Clinical Critical Care

E-ISSN 2774-0048

VOLUME 31 NUMBER 1
JANUARY-DECEMBER 2023

Clinical Critical Care
Volume 31, Article ID e230018, 6 pages
https://doi.org/10.54205/ccc.v31.264920
REVIEW
eISSN 2774-0048

Geo–economic variations in care for invasively ventilated patients: The potential benefits of closed–loop ventilation in resource–limited settings

Marcus J. Schultz[1,2,3,4], Kaouther Saihi[5], Rajyabardhan Pattnaik[6], Gentle S. Shrestha[7], Laura A. Buiteman–Kruizinga[1,8]

[1]Department of Intensive Care, Amsterdam University Medical Centers, location 'AMC', Amsterdam, the Netherlands, [2]Mahidol–Oxford Tropical Medicine Research Unit (MORU), Mahidol University, Bangkok, Thailand, [3]Nuffield Department of Medicine, University of Oxford, Oxford, UK, [4]Department of Research and New Technologies, Hamilton Medical AG, Bonaduz, Switzerland, [5]Product Management Respiratory Care Devices, Hamilton Medical AG, Bonaduz, Switzerland, [6]Department of Intensive Care Medicine, Ispat General Hospital, Rourkela, Sundargarh, Odisha, India, [7]Department of Critical Care Medicine, Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu, Nepal, [8]Department of Intensive Care, Reinier de Graaf Hospital, Delft, the Netherlands

OPEN ACCESS
Citation:
Schultz MJ, Saihi K, Pattnaik R, Shrestha GS, Buiteman–Kruizinga LA. Geo–economic variations in care for invasively ventilated patients: The potential benefits of closed–loop ventilation in resource–limited settings. Clin Crit Care 2023; 31: e230018.

Received: August 26, 2023
Revised: October 11, 2023
Accepted: October 16, 2023

Copyright:
© 2021 The Thai Society of Critical Care Medicine. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement:
The data and code were available upon reasonable request (Marcus J Schultz, email address: marcus.j.schultz@gmail.com)

Funding:
No funding support.

Competing interests:
Marcus J. Schulz and Kaouther Saihi worked at Hamilton Medical AG, Bonaduz, Switzerland till early 2023.

Corresponding author:
Marcus J Schultz
Department of Intensive Care, Amsterdam University Medical Centers, location 'AMC', Amsterdam, the Netherlands.
E-mail: marcus.j.schultz@gmail.com

ABSTRACT:

Lung–protective ventilation for invasively ventilated patients mimics normal breathing in which a low tidal volume is delivered at a specific respiratory rate with a limited inspiratory pressure on top of a sufficient level of positive end–expiratory pressure. It has been thoroughly demonstrated that despite being an expensive procedure, invasive ventilation when applied in a lung-protective way has a strong potential to improve the outcome of critically ill patients. However, implementing lung–protective ventilation has several challenges, including the fact that it can be quite time–consuming. One way to facilitate the use of lung–protective ventilation is to automate the settings involved with this strategy with closed–loop ventilation. In this review, we compare the epidemiology, ventilator management, and outcomes in critically ill ICU patients between middle–income countries and high–income countries and focus on the potentials and risks of closed–loop ventilation in middle–income countries.

Keywords: ICU; Critical care; Ventilation; Geo-economic variation; Closed-loop; Automated ventilation

INTRODUCTION

Invasive ventilation is one of the cornerstones of respiratory support for critically ill patients. Half a century ago, the initial targets of invasive ventilation were to provide sufficient alveolar ventilation and maintain lung recruitment [1]. Some 25 years ago, it became clear that lung protection was just as important, if not more so [2]. With this knowledge, national and international guidelines started to advocate lung protection, and lung–protective ventilation became the norm in intensive care units (ICU) worldwide [3]. Approximately 10 years later, closed–loop ventilation was introduced [4]. With closed–loop ventilation, a group of algorithms implemented within the ventilator titrate automatically key ventilator settings that otherwise need to be set and adjusted manually by the healthcare professional. Evidence for the benefits of closed–loop ventilation has steadily grown in recent years [4].

