information and provide clinicians with more meaningful and actionable information, less artifact, and fewer false alarms. Machine learning algorithms, for example, have been used with success to distinguish real events from artifact in online multisignal vital sign monitoring data streams.[12] They may also better predict clinical deterioration than current Early Warning Score systems.[9]

Conclusions

Avoidable deaths on hospital wards remain all too common. Many should be prevented by continuous vital sign monitoring. Wireless and wearable sensors can help as patients poorly tolerate tethered monitors.[13] Although many technical solutions already exist to monitor vital signs wirelessly, validation studies remain scarce. Major trials are needed to determine whether wireless and wearable sensors accurately monitor vital signs, avoid excessive false alarms, detect clinical deterioration sufficiently early to allow effective intervention, and reduce serious adverse outcomes.

Authors' contributions

Writing/revising editorial: both authors.

Declaration of interest

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References

1. Pearse RM, Moreno RP, Bauer P, et al. Mortality after surgery in Europe: a 7 day cohort study. *Lancet* 2012; **380**: 1059–65
2. Nolan JP, Soar J, Smith GB, et al. Incidence and outcome of in-hospital cardiac arrest in the United Kingdom national cardiac arrest audit. *Resuscitation* 2014; **85**: 987–92
3. Sun Z, Sessler DI, Dalton JE, et al. Postoperative hypoxemia is common and persistent: a prospective blinded observational study. *Anesth Analg* 2015; **121**: 709–15
4. Sessler DI, Meyhoff CS, Zimmerman NM, et al. Period-dependent associations between hypotension during and for 4 days after noncardiac surgery and a composite of myocardial infarction and death: a substudy of the POISE-2 trial. *Anesthesiology* 2018; **128**: 317–27
5. Taenzer AH, Pyke JB, McGrath SP, et al. Impact of pulse oximetry surveillance on rescue events and intensive care unit transfers: a before-and-after concurrence study. *Anesthesiology* 2010; **112**: 282–7
6. Brown H, Terrence J, Vasquez P, et al. Continuous monitoring in an inpatient medical–surgical unit: a controlled clinical trial. *Am J Med* 2014; **127**: 226–32
7. Subbe CP, Duller B, Bellomo R. Effect of an automated notification system for deteriorating ward patients on clinical outcomes. *Crit Care* 2017; **21**: 52
8. Barrett PM, Komatireddy R, Haaser S, et al. Comparison of 24-hour Holter monitoring with 14-day novel adhesive patch electrocardiographic monitoring. *Am J Med* 2014; **127**. 95.e11–7
9. Churpek MM, Yuen TC, Winslow C, et al. Multicenter comparison of machine learning methods and conventional regression for predicting clinical deterioration on the wards. *Crit Care Med* 2016; **44**: 368–74
10. Pei L, Huang Y, Mao G, Sessler DI. Axillary temperature, as recorded by the iThermonitor WT701, well represents core temperature in adults having noncardiac surgery. *Anesth Analg* 2018; **126**: 833–8
11. Michard F, Sessler DI, Saugel B. Non-invasive arterial pressure monitoring revisited. *Intensive Care Med* 2018. https://doi.org/10.1007/s00134-018-5108-x. Access Published March 7
12. Chen L, Dubrawski A, Wang D, et al. Using supervised machine learning to classify real alerts and artifact in online multisignal vital sign monitoring data. *Crit Care Med* 2016; **44**: e456–63
13. Michard F, Gan TJ, Kehlet H. Digital innovations and emerging technologies for enhanced recovery programmes. *Br J Anaesth* 2017; **119**: 31–9

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Bedside assessment of lung aeration and stretch

A. Fernandez-Bustamante[1,2] and M. F. Vidal Melo[3,*]

[1]Department of Anesthesiology, University of Colorado School of Medicine, Aurora, CO, USA, [2]Webb Waring Center, University of Colorado School of Medicine, Aurora, CO, USA and [3]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

