Topic: Ventilation management and dealing with asynchronous ventilation during attempted weaning trials

Associate Editor Graeme A'Court interviewed Geoff Shaw MBChB, FANZCA, FCICM, Hon FEngNZ from Christchurch in New Zealand. Dr. Shaw is an intensive care specialist and Professor at the University of Otago, Christchurch and an Adjunct Professor in the Department of Mechanical Engineering, College of Engineering, University of Canterbury.
He is the Editor in Chief of the Journal of Mechanical Ventilation and the first clinician to be made an honorary fellow of the Institute of Professional Engineers of New Zealand.

Q1: Please tell me about how you developed an interest in mechanical ventilation and the management of patient-ventilator asynchrony?

Answer: I have often felt most of the clinical trials in ventilation have focused on how patients are initially ventilated, rather than considering the much longer processes of weaning and discontinuation. Over 90% of time spent on mechanical ventilation is during weaning; this is where things often go wrong. The problem is that weaning is extremely complex. When patients are transitioned to spontaneous breathing, we need to consider their heterogeneous lung mechanics, their own mechanical power and control of breathing, and how all of these unknowns impact on their resolving lung injury. I think of ventilator asynchrony as the result of maladaptive patient responses to altered pulmonary mechanics, coupled with suboptimal and /or mismatched support from the ventilator. Weaning is hard to get right for many reasons. First, we generally have a poor understanding of the algorithms that control mechanical ventilation. Secondly, we have an incomplete understanding of the patient's evolving lung condition and their maladaptive responses. And finally, even if we mastered all of the above, how should we proceed? There is very little clinical practice guidance on weaning. So much to ponder. This is why it so interesting!

Q2: As weaning is a transition from controlled ventilation through to spontaneous breathing which control modes do you normally use?

Answer: Typically, I use a Bi-level or equivalent pressure-controlled (PC) mode with pressure support (PS) i.e. IMV. I reduce the respiratory rate, while the patient's spontaneous efforts are progressively supported by the ventilator. I initially set the PS level to equal the driving pressure (DP) used in the Bi-level mode.

Q3: Can you please describe your strategies to minimize or address patient-ventilator asynchrony?

Answer: Ventilator asynchrony is best conceptualized as a mismatch between the patient's own ventilation set points and the delivered support. First, we need to consider two things. Is it possible to match the patient's demands, and secondly would the resultant ventilation strategy be safe.

Frequently, during this transition, patients have a high ventilatory drive, which may cause further lung injury (patient self-inflicted lung injury; P-SILI. [1] It is not uncommon to find a struggling patient with a high minute ventilation, and a low $PaCO_2$, being given additional support. Instead, first, they should receive interventions to reduce their respiratory drive, such as further sedation, analgesia, and/or correction of any metabolic acidemia.

High transpulmonary pressures result in excess stress leading to strain injury to the lung. Amato and colleagues have shown strain injury may not equally distribute across the lung. Instead, it can be amplified in basal juxta-diaphragmatic regions during spontaneously breathing, through occult pendelluft. [2] This is an important concept. Sustained respiratory distress during transition needs to be carefully assessed. If the above measures, such as increasing opioids and sedation are ineffective, re-paralyzing should be considered. The weaning process needs to be suspended until there is improvement in lung condition. Once a patient is paralyzed, I often try to retrospectively estimate the DP, generated by the patient's spontaneous efforts (Pmus). Once sedated and paralyzed, I increase the DP of the ventilator to produce a tidal volume (V_T) similar to that reached during spontaneous breathing. The DPs are not uncommonly eye-wateringly high; sometimes in excess of 30 cmH_2O. The insights I have gained have reduced my threshold to abort trails of spontaneous breathing when I have any concerns about the potential for lung injury. Patient -ventilator asynchrony is a red flag.

Others have described using inspiratory threshold occlusion to estimate DP, however a simpler observational method sometimes can be used when patients are weaned with PS and PC breaths. Often, two *different* V_T are produced corresponding to either a PS breath or a PC breath. The ratio of the (V_T) volume of the PS breath to the V_T of the -PC breath multiplied by the controlled DP approximates the Pmus produced by a spontaneous breath.

$V_{T\ press\ support}$ / $V_{T\ press\ control}$) x $\Delta P = \Delta P_{spont}$

For example, I recently managed an intubated spontaneous breathing patient, with Pneumocystis jirovecii pneumonia, who had a small pneumothorax. During a controlled breath (DP = 15 cmH_2O) *without* any spontaneous effort, the resulting V_T was 330 ml. However, their spontaneous breaths were up to 800 ml. Thus, the estimated DP generated by the spontaneous breathing effort was 800/330 x 15 = 36 cmH_2O! Needless to say, the patient was re-sedated and paralyzed.

