Dilemmas in Covid-19 Respiratory Distress: Early vs Late Intubation; High Tidal Volume and Low PEEP vs Traditional Approach?

Abstract

Background: This article discusses the challenges and controversies in the management of the unique respiratory failure caused by COVID-19 pneumonia. Many uncertainties prevail in the treatment of this disease. There remains no clear consensus on the timing of intubation and trial of noninvasive therapies prior to intubation. We will discuss here the surrogate markers of deteriorating respiratory function and pulmonary infiltrates that could be utilized to prevent delayed intubation. We also discuss the proposal by Gattinoni et al. in employing a rather high tidal volume and low PEEP technique.

Main study: We review the importance of consideration of work of breathing, P-SILI and ultrasound lung in decision-making process. We discuss the ill effects of high tidal volumes in inducing lung strain with larger dynamic deformations and the benefit of high PEEP in homogenizing the strain distribution. The article proposes that the ground glass opacities seen in COVID-19 pneumonia could pose as ‘stress raisers’? If so, there may be importance to high PEEP in the L phenotype despite lower recruitability. The article also questions the appropriate tidal volume to be applied to this ‘larger baby lung’ in L phenotype.

Conclusion: Measures to avoid delays in recognition of need for intubation and escalation of care are key to avoid further damage from P-SILI. Clinical assessment of work of breathing and intubating at the earliest signs of respiratory distress may prevent P-SILI. While optimum ventilation strategy for ‘L’ phenotype remains a matter of ongoing discussion, risks of inducing lung injury with the approach employing the high tidal volume and low PEEP technique need to considered. The COVID-19 respiratory failure poses more questions and challenges our traditional protocols of ARDS management. Perhaps, forgoing protocols and a more individualized and prescribed mechanical ventilation setting may not only show more respect and appreciation for its varied presentations but may also translate into better patient outcomes.

Keywords: Covid-19, Early intubation, P-SILI, Pendulluft, Lung stress/strain, H and L phenotype, High tidal volume, Low PEEP.

Abbreviations: HFNC- High Flow Nasal Cannula; BiPAP- Bilevel Positive Airway Pressure; NIPPV- Non-Invasive Positive Pressure Ventilation; ARDS- Acute Respiratory Distress Syndrome; P-SILI- Patient Self Inflicted Lung Injury; CXR- Chest X-ray; US- Ultrasound; VILI- Ventilator Induced Lung Injury.
**Introduction**

COVID-19 has provoked us to rethink our basics of critical care medicine- when to intubate? Several propositions have been made, with some models suggesting early intubation after failure of conventional oxygen therapy with nasal cannula, omitting trial of High flow nasal cannula (HFNC) or Bilevel Positive Airway Pressure (BiPAP) while other protocols suggesting that early intubation is unfavorable and recommend to allow trial of HFNC. The counter statement to the use of these devices is that failing to recognize the need for intubation on these respiratory support modalities may result in an increase in mortality.

If there is one thing that this disease has impressed us with is, it is its non-uniformity. We have to appreciate and understand the varied pathophysiology, nuances and presentations that it is capable of. Likewise, the approach has to be tailored to an individual’s pathophysiology. Happy hypoxemia (severe hypoxia without dyspnea), while not a new phenomenon, is being encountered more in COVID-19 pneumonia and is making us reconsider how we manage this type of respiratory failure. When to intubate them still remains a topic of debate.

**Intubate early vs late?**

Gattinoni et al. proposed two phenotypes “L” and “H” [1]. Some authors have used alternate terms as “compliant lung” and “stiff lung”. While ARDS is not a novel disease and the society guidelines on ARDS management are uniform, coronavirus is a novel disease with non-uniform presentations posing unique questions in its management. Several patients present with complaint lungs and significantly less parenchymal involvement on CT scan, yet with profound hypoxemia. Patients, especially those that have been ‘toughening out’ for weeks at home, may present with “H” phenotype or “stiff lungs”. These variants may present as a continuum. We see patients presenting with either ends of the spectrum as well in phases of transition between the two. In this article, we will refer to them as “L” and “H” phenotypes as originally proposed by Gattinoni et al. [1]. The CT scan and lung ultrasound can help identify between the two phenotypes.

L type patients have been proposed to be hypoxic due to low V/Q ratio. The gas volume is fairly normal, hence they may not be dyspneic. These so-called “happy hypoxics” can respond well to conventional oxygen therapy. If still hypoxic, escalation to HFNC could be the next best step in this subset and may reduce the need for invasive ventilation. It remains unclear if the benefits of escalation to non-invasive positive pressure ventilation (NIPPV) outweigh the potentially higher risk of aerosolization of this method in “happy hypoxics”. In patients progressing to acute respiratory distress syndrome (ARDS), alveolar and interstitial edema causes dead space and impairs the ability to effectively clear CO₂. This results in a dissociation between pulmonary ventilation and the drive to expel CO₂. More gas volume needs to be inhaled to compensate for the impairment of gas exchange resulting in awareness of breathing. The diseased alveoli become less compliant and more work of breathing needs to be performed to overcome the increased elastance. Dyspnea, thus, results due to a combination of impairment of gas exchange, ineffective CO₂ clearance and stiff lungs [2].