*Corresponding author. E-mail: VidalMelo.Marcos@mgh.harvard.edu

Knowledge on lung physiology and lung injury mechanisms related to positive pressure ventilation has evolved from animal models advancing the concepts of volutrauma, barotrauma, atelectrauma, and biotrauma[1,2] to applications in mechanically ventilated patients in the ICU and, more recently, in the operating room to reduce pulmonary complications.[3] A defining point in the field was the demonstration that, in patients with acute respiratory distress syndrome (ARDS), protecting the lungs by using lower tidal volumes V_T (i.e. V_T scaled to lung size as 6 ml kg^{-1} of predicted body weight) had a substantial impact on patient outcomes in the ICU.[4] The benefit was presumably derived from limitation of lung stretch, and the practice of lower V_T has been adopted in ICUs and operating rooms,[5] although still not universally implemented.[6] The use of lower plateau pressures and higher PEEP was an additional principle that accompanied lower V_T composing the so-called protective ventilatory strategies. Yet, knowledge of the interplay between these variables is still incomplete, and a large registry-based study suggested that lower V_T combined with insufficient PEEP may worsen outcomes.[7]

Attempts to understand how injurious conditions during mechanical ventilation produce lung injury led investigators to apply engineering concepts. Volumetric strain, the change in lung volume divided by the initial reference volume, is one of those concepts.[8] Such a concept is expected to be relevant clinically, as, even if the total lung size were similar for different patients, the presence of atelectasis in some patients results in only a fraction of the lung receiving the total V_T, likely producing a more injurious condition than when V_T is distributed to the whole lung. For instance, it is intuitive that V_T=500 ml would be more injurious in a patient with a very small functional residual capacity (FRC) of 500 ml as in ARDS (volumetric strain=500/500=100%) than in a patient with a normal FRC of 2000 ml (volumetric strain=500/2000=25%).

Lung strain is composed of both a static and a dynamic component. The FRC can be understood as the resting lung volume in the absence of any additional external interventions (i.e. at PEEP of 0 cm H_2O). Considering the initial lung volume to calculate strain as FRC, static lung strain derives from the presence of an end-expiratory lung volume (EELV) different from FRC as a result of the additional lung volume resulting from the application of PEEP.[9,10] The dynamic component, dynamic lung strain, is a consequence of tidal ventilation. Not only large whole-lung dynamic strains are associated with lung injury, but also regional dynamic strains are related to local inflammation.[11] Minimisation of dynamic lung strain is, consequently, a result of the implementation of lower V_T strategies, and consistent with preclinical data relating lung inflammation and injury with dynamic volumetric strain, either combined with lung blood volume[12] or in isolation.[11]

A recent advance in the field is evidence that V_T normalised to respiratory system compliance (V_T/C_{RS}) represents the ventilation variable that best stratifies for survival in ARDS patients.[13] The ratio V_T/C_{RS} defines the driving pressure (ΔP), which can be estimated from the difference between plateau pressure and PEEP in the absence of respiratory effort, as in fully paralysed patients. In ARDS patients, changes in V_T and PEEP were not by themselves predictive of survival, except when they resulted in ΔP changes.[13] Such results appear to challenge initial findings on the role of reduced V_T to improve survival. A registry-based study on a large population of surgical patients undergoing general anaesthesia with mechanical ventilation also proposed driving pressure as an important correlate for major postoperative pulmonary complications,[14] which are still prevalent in the protective ventilation era.[15] The predictive value of driving pressure for major postoperative pulmonary complications was also superior to V_T by itself.[14] The relevance of driving pressure as a predictor of postoperative pulmonary complications was further emphasised in a meta-analysis of randomised clinical trial data of studies on intraoperative mechanical ventilation.[16] In all these studies, the reason why V_T/C_{RS} would be such a relevant variable was its interpretation as a measure of whole lung strain easily obtained with clinical measurements. This is based on the presumption that C_{RS} is a measure of aerated lung volume.[13,14,17] Whilst regional strain can occur even in the presence of acceptable global strain,[10] and values of regional lung strain below global thresholds are still associated with regional lung inflammation,[12] global estimates are certainly a valuable measure compared with the assessment of V_T by itself or normalised to lung size.[13,14]