More accurate way to estimate the amount of the patient's effort (Pmus) is using an esophageal balloon manometry or using the equation of motion: Pvent + Pmus = Elastance (E) x Volume (V) + Resistance (R) x Flow (V')
Assuming elastance and resistance is the same during passive and active conditions
In the example above:
Pvent (15 cmH2O) = E (33) X V (0.33) + R (10) X V' (0.6)
Pvent (15 cmH2O) + Pmus (?) = E (33) X V (0.8) + R (10) X V' (0.6)
Pvent (15 cmH2O) + Pmus (?) = 30 cmH2O
Other simplified way to estimate Pmus is from the P0.1 [3]
Pmus = -2.99 x (P0.1) + 0.53

There are many fishhooks during transition, which may contribute to ventilator-induced lung injury. Ventilator asynchrony and its associated risk of lung injury is likely a major contributor to poorer outcomes from mechanical ventilation.

Q4: How do you adjust rise time and expiratory trigger (cycling) to treat or minimize asynchrony?

Answer: Generally, I have had little success by adjusting the rise time to meet patient inspiratory demand. However, increasing the flow thresholds for cycling off PS can unmask unrecognized rapid respiratory rates. Unfortunately, short of re-sedation, there is little that can be done for an asynchronous tachypneic patient.

Q5: What are your thoughts of the use of driving pressure, mechanical power, peak pressure limitation, 6 ml/kg or adjusting the tidal volume based on lung compliance?

Answer: I feel 'compliance' is an unfortunate term, as it creates the illusion the lung is stiffer, when is it just simply too small. The baby lung paradigm of Gattinoni and colleagues provides a much more useful construct.[4] I use a PCV mode, so (V_T) are always proportionate to the available lung volume.

Mechanical power provides an attractive approach towards minimizing lung injury, because it accounts for the energy dissipation within the lung. Observational studies [5] have shown association with mortality, but there are no interventional studies yet to support this. However, there are a multitude of methods used to estimate this metric, but the contributions of DP, respiratory rate, compliance, resistance, and PEEP to lung injury are unclear. It is also difficult to calculate mechanical power at the bedside unless a ventilator is programmed to do this.

Automated ventilation, such as AVM2, which optimizes V_T and frequency to lowest mechanical power, makes sense. [6] However, until we can incorporate new ventilation algorithms into standard practice, in the same way as we can apply new drug therapeutics, significant improvements in outcomes of mechanical ventilation will be very difficult to achieve. We need to de-couple software from the hardware, which is an anathema to many ventilator manufactures.

Q6: How do you set "optimal" PEEP? Is it based on improving PaO_2, mechanics, or trying to have an open lung strategy?

Answer: The problem is that optimal PEEP depends on recruitment, and recruitment depends on PEEP. Does it even exist? The optimal PEEP in a non-recruited lung might not necessarily be the optimal PEEP in a newly recruited lung.

Optimal PEEP has been conceptualized as the lowest expiratory pressure corresponding to the maximum compliance. However, determining the highest compliance is extremely difficult because the PEEP-compliance curve is a very flat inverted 'U'. Moreover, if de-recruitment occurs as the PEEP is being reduced, this will flatten the curve even further. Estimating optimal PEEP based on bedside pulmonary measurements lacks precision, so aiming for optimal compliance, using standard tools at the bedside is probably a fool's game. What we really want is a level of PEEP than is just enough to prevent airway closure. Can we do this?

If a newly admitted patient to the ICU has a diagnosis that would suggest early ARDS or cardiogenic pulmonary oedema, I will often carry out the *incremental* phase of stepwise recruitment maneuver.

Having ensured the patient is volume replete; I use PEEP increments to primarily *assess for* recruitability. PEEP should never be increased in patients who are not recruitable. Following paralysis, I set the DP to 15 cmH_2O and increase PEEP by 4 cm H_2O increments from the current

baseline. At each PEEP increment I watch each expired V_T, for any increase. When the V_T stop increasing, I move to the next PEEP level. I stop the incremental phase of the recruitment maneuver when the V_T stops increasing, or when I have a reached a peak inspiratory pressure of about 45 cmH_2O.

I do not use a decremental reduction in PEEP to assess compliance. Instead, I reduce to PEEP to around 20 cm H_2O, noting the new V_T for that PEEP level and DP.

A gradual reduction in V_T suggests progressive alveolar collapse. Occasionally the incremental PEEP titration needs to be repeated, but this time landing on a higher PEEP level. I decrease the PEEP level by no more than 2 cm every six to twelve hours. The PEEP level is clinically re-evaluated each day. With improvement in compliance and saturations PEEP levels are empirically gradually reduced over the next few days. I feel this iterative approach is physiologically well grounded and accommodates the imprecision of PEEP selection at the bedside using current technologies.

