

10-1-2017

Impact of Physician Education and Availability of Parameters Regarding Esophageal Pressure and Transpulmonary Pressure on Clinical Decisions Involving Ventilator Management

Lonny Ashworth
Boise State University

Publication Information

Ashworth, Lonny. (2017). "Impact of Physician Education and Availability of Parameters Regarding Esophageal Pressure and Transpulmonary Pressure on Clinical Decisions Involving Ventilator Management". *Journal of Critical Care*, 41, 112-118.
<https://doi.org/10.1016/j.jcrc.2017.04.021>



This document was originally published in *Journal of Critical Care* by Elsevier. This work is provided under a Creative Commons Attribution-NonCommercial-No Derivatives 4.0 license. Details regarding the use of this work can be found at: <http://creativecommons.org/licenses/by-nc-nd/4.0/>. doi: 10.1016/j.jcrc.2017.04.021



Impact of physician education and availability of parameters regarding esophageal pressure and transpulmonary pressure on clinical decisions involving ventilator management

Yasuhiro Norisue, MD^{a,*}, Lonny Ashworth, MEd RRT FAARC^b, Takaki Naito, MD^a, Jun Kataoka, MD^a, Muneyuki Takeuchi, MD, PhD^c, Sunao Usami, CE^a, Junko Takada, PT RRT^a, Shigeki Fujitani, MD PhD^d

^a Department of Pulmonary and Critical Care Medicine, Tokyo Bay Urayasu Ichikawa Medical Center, Chiba, Japan

^b Department of Respiratory Care, Boise State University, Boise, ID, USA

^c Department of Anesthesia and Critical Care Medicine, Osaka Medical Center and Research Institute for Maternal and Child Health, Osaka, Japan

^d Department of Emergency and Critical Care Medicine, St. Marianna University Hospital, Kanagawa, Japan

ARTICLE INFO

Available online xxxx

Keywords:

Esophageal pressure
Transpulmonary pressure
Mechanical ventilation
Education
Simulation
PEEP
Inspiratory effort
Missed trigger
Work of breathing

ABSTRACT

Purpose: This study investigated the effects of physician education and the availability of P_{eso} and P_{L} data on physicians' decisions regarding ventilator management during specific simulated clinical conditions.

Materials and methods: The study was a prospective, before–after study using a case scenario–based questionnaire and a case simulator device comprising an Avea ventilator and an artificial lung and esophagus, which was connected to a Series 1101 Electronic Breathing Simulator. The 99 physicians participating in the study were provided with five simulated cases with on-time ventilator graphics without P_{eso} and P_{L} and completed a questionnaire on decisions they would make regarding ventilator management of the cases. Then, after receiving instruction on P_{eso} and P_{L} , they were given the same cases along with ventilator graphics that included P_{eso} and P_{L} .

Results: After receiving instruction and data on P_{eso} and P_{L} , statistically significant numbers of physicians changed their answers regarding ventilator management decisions in all five cases.

Conclusions: Providing education and data for P_{eso} and P_{L} had a significant effect on physician decisions regarding ventilator management in simulated cases. The use of case scenario–based education with simulator devices for physicians may hasten worldwide understanding and clinical application of P_{eso} and P_{L} .

© 2017 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Background

Transpulmonary pressure (P_{L}) is the difference between alveolar pressure and intrapleural pressure. P_{L} is known as the actual “lung-distending pressure” and the main force that promotes alveolar recruitment and lung inflation [1,2]. It has been demonstrated that changes in intrapleural pressure are similar to changes in esophageal pressure (P_{eso}) and P_{eso} has been used as a surrogate for intrapleural pressure [3–5]. Esophageal pressure is also regarded as the gold standard for measuring inspiratory effort and work of breathing [6,7]. Several studies have shown the potential benefits of measuring P_{eso} in various clinical settings such as monitoring respiratory muscle activity and synchrony

during assisted ventilation or titrating PEEP in patient with ARDS, potentially preventing alveolar collapse and atelectrauma [5,8–11]. Although the use of P_{eso} and P_{L} monitoring is increasing worldwide [5, 12], many physicians caring for critically ill patients receiving mechanical ventilation lack knowledge of P_{L} and thus do not use it to monitor their patients. Additionally, very few physicians in Japan actually monitor P_{eso} or P_{L} as part of their ventilator management. We hypothesized that providing data for P_{eso} and P_{L} after instruction on how to use these parameters may have a significant impact on physicians' clinical decisions involving mechanical ventilator management. This before–after study investigated the effect of providing physician education and patient P_{eso} and P_{L} data on physicians' decisions regarding ventilator management during specific, simulated clinical conditions.