In the current issue of the *British Journal of Anaesthesia*, Grieco and colleagues[18] present a clinical physiology study in non-obese ASA physical status 1 and 2 patients undergoing lower or upper abdominal surgery 'to determine whether C_{RS} and ΔP reflect lung aerated volume and dynamic strain during general anaesthesia'. Patients (*n*=20) received PEEP of 2, 7, or 12 cm H_2O randomly for 40 min during abdominal surgery, with C_{RS}, driving pressure, and estimates of EELV evaluated using a modified nitrogen wash-out and wash-in technique. From this and estimates of FRC based on demographjc data, the authors derived static and dynamic strains. Consequently, the authors tested some of the previous results and assumptions used in the interpretation of those large outcome studies.

Direct measurements of advanced respiratory variables during intraoperative conditions are relatively limited, and report of such data is consequently welcome. Grieco and colleagues[18] report that aerated EELV was less than the predicted awake spontaneously breathing supine FRC in 65% of patients at PEEP of 2 cm H_2O and in 45% of patients at PEEP of 5 cm H_2O. Thus, the recent recommendation for PEEP of $\leq$2 cm H_2O during open abdominal surgery in non-obese surgical patients[19,20] would be expected to produce lung de-recruitment in a significant proportion of patients. This could contribute to the observed increase in 30-day postoperative mortality in patients ventilated with low V_T and low PEEP.[7]

It is also remarkable that a median lung recruitment of 445 ml was obtained at PEEP of 7 cm H_2O compared with PEEP of 2 cm H_2O. This is comparable with the 15–20% reduction in FRC after the induction of general anaesthesia,[21] suggesting that, in this small group of patients, PEEP of 7 cm H_2O allowed the recovery of a substantial amount of lung volume usually lost during the induction of anaesthesia. Lung recruitment was much smaller (107 ml) between PEEP of 7 and 12 cm H_2O. Such findings match well with CT imaging studies reporting reduced EELV after the induction of general anaesthesia with mechanical ventilation, with 16–20% of lung tissue showing no or poor aeration.[22] CT imaging studies have also shown that airway pressures may need to be above 40 cm H_2O for at least 7–8 s to recruit previously collapsed lung areas in at-risk patients.[23,24] Thus, the observation of lung recruitment at PEEP of 7 cm H_2O in the absence of a specific recruitment manoeuvre suggests a sizeable number of alveolar units with low opening pressures in normal adult lungs. An additional interesting observation was the constant cardiac output for PEEP of 2–12 cm H_2O suggesting limited haemodynamic impact of these PEEP values in this group of patients.

Grieco and colleagues attempted to achieve their aim by studying correlations between C_{RS} and aerated EELV, and between ΔP and dynamic strains overall and at each PEEP level.[18] A major point is the importance of the FRC predicted from demographic data. Better correlations were found for measured aerated lung volumes below predicted FRC than above it, but it is not clear if the multiple correlations were part of the original analysis plan or an observation achieved *a posteriori*. Elucidation of the dependence of these correlations on predicted FRC would appear of great relevance to understanding and potentially limiting the use of the presumptions of the correlations in the cited outcome studies.[13,14,16] Indeed, the fractional contributions of individual lung regions at different levels of EELV would influence the correlation. This information could also be valuable in the search for the ideal management of PEEP.[20,25,26] The dependence of the results on FRC appears to conflict with findings in ARDS patients that ΔP reductions were significantly associated with better survival irrespective of baseline elastance (the inverse of compliance) of the respiratory system,[13] suggesting an effect throughout all ranges of lung expansion, not only that indicated by Grieco and colleagues.[18] Previous imaging studies also reported significant correlations between compliance and aerated lung volume in patients with acute respiratory failure at a wide range of pressures, with correlation values similar or better than those presented by Grieco and colleagues[18] in their 'best' conditions (i.e. at aerated lung volumes less than the predicted FRC).[17] Whether such apparent conflicting results are attributable to physiological differences between surgical patients with initially normal lungs and ARDS patients or to other issues will require further clarification. An additional important limitation of these findings is that the applicability of the results would require knowledge of the patient's aerated EELV and FRC, but such knowledge would be unusual, and assumed expected values would be required to apply the reported results.

