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MANAGEMENT & PRACTICE

INTENSIVE CARE - EMERGENCY MEDICINE - ANAESTHESIOLOGY

VOLUME 21 - ISSUE 1 - 2021

**SPECIAL SUPPLEMENT**
Sedation in Critically-Ill COVID-19 Patients

# 20 Lessons from 2020



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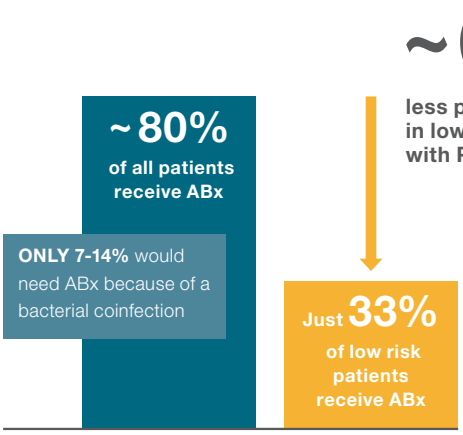


**Antibiotic treatment of COVID-19 patients[1]**

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# 20 Lessons from 2020

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ICU_Management

The COVID-19 pandemic has had a significant impact on ICUs and critical care healthcare providers all across the globe. As of this week, 110 million people have been infected with the virus worldwide, and 2.4 million have died. Many of the infected patients need hospitalisation and admission to the ICU. A high percentage of severely ill patients with COVID-19 require mechanical ventilation. Hence, ICUs have had their work cut out for them and have faced many challenges, including the management of high patient flow, appropriate allocation of resources, the need to balance care of patients with COVID-19 and those with other critical illnesses, restructuring workflows, and ensuring the safety of healthcare workers, patients and their families.

As ICU workers around the world deal with the rapidly changing situation of COVID-19, there is a need for clinicians to evaluate and review how we performed during this crisis, what we did well and what we could have done better. It is time to evaluate the data and synthesise evidence-based guidelines to better guide the management of patients with COVID-19.

In this issue, our contributors talk about **20 Lessons from 2020.** Nicole Juffermans and I talk about these lessons with a focus on the ICU perspective. This year has been quite unusual, and we review what happened and what lessons we learned from our combined experiences.

Audrey De Jong, Yassir Aarab and Samir Jaber evaluate whether videolaryngoscopy is the new gold standard for intubation following the COVID-19 crisis while Andrej Michalsen and Kateřina Rusinová question whether prioritisation decisions are really a physicians' problem.

Vitaly Herasevich, Jeremy Clain and Brian Pickering provide an overview of the large-scale transition to telemedicine during the COVID-19 pandemic and how telemedicine could rapidly transform healthcare.

Lukas Martin, Arne Peine, Gernot Marx and Johannes Bickenbach highlight the use and challenges of digitalisation and artificial intelligence and how the focus should be on providing less rather than more data. Orlando Ruben Perez-Nieto and co-authors talk about prone position in awake, non-intubated patients with ARDS.

Ashish Khanna, Piyush Mathur, Jacek Cywinski and Kamal Maheshwari discuss the prevention of perioperative patient harm and the importance of continuous and better patient monitoring for early detection and prevention. Jodi Allen, Gabrielle Rossano and Jackie McRae describe the experiences of Speech and Language Therapy and the upper airway challenges associated with extubation and oral management in COVID-19 patients.

2020 was a challenging year, and as we continue to manage the second wave, we know that there are things that must change. Critical care providers all over the world have faced distress and burnout. Patients and families are equally stressed. There is the challenge of limited resources and critical decisions. Changes must be made, and as we persevere, I am confident that we will come out stronger and better.

As always, if you would like to get in touch, please email JLVincent@icu-management.org

**Jean-Louis Vincent**

# 20 LESSONS FROM 2020

## COVER STORY



## IN EVERY ISSUE



## SPECIAL SUPPLEMENT (pp. 5-12)


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## POINT OF VIEW

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# Sedation in Critically-Ill COVID-19 Patients

Report of a Symposium Presented at LIVES 2020
33rd Congress of the European Society of Intensive Care Medicine