2. Methods

2.1. Study design and objectives

This prospective, before–after study utilized a simulated case scenario–based questionnaire and case simulator device to investigate the

Abbreviations: P_{L} , transpulmonary pressure; P_{eso} , esophageal pressure; PEEP, positive end-expiratory pressure; APRV, airway pressure release ventilation; PRVC, pressure-regulated volume control.

* Corresponding author at: Department of Pulmonary Critical Care Medicine, Tokyo Bay Urayasu Ichikawa Medical Center, 3–4–32 Todajima Urayasu City, Chiba 2790001, Japan.
E-mail address: yasuhiro@jadecom.jp (Y. Norisue).

Table 1
Main points of lecture given to participants.

- [1] P_L is the difference between alveolar pressure and intrapleural pressure.
- [2] P_L reflects actual stress on alveoli.
- [3] P_L can be substantially lower than the set or measured airway pressure if intrapleural pressure is high.
- [4] A negative P_L may indicate collapsed alveoli.
- [5] Peak P_L can be substantially higher than the set or measured airway pressure if inspiratory effort is strong in a patient with negative intrapleural pressure.
- [6] There is no absolute cut-off value that is considered safe for P_L , although a value of <25 cm H_2O is suggested for ARDS patients.
- [7] There is no absolute cut-off value that is considered safe for delta P_L , although a value of <12 cm H_2O is suggested for ARDS patients.
- [8] A negative deflection in P_{eso} reflects a patient's inspiratory effort.

impact of education and availability of patient P_{eso} and P_L data on physicians' clinical decisions regarding ventilator management. The study was approved by the Institutional Review Board at Tokyo Bay Urayasu Ichikawa Medical Center. The Japanese Society of Education for Physicians and Trainees in Intensive Care (JSEPTIC) email list, which includes approximately 4600 members in Japan and provides opportunities to freely exchange information about intensive care, was used to recruit physicians who were interested in participating in the study at the study sites. The 99 Japanese physicians who participated in the study were instructed to return the questionnaire only if they agreed to participate and provide their answers for this study.

2.2. Case simulator device and case presentation

The case simulator device comprised an Avea ventilator (CareFusion, San Diego, CA) and an artificial lung and esophagus (artificial thorax) connected to a Series 1101 Electronic Breathing Simulator (Hans Rudolph, Shawnee, KS) and was used to simulate various levels of inspiratory effort (Supplementary Fig. 1). A continuous positive airway pressure device (POINT CPAP, Hoffrichter, Schwerin, Germany) was connected to the artificial thorax in **Case 1** to increase intrapleural pressure.

Participants were provided with real-time ventilator graphics (Supplementary Fig. 2–6) produced by the simulator while they selected their answers for five simulated case scenarios (Appendix 1) involving critically ill, mechanically ventilated patients. Only the graphics from the ventilator display were provided on the central screen at the front of the room. All parameters and indices were given to the participants in a written handout, because reproducing each of the parameters and

indices on the artificial lung was impossible due to its low compliance and low volume.

2.3. Simulated case scenarios (see Appendix 1 for detail)

Case 1 (assessed with Question 3): This case involved determination of optimal positive end-expiratory pressure (PEEP) in a hypoxic patient with plateau pressure 30 cm H_2O , PEEP 5 cm H_2O . Tidal volume was low despite inspiratory pressure of 25 cm H_2O due to elevated intrapleural pressures and abdominal compartment syndrome, which resulted in negative end-expiratory P_L and atelectasis.

Case 2 (assessed with Question 4): This case involved a decision whether to use neuromuscular blockade in a patient on pressure control ventilation with severe acute respiratory distress syndrome (ARDS) characterized by strong inspiratory effort and, therefore, high P_L (>35 cm H_2O).

Case 3 (assessed with Question 5): This case involved detection of trigger asynchrony resulting in missed triggers in a patient with auto-PEEP, which, although detectable on the flow versus time waveform, was more obvious on the P_{eso} versus time waveform.

Case 4 (assessed with Question 6): This case involved a decision whether to discontinue airway pressure release ventilation (APRV) in a patient with ARDS and strong inspiratory effort resulting in high P_L (>35 cm H_2O), even though peak airway pressure was <30 cm H_2O .

Case 5 (assessed with Question 7): This case involved a decision whether to discontinue pressure regulated volume control (PRVC) in a patient with ARDS and strong inspiratory effort, resulting in prominent negative inspiratory P_{eso} and low peak inspiratory pressure.

