Heart & Lung 000 (2019) 1–8

Contents lists available at ScienceDirect

Heart & Lung

journal homepage: www.heartandlung.com

Airway and transpulmonary driving pressures and mechanical powers selected by INTELLiVENT-ASV in passive, mechanically ventilated ICU patients

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ARTICLE INFO

Article History:
Received 18 June 2019
Revised 31 October 2019
Accepted 1 November 2019
Available online xxx

Keywords:
Mechanical ventilation
Driving pressure
Mechanical power
Transpulmonary pressure

ABSTRACT

Background: Driving pressure (ΔP) and mechanical power (MP) are predictors of the risk of ventilation- induced lung injuries (VILI) in mechanically ventilated patients. INTELLiVENT-ASV® is a closed-loop ventilation mode that automatically adjusts respiratory rate and tidal volume, according to the patient's respiratory mechanics.
Objectives: This prospective observational study investigated ΔP and MP (and also transpulmonary ΔP (ΔP_L) and MP (MP_L) for a subgroup of patients) delivered by INTELLiVENT-ASV.
Methods: Adult patients admitted to the ICU were included if they were sedated and met the criteria for a single lung condition (normal lungs, COPD, or ARDS). INTELLiVENT-ASV was used with default target settings. If PEEP was above 16 cmH2O, the recruitment strategy used transpulmonary pressure as a reference, and ΔP_L and MP_L were computed. Measurements were made once for each patient.
Results: Of the 255 patients included, 98 patients were classified as normal-lungs, 28 as COPD, and 129 as ARDS patients. The median ΔP was 8 (7 – 10), 10 (8 – 12), and 9 (8 – 11) cmH2O for normal-lungs, COPD, and ARDS patients, respectively. The median MP was 9.1 (4.9 – 13.5), 11.8 (8.6 – 16.5), and 8.8 (5.6 – 13.8) J/min for normal-lungs, COPD, and ARDS patients, respectively. For the 19 patients managed with transpulmonary pressure ΔP_L was 6 (4 – 7) cmH2O and MP_L was 3.6 (3.1 – 4.4) J/min.
Conclusions: In this short term observation study, INTELLiVENT-ASV selected ΔP and MP considered in safe ranges for lung protection. In a subgroup of ARDS patients, the combination of a recruitment strategy and INTELLiVENT-ASV resulted in an apparently safe ΔP_L and MP_L.

Introduction

Mechanical ventilation may induce lung injuries caused by excessive stress, strain, or atelectrauma.[1] Driving pressure (ΔP) is the change in elastic pressure during tidal ventilation, which can easily be measured at the bedside in passive patients as the difference between plateau pressure (P_{PLAT}) and total positive end-expiratory pressure ($PEEP_{TOT}$).[2,3] Driving pressure assesses the strain applied to the lungs,[4] can be used to detect lung overstress,[5] and is an important variable to consider when measuring the effect of mechanical ventilation on patient outcomes. For patients with acute respiratory distress syndrome (ARDS) mechanically ventilated with a low tidal volume (VT), ΔP is the ventilator variable associated most strongly with mortality.[6] Prospective observational data suggest an increased risk of death for ARDS patients with ΔP above 14 cmH2O.[7] To date, no study have been carried out to investigate whether interventions in ΔP are associated with any clinical benefit. However, it seems reasonable to monitor ΔP in ARDS patients in order to assess the risk of ventilator-induced lung injuries (VILI) and to try to keep it below 14 cmH2O.[2] Interestingly, ΔP has also been shown to be a strong predictor of pulmonary complications in brain-injured patients[8] and in patients undergoing mechanical ventilation for general anesthesia.[9]

Driving pressure measured using airway pressure combines the elastic change in pressure required to inflate the lung and the chest wall. Transpulmonary driving pressure (ΔP_L) can be calculated by means of esophageal pressure measurement as the difference between transpulmonary pressure at end-inspiration ($P_{L\ EI}$) and end-expiration ($P_{L\ EE}$), and may be more precise than ΔP for assessing the risk of VILI. Preliminary data show that ΔP_L of less than 8 cmH2O after 24 h of mechanical ventilation is associated with improved survival in ARDS patients.[10]

Mechanical power (MP) represents the energy load transferred from the ventilator to the respiratory system. It is a composite variable determined by the ventilator-related contributors to VILI, namely VT, ΔP, inspiratory flow, respiratory rate (RR), and PEEP.[11]

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https://doi.org/10.1016/j.hrtlng.2019.11.001
0147-9563/

MP could provide a useful bedside integrative index of mechanical VILI risk but it would need to be adapted to account for the difference in lung size, degree of inhomogeneity, and local distribution of stress and strain.[12] Despite these limitations, an experimental study in normal pigs ventilated with different combination of VT and RR found that VILI occurred for a transpulmonary MP over 12 J/min.[13] A retrospective analysis of 787 ARDS patients reported that survival was significantly higher in patients with MP below 12 J/min on the first day of mechanical ventilation.[14] A retrospective analysis of 1705 patients admitted in the ICU without ARDS reported that the incidence of secondary ARDS was higher when MP was over 12 J/min on the first days of mechanical ventilation.[15] As only the energy dissipated within the lung parenchyma may contribute to VILI, calculation of tranpulmonary MP (MP_L) should better assess the risk of VILI.[16]