**Moderator**
**Vito Marco Ranieri** *(Bologna, Italy)*

**Speakers**

***Why Do We Need Sedation in Critically-Ill COVID-19 Patients?***
**Salvatore Maurizio Maggiore** *(Chieti, Italy)*

***How Should We Manage Sedation in Critically-Ill COVID-19 Patients?***
**Boris Jung** *(Montpellier, France)*

**The COVID-19 pandemic has wreaked havoc across the globe. Clinicians worldwide have been battling the pandemic while managing critically-ill patients infected with the coronavirus. Critical cases of COVID-19 are characterised by respiratory failure, septic shock and multiple organ dysfunction. Sedation of critically-ill patients is a complex intervention, especially keeping in mind that COVID-19 is a new disease and determining optimum levels of sedation through the course of the infection remains challenging for clinicians.**

**This symposium discussed sedation in critically-ill COVID-19 patients and provided an overview of the need for sedation, when to sedate and how to manage sedation in these patients. The symposium concluded with a Question and Answer session where experts answered important questions regarding sedation and management of these patients.**

Supplement in collaboration with Aspen Pharma

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# Why Do We Need Sedation in Critically-Ill COVID-19 Patients?

COVID-19 patients present to the hospital with lung involvement and interstitial pneumonia eventually associated with lung collapse. The clinical picture is dominated by severe hypoxaemia without dyspnoea/tachypneoa and normal respiratory mechanics; this condition has been defined as silent hypoxia. The picture may evolve, and these patients may present with severe refractory hypoxaemia associated with dyspnoea/tachypnoea, use of accessory muscles of respiration, and respiratory mechanics impairment.

Silent hypoxia is linked to the mechanism of dyspnoea. Dyspnoea occurs due to a perceived mismatch between the outgoing efferent signals from the respiratory centre to the ventilatory muscles and incoming afferent signals from the lungs and the chest wall to the respiratory centre. These afferent signals may be triggered by hypercapnia or severe hypoxaemia, airway and interstitial inflammation and impaired lung mechanics. COVID-19 patients can have impairment of lung function, both at the alveolar level and at the intravascular level but a very low level of oxygenation (as low as 30 mmHg) needs to be reached to have dyspnoea, which is mediated by an increase in $CO_2$, in minute ventilation and in the effort to breathe. In the beginning, patients can be treated with simple oxygen therapy followed by mechanical respiratory support as needed (Dhont et al. 2020).

## Goals of Mechanical Respiratory Support in COVID-19 Patients

The most important goals of mechanical respiratory support are:

- To improve oxygenation
- To support the respiratory muscles
- To prevent additional lung injury

## Noninvasive Support and Guidelines in Hypoxaemic Acute Respiratory Failure

Besides standard oxygenation techniques, different forms of non-invasive support can be used in hypoxaemic patients. These include Nasal High Flow (NHF), continuous positive airway pressure (CPAP), and non-invasive positive pressure ventilation (NIPPV). NHF delivers high gas flow and is a technique that can increase the airway pressure and can generate a positive end-expiratory pressure (PEEP). With CPAP, a single value of airway pressure is set and this pressure is usually higher than that provided by NHF. With NIPPV two levels of pressure are set: the lowest is maintained during expiration and the highest is reached during inspiration to support the respiratory muscles.

COVID-19 is a new disease. The ERS/ATS clinical practice guidelines for use of noninvasive ventilation in hypoxaemic acute respiratory failure should be referred to when dealing with this patient population. Several studies show conflicting results, and overall there is no effect of NIV on mortality. Given the uncertainty of evidence, the guidelines state that it was not possible to offer any reccomendation about the use of NIPPV in hypoxaemic patients (Rochwerg et al. 2017).