The authors acknowledge other limitations to their study. The absence of measurements of trans-pulmonary pressure, the pressure effectively distending the lungs and likely responsible for lung injury,[27] limits insight into the effect of the utilised PEEP and meaning of the resulting EELV. Availability of regional assessments of lung expansion as obtainable with different imaging techniques would be helpful to understand better how the global changes produced on EELV by PEEP effectively redistribute lung expansion, and thus, strain.[12]

The goal of Grieco and colleagues[18] to identify and understand if and which measures of global lung mechanics reflect more complex physiological variables during mechanical ventilation is certainly relevant. The correlations reported by these authors agree with previous studies and current assumptions related to the interpretation of driving pressures as a measure of whole-lung global strain and of C_{RS} as an indirect measure of aerated lung volume. The results also raise concerns that the validity of those assumptions has limits. Future investigations with physiology-based hypotheses will be required to advance the understanding of such issues, and to allow the development of tools that are meaningful and available to the clinician adjusting ventilatory settings. The search for such bedside tools to identify the optimal intraoperative PEEP management continues.[28,29]

Authors' contributions

Study conception: both authors.
Writing of final manuscript: both authors.

Declaration of interest

The authors declare that they have no conflicts of interest.

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References

1. Dreyfuss D, Saumon G. Ventilator-induced lung injury: lessons from experimental studies. *Am J Respir Crit Care Med* 1998; **157**: 294–323
2. Dos Santos CC, Slutsky AS. Invited review: mechanisms of ventilator-induced lung injury: a perspective. *J Appl Physiol* 2000; **89**: 1645–55
3. Miskovic A, Lumb AB. Postoperative pulmonary complications. *Br J Anaesth* 2017; **118**: 317–34
4. Acute Respiratory Distress Syndrome Network, Brower RG, Matthay MA, et al. 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**: 1301–8
5. Wanderer JP, Ehrenfeld JM, Epstein RH, et al. Temporal trends and current practice patterns for intraoperative ventilation at U.S. academic medical centers: a retrospective study. *BMC Anesthesiol* 2015; **15**: 40
6. Bellani G, Laffey JG, Pham T, 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**: 788–800
7. Levin MA, McCormick PJ, Lin HM, Hosseinian L, Fischer GW. Low intraoperative tidal volume ventilation with minimal PEEP is associated with increased mortality. *Br J Anaesth* 2014; **113**: 97–108
8. Fung YC. Stress, deformation, and atelectasis of the lung. *Circ Res* 1975; **37**: 481–96
9. Protti A, Cressoni M, Santini A, et al. Lung stress and strain during mechanical ventilation: any safe threshold? *Am J Respir Crit Care Med* 2011; **183**: 1354–62
10. Paula LF, Wellman TJ, Winkler T, et al. Regional tidal lung strain in mechanically ventilated normal lungs. *J Appl Physiol* 2016; **121**: 1335–47
11. Wellman TJ, Winkler T, Costa EL, et al. Effect of local tidal lung strain on inflammation in normal and lipopolysaccharide-exposed sheep*. *Crit Care Med* 2014; **42**: e491–500
12. Motta-Ribeiro GC, Hashimoto S, Winkler T, et al. Deterioration of regional lung strain and inflammation during early lung injury. *Am J Respir Crit Care Med* 2018 May 22. https://doi.org/10.1164/rccm.201710-2038OC [Epub ahead of print] PMID: 29787304
13. Amato MB, Meade MO, Slutsky AS, et al. Driving pressure and survival in the acute respiratory distress syndrome. *N Engl J Med* 2015; **372**: 747–55
14. Ladha K, Vidal Melo MF, McLean DJ, et al. Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: hospital based registry study. *BMJ* 2015; **351**: h3646
15. Fernandez-Bustamante A, Frendl G, Sprung J, et al. Postoperative pulmonary complications, early mortality, and hospital stay following noncardiothoracic surgery: a multicenter study by the Perioperative Research Network investigators. *JAMA Surg* 2017; **152**: 157–66