INTELLiVENT-ASV is a fully closed-loop ventilation mode that automatically controls ventilation and oxygenation settings to reach targets set by the user.[17] Minute ventilation is adjusted to reach the target end-tidal CO2 ($P_{ET}CO2$), while VT and RR are determined according to the respiratory mechanics, namely the expiratory time constant (RC_{EXP}), based on the minimal work of breathing principle described by Otis.[18,19] In passive patients, INTELLiVENT-ASV functions as an adaptive pressure-control mode, adjusting the inspiratory pressure to reach the target VT. The ASV algorithm was modified in 2016 (ASV1.1) to introduce the concept of the minimal force of breathing in addition to the minimal work of breathing.[20] The minimal force of breathing corresponds to the minimal inspiratory pressure (P_{INS}) applied to the respiratory system. Thus ΔP is controlled indirectly by the ventilator and adjusted according to the respiratory mechanics.

The safety, feasibility, and ventilation variables selected by INTELLiVENT-ASV have already been reported previously.[17,21–23] However, all these studies used the former version of the ASV algorithm and none of them reported results for ΔP, ΔP_L, MP, and MP_L. The objective of the present study was to assess whether the automatic ventilator settings selected by INTELLiVENT-ASV using the new version of ASV (1.1) pose a risk of VILI, or can in fact be considered as lung protective. During this clinical trial, we measured the airway and transpulmonary ΔP and MP selected by INTELLiVENT-ASV in patients mechanically ventilated in the intensive care unit (ICU) with a range of different lung conditions.

Methods

A large observational study focusing on respiratory mechanics was conducted in the 16-bed medical-surgical adult ICU of the Sainte Musse Hospital in Toulon (France) from June 2015 to November 2016.[24] The present study is a subgroup analysis of all patients mechanically ventilated with INTELLiVENT-ASV (ASV1.1) included between January 2016 and November 2016. The institutional review board approved the protocol, which was also declared to the Commission Nationale Informatique et Liberté (CNIL). According to French regulations, signed consent was waived. Each patient's next of kin was provided with written information about the study and had the opportunity to refuse the patient's participation.

Patients

Consecutive adult patients admitted to the ICU were included if they were sedated (Richmond agitation-sedation scale −4 or −5), had been mechanically ventilated for less than 48 h without any spontaneous breathing activity, and met the criteria for a single lung condition (normal lungs, chronic obstructive respiratory disease (COPD), or ARDS). Exclusion criteria were pregnancy, a body mass index (BMI) of more than 30 kg/m^2, severe hemodynamic impairment, bronchopleural fistula, brain death, or a mix of lung conditions (e.g., COPD with ARDS). Sedation and myorelaxant were prescribed by the physician in charge of the patient in the form of sufentanil combined with midazolam or propofol, and cisatracurium, respectively. Patients were placed in a semi-recumbent position (30° to 45°) and mechanically ventilated with a HAMILTON-S1 ventilator (Hamilton Medical AG, Bonaduz, Switzerland; software version 2.60) in controlled mode using INTELLiVENT-ASV with ASV1.1 activated.

Ventilator settings

Ventilator settings were determined by the physician in charge of the patient according to the ICU's protocol. INTELLiVENT-ASV was used with $P_{ET}CO2$ and oxygen saturation measured by pulse oximetry (SpO2) with default target ranges for each selected condition. PEEP was automatically adjusted by INTELLiVENT-ASV for normal-lung, COPD, and mild ARDS patients with a PEEP range set at 5 – 10 cm H2O. For moderate and severe ARDS patients, an open-lung strategy combining a recruitment maneuver (sustained inflation at 40 cmH2O for 10 s[25]) followed by a decremental PEEP trial focusing on oxygenation (SpO2) was implemented.[26] PEEP was then set manually. Where the PEEP setting as determined by the decremental PEEP trial was higher than 16 cmH2O, an esophageal catheter was inserted and the correct position verified by an occlusion test.[27] Another sustained inflation recruitment maneuver was then performed targeting a transpulmonary pressure (P_L) of 20 cmH2O for 10 s,[28] and subsequently a decremental PEEP trial targeting $P_{L\ EE}$ of 2 cmH2O was carried out.[29] Peak pressure (P_{PEAK}) was limited to 35 cmH2O for all patients in order to make sure that VT and ΔP selected were the results of ASV selection and not of any pressure limitation by the clinicians.

Measurements, collected data, and calculations

Airway pressure and flow were measured using the ventilator's proximal pneumotachograph (single-use flow sensor, PN 279331, Hamilton Medical AG, Bonaduz, Switzerland, linear between −120 and +120 l/min with $a \pm 5\%$ error of measure) inserted between the endotracheal tube and the Y-piece. Volume was obtained by integration of the flow signal.

The time of data collection was chosen to be separate from other nursing care and medical procedures. In addition, measurements were performed at least one hour after the last manual change of ventilator setting. Airway and esophageal pressures were measured at end-inspiration and end-expiration using a 3-second end-inspiratory and end-expiratory occlusion, respectively[3] together with an arterial blood gas (ABG) measurement. Static compliance (C_{STAT}) was calculated as VT/ (P_{PLAT}-$PEEP_{TOT}$), and ΔP was calculated as the difference between P_{PLAT} and $PEEP_{TOT}$. Inspiratory resistance (R_{INS}) was measured by the least square fitting method over the full respiratory cycle.[30] MP expressed in J/min was calculated according to the extended formula[11]

$$MP = 0.098.RR.\left\{VT^2.[1/2.E_{RS} + RR.((1 + I/E)/(60 + I/E)).R_{INS}] + VT.PEEP\right\} \quad (1)$$

Where 0.098 is the conversion factor from Liters*cmH2O to Joule, E_{RS} is the respiratory system elastance calculated as the inverse of C_{STAT}, and I/E is the inspiratory-to-expiratory time ratio.