Invasive ventilation faces several difficulties when resources are scarce [5, 6]. The costs of invasive ventilation are substantial in low– and middle–income countries (LMIC) [7], probably because of the relative high costs for the healthcare professionals needed to apply this intervention. Due to shortages of trained healthcare professionals, respiratory monitoring is often severely limited in ICUs with restricted resources [8]. Closed–loop ventilation could be helpful here as it ensures the use of optimal ventilator settings and reduces the workloads of the frequently overloaded healthcare professionals in LMIC.

In this review, following a succinct description of ventilator settings that are key in lung protection and an overview of currently available closed–loop ventilation modes for use in critically ill patients, we compare the epidemiology, ventilator management, and outcomes in critically ill ICU patients in middle–income countries (MIC) with high–income countries (HIC). We will end this review with a discussion of what we now need to know about the potential and risks of closed–loop ventilation in resource–limited settings.

KEY MESSAGES:

- Lung–protective ventilation has a strong potential to improve the outcome of critically ill patients but comes with challenges.
- There are some, but only minor differences in the epidemiology and ventilator management between MIC and HIC.
- Automated or closed–loop ventilation has the potential to improve the use of lung–protective ventilation and maybe even the workload associated with it.

KEY ELEMENTS OF LUNG–PROTECTIVE VENTILATION

The most important and easy element to apply for lung–protective ventilation is low tidal volume (VT) that is sized to the predicted body weight (PBW), i.e., < 8 ml/kg PBW, with a low inspiratory pressure (Pinsp), i.e., < 30 cm H_2O. Use of a low VT with a low Pinsp has repeatedly been shown to reduce mortality in patients with various forms of acute respiratory distress syndrome [9, 10]. In patients without ARDS, research showed that a somewhat higher VT, i.e., up to 10 ml/kg PBW, can also be accepted in patients with uninjured lungs [11], probably because these patients can breathe spontaneously more often and therefore may have a larger lung volume. One limitation of the use of low VT is the risk of arterial hypercapnia, which needs to be compensated with a sufficient rise in the respiratory rate (RR).

Another approach to protecting the lungs of critically ill patients is the use of low fractions of inspired oxygen (FiO_2), to reduce the direct harmful effects of oxygen on pulmonary tissue [12]. With this approach, arterial hyperoxemia is prevented by restricted FiO_2 levels, but one caveat of this approach is the risk of acute or unrecognized arterial hypoxemia.

Invasive ventilation that results in a low driving pressure (ΔP) may also prevent lung injury, improving the outcome of invasively ventilated critically ill patients [13-15]. Direct evidence for the benefit of a strategy that targets a low ΔP, however, remains scarce. Besides, targeting a low ΔP can be challenging––a higher PEEP strategy, with or without recruitment maneuvers, may decrease ΔP if it increases the size of the functional lung, but this approach may increase ΔP if it does not recruit collapsed lung units or instead causes pulmonary overdistention. This could be one of the reasons for the neutral [16-18] and at times, even conflicting findings [19, 20] in studies and meta–analyses [21, 22] of PEEP and recruitment maneuvers in critically ill patients. Probably, a personalized approach is better [23, 24]. While it is generally agreed that the use of a higher PEEP strategy, i.e., with PEEP > 10 cm H_2O, benefits patients with ARDS [3, 25], there is evidence against using a higher PEEP strategy in patients with uninjured lungs [26]. Evidence for the benefit of recruitment maneuvers in patients without ARDS is completely lacking.

The mechanical power of ventilation (MP) is receiving increasing attention as there is a clear and independent association between MP and outcomein patients with ARDS and in patients without ARDS [14, 15, 27]. Mechanical ventilation is associated with substantial dissipation of energy, probably resulting in 'heat' or inflammation, potentially leading to injury to lung tissue [14]. MP incorporates VT, Pinsp and ΔP, inspiratory flow, and RR, and reflects the energy transferred to the respiratory system per minute. There are several equations in use for calculating MP, the most frequently used is:

$$MP\ (J/Min) = 0.098 * VT\ [L] * RR * (Ppeak\ [cm\ H_2O] - 0.5 * \Delta P\ [cm\ H_2O])$$

Targeting a low MP is by far the most challenging and complicated aspect of lung–protective ventilation. MP involves a complicated calculation. It is also unclear which of these factors should be given priority. The most challenging aspect is undoubtedly that altering one parameter may necessitate altering another, and these adjustments may actually have opposing impacts on MP. For instance, reducing VT to lower the MP may trigger the use of a higher RR, yet doing so may actually raise the MP.

