SARS CoV-2

The current pandemic with SARS CoV-2 represents the realization of imagined scenarios with serious consequences. The current viral interstitial pneumonia has resulted in severe hypoxemic respiratory failure, overcrowded ICUs, equipment and personnel shortages, and significant mortality. Projections for patient volumes are expected to overrun critical care capabilities, with shortages of PPE, staff, and ventilators dominating discussions in local hospitals and the news media.

We provide a synthesis of the current experience coming from China, Italy and the US (Seattle & New York) and some common sense approaches from past lessons learned. These discussions are prompted by the frequent questions we receive by email and phone. Whenever possible, the statements here are supported by the most recent findings. At the time of this writing, the statement from the Society of Critical Care Medicine (SCCM) has been published addressing many issues related to treatment of ventilated patients.

We reiterate those major recommendations:

1. **Maintain strict infectious disease precautions.**

2. **In severe respiratory distress, do NOT delay intubation.**

3. **In patients with early hypoxemia, consider high flow nasal oxygen. This is controversial, with some concerns regarding environmental contamination. If used, there should be a low threshold for failure and urgent intubation. Some clinicians will elect to avoid high flow nasal cannula.* Environmental controls should be considered with an emphasis on caregiver protection.**

4. **The use of NIV is associated with a high rate of failure. Because of high failure rate and the possibility of environmental contamination, we suggest avoiding NIV. (If NIV is used a low threshold for failure; e.g., no improvement in 1-2 hours should prompt intubation).***

5. **Mechanical ventilation should follow the ARDSnet recommendations:**

   a. **Tidal volumes of 4-8 ml/kg of predicted body weight (volume or pressure control).**

   b. **CMV-assist control is recommended due to often heavy sedation requirements.**

   c. **Plateau pressure less than 30 cm H_2O.**

   d. **PEEP/FIO_2 Table from ARDSnet (high PEEP).**

6. **In the face of refractory hypoxemia (PaO_2/FIO_2 < 150) – prone positioning is the first recommended therapy. We acknowledge the manpower needs and increased need for PPE associated with manual proning.**

What are the major findings in patients with SARS CoV-2 viral pneumonia requiring mechanical ventilation?

> Patients who require mechanical ventilation are severely ill. The intensity of treatment parallels treatment for any severe ARDS patient.

The preponderance of evidence is for severe hypoxemic respiratory failure in the most critically ill subjects. Of note, pulmonary compliance appears to be reduced but not to levels typically seen with ARDS. In a recent ESICM presentation, Pesenti reported on 672 patients from Lombardy, Italy.[1] In this cohort, the median PEEP was 14 cm H_2O with the majority of patients managed between 10 and 20 cm H_2O (25%-75% percentile 12 - 15 cm H_2O). The median FIO_2 was 0.55 with the 25%-75% percentiles of 0.45 and 0.70. Nearly 30% of patients required an FIO_2 of 0.70 or greater.

In the recent report from Seattle by Arentz et al,[2] in a series of 21 subjects, more than half had severe ARDS (57%) with a mean PaO_2/FIO_2 at admission of 169 (69-492) and a nadir PaO_2/FIO_2 108 (58-247).

These are one area where we are not in complete agreement with the SCCM document.

Humidification

> An HMEF or heated humidifier can be used in these subjects.

While heated humidification has advantages, the use of a heat and moisture exchanging filter (HMEF) can provide sufficient humidification while also protecting staff and the environment. These can be standard filters or HEPA filters. Caution: the use of HMEFs increases mechanical deadspace by ~30 mL, which for an average sized adult translates to 0.5 mL/kg and an increase in V_D/V_T of 8%. As V_D/V_T in moderate and severe ARDS typically is ~0.60 and ~0.70, these devices likely will require similar small adjustments in preset V_t to maintain alveolar ventilation.

During SARS-CoV-1 in Canada, following identification of the infection, patients testing positive for SARS were placed on ventilators with heated expiratory filters. The impact on transmission following this change was difficult to measure.