16. Neto AS, Hemmes SN, Barbas CS, et al. Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: a meta-analysis of individual patient data. *Lancet Respir Med* 2016; **4**: 272–80
17. Gattinoni L, Pesenti A, Avalli L, Rossi F, Bombino M. Pressure-volume curve of total respiratory system in acute respiratory failure. Computed tomographic scan study. *Am Rev Respir Dis* 1987; **136**: 730–6
18. Grieco DL, Russo A, Romanò B, et al. Lung volumes, respiratory mechanics and dynamic strain during general anaesthesia. *Br J Anaesth* 2018; **121**: 1156–65
19. Guldner A, Kiss T, Serpa Neto A, et al. Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. *Anesthesiology* 2015; **123**: 692–713
20. Prove Network Investigators for the Clinical Trial Network of the European Society of Anaesthesiology, Hemmes SN, Gama de Abreu M, Pelosi P, Schultz MJ. High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial): a multicentre randomised controlled trial. *Lancet* 2014; **384**: 495–503
21. Hedenstierna G, Strandberg A, Brismar B, Lundquist H, Svensson L, Tokics L. Functional residual capacity, thoracoabdominal dimensions, and central blood volume during general anesthesia with muscle paralysis and mechanical ventilation. *Anesthesiology* 1985; **62**: 247–54
22. Reber A, Engberg G, Sporre B, et al. Volumetric analysis of aeration in the lungs during general anaesthesia. *Br J Anaesth* 1996; **76**: 760–6
23. Whalen FX, Gajic O, Thompson GB, et al. The effects of the alveolar recruitment maneuver and positive end-expiratory pressure on arterial oxygenation during laparoscopic bariatric surgery. *Anesth Analg* 2006; **102**: 298–305
24. Rothen HU, Neumann P, Berglund JE, Valtysson J, Magnusson A, Hedenstierna G. Dynamics of re-expansion of atelectasis during general anaesthesia. *Br J Anaesth* 1999; **82**: 551–6
25. Ferrando C, Soro M, Unzueta C, et al. Individualised perioperative open-lung approach versus standard protective ventilation in abdominal surgery (iPROVE): a randomised controlled trial. *Lancet Respir Med* 2018; **6**: 193–203
26. de Jong MAC, Ladha KS, Vidal Melo MF, et al. Differential effects of intraoperative positive end-expiratory pressure (PEEP) on respiratory outcome in major abdominal surgery versus craniotomy. *Ann Surg* 2016; **264**: 362–9
27. Mauri T, Yoshida T, Bellani G, et al. Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives. *Intensive Care Med* 2016; **42**: 1360–73
28. Blankman P, Shono A, Hermans BJ, Wesselius T, Hasan D, Gommers D. Detection of optimal PEEP for equal distribution of tidal volume by volumetric capnography and electrical impedance tomography during decreasing levels of PEEP in post cardiac-surgery patients. *Br J Anaesth* 2016; **116**: 862–9
29. Nestler C, Simon P, Petroff D, et al. Individualized positive end-expiratory pressure in obese patients during general anaesthesia: a randomized controlled clinical trial using electrical impedance tomography. *Br J Anaesth* 2017; **119**: 1194–205