The ever-changing pulmonary condition makes it even more difficult to maintain all the above settings within safe ranges.

CLOSED–LOOP VENTILATION

With closed–loop ventilation, software algorithms within the ventilator are able to adjust certain ventilator settings that otherwise need to be chosen and adjusted by the bedside clinician. There are several examples of commercially available closed–loop ventilation modes, with similarities and differences between them (see Figure 1) [4].

'Proportional Assist Ventilation+' (PAV+)™, available at ventilators of Puritan Bennett™ (Puritan Bennett, Minneapolis, USA), and 'Neurally Adjusted Ventilatory Assist' (NAVA)™, available at ventilators of Maquet™ (Getinge, Goteborg, Sweden), have in common that they

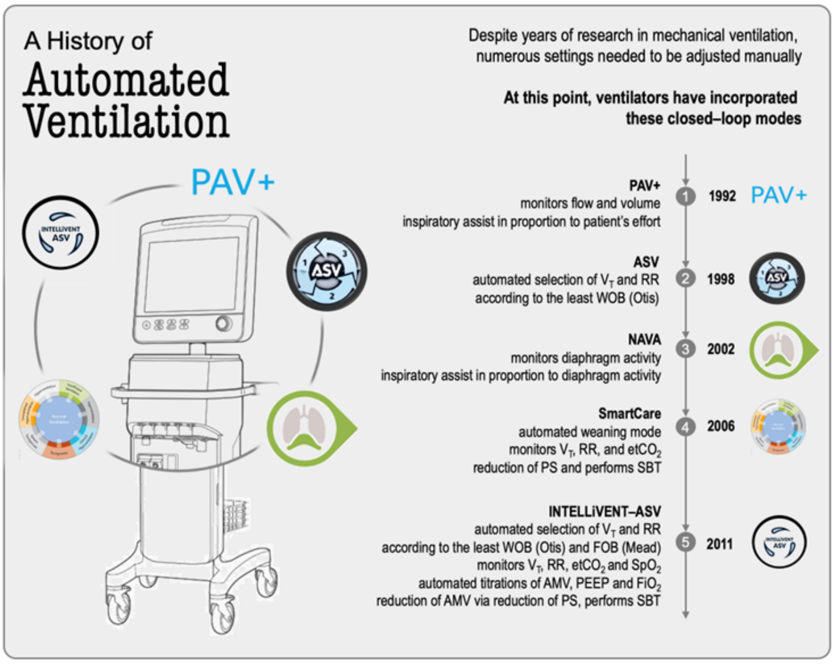

Figure 1. A timeline of close–loop ventilation, with a description of each ventilation modes that are currently available: proportional Assist Ventilation with load–adjustable gain factors, SmartCare, Neurally Adjusted Ventilatory Assist ventilation (NAVA), and Adaptive Support Ventilation (ASV) and its successor INTELLiVENT–ASV (Adapted and modified from Buiteman-Kruizinga et al [4]). Abbreviations: VT: tidal volume; RR: respiratory rate; $etCO_2$: end-tidal carbon dioxide; PS: pressure support; SBT: spontaneous breathing trial; WOB: Work of Breathing; FOB: Force of Breathing; SpO_2: pulse oximetry; FiO_2: fraction of inspired oxygen.

deliver proportional assistance and measure patient efforts. SmartCare™, available at ventilators of Dräger™ (Dräger, Lübeck, Germany), and 'Adaptive Support Ventilation' (ASV)™ and its successor 'INTELLiVENT–ASV'™, available at ventilators of Hamilton Medical™ (Hamilton Medical AG, Bonaduz, Switzerland), have in common that they integrate algorithms to target alveolar ventilation and oxygenation goals considering changes in lung mechanics.