$P_{L\ EI}$ and $P_{L\ EE}$ were calculated as the difference between airway and esophageal pressures during the end-inspiratory and end-expiratory occlusions, respectively. ΔP_L was calculated as the difference between $P_{L\ EI}$ and $P_{L\ EE}$. MP_L expressed in J/min was calculated according to the following formula[16]

$$MP_L = 0.098.RR.\left\{VT^2.1/2.E_L + VT.PEEP\right\}$$

Where E_L is the lung elastance calculated as ΔP_L / VT.

Patients were classified according to their lung condition as either normal-lung, COPD, or ARDS. Normal-lung patients were classified as

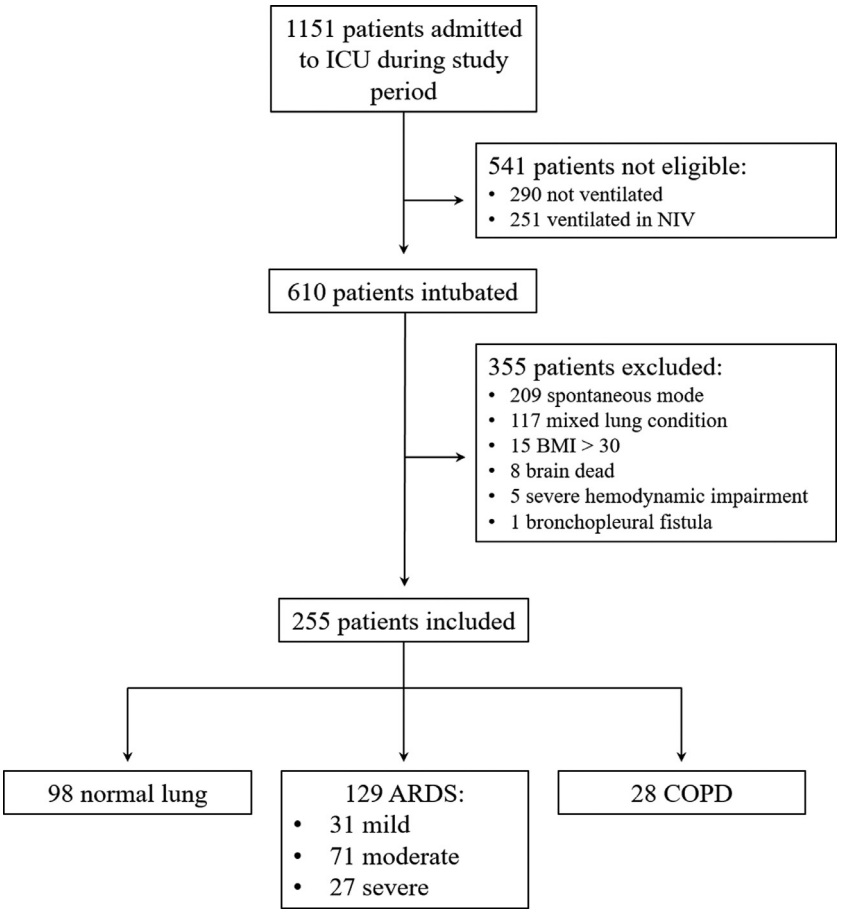

Fig. 1. Patient flow chart.

those with no underlying respiratory disease, a normal chest radiography on the day of inclusion, and a ratio of partial pressure of arterial oxygen (PaO2) over the inspiratory fraction of oxygen (FiO2) of 300 mmHg or higher[31]; ARDS was defined according to the Berlin definition by means of an arterial blood gas (ABG) measurement made at 5 cmH2O of PEEP[32]; COPD was defined according to the "GOLD" criteria.[33]

Statistical methods

In order to perform subgroup analysis, the study was planned to conclude after the inclusion of at least 80 normal-lung patients, 25 ARDS patients for each severity subgroup, and 25 COPD patients.

Values are expressed as medians (25th–75th interquartile range). Kruskal-Wallis analysis of variance (ANOVA) was used to compare values between each type of lung conditions and each ARDS severity groups. Statistical analysis was performed using SigmaPlot software (version 11.0, SPSS, Inc., Chicago, IL, USA). Statistical significance was assumed for *P* value no greater than 0.05.

Results

Among the 255 patients included, 98 patients were classified as normal lungs, 28 as COPD, and 129 as ARDS patients. A flow diagram and characteristics of the patients at inclusion are presented in Fig. 1 and Table 1, respectively. Ventilator settings, respiratory mechanics and ABG results are presented in Table 2.

The median ΔP was 8 (7 – 10), 9 (8 – 11), and 10 (8 – 12) cmH2O for normal lungs, ARDS, and COPD patients, respectively ($p < 0.001$). Within the group of ARDS patients, the median ΔP was 9 (9–11), 9 (8–12), and 10 (9–12) cmH2O, respectively for mild, moderate, and severe conditions ($p = 0.54$).