2.4. Pre-questionnaire

All questionnaires were completed anonymously. The questionnaire consisted of two questions pertaining to the respondents' background (specialty and postgraduate year; Questions 1 and 2) and five questions on their decisions regarding ventilator management in the five simulated case scenarios (Appendix 2). The participants were informed that there were no clearly correct answers. They were also instructed to choose the answer from the provided choices that they felt were the decisions that they would make in actual clinical practice for each simulated case scenario although there may be other appropriate responses beside the choices.

The case scenarios and graphics included the clinical parameters considered necessary when making changes in ventilator

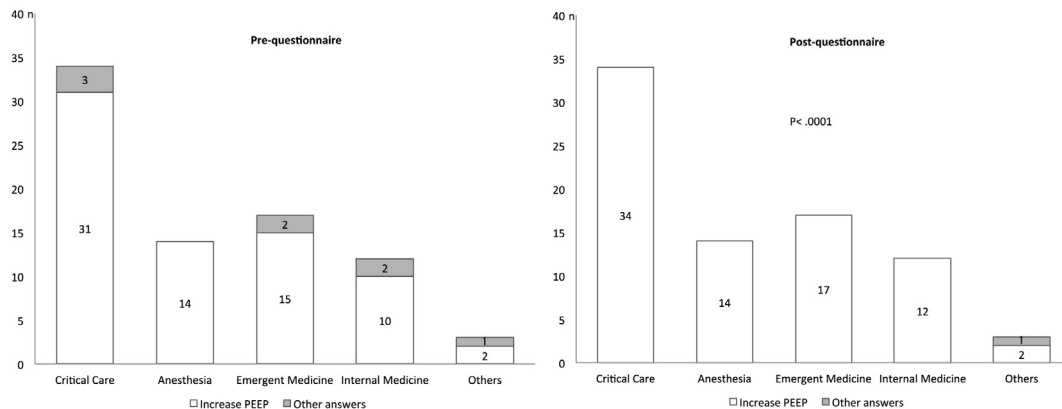


Fig. 1. The numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires for Case 1.

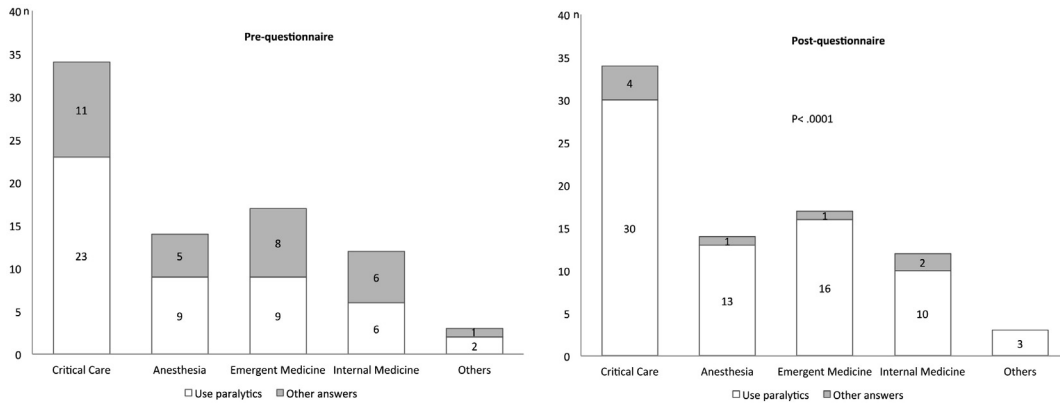


Fig. 2. The numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires for Case 2.

management, such as vital signs, physical findings, arterial blood gas analysis, and airway pressures. No information related to P_{es0} , P_L , or the graphic display of P_{es0} , P_L was provided (Supplementary Fig. 2a–6a).

2.5. Lecture on P_{es0} and P_L

After participants completed the questionnaire, they attended a 40-min lecture focusing on current knowledge and perspectives regarding P_{es0} and P_L and the application of this information to the clinical setting [2,5,8–11,13–16]. Table 1 shows the points emphasized in the lecture.

2.6. Post-questionnaire

After the lecture, the same simulated case scenarios were provided to the participants, along with the same questionnaire; however, the graphics provided included P_{es0} and P_L for all the specific simulated case scenarios (Supplementary Fig. 2b–6b).