To date, COVID-19 has not been associated with increased airway secretions. We do not know if using an HMEF makes an expiratory filter redundant. An expiratory filter may provide additional protection of the environment. CAUTION: Expiratory filter resistance may increase with use of heated humidification and time. Observe the patient for signs of increased expiratory resistance (PEEPi, expiratory flow limitation).

Can the SNS stockpile ventilators manage patients with COVID-19?

> The LTV-1200 and the Impact 754 can both be used to treat the majority of patients described to date. **(Please see the videos for use at the AARC website.)**

The SNS ventilators include the LTV-1200, the Impact 754 and the LP-10. The LTV-1200 and Impact 754 can deliver the required tidal volumes, FIO_2, and PEEP to maintain the majority of patients based on the current clinical presentation. Both devices have been used to manage ARDS patients during military transport and in disaster operations. Both are capable of delivering a PEEP of 20 cm H_2O and near 100% oxygen. The LTV-1200 is the most common and newest device in the stockpile and we believe will likely be issued first.

The LP-10 is a piston-based home care ventilator with only a low flow oxygen inlet and the addition of PEEP with an external valve. The LP-10 can only provide volume ventilation. Three factors limit utility of this ventilator for hypoxemic respiratory failure: its limited FIO_2 range, inability to select and maintain a set FIO_2 and it's requirement for an external PEEP valve.

Notes regarding function:

1. The maximum peak flow of the Impact 754 is 60 L/min using a constant flow waveform. The 754 only provides volume ventilation. Patients with high inspiratory flow demands may have flow asynchrony.
2. Tidal volume delivery with the 754 at the low end is improved with the use of external air bypassing the internal compressor.
3. None of the ventilators in the stockpile have an expiratory filter. Placement of an expiratory filter will be important prior to use on infectious patients.
4. All the SNS ventilators have a room air inlet for the compressor and inlet filters should be added to the 754 and the LP-10. The LTV-1200 has an internal filter.

Can bilevel ventilators be used for invasive ventilation?

> CPAP machines designed for obstructive sleep apnea cannot be repurposed as ventilators by clinicians. However, bilevel devices are ventilators and can be used for invasive ventilation.

There have been suggestions in the media that CPAP machines designed to treat obstructive sleep apnea can be repurposed as ventilators. This is not something that a respiratory therapist can do and this should not be attempted.

It is possible for bilevel devices, including those used in the hospital and those used in the home, to be used for invasive mechanical ventilation. Some, but not all, bilevel devices are FDA-cleared for use as an invasive ventilator. These ventilators are commonly used for chronic respiratory failure and some sleep disorders.

Bilevel ventilators do not have an active exhalation valve. Of concern is aerosol generation from the leak port. This is a legitimate concern. There are commercially available filters that can be fitted to the leak port. Check with the manufacturer to purchase these for your circuits before using this ventilator type on a patient with COVID-19.

We recommend active humidification when a bilevel ventilator is used for invasive respiratory support. Alternatively, a heat-and-moister exchanger (HME) can be used. If using an HME, ideally an HME-filter is used and this might obviate the need for a filter on the leak port.

On bilevel ventilators, the level of respiratory support is determined by the difference between IPAP and EPAP. This difference is the level of pressure support or pressure control. The level of EPAP (PEEP) can be increased as needed to support hypoxemic respiratory failure, but it is important to remember that IPAP must be increased when EPAP is increased (and vice versa).

FIO$_2$ can be set directly on some bilevel ventilators. For others, oxygen is titrated into the system. For oxygen titration, follow the instructions of the manufacturer.

As with any ventilator, lung protective ventilation strategies should be used. If the ventilator displays tidal volume, target 6 mL/kg predicted body weight and a driving pressure (IPAP-EPAP) less than 15 cm H$_2$O. Titrate PEEP appropriately, such as with the high PEEP ARDSnet table.