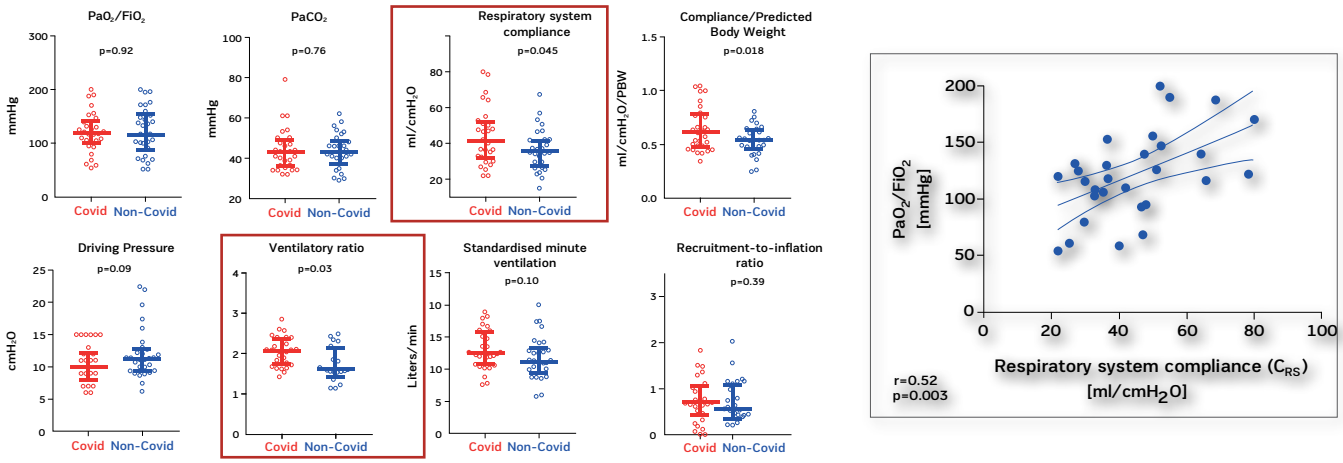


**Figure 1.** COVID-19 ARDS vs. ARDS from other aetiologies. Adapted from Grieco et al. 2020

Results of a recent meta-analysis may further help to guide NIPPV use in hypoxaemic patients, including those with COVID-19. Findings show that, as compared with standard oxygen, NIPPV may reduce mortality, particularly when it is delivered with helmet. As compared with both face mask NIPPV and NHF, helmet NIPPV might give better results, thus being preferable in patients with hypoxaemic respiratory failure (Ferreyro et al. 2020).

New guidelines were released regarding the use of NHF in hypoxaemic respiratory failure. Based on the results of the meta-analysis, the panel gave a strong recommendation for the use of NHF compared to standard oxygenation in these patients (Rochwerg et al. 2020).

There are risks associated with noninvasive respiratory support. These include:

- Environmental contamination
- Intubation delay
- Patient self-inflicted lung injury, due to high respiratory drive (Brochard et al. 2017).

## Sedation and Analgesia During NIPPV

Sedation can manipulate respiratory drive, typically very high in COVID-19 patients, when breathing spontaneously. However, it is important to remember that the results of using analgosedation are not always positive. A study by Muriel et al. (2015) suggests that compared to no sedation, use of analgesia, sedation or both was associated with an increase in NIPPV failure and 28-day mortality. Therefore, sedation in COVID-19 patients during NIPPV is not recommended, especially because many of these patients may not have dyspnoea. If the patient's condition worsens, the only solution is to use intubation and invasive mechanical ventilation.

## COVID-19 ARDS vs. ARDS From Other Aetiologies

It is being debated if COVID-19 ARDS is similar to traditional ARDS or different. At the beginning of the pandemic, these data were not available, but more data have been produced since then. In a study by Grieco et al. (2020), 30 patients with moderate to severe COVID-19 related ARDS were matched with 30 other patients with ARDS from other aetiologies. All patients were studied within 24 hours from intubation. Two PEEP levels were applied – 5 and 15 $cmH_20$ to assess the response of these patients to PEEP and lung recruitability.

Several parameters were compared between COVID-19 and non-COVID-19 patients **(Figure 1)**. From a clinical point of view, all measured parameters, including gas exchange, compliance, driving pressure, ventilatory ratio (a measure of deadspace), minute ventilation and the recruitment-to-inflation ratio (a measure of recruitability), were similar in COVID-19 and non-COVID-19 patients, although compliance and ventilatory ratio were statistically higher in COVID-19 patients. It is important to note that all these parameters showed a high variability both in COVID-19 and in non-COVID-19 patients. In COVID-19 patients, a direct correlation was also observed between compliance and oxygenation. Because compliance is an index of lung aeration, this correlation indicates that oxygenation improved with improving lung aeration, as it has been described in traditional ARDS (Grieco et al. 2020).