The median MP was 9.1 (4.9 – 13.5), 8.8 (5.6 – 13.8), and 11.8 (8.6 – 16.5) J/min for normal lungs, ARDS, and COPD patients, respectively ($p = 0.06$). Within the group of ARDS patients, the median MP was 9.6 (8.0 – 12.2), 8.2 (5.1 – 13.8), and 9.8 (6.5 – 14.2) J/min, respectively for mild, moderate, and severe conditions ($p = 0.37$).

The median VT was 6.9 (6.2–7.7), 6.3 (5.5–6.9), and 7.7 (7.1–10.3) mL/kg ideal body weight (IBW) for normal lungs, ARDS, and COPD patients, respectively ($p < 0.001$). Results for ΔP, MP, VT, and P_{PLAT} are presented in Tables 3 and 4 and Figs. 2 and 3.

Esophageal pressure measurement was performed in 19 ARDS patients (11 severe and 8 moderate). The median ΔP_L and MP_L were 6 (4 – 7) cmH2O and 3.6 (3.1 – 4.4) J/min, respectively (Table 5).

Discussion

This prospective observational study reports a ΔP below 14 cmH2O in most of the patients when using INTELLiVENT-ASV in passive, mechanically ventilated ICU patients with a normal-lung, ARDS or COPD condition. In a subgroup of moderate and severe ARDS patients, the ΔP_L selected by INTELLiVENT-ASV was below 8 cmH2O. Interpretation of MP and MP_L is more difficult as there is no safety threshold determined for humans.

Mechanical ventilation may induce lung injuries that subsequently have severe clinical consequences, such as higher mortality in ARDS patients,[34] a higher risk of secondary ARDS in patients with normal lungs,[35] and a higher risk of pulmonary complications in surgical patients.[9] In ARDS patients, results have shown that ventilation with a low VT in the range of 4 – 8 mL/kg IBW is

Table 1
Patients' characteristics at inclusion

	All patients	Normal lungs	COPD	ARDS			
				All	Mild	Moderate	Severe
Number	255	98	28	129	31	71	27
Sex ratio (%M/%F)	67/33	66/34	89/11	62/38	58/42	59/41	75/25
Age (years)	67 (55 – 75)	66 (53 – 73)	66 (59 – 76)	68 (55 – 78)	67 (56 – 76)	68 (54 – 78)	68 (58 – 79)
BMI (kg/m^2)	25 (22 – 29)	25 (22 – 28)	23 (22 – 27)	26 (22 – 29)	26 (21 – 29)	27 (23 – 29)	26 (22 – 29)
IBW (kg)	66 (57 – 72)	66 (59 – 73)	68 (64 – 72)	65 (55 – 72)	65 (55 – 72)	65 (56 – 72)	66 (52 – 72)
SAPS II	57 (47 – 69)	56 (45 – 68)	54 (46 – 67)	60 (50 – 72)	57 (49 – 66)	61 (49 – 73)	62 (53 – 74)

Data are median (25th–75th quartiles). COPD: Chronic Obstructive Pulmonary Disease; ARDS: Acute Respiratory Disease Syndrome; BMI: Body mass index; IBW: Ideal body weight; SAPS: Simplified Acute Physiological Score.

Table 2
Ventilator settings, static compliance and arterial blood gas results

	All patients	Normal lungs	COPD	ARDS			
				All	Mild	Moderate	Severe
Number	255	98	28	129	31	71	27
MV (L/min)	8.0 (6.4 – 9.8)	7.9 (6.2 – 9.7)	7.2 (6.1 – 8.6)	8.2 (6.5 – 10.3)	8.4 (7.4 – 10.1)	7.9 (6.3 – 10.7)	8.3 (6.7 – 9.7)
RR (breath/min)	20 (17 – 22)	19 (16 – 21)	14 (9 – 17)	21 (19 – 25)	21 (19 – 23)	22 (19 – 26)	22 (20 – 28)
PEEP (cmH2O)	8 (5 – 12)	5 (5 – 7)	8 (5 – 11)	12 (9 – 15)	10 (8 – 13)	12 (9 – 15)	14 (12 – 17)
FiO2 (%)	30 (26 – 41)	25 (21 – 29)	36 (28 – 43)	37 (29 – 49)	31 (28 – 37)	41 (32 – 50)	43 (32 – 69)
C_{STAT} (mL/cmH2O)	47 (36 – 62)	54 (44 – 69)	63 (42 – 75)	41 (32 – 53)	44 (36 – 53)	38 (29 – 54)	38 (32 – 46)
pH	7.35 (7.28 – 7.41)	7.39 (7.34 – 7.43)	7.32 (7.25 – 7.38)	7.32 (7.26 – 7.39)	7.33 (7.28 – 7.37)	7.33 (7.25 – 7.40)	7.30 (7.25 – 7.35)
PaO2 (mm Hg)	83 (73 – 94)	89 (82 – 95)	78 (63 – 97)	78 (72 – 90)	78 (72 – 83)	79 (73 – 93)	78 (67 – 92)
PaCO2 (mm Hg)	41 (37 – 47)	37 (36 – 39)	51 (46 – 56)	44 (39 – 51)	40 (37 – 47)	44 (40 – 51)	49 (44 – 56)
SaO2 (%)	96 (94 – 97)	97 (96 – 98)	95 (92 – 98)	95 (94 – 96)	96 (94 – 97)	95 (94 – 97)	94 (93 – 95)
PaO2/ FiO2 (mm Hg)	267 (194 – 345)	351 (304 – 411)	217 (149 – 314)	207 (159 – 260)	261 (228 – 285)	194 (156 – 244)	191 (117 – 241)

Data are median (25th–75th quartiles). COPD: Chronic Obstructive Pulmonary Disease; ARDS: Acute Respiratory Disease Syndrome. MV: Minute volume; RR: respiratory rate; C_{STAT}: static compliance.