2.7. Statistical analysis

Continuous variables are expressed as mean and standard deviation (SD). Discrete variables are summarized as percentages. Dichotomous variables were analyzed and compared using the McNemar test. The software package EZR (Saitama Medical Center, Jichi

Medical University) was used to perform the statistical analysis. A P value of <0.05 was considered to indicate statistical significance.

3. Results

3.1. Participants

Of the 99 physician participants, 12 did not return their questionnaires (recovery rate 88%), and 7 questionnaires could not be analyzed because of missing data; hence, 92% (80/87) of the returned questionnaires were analyzed. Of the returned questionnaires, 42.5% (34/80) were critical care physicians, 17.5% (14/80) were anesthesiologists, 21.25% (17/80) were emergency medicine physicians, 15% (8/80) were general internal medicine physicians, 1.25% (1/80) was a surgeon, and 2.5% (2/80) were residents who had not yet selected a specialty. The mean (SD) and median postgraduate year (PGY) of the respondents were 13.6 (7.43) years and 12 years, respectively; 7.5% (6/80) were in PGY 1–5, 30% (24/80) were in PGY 6–10, 32.5% (26/80) were in PGY 11–15, and 30% (24/80) were in PGY 16 or later.

Case 1. Determining optimal PEEP level in a patient with elevated end-expiratory intrapleural pressure and negative P_L .

For Case 1, the numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires, are shown in Fig. 1. Overall, 14% of physicians chose an answer other than “increasing PEEP” before the lecture without information on P_{es0} and

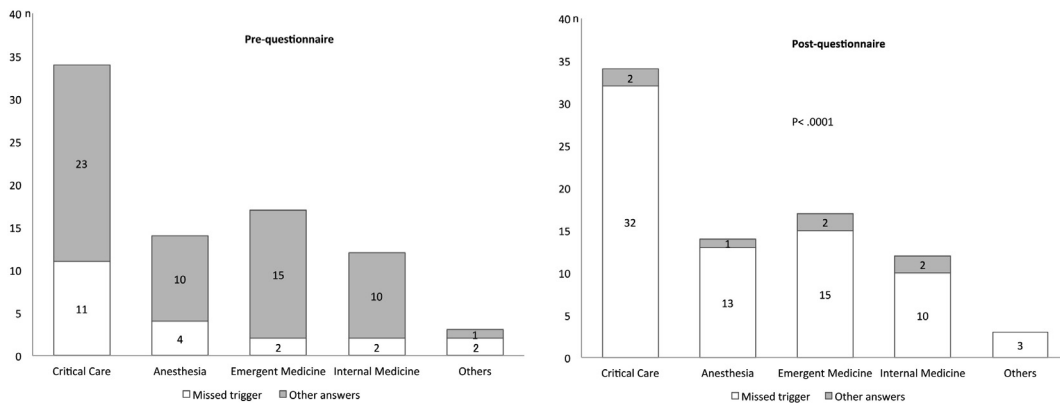


Fig. 3. The numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires for Case 3.

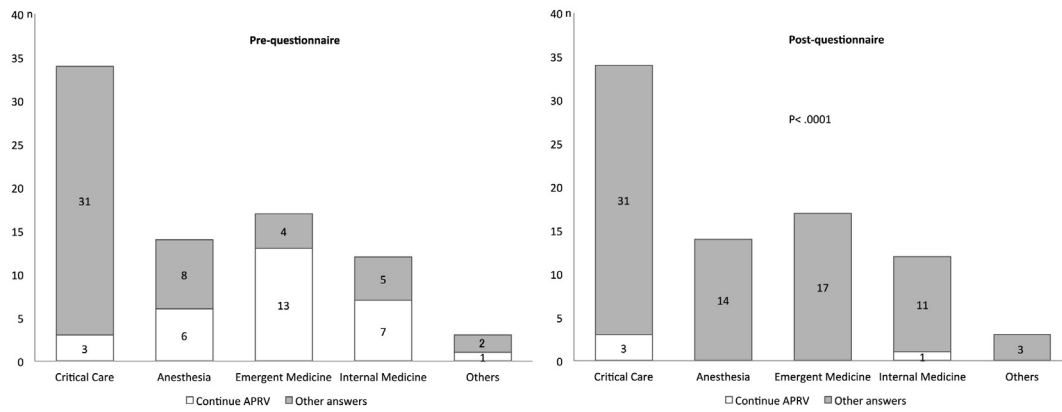


Fig. 4. The numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires for Case 4.

P_L , whereas 1.8% chose such responses after attending the lecture and receiving data on P_{eso} and P_L ($P < 0.0023$).