For safety, alarms should be set appropriately when any bilevel ventilator is used. Continuous pulse oximetry should also be used, with alarms set appropriately.

We suggest that use of bilevel ventilators for invasive support should be triaged. Ideally, they should be used for patients who do not have COVID-19, thus freeing critical care ventilators for patients with COVID-19 hypoxemic respiratory failure.

Triage ventilator performance to patient illness

> Use the highest technology equipment for the most severely ill patients.

As with any asset, the ventilators at your disposal should be triaged for use, matching the device capabilities with the severity of patient illness. The patients with the most severe hypoxemia requiring high PEEP and high FIO$_2$, with reduced compliance, should be triaged to ICU ventilators. Patients requiring ventilation for non-COVID related illness can be managed with portable devices and less sophisticated devices in your inventory. The SNS ventilators can be woven into that matrix which includes the use of anesthesia workstations.

Can I ventilate more than one patient with a single ventilator?

> Do not attempt to ventilate multiple patients with a single ventilator. As a last-ditch effort, an attempt to ventilate 2 subjects with similar compliance might be attempted after approval of local Ethics Committee and/or Institutional Review Board (IRB).

The interest in ventilating multiple patients on a given ventilator has been piqued by well-intended but potentially dangerous internet videos. The first modern descriptions for 4 patients per ventilator were advanced by Neyman et al[3] in 2006 and Paladino[4] in 2008. In each instance Branson, Rubinson and others have cautioned against the use of this technique. At present we recommend that you **DO NOT** attempt to ventilate 4 patients with a single ventilator.[5-7]

Of note, the jump to 4 patients without considering just 2 patients is nonsensical due to the complexity of this approach. We hope to provide more guidance on the safest possible application of a single ventilator for 2 patients in the near future.

Regarding the 4-patient scenario, the patients would have to be arranged around the ventilator like spokes abound a hub. This positioning moves the patient away from the supplies of oxygen, air, and vacuum at the head of the bed. It also places the patients in close proximity for transfer of other organisms. It cannot be done in separate rooms. One of our concerns is that in attempt to position patients, extra dead space (resulting in hypercarbia) or longer tubing contributing to compressible volume could be dangerous.

We do not find that matching patients by size is relevant, however matching by compliance, driving pressure, PEEP, and FIO$_2$ are far more important. Patients have to be heavily sedated and paralyzed. Spontaneous breathing by a single patient sensed by the ventilator would set the respiratory frequency for all the others. Worse, the added circuit volume could preclude triggering (note the internet presentations suggest making the ventilator less sensitive) and may cause the patients to share gas between circuits in the absence of one-way valves. Pendelluft between patients is not out of the question resulting in rebreathing, cross infection, and over-distension. The reasons not to ventilate 4 subjects with 1 ventilator are too numerous to mention. An abbreviated list is shown below:

1. The added circuit volume defeats the operational self-test (the test fails). You have to operate the ventilator without a successful test adding to errors in the measurement.

2. Additional external monitoring is required – the ventilator monitors only the average pressures and volume. The system prevents monitoring changes in the individual patients.

3. Even if respiratory mechanics of all 4 patients are the same at initiation, if one becomes sicker, one stays the same, two are getting better, the distribution of gas to each patient is unequal and unmonitored. The sickest patient gets the smallest V$_T$ and the improving patient gets the largest V$_T$. This was clearly evident in the study by Paladino[4] wherein all four sheep were observed to have episodes of pronounced decreases in PaO$_2$ and acute hypercapnia likely signifying underventilation resulting from substantial changes in chest mechanics between the animals.

4. Ventilator weaning or ventilator discontinuation is impossible and the patient who is improving has to be switched to a single ventilator.