Table 3
Tidal volume, plateau pressure, driving pressure, and mechanical power results according to lung condition

	All patients	1 Normal lungs	2 COPD	3 ARDS	P (ANOVA)	Post hoc comparison ($p \leq 0.05$)
Number	255	98	28	129		
VT (mL/kg IBW)	6.7 (5.8 – 7.6)	6.9 (6.2 – 7.7)	7.7 (7.1 – 10.3)	6.3 (5.5 – 6.9)	< 0.001	1 vs. 2, 1 vs. 3, 2 vs. 3
P_{PLAT} (cmH2O)	19 (15 – 24)	15 (13 – 17)	21 (17 – 23)	23 (19 – 25)	< 0.001	1 vs. 2, 1 vs. 3
ΔP (cmH2O)	9 (7 – 11)	8 (7 – 10)	10 (8 – 12)	9 (8 – 11)	< 0.001	1 vs. 3
MP (J/min)	9.2 (5.4 – 14.5)	9.1 (4.9 – 13.5)	11.8 (8.6 – 16.5)	8.8 (5.6 – 13.8)	0.06	

Data are median (25th–75th quartiles). COPD: Chronic Obstructive Pulmonary Disease; ARDS: Acute Respiratory Disease Syndrome; VT: Tidal volume; IBW: Ideal body weight; P_{PLAT}: Plateau pressure, ΔP: Driving pressure, MP: mechanical power, vs: versus. Comparisons used a Kruskal-Wallis analysis of variance (ANOVA) with a Dunn's post hoc test. Vs.

associated with better outcomes.[30] Within this range of low VT, outcomes may also be improved if ΔP is below 14 cm H2O.[7] The INTELLiVENT-ASV mode selects VT according to three parameters: Minute volume required to reach the $P_{ET}CO2$ set by the user, anatomical dead space, and respiratory mechanics. For any given minute volume and dead space, the selected VT depends on resistance and C_{STAT}. If resistance remains stable, a decrease in C_{STAT} will result in a lower VT. Interestingly, the ratio of VT to C_{STAT} (ΔP) in this study was around 9 (7 – 11) cmH2O for all three lung conditions. This result is below the accepted threshold of 14 cmH2O that is associated with better outcomes and can therefore be considered as lung protective.[7] Only 4 patients out of 255 were

Table 4
Tidal volume, plateau pressure, driving pressure, and mechanical power results in the subgroup of ARDS patients

	All ARDS patients	1 Mild ARDS	2 Moderate ARDS	3 Severe ARDS	P (ANOVA)	Post hoc comparison ($p \leq 0.05$)
Number	129	31	71	27		
VT (mL/kg IBW)	6.3 (5.5 – 6.9)	6.6 (6.0 – 7.3)	6.0 (5.4 – 6.8)	5.9 (5.3 – 6.8)	0.041	1 vs. 2
P_{PLAT} (cmH2O)	23 (19 – 25)	21 (18 – 25)	22 (19 – 25)	25 (23 – 28)	0.002	1 vs. 3, 2 vs. 3
ΔP (cmH2O)	9 (8 – 11)	9 (9 – 11)	9 (8 – 12)	10 (8 – 11)	0.54	
MP (J/min)	8.8 (5.6 – 13.8)	9.6 (8.0 – 12.2)	8.2 (5.1 – 13.8)	9.8 (6.5 – 14.2)	0.37	

Data are median (25th–75th quartiles). ARDS: Acute Respiratory Disease Syndrome; VT: Tidal volume; IBW: Ideal body weight; P_{PLAT}: Plateau pressure, ΔP: Driving pressure, MP: mechanical power, vs: versus. Comparisons used a Kruskal-Wallis analysis of variance (ANOVA) with a Dunn's post hoc test.

ventilated with ΔP above 15 cmH2O, all of them in ARDS condition (Fig. 2).

Interpretation of MP results is difficult as there is no safety threshold determined for ICU patients. MP represents the energy load provided by the ventilator to the respiratory system which react to it according to its anatomical structure and pathophysiological status.[16] The risk of VILI for a given MP depends on the volume of aerated lung, lung heterogeneity, local distribution of stress and strain, and the chest wall mechanics.[12] Despite all these limitations, it has been demonstrated that computed MP using the extended formula based on the equation of motion provide results well correlated with measured MP.[11] Two studies in ARDS and non ARDS patients reported better outcomes for patients ventilated with a calculated MP below 12 J/min.[14,15] The association between MP and mortality was examined retrospectively in 8207 patients receiving mechanical ventilation for at least 48 h in ICU. There was a consistent increase in the risk of death with MP higher than 17 J/min.[35] In the present study, calculated MP provided in INTELLiVENT-ASV was below 17 J/min for most of the patients and was lower than the values reported in previous clinical studies.[11,14,15,36,37] These results is the consequence of