In non-intubated patients, it is difficult to assess for recruitability and lung elastance. Work of breathing can be surrogate marker of compliance of the lungs. Because of alveolar and interstitial edema, the lung volume available for gas exchange is significantly reduced. Since the patients are not able to inhale the gas volume they expect, they feel short of breath. Persistent hypoxia in this subgroup exhibiting respiratory distress is less likely to result in resolution unless positive end expiratory pressure (PEEP) is provided to recruit the dependent fluid filled alveoli and reduce the shunting. HFNC may be less likely to succeed in reducing the need for intubation in this subset. Early intubation strategy might apply well in this category without the intermediate steps of HFNC or NIPPV.

The phenotypes and presentations of COVID19 pneumonia are not static; they can be rather dynamic throughout the clinical course. Often, patients presenting as L type can progress to H type, which is an unfavorable course that we may want to avert. This could be, at least partly attributed to patient self-inflicted lung injury (P-SILI). With transition to H type, multiple lung units begin to collapse and now remain unavailable for gas exchange. Increase in dead space leads to increase in respiratory drive and minute ventilation, now causing increased work of breathing. Excessive negative intrathoracic pressures from excess work of breathing can generate potentially injurious transpulmonary pressure swings, thus inflicting P-SILI. In normal lungs, local changes in pleural pressure are generalized over the whole pleural surface. In patients with existing lung injury, negative forces generated by the respiratory muscles may lead to injurious effects on a regional level. In addition, the increase in transmural pulmonary vascular pressure swings caused by inspiratory effort may worsen vascular leakage [3,4]. Furthermore, strong spontaneous respiratory efforts in an already injured lung can cause pendelluft due to more localized changes in pleural pressures in dependent regions since the negative pressures from diaphragmatic contraction are not distributed uniformly [5]. Should endotracheal intubation be rather applied early forgoing trial of HFNC or BiPAP to minimize progression of acute lung injury from P-SILI? In early phase of transition, without significant work of breathing, but increasing alveolar edema as determined by imaging or lung ultrasound, HFNC may have a role in reducing the amount physiological and anatomical dead space and thereby reducing the respiratory drive and minimize progression to patient self-inflicted lung injury (P-SILI).

Below is an example of a patient who presented to the emergency department with moderate respiratory distress and work of breathing. She was given a trial of non-rebreather and BiPAP, failing which, she was intubated 5 hours later. The chest X-ray (CXR) at the time of intubation shows remarkable progression of infiltrates since the admission CXR. While worsening pneumonia could have contributed to her CXR findings, it is hard to overlook the contribution of P-SILI to her worsening pulmonary infiltrates (Figure 1).

Thus, P-SILI is especially important in today’s scenario. If intubated after such significant worsening has occurred, the patient may be subject to a rather prolonged period of mechanical ventilation. Shorter duration of ventilation is particularly advantageous in the current pandemic setting, which is resource limited.
Lung ultrasound (US) can also be utilized as an effective tool to follow progression of disease, since it is not practical to obtain frequent CT scans or CXRs. Since COVID-19 pneumonia is frequently patchy and focal, a lawn-mower approach gliding the US probe over the entire chest will help capture a good proportion of pleura and lung tissue. Progression of disease to multiple quadrants, coalescence of B lines, increasing number of B lines, white lung, worsening pleural irregularities and interruptions, alveolar consolidation pattern are an important clue to disease progression and diffuse involvement of pneumonia [6]. Now with less available lung for ventilation, these patients should be closely observed for developing dyspnea, if they are not so already. In patients presenting with limited pulmonary disease, lung US can aid in recognition of transition to full blown ARDS.

We need to respond to the patient’s underlying pathophysiology, as delay in intubation can lead to worse outcomes. A cookie cutter approach is not the answer. The benefit of HFNC with regards to averting intubation can be applied to selected patients on a case-by-case basis. Many patients requiring high FiO2 on HFNC for several days are being discharged home successfully. However, once dyspnea sets in, a significant number of patients continue to progress to the point of intubation. Rapid shallow breathing in itself can decrease alveolar ventilation by increasing the anatomical dead space and ultimately fatigue of the respiratory pump (diaphragm and chest wall). While a blueprinted protocol of early intubation for all may not be best practice, it is crucial to recognize early patients that are at higher risk of decompensation requiring intubation. In fact, delaying intubation might be detrimental and can further worsen the interstitial and alveolar edema and acute lung injury. Clinical assessment of work of breathing and intubating at the earliest signs of respiratory distress may prevent further P-SILI, and timely intubation could lead to shorter duration of mechanical ventilation.