Case 2. Deciding whether to use neuromuscular blockade in a patient with severe ARDS, strong inspiratory effort, and high P_L (> 35 cm H_2O) but with a peak airway pressure < 30 cm H_2O .

For Case 2, the numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires, are shown in Fig. 2. Overall, 52.6% and 89.5% of physicians chose “using neuromuscular blockade” on the pre- and post-questionnaires, respectively ($P < 0.001$).

Case 3. Detecting patient-ventilator asynchrony with missed triggers in a patient with auto-PEEP.

For Case 3, the numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires, are shown in Fig. 3. Overall, 19.3% and 89.5% of physicians chose “missed trigger” on the pre- and post-questionnaires, respectively ($P < 0.001$).

Case 4. Determining whether to discontinue APRV in a patient with ARDS and strong inspiratory effort resulting in high P_L (> 35 cm H_2O), although peak airway pressure was < 30 cm H_2O .

For Case 4, the numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires, are shown in Fig. 4. Overall, 56.1% and 7% of physicians decided to “continue APRV mode” on the pre- and post-questionnaires, respectively ($P < 0.001$).

Case 5. Determining whether to discontinue PRVC-AC in a patient with ARDS, strong inspiratory effort, and prominent negative inspiratory P_{eso} , resulting in low peak inspiratory pressure.

For Case 5, the numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires, are shown in Fig. 5. Overall, 14% and 3.5% of physicians decided to “continue PRVC-AC” on the pre- and post-questionnaires, respectively ($P = 0.0012$).

4. Discussion

This is the first study to show that providing education and patient data on P_{eso} and P_L significantly affected physician decision-making. After receiving instruction on P_{eso} and P_L a significant number of physicians changed their answers regarding ventilator management in the five simulated cases.

This study demonstrates that new concepts and information can significantly affect clinical decision-making, even among experienced physicians. With the exception of data on P_{eso} and P_L , the pre-questionnaire included the principal information necessary for participants to make suitable decisions. These included factors such as distended abdomen with high airway pressure in Case 1, a strong inspiratory effort in Cases 2, 4 and 5, and flow versus time waveforms in Case 3. A better understanding of P_L and the availability of patient P_{eso} and P_L data and graphics had a significant effect on physicians' decision-making. Clarifying whether or not the changes in their decisions based on P_{eo} and P_L will result in better outcomes in real clinical setting requires further investigation.

In situations such as Case 1, where end-expiratory pressure outside the lungs (intrapleural pressure) is higher than the pressure inside the lungs (airway pressure), some physicians may think that alveoli are open because PEEP is positive. Some physicians may also have fear of barotrauma by increasing PEEP, which results in plateau pressure > 30 cm H_2O . The significant change in physicians' responses after the

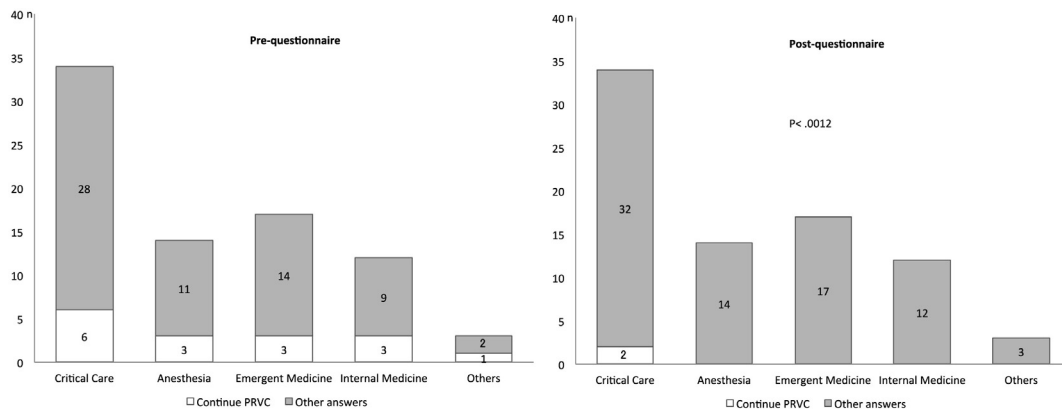


Fig. 5. The numbers and specialties of physicians who chose each response, on the pre- and post-questionnaires for Case 5.

intervention appears to reflect an improved understanding of P_L . Moreover, without specific modalities such as P_{eso} monitoring, even if negative P_L is suspected because of abdominal distension, it is unclear if the current PEEP level is sufficient to keep alveoli open [10,12,13].