Evidence for the benefits of closed–loop ventilation is steadily growing. First, they may improve safety by preventing unwanted deteriorations in gas exchange, i.e., severe hypoxemia or dyscapnia. Second, they can increase the effectiveness by setting and titrating settings so that lung–protection is guaranteed, at least according to current insights. Third, they may increase efficacy by facilitating the weaning process, which may translate to earlier liberation from the ventilator and maybe even better survival.

PAV+™ has been found to decrease ΔP, by decreasing VT when the functional lung size decreases and by increasing VT only when the functional lung size increases [28]. SmartCare™ and PAV+™ have been found to decrease the duration of weaning [29, 30], and to shorten the duration of ventilation and stay in the ICU [30], and NAVA™ may even increase survival [30]. INTELLiVENT–ASV™ has been found to be safe and effective with regards to the titration of VT and Pinsp [31], FiO_2 [32], and ΔP and MP [33]. INTELLiVENT–ASV™ provides ventilation with more time spent in desired clinical target zones and with lower ΔP and less MP in various patient categories [34-36].

GEO–ECONOMIC VARIATIONS IN CARE FOR INVASIVELY VENTILATED PATIENTS

Two recently reported studies may help understand if the epidemiology, ventilator management, and outcome of invasively ventilated critically ill patients are different in middle–income countries (MIC) when compared with high–income countries (HIC) [37, 38].

The 'Large observational study to understand the global impact of severe acute respiratory failure' (LUNG–SAFE) was a worldwide multicenter, prospective cohort study focusing on ventilator management in ARDS patients [3]. The enrollment window for LUNG–SAFE included four consecutive winter weeks, chosen by each participating ICU, during February–March 2014 in the Northern Hemisphere and June–August 2014 in the Southern Hemisphere. The LUNG–SAFE investigators recruited 2813 patients with ARDS in 459 ICUs worldwide, with 546 patients from 120 MIC and 2267 patients from 339 HIC [38]. The PRoVENT–iMiC study was an international, multicenter prospective cohort study in Asia, focusing on ventilator management in critically ill patients without ARDS [39]. Like LUNG–SAFE, the enrollment window of the PRoVENT–iMiC study included four weeks, chosen by each country investigator, in November 2017–December 2018. The PRoVENT–iMiC study investigators managed to recruit a sample of 1315 patients in 54 ICUs in Asia [40]. The individual patient data of patients without ARDS in the PRoVENT–iMiC study were merged with data from patients without ARDS in LUNG–SAFE and two other prospective cohort studies [41, 42]. The merged sample included 3852 patients without ARDS, 2345 in 27 LMICs and ,1507 in 27 HICs [37].

Epidemiology

Compared to HIC, patients in MIC were younger and had a lower body mass [37, 38]. ARDS patients in MIC were less likely to have a pre–existing comorbidity like diabetes mellitus, chronic kidney failure, or liver disease, and more likely to have heart failure than patients in HIC [38]. Patients without ARDS in the MIC more often had diabetes mellitus or active cancer and less often had chronic obstructive pulmonary disease or heart failure than patients in the HIC [37].

The primary risk factor for ARDS was pneumonia, which did not differ between ARDS patients and patients without ARDS nor between MIC and HIC [37, 38]. Compared to HIC, extrapulmonary sepsis was more common in patients in MIC [37, 38]. In patients with ARDS, there were noticeable differences between MIC and HIC in the frequency of pancreatitis, inhalation injury, and trauma [38]. Patients without ARDS were more often admitted for pneumonia and less often for gastric aspiration or pulmonary contusion [37].

According to Sequential Organ Failure Assessment (SOFA) scores, patients with ARDS in MIC were slightly sicker than patients with ARDS in HIC. In patients without ARDS, SOFA scores at admission were not different between MIC and HIC.

Ventilator management

The proportion of ARDS patients receiving ventilation with a low VT and a low Pinsp was not different in MIC compared to HIC [38]. Ventilation with a low FiO_2 was more common in HIC than in MIC, and PEEP was more often low and less often high in MIC than in HIC. The use of recruitment maneuvers was lower in HIC than in MIC. A low ΔP occurred more often in MIC than in HIC. MP was not reported in this study.