As far as response to PEEP is concerned, the results were similar in both COVID-19 and non-COVID-19 cohorts. High-level PEEP improved oxygenation in both cohorts. There was a similar response in terms of ventilatory ratio, compliance and driving pressure in both cohorts. High PEEP resulted in a greater improvement of oxygenation in COVID-19 patients compared to traditional ARDS, but the improvement in oxygenation was not related to the index of recruitability. Recruitability was correlated to a decrease in $PCO_2$. Overall, findings from this study show that after the establishment of mechanical ventilation, patients with COVID-19 show a conventional ARDS phenotype (heterogeneity in respiratory mechanics, aeration loss related to the degree of hypoxaemia and inter-individually variable recruitability) and that clinicians treating COVID-19 patients should adhere to recent guidelines regarding standard ARDS management (Grieco et al. 2020).

These findings have been confirmed by another study conducted in 301 COVID-19 ARDS patients who were compared to 2634 traditional ARDS patients. In both groups, compliance was highly variable and values were very similar from a clinical perspective, although slightly higher in COVID-19 patients. Total lung weight was also similar. Authors also described lung thrombo-embolic events in COVID-19 patients, particularly when high compliance was associated with high levels of D-dimers, and these thrombo-embolic phenomena have been described also in traditional ARDS. Study authors concluded that patients with COVID-19 associated ARDS

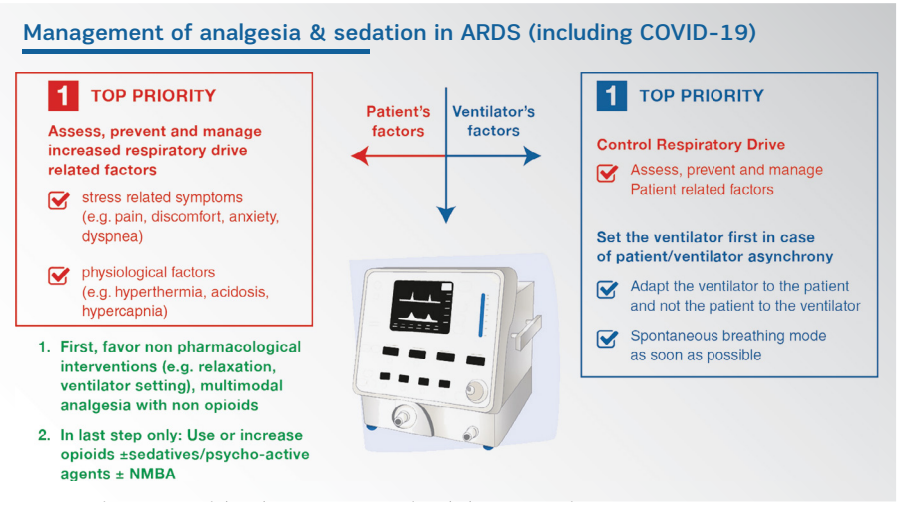


**Figure 2.** Management of analgesia and sedation in ARDS. Source: Chanques et al. 2020

have a form of injury that, in many aspects, is similar to that of those with ARDS unrelated to COVID-19 (Grasselli et al. 2020).

## Protective Ventilation in COVID-19 ARDS

Following the previous reasoning, it is important, also in COVID-19 related ARDS, to follow the official clinical practice guidelines of the American Thoracic Society (ATS), European Society of Intensive Care Medicine (ESICM), and Society of Critical Care Medicine (SCCM) (Fan et al. 2017), for the management of mechanical ventilation in ARDS, which recommend:

- To use low tidal volume (4-8 ml/kg PBW) and low plateau pressures (<30 cmH20)
- To use prone position in severe ARDS (>12 h/day) and suggest to use higher PEEP and recruitment manoeuvres in moderate-severe ARDS.

However, it is important to individualise ventilation strategies in both traditional and COVID-19 ARDS patients. This should be done taking into consideration the risks associated with aggressive mechanical ventilation, including shear stress, overdistention, or increase in intrathoracic pressure, which can further injure the lung and have been linked to the spillover of bacteria and inflammatory mediators from the lung into systemic circulation. This can cause damage to the distal organs leading to multi-organ failure (Slutsky and Tremblay 1998).

In fact, it is known that aggressive mechanical ventilation can have harmful effects on the patient. For example, a Brazilian study compared the use of an aggressive ventilator strategy, with lung recruitment manoeuvres and a high PEEP level, in patients with ARDS to a low/moderate PEEP level strategy. Findings from this study show that aggressive mechanical ventilation was associated with increased mortality and an increase in complications like pneumothorax, barotrauma and shock, suggesting that an aggressive mechanical ventilation strategy may have deleterious effects also at the cardiovascular level (Cavalcanti et al. 2017).