**High tidal volume and low PEEP vs low tidal volume and high PEEP?**

Gattinoni and colleagues mention the use of higher tidal volumes in L phenotypes, which did take a lot of us by surprise. It is at odds with years of research in critical care endorsing low tidal volume ventilation as a standard of care. The high tidal volume and low PEEP strategy proposed refutes their own studies showing dynamic strain due to high tidal volumes is more injurious than static strain from high PEEP. As demonstrated by Gattinoni et al, global strain and overall inflation of the lungs is not the sole determining factor of lung injury, rather the manner in which it was achieved also holds significance [7,8]. Large dynamic deformations are more injurious than the same level of strain induced by static inflation.

The established principles of limiting large deformations by restricting tidal volumes and minimizing lung inhomogeneities by adequate static inflation using an adequate PEEP level would not stand the test of L-types ARDS?

While there may be larger proportions of disease-spared normal lung tissue, wouldn’t the focal areas of ground glass opacities act as ‘stress raisers’? Lung being a viscoelastic substance, the stress is proportional to the velocity of deformation and is higher during the dynamic phase [9,10]. At a constant respiratory rate, higher volume change per unit time, as with higher tidal volume, can augment the stress, and hence the risk of rupture, across the viscous lung. Tidal inflation pattern that employs small and slow cyclic strain rather than large and rapid deformations is crucial to maintaining the integrity of the parenchymal micro-architecture. This effect is further amplified at the interface of the injured and normal lung regions. The mechanical interdependence of the air spaces in a visco-elastic substance causes amplification of stress in a non-homogenous lung, with significantly higher stress borne at the interface of closed and open lung units [11]. Even though the focal ground glass opacities may involve relatively smaller lung regions, they can act as ‘stress raisers’ or ‘pressure multipliers’ and initiate the process of ventilator induced lung injury (VILI).

So, while it is true that the ventilable lung volume in L-type ARDS is not so small, should we really be using larger tidal volumes to ventilate this ‘greater baby lung’? In an experiment estimating strains at different levels of tidal volume and PEEP in mechanically ventilated normal lungs, strain increased with larger tidal volume, albeit with regional variations. The maximum volumetric strain occurred at mid and dependent lung regions implying different
regions have different risks of strain and injury. PEEP, on the other hand, was noted to homogenize the spatial distribution of regional strain and reduce inflammation [12].

While 9 ml/kg IBW (ideal body weight) may not be appropriate, applying 4-5 ml/kg IBW tidal volume may be increasing dead space ventilation since it is not a truly ‘baby’ sized lung volume. Radiological imaging may provide an insight into the ‘baby lung volume’ available for ventilation. Further titration towards achieving low transpulmonary and driving pressures may allow for optimum ventilation strategy. In those requiring FiO2 0.9-1.0, should we apply PEEP upwards of 15-20 as per the ARDSnet? Whereas high PEEP is important for the reasons mentioned above, how high is the appropriate and acceptable PEEP parameter in L-type so as to balance the benefit of homogenizing the stress and strain across the lung versus the risk of over distension of the rather larger available open lung units? The COVID-19 ARDS poses more questions and challenges our traditional protocols of ARDS management. Perhaps, forgoing protocols and a more individualized and prescribed mechanical ventilation setting may not only show more respect and appreciation for its varied presentations but may also translate into better patient outcomes.

Conclusion

Several challenges remain in the management of this rather unique respiratory failure. This is reflected in the wide variation in protocols implemented at various institutions. Timing of intubation could play a key role in overall outcomes and should be a subject of further research. Work of breathing can be regarded as a surrogate marker of lung compliance in non-intubated patients. In patients with increased work of breathing, P-SILI could cause worsening of edema and infiltrates during prolonged trial of noninvasive respiratory support. Being mindful to prevent further lung damage from P-SILI in this subset by timely recognition of respiratory distress and early intubation may result in shorter duration of mechanical ventilation and improved outcomes. Given the variable and dynamic presentations and phenotypes, it remains unclear if standard ARDSnet protocols apply to all patients. Focal ground glass opacities can act as stress raisers and thus, may necessitate adequate PEEP application to restore lung homogeneity and reduce strain. In patients that have not progressed to ARDS and with ‘larger baby lung’ volumes, appropriate tidal volume application is a matter of debate. Employing low tidal volumes may still be beneficial to avoid large dynamic deformations, and mitigate lung stress and lung injury.

Declarations

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References