In situations such as Case 2, a patient with strong inspiratory effort and large tidal volumes, physicians will sometimes allow or ignore potential volutrauma because “the plateau pressure is less than 30 cm H_2O and that’s how they want to breathe”, especially when using pressure-targeted modes. When provided with information indicating high P_L (far >30 cm H_2O) due to negative intrapleural pressure, physicians might appreciate the potential strain and barotrauma, even at an airway pressure of <30 cm H_2O [17,18].

In situations such as Case 3, a patient with missed triggers on a flow versus time waveform because of auto-PEEP, physicians sometimes miss the asynchrony. This may be due in part to the positive change in the expiratory flow versus time waveform, which is not sufficiently intuitive to be associated with patient inspiratory effort. A negative change in P_{eso} that does not trigger a ventilator breath might be more intuitive and easier to associate with missed triggers [16].

In situations such as Cases 4 and 5, where all visible parameters such as airway pressures and tidal volumes are within permissive ranges on sophisticated modes, physicians may feel that they lack a rationale for changing ventilation mode. However, if P_{eso} data are available, physicians may decide to change ventilation mode after visualizing patient exertion during breathing and high P_L , as in Case 4 [19]. Although the P_L was set high in Case 4, to highlight the importance of awareness of possible high P_L due to strong inspiratory effort with overinflated lungs and low chest wall compliance, the case was not designed as an argument against the general use of APRV. In Case 5, the prominent negative deflection of P_{eso} may have reminded physicians of the patient’s strong inspiratory effort with insufficient inspiratory support from the ventilator during PRVC mode, which frequently occurs in actual practice, particularly in acute settings [20].

This study has several limitations. First, because this is a before–after study, exposure to the same case twice may have influenced the participants’ understanding of the cases. Second, it is not possible to determine which component, education or information on P_{eso} and P_L or both, was more strongly associated with the results. Third, because the artificial lung had low compliance and low volume, the graphics provided to the participants were somewhat different from those seen in real practice. Finally, the study design might have encouraged “artificial” participant responses; however, participants were instructed to select responses that reflected what they would do in actual clinical practice.

5. Conclusions

This study showed that an improved understanding of, and patient information related to, P_{eso} and P_L had a significant impact on physicians’ decision-making regarding ventilator management in simulated cases with high intrapleural pressure and collapsed alveoli, high P_L with strong inspiratory effort, asynchrony with missed triggers, high P_L during APRV, and strong inspiratory effort during PRVC. Use of case scenario–based education with simulator devices for physicians may hasten worldwide understanding and clinical application of P_{eso} and P_L .

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.jcrc.2017.04.021>.

Authors’ contributions

All authors participated in the design of the study, data interpretation, and manuscript preparation. Y. N. is the principal investigator and was responsible for budget management, regulatory compliance, participant recruitment, data collection, and analyses, and manuscript preparation. L.A., T.N., J.K., S.U., J.T. and S.F. contributed to study coordination, data collection, entry, and analyses. All authors read and approved the manuscript.

Declaration of conflicting interests

All the authors declared no industry relationships in the past two years or no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not for profit sectors.

Acknowledgments

We thank Critical Care Patients Safety Network for renting the Series 1101 Electronic Breathing Simulator for the study and IMI Corporation for providing the Avea ventilator system and a conference room on the days of the study.

Appendix 1

Case 1

- 60 year-old male, height 165 cm, body weight 90 kg
- Admitted for acute pancreatitis
- Received multiple boluses of crystalloid solution for decreased urine output
- Intubated for worsening oxygenation and respiratory status
- Very distended abdomen
- Ventilator settings: AC-PC, P_i (above PEEP) 25 cm H_2O , f 20/min, PEEP 5 cm H_2O , FiO_2 1.0
- Measured parameters and graphics: SpO_2 88%, Respiratory rate 20/min, Ppeak 30 cm H_2O , Tidal volume 0.35 L, Minute ventilation 7.1 L/min

Case 2

- 72 year-old male, height 170 cm, body weight 63 kg
- Admitted for severe community-acquired pneumonia
- Intubated for worsening oxygenation and respiratory status
- Very strong inspiratory effort
- Ventilator settings: AC-PC, P_i (above PEEP) 5 cm H_2O , f 20/min, PEEP 15 cm H_2O , FiO_2 1.0
- Measured parameters and graphics: SpO_2 96%, Respiratory rate 25/min, Ppeak 20 cm H_2O , Tidal volume 750 mL, Minute ventilation 18.8 L/min