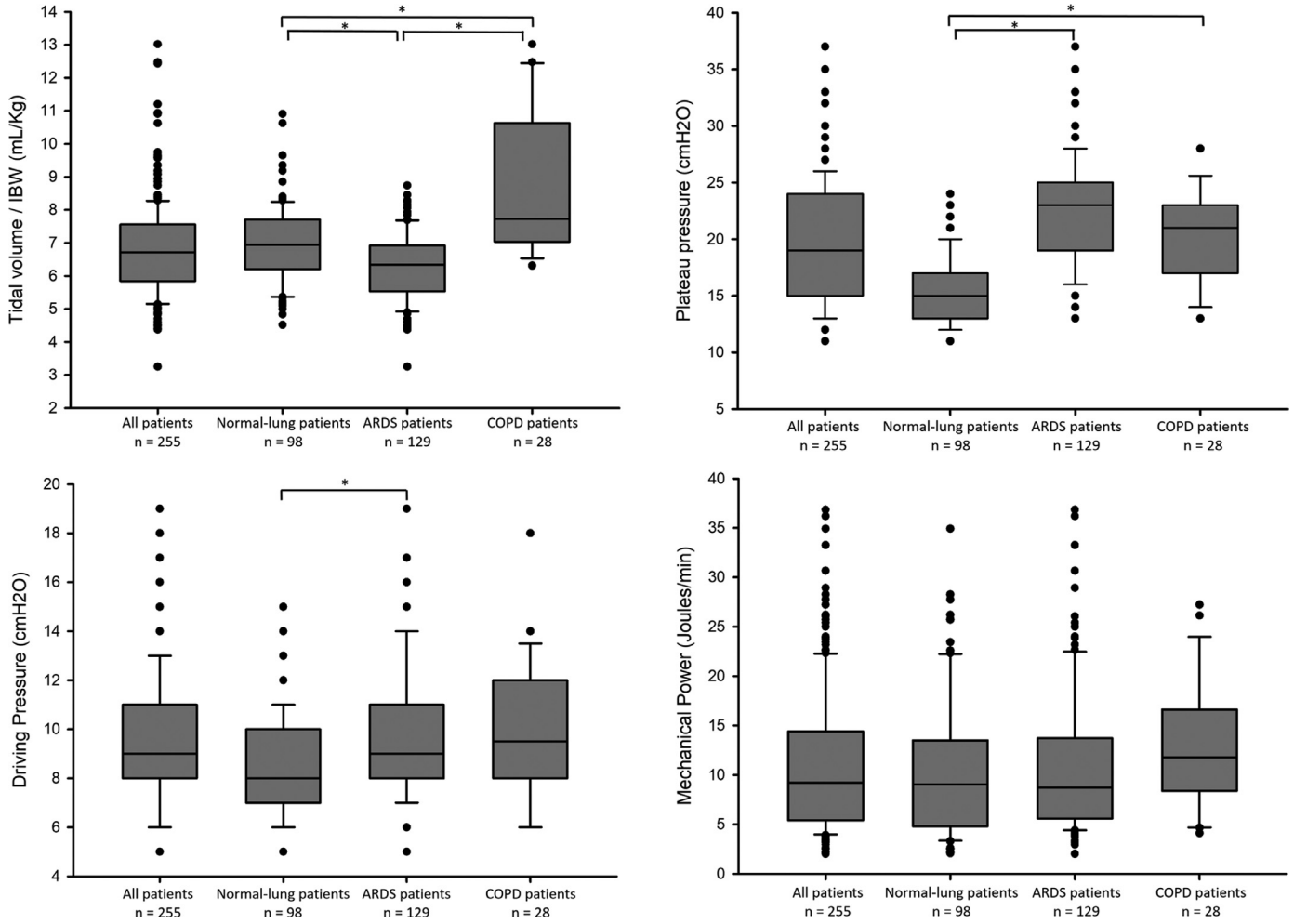

Fig. 2. Tidal volume, plateau pressure, driving pressure and mechanical power according to lung condition. Box plots represent median with 25th-75th percentiles. Whisker caps represents 10th-90th percentiles. Black circles represent outliers. Comparisons used a Kruskal-Wallis analysis of variance with a Dunn's post hoc test. *$P \leq 0.05$. ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; IBW, ideal body weight.