The proportion of patients without ARDS receiving lung–protective ventilation with a low VT was comparable between MIC and HIC [37]. VT expressed in ml/kg actual bodyweight and PBW was also not different between patients in MIC and HIC, but the applied absolute median VT used in MIC was lower. The fraction of inspired oxygen, Pinsp, and ΔP were not different in MIC from HIC. PEEP was higher in HIC, but the difference was minimal. In this study also, MP was not reported.

Outcomes

Adjusted rate ratios for duration of invasive ventilation and length of ICU stay in ARDS patients were significantly higher in HIC, and adjusted odds ratios for ICU and hospital death were significantly lower in HIC. These differences, however, were not dependent on geo–economic variations in ventilation. Mortality was independently associated with gross domestic product.

ICU mortality was approximately 1.5 times higher in patients without ARDS from MIC than from HIC [37]. The higher probability of death in patients with MIC was particularly pronounced in patients with lower SOFA scores. Crude ICU mortality was inversely associated with gross domestic product per capita.

Interpretation

From these two conveniently sized studies, it can be concluded that there are some, but only minor, case–mix differences between MIC and HIC. This at least suggests that ventilation strategies in MIC should not necessarily differ from those in HIC. And indeed, there are some, but again, only minor differences in ventilator management, mainly in patients with ARDS. Outcomes, however, are different: critically ill patients in HIC have better chances of liberation from the ventilator and eventually survival.

LUNG–SAFE, as well as the other meta–analyzed studies of ventilation in critically ill patients, may have suffered from observation bias and reporting biases. It is important to note that the investigators had no access to the patient data. The findings could also be biased when resource–rich ICUs might have been overrepresented. Large public hospitals, known for their large patient loads in relation to available healthcare professionals and potential worse adherence to guidelines, were underrepresented. Last but not least, these studies did include only one low–income country, probably underscoring the resource–dense nature of critical care.

Nevertheless, the differences in outcome between MIC and HIC are large and could reflect a situation where scarce healthcare professionals are having difficulties in adhering to other guidelines. If this is true, one approach could be to reduce workload associated with invasive ventilation, so that there is more time to improve other patient care.

FUTURE RESEARCH IN CLOSED–LOOP VENTILATION

As outlined above, certain parts of lung–protective ventilation are complex and time–consuming. In an area with shortages of healthcare professionals, as in resource–limited settings, there is a great need for automation. This need may even increase. In HIC, there are clear signs that demand, i.e., numbers of critically ill patients, will continue to grow, while supply, i.e., healthcare professionals, will remain near constant, resulting in deficits of ICU nurses and doctors at the bedside [43, 44]. The recent pandemic taught us that ICU systems can easily become disrupted, perhaps most of all because of the already scarcely available ICU nurses.

Benefits of closed–loop ventilation not only include its safety, effectiveness, and efficacy. It can be speculated that the introduction of closed–loop ventilation in LMIC could also reduce workloads. We are highly uncertain, however, how to measure workload. The use of closed–loop ventilation may be associated with a reduction in the number of interactions between healthcare professionals and ventilators [45], but this does not necessarily mean it reduces workloads.

Unfortunately, most if not all studies of automated ventilation do not well report the adverse events that may come with the use of closed–loop ventilation modes. Adverse events, though, may occur, especially outside of a research environment. Examples of risks include unwanted deteriorations in gas exchanges if alarms are improperly set, and also unwanted, and even unsafe, (automated) ventilator settings if the limits for the software are set too wide.

One associated caveat is that the introduction of closed–loop ventilation itself will initially increase the workload. Indeed, automated ventilation requires a change in the role of caregivers, keeping in mind that with these modes, deteriorations in gas exchange may also happen, and that limits need to be set properly. Also, alarm settings can be set wrong, i.e., too loose or too tight. Regarding the last, with closed–loop ventilation, there could be an increase in the number of alarms, thereby increasing workloads. Thus, apart from investments in education and training, in the beginning it could be more time–consuming to work with a closed–loop system.