Case 3

- 80 year-old male, height 172 cm, body weight 80 kg
- Admitted and intubated for COPD exacerbation
- Prolonged expiratory phase on physical examination
- Ventilator settings: AC-PC, P_i (above PEEP) 12 cm H_2O , f 16/min, PEEP 5 cm H_2O , FiO_2 0.21
- Measured parameters and graphics: SpO_2 92%, Respiratory rate 16/min, Ppeak 18 cm H_2O , Tidal volume 501 mL, Minute ventilation 8.2 L/min

Case 4

- 67 year-old male height 174 cm, body weight 90 kg
- Admitted for septic shock due to intestinal perforation
- Intubated for possible aspiration and severe ARDS
- Started on APRV
- Ventilator settings: APRV, P_{high} 25 cm H_2O , P_{low} 0 cm H_2O , Time high 5.4 s, Time low 0.6 s, FiO_2 0.8, preserved spontaneous breathing

- Measured parameters and graphics: SpO₂ 92%, Respiratory rate 16/min, Ppeak 25 cm H₂O, Tidal volume 380 mL, Minute ventilation 8.2 L/min

Case 5

- 78 year-old male, height 165 cm, body weight 90 kg
- Admitted and intubated for aspiration pneumonia and ARDS
- Strong inspiratory effort
- Ventilator settings: PRVC, Tidal volume 420 mL, f 20/min, PEEP 12 cm H₂O, FiO₂ 0.6
- Measured parameters and graphics: SpO₂ 96%, Respiratory rate 24/min, Ppeak 16 cm H₂O, Tidal volume 410–420 mL, Minute ventilation 10 L/min

AC-PC: Assist control pressure control, Pi: Inspiratory pressure, PEEP: Positive end-expiratory pressure, APRV: Airway pressure release ventilation, PRVC: Pressure regulated volume control

Appendix 2

Questionnaire

Answer the following questions based on what you believe are the right decisions for patients in a real setting. Choose only one answer for each question. Return this questionnaire only if you agree to provide your answers as a part of data for our study.

Pre-questionnaire

Question 1.

What is your specialty?

- Critical care
- Anesthesiology
- Emergency medicine
- Internal medicine
- Surgery
- Resident physician postgraduate-year (PGY) <6

Question 2.

What is your PGY?

()

Question 3. (Case 1)

How would you change PEEP?

- Continue the same level of PEEP
- Increase PEEP
- Decrease PEEP
- Don't know

Question 4. (Case 2)

Would you use a neuromuscular blocker?

- Yes
- No
- Don't know

Question 5. (Case 3)

What asynchrony does this patient have?

- Auto-trigger
- Missed trigger
- Double trigger
- Premature termination of inspiratory support
- Late termination of inspiratory support
- Other (Describe:)
- Don't know

Question 6. (Case 4)

What intervention would you do?

- Observe without specific interventions
- Increase analgesics and/or sedatives
- Use neuromuscular blockade
- Discontinue APRV
- Other (Describe:)
- Don't know

Question 7. (Case 5)

What change would you make?

- No change and continue APRV
- Change to AC-PC
- Change to AC-VC
- Change to PSV (CPAP with PS)
- Change to other mode (Describe:)
- Don't know

Stop here.

Post-questionnaire

Question 1 (skip if you already answered in pre-questionnaire)

What is your specialty?

- Critical care
- Anesthesiology
- Emergency medicine
- Internal medicine
- Surgery
- Resident physician postgraduate-year (PGY) <6

Question 2 (skip if you already answered in pre-questionnaire)

What is your PGY?

()

Question 3. (Case 1)

How would you change PEEP?

- Continue the same level of PEEP
- Increase PEEP
- Decrease PEEP
- Don't know

Question 4. (Case 2)

Would you use a neuromuscular blocker?

- Yes
- No
- Don't know

Question 5. (Case 3)

What asynchrony does this patient have?

- Auto-trigger
- Missed trigger
- Double trigger
- Premature termination of inspiratory support
- Late termination of inspiratory support
- Other (Describe:)
- Don't know

Question 6. (Case 4)

What intervention would you do?

- Observe without specific interventions
- Increase analgesics and/or sedatives
- Use neuromuscular blockade

- Discontinue APRV
- Other (Describe:)
- Don't know

Question 7. (Case 5)

What change would you make?