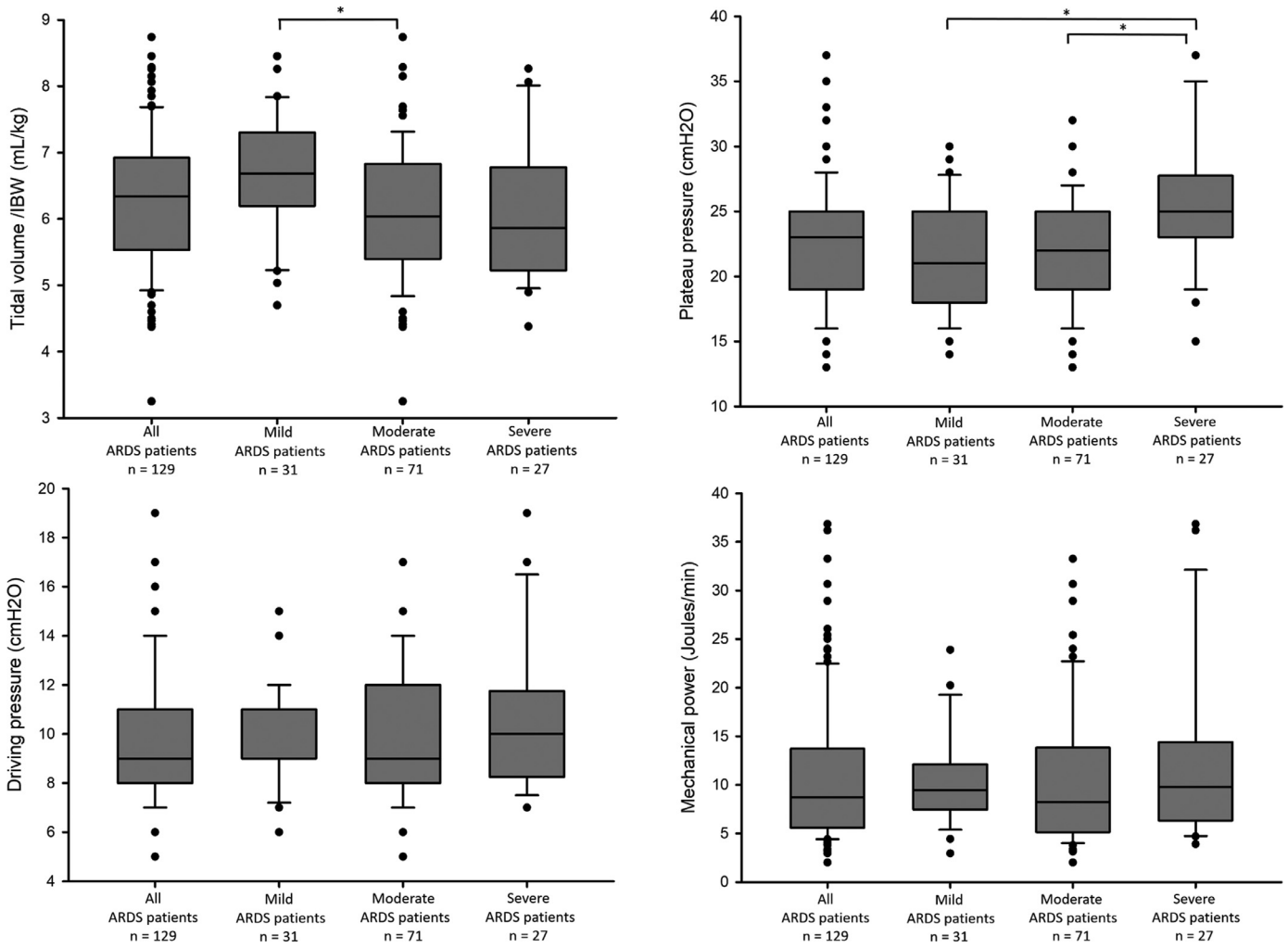

Fig. 3. Tidal volume, plateau pressure, driving pressure and mechanical power in the subgroup of ARDS patients. Box plots represent median with 25th-75th percentiles. Whisker caps represents 10th-90th percentiles. Black circles represent outliers. Comparisons used a Kruskal-Wallis analysis of variance with a Dunn's post hoc test. $^{*}P \leq 0.05$. ARDS, acute respiratory distress syndrome; IBW, and ideal body weight.

INTELLiVENT-ASV algorithm that select a permissive hypercapnia strategy when peak pressure is above 25 cmH2O, and the ASV 1.1 algorithm that minimizes work and force of breathing. We can then conclude that MP provided by INTELLiVENT-ASV seems in the safe range. Interestingly, MP was not statistically different according to lung condition nor ARDS severity (Figs. 2 and 3).

Lung protection should be a strategy implemented in all mechanically ventilated patients, regardless of their lung condition. Because this study included patients with very different respiratory mechanics (C_{STAT} from 11 to 90 ml/cmH2O), we conclude that INTELLiVENT-ASV can be trusted to select a safe ventilation in most mechanically ventilated ICU patients.

In moderate to severe ARDS patients, the chest-wall mechanics may be impaired. As a result, the elastic pressure required to distend the chest wall will increase, which also increases ΔP. As ΔP_L may be a better measure of the risk of lung injury, it is useful to partition ΔP into its lung (ΔP_L) and chest-wall components. The results of the present study show that after a recruitment maneuver and PEEP setting guided by transpulmonary pressure, INTELLiVENT-ASV selected ΔP_L at 6 (4 – 7) cm H2O. There is not extensive data on ΔP_L to be found in the literature; however a retrospective analysis of the EPVent study demonstrated that a ΔP_L below 10 cmH2O is associated with better outcomes in ARDS patients.[10] The present study demonstrates that a recruitment strategy guided by transpulmonary pressure combined with the use of INTELLiVENT-ASV results in a lung-protective ΔP_L. For the same reason, MP_L should be a better assessement of the risk of VILI than MP because it removes the energy required to move the chest wall and the energy dissipated in endotracheal tube and tracheobronchial tree during inspiration.[13] In an experimental study with normal pigs, VILI occurred when measured MP_L was over 12 J/min.[13] Calculated MP_L reported in this study was far below this threshold but we can't draw any conclusion because there is no safety threshold for patients. In addition, MP_L should be normalized to the volume of aerated lung tissue to compare the results.[16] However, given the small number of patients managed with esophageal pressure in this study, the result should be considered as preliminary. Larger comparative studies will be needed to confirm whether this apparently safe ΔP_L and MP_L are associated with an improvement in clinical outcomes.