More work needs to be done. While studies thus far show that closed–loop ventilation systems are effective in invasively ventilated patients, it must be realized that evidence via randomized clinical trials is mainly present in 'simple to ventilate' patients, like those receiving postoperative ventilation after cardiac surgery. More studies are needed, and we ourselves are performing a study named 'Effects of Automated Closed-loop VenTilation versus Conventional Ventilation on Duration and Quality of Ventilation' (ACTiVE), an international, multicenter, two–group randomized clinical superiority trial in 1200 patients with an anticipated duration of ventilation of > 24 hours (clinicaltrials.gov NCT04593810).

CONCLUSION

Closed–loop ventilation is finding its way into the ICU arena. Closed–loop ventilation is safe, and it has a great potential to improve lung protection in critically ill patients. In the context of the shortages of healthcare professionals in resource–limited settings, research on closed–loop ventilation should now also focus on workloads. Research also needs to evaluate its feasibility and effectiveness in these settings. If closed–loop ventilation reduces the workload associated with safe and lung–protective invasive ventilation, it creates a chance for improvements in other parts of care, thereby hopefully improving the outcome of patients in settings with scarce resources.

REFERENCES

1. MacIntyre N, Rackley C, Khusid F. Fifty Years of Mechanical Ventilation-1970s to 2020. Crit Care Med. 2021;49(4):558-74.
2. Slutsky AS, Ranieri VM. Ventilator-Induced Lung Injury. New England Journal of Medicine. 2013;369(22):2126-36.
3. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. Jama. 2016;315(8):788-800.
4. Buiteman-Kruizinga LA, Serpa Neto A, Schultz MJ. Automation to improve lung protection. Intensive Care Med. 2022;48(7):943-6.
5. Serpa Neto A, Checkley W, Sivakorn C, Hashmi M, Papali A, Schultz MJ. Pragmatic Recommendations for the Management of Acute Respiratory Failure and Mechanical Ventilation in Patients with COVID-19 in Low- and Middle-Income Countries. Am J Trop Med Hyg. 2021;104(3_Suppl):60-71.
6. Serpa Neto A, Schultz MJ, Festic E. Ventilatory support of patients with sepsis or septic shock in resource-limited settings. Intensive Care Med. 2016;42(1):100-3.
7. Hung TM, Van Hao N, Yen LM, McBride A, Dat VQ, van Doorn HR, et al. Direct Medical Costs of Tetanus, Dengue, and Sepsis Patients in an Intensive Care Unit in Vietnam. Front Public Health. 2022;10:893200.
8. Schultz MJ, Dunser MW, Dondorp AM, Adhikari NK, Iyer S, Kwizera A, et al. Current challenges in the management of sepsis in ICUs in resource-poor settings and suggestions for the future. Intensive Care Med. 2017;43(5):612-24.
9. Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342(18):1301-8.
10. Botta M, Tsonas AM, Pillay J, Boers LS, Algera AG, Bos LDJ, et al. Ventilation management and clinical outcomes in invasively ventilated patients with COVID-19 (PRoVENT-COVID): a national, multicentre, observational cohort study. Lancet Respir Med. 2021;9(2):139-48.