5. During airway suctioning of one patient, ventilation of the other patient is interrupted.

6. There are longer term consequences to this approach that paradoxically could worsen the supply of ventilators during a pandemic. Chief among these is that prolonged use (i.e. > 48 hr) of paralytic agents may be associated with ICU acquired weakness that prolongs the need for mechanical ventilation. This becomes particularly worrisome as the median duration of mechanical ventilation in SARS and MERS ranges between 8-31 days. In addition, the ability to reduce mechanical ventilation duration and ICU length of stay is inextricably related to the ability to perform spontaneous breathing trials and daily sedation interruptions. This process is stymied by having more than one patient tethered to the same ventilator. To address this issue would require changing the ventilator used for the patient(s) who "appear" to be recovering faster and would consume an extraordinary amount of clinician time and logistics in a situation when intensive care resources are under maximal stress.

7. We refute the "it's better than nothing defense," as in a cohort of 4 patients, one of whom may die regardless of maximal efforts, the deterioration in that subject may lead to injury in the other three.

8. We suggest that these videos be removed from the internet as they promote a very inexperienced and cavalier approach to a very complicated issue fraught with patient harm.

9. Before any unconventional approaches like this are used, they MUST be approved by the appropriate Ethics Committees and, in some cases, the Institutional Review Board. Failure to do so could result in severe penalties.

What about using artificial resuscitators or minimal function mechanical ventilators?

> Artificial resuscitators have little utility in caring for the subjects requiring mechanical ventilation in this scenario.

The use of disposable and limited function ventilators unable to control V_T, PEEP, or FIO_2 and those with limited inspiratory flow capabilities (limiting the total rate) are not viable candidates for this illness. Again, the "it's better than nothing" or "these can be used in the least ill patients" may not apply. The least ill patients do not require intubation. Those that require intubation, require a ventilator capable of meeting the parameters outlined in the ARDSnet treatment guidelines. Of note, artificial resuscitators are only intended for use as life support when attended one caregiver to one patient. And these devices have been shown to fail without alarm with changes in position.[8]

We have similar concerns with the multitude of potential DIY (Do it yourself) projects and hack challenges to create a 'simple' open source ventilator. Mechanical ventilation in this scenario requires a ventilator capable of managing ARDS including PEEP 10-20 cm H_2O, VT 300-600 ml and minute volume of 10-15 L/min. Failure to meet these requirements will not allow support of the these critically ill patients.[9]

What about an inhaled vasodilator?

> Inhaled vasodilators should not be used routinely. Aerosolized vasodilators should be avoided.

The profound hypoxemia associated with SARS-CoV-2 may respond to an inhaled vasodilator. We agree that **routine** use of an inhaled vasodilator is not supported or warranted. However, in the absence of a response to PEEP, lung recruitment, or prone position (or a patient unable to be proned) an inhaled vasodilator might be considered for refractory hypoxemia. The study from Seattle used aerosolized vasodilators in several patients.[1] Given the mode of transmission of the virus, the use of an aerosolized vasodilator might be unwise. Additionally, the requirement for an expiratory filter to prevent accumulation of aerosol in the expiratory valve will require breaking the circuit to change at predetermined intervals. In the current environment, changing filters may result in loss of lung recruitment as well as result in unnecessary exposure of the caregivers. The use of inhaled nitric oxide could be given a short trial. We suggest this be a short trial with pre-established criteria for continued used or discontinuation. We also look forward to improved access and reduced costs for this therapy in the midst of this pandemic.

Aerosol therapy – nebulizers or pressurized metered dose inhalers

> Most patients with COVID-19 do not need inhaled bronchodilator therapy.

The use of a nebulizer may increase the transfer of particles into the environment and decrease the life of expiratory circuit filters. The use of pMDIs to deliver bronchodilators may be more prudent. However, there is no role for inhaled bronchodilators in patients with COVID-19 unless the patent has co-morbid asthma or COPD.

Non-ventilated patients

Much of the discussion and concern during this pandemic is associated with mechanically ventilated patients. It is important to remember that standard oxygen therapy has been indicated in over 75% of hospitalized subjects.

