices) were measured at each PEEP level. Their results showed that ventilation above UDP was related to an increase in PaO_2 when compared to ventilation above the LIP. According to computed tomography, when PEEP was set to the UDP; there was an increase in the volume of aerated lung tissue and a decrease in the volume of nonaerated lung. According to changes in hemodynamics, they did not observe changes in arterial pressures or heart rate during the study [15].

Conclusions:

PEEP adjusted according to UDP showed significant increase in static compliance and PaO_2/ FIO_2 ratio and significant decrease in peak airway pressure, plateau pressure and mean airway pressure values in comparison with PEEP adjusted according to LIP with non significant change in the hemodynamics.

Conflicts of interest:

No conflicts of interest declared.

Authors' contributions:

All authors had equal role in design, work, statistical analysis and manuscript writing.

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نقطة الإنحراف العليا مقابل نقطة الإنعطاف السفلى على منحنى (الضغط-الحجم) لتحديد الضغط الموجب الآمثل عند نهاية الزفير فى مرضى متلازمة الضيقة التنفسية الحادة

المقدمة: الضغط الموجب الآمثل عند نهاية الزفير هو الذى ينتج أقصى تحسين بالوظائف الرئوية والحفاظ على سلامة الممرات الهوائية وبالتالى يحسن من نسبة الآكسجين الواصل للآنسجة بدون تأثير سلبى على ديناميكية الدم وهناك وسائل عدة لتحديد الضغط الموجب الآمثل عند نهاية الزفير منها وضعه إعتمادا على نقطة الإنعطاف السفلى على منحنى (الضغط-الحجم) وبالرغم من ذلك فإن الدراسات الحديثة أوضحت أن نقطة الإنعطاف السفلى لا ترتبط بدقة للضغط الموجب الآمثل عند نهاية الزفير وإن إعادة تمدد وحدات الرئة التى إنكمشت مسبقا يستمر على الجزء الخطى أعلى نقطة الإنعطاف السفلى على منحنى (الضغط-الحجم) وإن إنكماش الوحدات التى تم تمددها لا يتم إلا عند ضغط أقل من نقطة الإنحراف العليا وأن هذه النقطة مرتبطة دائما بأكبر نسبة وحدات رئوية عاملة مقارنة بنقطة الإنعطاف السفلى.

الغرض من البحث: عمل مقارنة بين نقطة الإنحراف العليا ونقطة الإنعطاف السفلى بإستخدام منحنى الضغط والحجم لتحديد الضغط الموجب الآمثل عند نهاية الرفير مسترشدا بميكانيكا الرئة وعامل أكسجة الدم وديناميكا الدم.

النتائج: أظهرت النتائج أن الضغط الإيجابى الآمثل عند نهاية الزفير الذى تم تحديده حسب نقطة الإنحراف العليا قد أعطى زيادة ملحوظة بالنسبة لإمتثال الرئة الثابت ونسبة أكسجة الدم/نسبة تشبع الدم ونقص ملحوظ بالنسبة لذورة الضغط الهوائى ومتوسط الضغط الهوائى والضغط الهضبى مقارنة بالضغط الإيجابى الآمثل عند نهاية الزفير الذى تم تحديده حسب نقطة الإنعطاف السفلى مع عدم وجود أى تغير ملحوظ بينهما بالنسبة لديناميكية الدم.

المستخلص من الرسالة: الضغط الإيجابى الآمثل عند نهاية الزفير الذى تم تحديده حسب نقطة الإنحراف العليا كان الآفضل بالنسبة لأكسجة الدم، ميكانيكا الرئة وإستقرار الدورة الدموية.