11. Simonis FD, Serpa Neto A, Binnekade JM, Braber A, Bruin KCM, Determann RM, et al. Effect of a Low vs Intermediate Tidal Volume Strategy on Ventilator-Free Days in Intensive Care Unit Patients Without ARDS: A Randomized Clinical Trial. Jama. 2018;320(18):1872-80.
12. Helmerhorst HJ, Schultz MJ, van der Voort PH, de Jonge E, van Westerloo DJ. Bench-to-bedside review: the effects of hyperoxia during critical illness. Crit Care. 2015;19(1):284.
13. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med. 2015;372(8):747-55.
14. Serpa Neto A, Deliberato RO, Johnson AEW, Bos LD, Amorim P, Pereira SM, et al. Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts. Intensive Care Med. 2018;44(11):1914-22.
15. van Meenen DMP, Algera, AGA, Schuijt, MTU, Simonis, FD, van der Hoeven, SM, Serpa Neto, A, Gama de Abreu, M, Pelosi, P, Paulus, F, Schultz, MJ. Effect of Mechanical Power on Mortality in Invasively Ventilated ICU patients without ARDS––An Individual Patient Data–analysis of Three Randomized Clinical Trials. European Journal of Anesthesiology. 2022; in press.
16. Brower RG, Lanken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med. 2004;351(4):327-36.
17. Meade MO, Cook DJ, Guyatt GH, Slutsky AS, Arabi YM, Cooper DJ, et al. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. Jama. 2008;299(6):637-45.
18. Mercat A, Richard JC, Vielle B, Jaber S, Osman D, Diehl JL, et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. Jama. 2008;299(6):646-55.
19. Cavalcanti AB, Suzumura É A, Laranjeira LN, Paisani DM, Damiani LP, Guimarães HP, et al. Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. Jama. 2017;318(14):1335-45.
20. Briel M, Meade M, Mercat A, Brower RG, Talmor D, Walter SD, et al. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. Jama. 2010;303(9):865-73.
21. Ball L, Serpa Neto A, Trifiletti V, Mandelli M, Firpo I, Robba C, et al. Effects of higher PEEP and recruitment manoeuvres on mortality in patients with ARDS: a systematic review, meta-analysis, meta-regression and trial sequential analysis of randomized controlled trials. Intensive Care Med Exp. 2020;8(Suppl 1):39.
22. Dianti J, Tisminetzky M, Ferreyro BL, Englesakis M, Del Sorbo L, Sud S, et al. Association of Positive End-Expiratory Pressure and Lung Recruitment Selection Strategies with Mortality in Acute Respiratory Distress Syndrome: A Systematic Review and Network Meta-analysis. Am J Respir Crit Care Med. 2022;205(11):1300-10.
23. Constantin JM, Jabaudon M, Lefrant JY, Jaber S, Quenot JP, Langeron O, et al. Personalised mechanical ventilation tailored to lung morphology versus low positive end-expiratory pressure for patients with acute respiratory distress syndrome in France (the LIVE study): a multicentre, single-blind, randomised controlled trial. Lancet Respir Med. 2019;7(10):870-80.
24. Pelosi P, Ball L, Barbas CSV, Bellomo R, Burns KEA, Einav S, et al. Personalized mechanical ventilation in acute respiratory distress syndrome. Crit Care. 2021;25(1):250.
25. Laffey JG, Bellani G, Pham T, Fan E, Madotto F, Bajwa EK, et al. Potentially modifiable factors contributing to outcome from acute respi-