Table 5
Airway and transpulmonary driving pressures and mechanical powers results for the 19 ARDS patients managed with esophageal pressure measurement

	Respiratory system	Chest wall	Lung
ΔP (cmH2O)	9 (8 – 10)	2 (2 – 4)	6 (4 – 7)
MP (J/min)	7.6 (5.6 – 9.5)		3.6 (3.1 – 4.4)

Data are median (25th–75th quartiles). ΔP: Driving pressure; MP: mechanical power.

Recently, the LUNG SAFE study reported on current management of ARDS patients in ICU's around the world.[38] There, the VT selected manually by the clinician was higher than the VT reported in the present study, and the PEEP was lower. Interestingly, P_{PLAT} was similar in both studies, which means that the ΔP selected by clinicians was also higher than in the present study. The LUNG SAFE study also reported that only 34% of ARDS patients were actually recognized as such by clinicians at the time of fulfilling the ARDS criteria, which suggests that the diagnosis of ARDS was frequently delayed or missed altogether. Those patients with undiagnosed ARDS were ventilated with a significantly higher VT than patients with diagnosed ARDS. This common problem can be solved by closed-loop mechanical ventilation that takes into account the respiratory mechanics to select VT and ΔP, regardless of the diagnosis. Using a closed-loop ventilation mode that adjusts the VT according to the patient's respiratory mechanics may help the clinician to better apply lung-protective ventilation.

Several previous studies reported on the VT selected by ASV or INTELLiVENT-ASV for different lung conditions.[31,23] However, none of these previous studies reported on ΔP, ΔP_L, MP, or MP_L because neither parameter was a focus at that time. In addition, the present study was performed with the new version of ASV, which introduces the minimal force of breathing concept that is equivalent to the minimal P_{INS}.[20] As compared to our previous study in a different cohort of patients, it seems that VT has been reduced with this new version (normal lungs: 8.1 (7.3 – 8.9) versus 6.9 (6.2 – 7.7) mL/kg IBW; ARDS: 7.5 (6.9 – 7.9) versus 6.3 (5.5 – 6.9) mL/kg IBW; COPD: 9.9 (8.3 – 11.0) versus 7.7 (7.1 – 10.3) mL/kg IBW for ASV1.0 and ASV1.1, respectively).[23] P_{PLAT} was also reduced by an average of 3 cmH2O. It can therefore be concluded that this new version of ASV improves the lung protection provided by these closed-loop modes.

The main limitation of this study is that only one measurement was made per patient at a given time. This measurement was taken soon after ICU admission once the patient had been stabilized, and separately from any other nursing procedure. Therefore, these results do not reflect the average value over a longer period of time. Further studies with longer observation time are needed to confirm the safety of this ventilation mode. The second limitation is that only patients with a single lung condition were included. As shown in Fig. 1 by the number of patients excluded, a mixed lung condition (for example, ARDS in COPD patients) is common in mechanically ventilated patients. However, because this study included patients with a large range of respiratory mechanics, we can assume that the ΔP selected would be quite similar for a mixed lung condition. The third limitation concerns the calculation of MP which was not normalized for the volume of aerated lung or lung heterogeneity and did not consider the energy dissipated into the respiratory system during expiration.[16] Finally, the number of patients with esophageal pressure measurement was small and limited to severe ARDS.

This study was performed in a mixed ICU with a standard admitted population and standard ICU management. The results of the present study would probably be similar to results obtained in other ICUs, and may well be valid for most ICU patients because the closed-loop ventilation mode would apply similar ventilation parameters.

INTELLiVENT-ASV using ASV1.1 selects physiological variables that have been associated with improved outcomes in other analyses.[6,8,9,35] Safety and efficacy over longer period of ventilation and impact of these settings on the clinical outcomes will need to be tested in prospective comparative studies.

Conclusion

In this prospective, short term observational study on 255 passive ICU patients with normal lungs, COPD, and ARDS, INTELLiVENT-ASV selected ΔP and VT considered in the safe ranges for lung protection. MP results are difficult to interpret but seem also on the safe range. In a subgroup of moderate and severe ARDS patients managed with esophageal pressure measurement, the combination of a recruitment strategy and INTELLiVENT-ASV resulted in an apparently safe ΔP_L and MP_L. These results support the use of closed-loop mechanical ventilation to help the clinician apply lung-protective ventilation in ICU patients.

Institution

This study was conducted in the Service de Réanimation Polyvalente, Hôpital Sainte Musse, 54 Avenue Henri Sainte Claire Deville, 83056 Toulon, France.

Author's contribution

Jean-Michel Arnal searched the literature, designed the study, collected data, analyzed the data, and prepared the manuscript.

Mathieu Saoli searched the literature, designed the study, collected data, and reviewed the manuscript.

Aude Garnero searched the literature, designed the study, collected data, and reviewed the manuscript.

Previous presentation

ESICM 2016 in Milan

Conflict of interest

Jean-Michel Arnal is employed part-time as Medical Research Manager by Hamilton Medical AG.

Aude Garnero and Mathieu Saoli do not have any competing interests to disclose.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

None

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