Recommendations from the SCCM task force

Ventilation	
In adults with COVID-19, we suggest starting supplemental oxygen if the peripheral oxygen saturation (SPO$_2$) is < 92%, and **recommend** starting supplemental oxygen if SpO$_2$ is < 90%	Weak Strong
In adults with COVID-19 and **acute hypoxemic respiratory failure on oxygen**, we **recommend** that SpO$_2$ be maintained no higher than 96%.	Strong
For adults with COVID-19 and **acute hypoxemic respiratory failure** despite conventional oxygen therapy, we **suggest using** HFNC over conventional oxygen therapy.	Weak
In adults with COVID-19 and **acute hypoxemic respiratory failure**, we **suggest** using HFNC over NIPPV.	Weak
In adults with COVID-19 and **acute hypoxemic respiratory failure**, if HFNC is not available and there is no urgent indication for endotracheal intubation, we **suggest** a trial of NIPPV with close monitoring and short-interval assessment for worsening of respiratory failure.	Weak
We were not able to make a recommendation regarding the use of helmet NIPPV compared with mask NIPPV. It is an option, but we are not certain about its safety or efficacy in COVID-19.	No Recommendation
In adults with COVID-19 receiving NIPPV or HFNC, we **recommend** close monitoring for worsening of respiratory status, and early intubation in a controlled setting if worsening occurs.	Best practice statement
In mechanically ventilated adults with COVID-19 and ARDS, we **recommend** using low tidal volume (Vt) ventilation (Vt 4-8 mL/kg of predicted body weight), over higher tidal volumes (Vt>8 mL/kg).	Strong
For mechanically ventilated adults with COVID-19 and ARDS, we **recommend** targeting plateau pressures (Pplat) of < 30 cm H$_2$O.	Strong
For mechanically ventilated adults with COVID-19 and moderate to severe ARDS, we **suggest** using a higher PEEP strategy, over a lower PEEP strategy. **Remarks**: If using a higher PEEP strategy (i.e., PEEP > 10 cm H$_2$O), clinicians should monitor patients for barotrauma.	Strong

For mechanically ventilated adults with COVID-19 and ARDS, we **suggest** using a conservative fluid strategy over a liberal fluid strategy.	Weak
For mechanically ventilated adults with COVID-19 and **moderate to severe ARDS**, we **suggest** prone ventilation for **12 to 16 hours**, over no prone ventilation.	Weak
For mechanically ventilated adults with COVID-19 and **moderate to severe ARDS**: We **suggest** using, as needed, intermittent boluses of neuromuscular blocking agents (NMBA), over continuous NMBA infusion, to facilitate protective lung ventilation.	Weak
In the event of persistent ventilator dyssynchrony, the need for ongoing deep sedation, prone ventilation, or persistently high plateau pressures, we **suggest** using a continuous NMBA infusion for up to 48 hours.	Weak
In mechanically ventilated adults with COVID-19 ARDS, we **recommend against** the routine use of inhaled nitric oxide.	Weak
In mechanically ventilated adults with COVID-19, severe ARDS and hypoxemia despite optimizing ventilation and other rescue strategies, we **suggest** a trial of inhaled pulmonary vasodilator as a rescue therapy; if no rapid improvement in oxygenation is observed, the treatment should be tapered off.	Weak
For mechanically ventilated adults with COVID-19 and hypoxemia despite optimizing ventilation, we **suggest** using recruitment maneuvers, over not using recruitment maneuvers.	Weak
If recruitment maneuvers are used, we **recommend against** using staircase (incremental PEEP) recruitment maneuvers.	Strong
In mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimizing ventilation, use of rescue therapies, and proning, we suggest using **venovenous** (VV) ECMO if available, or referring the patient to an ECMO center. **Remark:** Due to the resource-intensive nature of ECMO, and the need for experienced centers and healthcare workers, and infrastructure, ECMO should only be considered in carefully selected patients with COVID-19 and severe ARDS.	Weak

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