- No change and continue APRV
- Change to AC-PC
- Change to AC-VC
- Change to PSV (CPAP with PS)
- Change to other mode (Describe:)
- Don't know

References

- [1] Gattinoni L, Carlesso E, Cadringer P, Valenza F, Vagginelli F, Chiumello D. Physical and biological triggers of ventilator-induced lung injury and its prevention. *Eur Respir J Suppl* 2003;47:15s–25s.
- [2] Protti A, Andreis DT, Monti M, Santini A, Sparacino CC, Langer T, et al. Lung stress and strain during mechanical ventilation: any difference between statics and dynamics? *Crit Care Med* 2013;41(4):1046–55.
- [3] Dornhorst AC, Leathart GL. A method of assessing the mechanical properties of lungs and air-passages. *Lancet* 1952;2(6725):109–11.
- [4] Cherniack RM, Farhi LE, Armstrong BW, Proctor DF. A comparison of esophageal and intrapleural pressure in man. *J Appl Physiol* 1955;8(2):203–11.
- [5] Akoumianaki E, Maggiore SM, Valenza F, Bellani G, Jubran A, Loring SH, et al. The application of esophageal pressure measurement in patients with respiratory failure. *Am J Respir Crit Care Med* 2014;189(5):520–31.
- [6] Argod J, Pepin JL, Smith RP, Levy P. Comparison of esophageal pressure with pulse transit time as a measure of respiratory effort for scoring obstructive nonapneic respiratory events. *Am J Respir Crit Care Med* 2000;162(1):87–93.
- [7] Bellani G, Pesenti A. Assessing effort and work of breathing. *Curr Opin Crit Care* 2014;20(3):352–8.
- [8] Talmor D, Sarge T, Malhotra A, O'Donnell CR, Ritz R, Lisbon A, et al. Mechanical ventilation guided by esophageal pressure in acute lung injury. *N Engl J Med* 2008;359(20):2095–104.
- [9] Talmor D, Sarge T, O'Donnell CR, Ritz R, Malhotra A, Lisbon A, et al. Esophageal and transpulmonary pressures in acute respiratory failure. *Crit Care Med* 2006;34(5):1389–94.
- [10] Loring SH, Pecchiari M, Della Valle P, Monaco A, Gentile G, D'Angelo E. Maintaining end-expiratory transpulmonary pressure prevents worsening of ventilator-induced lung injury caused by chest wall constriction in surfactant-depleted rats. *Crit Care Med* 2010;38(12):2358–64.
- [11] Pecchiari M, Loring SH, D'Angelo E. Esophageal pressure as an estimate of average pleural pressure with lung or chest distortion in rats. *Respir Physiol Neurobiol* 2013;186(2):229–35.
- [12] Mauri T, Yoshida T, Bellani G, Goligher EC, Carreaux G, Rittayamai N, et al. Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives. *Intensive Care Med* 2016.
- [13] Kubiak BD, Gatto LA, Jimenez EJ, Silva-Parra H, Snyder KP, Vieau CJ, et al. Plateau and transpulmonary pressure with elevated intra-abdominal pressure or atelectasis. *J Surg Res* 2010;159(1):e17–24.
- [14] Brochard L. Measurement of esophageal pressure at bedside: pros and cons. *Curr Opin Crit Care* 2014;20(1):39–46.
- [15] Grasso S, Terragni P, Birocco A, Urbino R, Del Sorbo L, Filippini C, et al. ECMO criteria for influenza A (H1N1)-associated ARDS: role of transpulmonary pressure. *Intensive Care Med* 2012;38(3):395–403.
- [16] Younes M, Brochard L, Grasso S, Kun J, Mancebo J, Ranieri M, et al. A method for monitoring and improving patient: ventilator interaction. *Intensive Care Med* 2007;33(8):1337–46.
- [17] Yoshida T, Uchiyama A, Matsuura N, Mashimo T, Fujino Y. Spontaneous breathing during lung-protective ventilation in an experimental acute lung injury model: high transpulmonary pressure associated with strong spontaneous breathing effort may worsen lung injury. *Crit Care Med* 2012;40(5):1578–85.
- [18] Yoshida T, Uchiyama A, Matsuura N, Mashimo T, Fujino Y. The comparison of spontaneous breathing and muscle paralysis in two different severities of experimental lung injury. *Crit Care Med* 2013;41(2):536–45.
- [19] Mireles-Cabodevila E, Kacmarek RM. Should airway pressure release ventilation be the primary mode in ARDS? *Respir Care* 2016;61(6):761–73.
- [20] Mireles-Cabodevila E, Chatburn RL. Work of breathing in adaptive pressure control continuous mandatory ventilation. *Respir Care* 2009;54(11):1467–72.