ratory distress syndrome: the LUNG SAFE study. Intensive Care Med. 2016;42(12):1865-76.

26. Algera AG, Pisani L, Serpa Neto A, den Boer SS, Bosch FFH, Bruin K, et al. Effect of a Lower vs Higher Positive End-Expiratory Pressure Strategy on Ventilator-Free Days in ICU Patients Without ARDS: A Randomized Clinical Trial. Jama. 2020;324(24):2509-20.
27. Urner M, Jüni P, Hansen B, Wettstein MS, Ferguson ND, Fan E. Time-varying intensity of mechanical ventilation and mortality in patients with acute respiratory failure: a registry-based, prospective cohort study. Lancet Respir Med. 2020;8(9):905-13.
28. Georgopoulos D, Xirouchaki N, Tzanakis N, Younes M. Data on respiratory variables in critically ill patients with acute respiratory failure placed on proportional assist ventilation with load adjustable gain factors (PAV+). Data Brief. 2016;8:484-93.
29. Burns KE, Lellouche F, Nisenbaum R, Lessard MR, Friedrich JO. Automated weaning and SBT systems versus non-automated weaning strategies for weaning time in invasively ventilated critically ill adults. Cochrane Database Syst Rev. 2014;2014(9):Cd008638.
30. Kampolis CF, Mermiri M, Mavrovounis G, Koutsoukou A, Loukeri AA, Pantazopoulos I. Comparison of advanced closed-loop ventilation modes with pressure support ventilation for weaning from mechanical ventilation in adults: A systematic review and meta-analysis. J Crit Care. 2021;68:1-9.
31. Botta M, Tsonas AM, Sinnige JS, De Bie AJR, Bindels A, Ball L, et al. Effect of Automated Closed-loop ventilation versus convenTional VEntilation on duration and quality of ventilation in critically ill patients (ACTiVE) - study protocol of a randomized clinical trial. Trials. 2022;23(1):348.
32. Lellouche F, Bouchard PA, Simard S, L'Her E, Wysocki M. Evaluation of fully automated ventilation: a randomized controlled study in post-cardiac surgery patients. Intensive Care Med. 2013;39(3):463-71.
33. Arnal JM, Saoli M, Garnero A. Airway and transpulmonary driving pressures and mechanical powers selected by INTELLiVENT-ASV in passive, mechanically ventilated ICU patients. Heart Lung. 2020;49(4):427-34.
34. De Bie AJR, Neto AS, van Meenen DM, Bouwman AR, Roos AN, Lameijer JR, et al. Fully automated postoperative ventilation in cardiac surgery patients: a randomised clinical trial. Br J Anaesth. 2020;125(5):739-49.
35. Wendel Garcia PD, Hofmaenner DA, Brugger SD, Acevedo CT, Bartussek J, Camen G, et al. Closed-Loop Versus Conventional Mechanical Ventilation in COVID-19 ARDS. J Intensive Care Med. 2021;36(10):1184-93.
36. Buiteman-Kruizinga LA, Mkadmi HE, Serpa Neto A, Kruizinga MD, Botta M, Schultz MJ, et al. Effect of INTELLiVENT-ASV versus Conventional Ventilation on Ventilation Intensity in Patients with COVID-19 ARDS-An Observational Study. J Clin Med. 2021;10(22).
37. Pisani L, Algera AG, Neto AS, Azevedo L, Pham T, Paulus F, et al. Geoeconomic variations in epidemiology, ventilation management, and outcomes in invasively ventilated intensive care unit patients without acute respiratory distress syndrome: a pooled analysis of four observational studies. Lancet Glob Health. 2022;10(2):e227-e35.
38. Laffey JG, Madotto F, Bellani G, Pham T, Fan E, Brochard L, et al. Geo-economic variations in epidemiology, patterns of care, and outcomes in patients with acute respiratory distress syndrome: insights from the LUNG SAFE prospective cohort study. Lancet Respir Med. 2017;5(8):627-38.
39. Pisani L, Algera AG, Serpa Neto A, Ahsan A, Beane A, Chittawatanarat K, et al. PRactice of VENTilation in Middle-Income Countries (PRoVENT-iMIC): rationale and protocol for a prospective international multicentre observational study in intensive care units in Asia. BMJ Open. 2018;8(4):e020841.
40. Pisani L, Algera AG, Serpa Neto A, Ahsan A, Beane A, Chittawatanarat K, et al. Epidemiological Characteristics, Ventilator Management, and Clinical Outcome in Patients Receiving Invasive Ventilation in Intensive Care Units from 10 Asian Middle-Income Countries (PRoVENT-iMiC): An International, Multicenter, Prospective Study. Am J Trop Med Hyg. 2021;104(3):1022-33.
41. Azevedo LC, Park M, Salluh JI, Rea-Neto A, Souza-Dantas VC, Varaschin P, et al. Clinical outcomes of patients requiring ventilatory support in Brazilian intensive care units: a multicenter, prospective, cohort study. Crit Care. 2013;17(2):R63.
42. Neto AS, Barbas CSV, Simonis FD, Artigas-Raventós A, Canet J, Determann RM, et al. Epidemiological characteristics, practice of ventilation, and clinical outcome in patients at risk of acute respiratory distress syndrome in intensive care units from 16 countries (PRoVENT): an international, multicentre, prospective study. Lancet Respir Med. 2016;4(11):882-93.
43. British Medical Association. Medical staffing in England: a defining moment for doctors and patients. London; 2021.
44. Angus DC, Kelley MA, Schmitz RJ, White A, Popovich J, Jr. Caring for the critically ill patient. Current and projected workforce requirements for care of the critically ill and patients with pulmonary disease: can we meet the requirements of an aging population? Jama. 2000;284(21):2762-70.
45. Bialais E, Wittebole X, Vignaux L, Roeseler J, Wysocki M, Meyer J, et al. Closed-loop ventilation mode (IntelliVent®-ASV) in intensive care unit: a randomized trial. Minerva Anestesiol. 2016;82(6):657-68.

To submit the next your paper with us at:

https://he02.tci-thaijo.org/index.php/ccc/about/submissions