Q7: Can you please describe your thoughts on the use of esophageal pressure monitoring as a strategy for lung recruitment and or setting PEEP?

Answer: Trans-alveolar pressure is the alveolar to pleural pressure difference. Esophageal pressure provides a reasonable estimate of pleural pressure, so trans-alveolar pressure can be readily determined at the bedside. In critically ill patients, pleural pressures are often positive due to pleural fluid and tissue oedema. This tends to collapse alveoli unless PEEP is greater than this. In a study of patients with severe ARDS from influenza, PEEP was titrated to keep the end expiratory trans-alveolar pressure always positive, which resulted in some patients avoiding ECMO. [7]

Despite promising results, most ICUs, including our own do does not use esophageal pressure monitoring. Costs, complexity of care, plus training requirements are barriers to implementing new technologies.

Q8: Which mode or strategy do you use for lung protection? Would you consider newer modes of ventilation “closed loop” that automatically adjust to match the changes of the patient’s lungs and as well maybe better synchrony?

Answer: In the absence of automated or closed loop ventilation, managing DP is the simplest and safest way to mitigate lung injury. In the simplest quasi-static model of alveolar mechanics V_T, a surrogate of lung strain, is proportional to compliance, which is a measure of the available lung volume for tidal ventilation:

V_T = Compliance x Driving Pressure

Limiting V_T to 6 ml/kg/PBW is very much embedded in the culture of intensive care; yet DP and compliance, *the product of which determines V_T*, are rarely contemplated at the bedside. The problem arises when the compliance is very low. For example, if the compliance is 15 cm / ml, in a 50 kg patient ventilated with a V_T of 6 ml/kg/PBW (300 ml), the driving pressure is 20 cmH_2O.

Thus, the ratio of V_T / compliance is important, which is, of course, the DP. It makes complete sense to limit DP, whereas limiting V_T may still cause lung injury.

DP is a major, but not the only metric contributing to lung injury. The notion of mechanical power, which also accounts for minute ventilation and resistance, will improve our ability to deliver lung-protective ventilation. However, it needs to be computed at the bedside, and ideally implemented as part of a closed loop system.

Q9: Can you please share your thoughts on the use of neuromuscular blockers and permissive hypercapnia as part of management for lung protective ventilation?

Answer: Acceptance of patients with a raised P_aCO_2 was probably the key barrier to using permissive hypercapnia since it was described by Hickling and colleagues in 1990. [8] This approach recognized prioritizing risk of lung injury over respiratory acidosis; the latter is generally very well tolerated. In the initial stages of mechanical ventilation minimizing lung injury, using paralysis, sedation and low tidal volumes often necessitates neuromuscular blockade (NMB). During transition to spontaneous breathing, patients will frequently develop high tidal volumes, respiratory rates, and dyssynchronous breathing. The reasons for this are highly complex, which makes management tricky. Unmeasured and uncontrolled lung strain will result in ventilator-associated lung injury. Neuromuscular blockade removes all of these problems and plays an important role in managing the weaning process.

Concerns about NMBs contributing to critical illness weakness and prolonged weaning have not been demonstrated in clinical trials. In the ACURASYS study, patients with ARDS who received neuromuscular blockade for the first 48 hours of mechanical ventilation had an improved survival. [9] There is clearly a trade-off between use of NMBs to reduce lung injury and inflammatory response, and their potential to aggravate the myopathies associated with critical illness.

Q10: Are prone positioning and extracorporeal support in your ICU practice? If so, can you please elaborate on lessons learned from experience?

Answer: All ICUs, which manage patients with severe hypoxemia, should be capable of implementing prone positioning. There is overwhelming basic science and clinical trial evidence to support this practice. With regard to extracorporeal support, this is not generally available outside of the country's largest city, Auckland (population 1.65 M, from a national population of 5.12 M) However there are plans to ensure that all the major centers will be able to offer VA ECMO.

Q11: In your opinion, what are the unanswered questions in the field of mechanical ventilation?

Answer: Having real-time estimates of lung recruitability, lung strain in all modes of ventilation, along with asynchrony detection, sitting alongside automated protocols are ventilation's Holy Grail. The initial way forward may be to parametrize those metrics, which define a patient-specific lung condition in real time. This is an example of a digital twin. [10] I hope such an approach will become the foundation on which automated ventilation is built. Predictions such as 'what happens when I turn this knob', can be made. However, should we still be turning knobs? Within 50 years, ventilation decisions will be based on patient-specific parameters; *optimized and automated* in real time.

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