Sedation may be useful to limit another risk of mechanical ventilation, that is patient ventilator dyssynchrony. If there is a mismatch between the patient's breath and ventilator-assisted breaths, and the ventilator's flow delivery does not match the patient's flow demand, it can generate a dyssynchrony, i.e. double cycling, which can have a negative impact on the patient. This can be managed by sedation while ensuring no oversedation or undersedation.

There is a relationship between ventilatory management and sedation management. A recent review of analgesia and sedation management in ARDS, including patients with COVID-19, highlights the importance of optimising sedation. As per this review, the most important priorities are to manage increased respiratory drive, and to optimise ventilation to avoid ventilator dyssynchrony (Chanques et al. 2020).

In conclusion, the primary reasons for sedation in COVID-19 patients include improving patient comfort (pain, anxiety and dyspnoea), enhancing patient safety (during special manoeuvres such as proning), facilitating lung-protective mechanical ventilation, and treating ventilator dyssynchrony by controlling the respiratory drive. Also, aims of sedation in all ARDS patients, including those with COVID-19, are to maintain patient interaction with staff and family and to promote early physical and cognitive recovery. ■

### Key Points

- NIPPV should be applied on an individual basis when managing COVID-19 patients, paying attention not to delay intubation if required.
- Sedation during NIPPV is generally not needed in COVID-19 patients.
- Patients with COVID-19 show a conventional ARDS phenotype and should be treated using guidelines regarding standard ARDS management.
- There is a relationship between ventilatory management and sedation management and the priorities should be to manage increased respiratory drive, to optimise ventilation and to avoid ventilator dyssynchrony.

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# How Should We Manage Sedation in Critically-Ill COVID-19 Patients?

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## Clinical Practice Guidelines

The Choosing Wisely top five guidelines published a few years ago by the Chest Association of Physicians, the American Thoracic Society, the Society of Critical Care Medicine, and the American Association of Critical Care Nurses state that mechanically ventilated patients should not be deeply sedated without a specific indication and without daily attempts to lighten sedation (Halpern et al. 2014). This is a very important recommendation, especially when discussing sedation in critically-ill COVID-19 patients.

Findings from a landmark study published by the Chicago Study Group 20 years ago showed that if daily sedation is interrupted in mechanically ventilated patients, the duration of mechanical ventilation can be shortened (Kress et al. 2000).

### Pain

The most recently published guidelines from 2018 recommend a checklist. The first step is to make sure that mechanically ventilated patients are not in pain. Pain should be measured using appropriate scales, and pain management should be initiated with intravenous opioid drugs but also non-opioid analgesics to spare the excessive use of opiates. The most commonly used scale is the Behavioral Pain Scale (BPS) that ranges from 3 to 12, 3 representing a patient with no pain at all and 12 being a patient experiencing very intense pain.

### Sedation

The next step, once the pain is treated, is sedation. The 2018 guidelines suggest that light sedation and not deep sedation should be used in critically-ill mechanically ventilated adults. Light sedation is associated with a shorter duration of invasive mechanical ventilation and reduced tracheotomy rates (Devlin et al. 2018).

In a multi-centre study, authors showed that most of the patients were deeply sedated in their first 48 hours of the ICU stay. However, this proportion decreased with time. In this study, deep sedation was associated with a longer time to extubation and a lower survival rate. Deep sedation was also associated with a higher mortality rate three months after the ICU stay (Shehabi et al. 2012).

Light sedation can be defined using scales. One of the most used scales is the Richmond Agitation and Sedation Scale, known as the RASS scale. Light sedation is between -2 to +1. Light sedation and sometimes even no sedation can be performed in many mechanically ventilated patients. In a randomised trial published in 2020 in the New England Journal of Medicine, the authors showed that no sedation or light sedation could be performed in many patients admitted to the ICU, those who are mechanically ventilated and even with pneumonia or ARDS (Olsen et al. 2020). As shown in **Figure 1,** results from the study show that in the light sedation group, the mean RASS score was between -2 and -3 in most patients. An important thing to note is that in these ICUs in Scandinavia mostly, the patient to nurse ratio was 1:1, meaning that the nurses were readily available to make sure that the patient wouldn't self-extubate or be at risk of severe agitation.

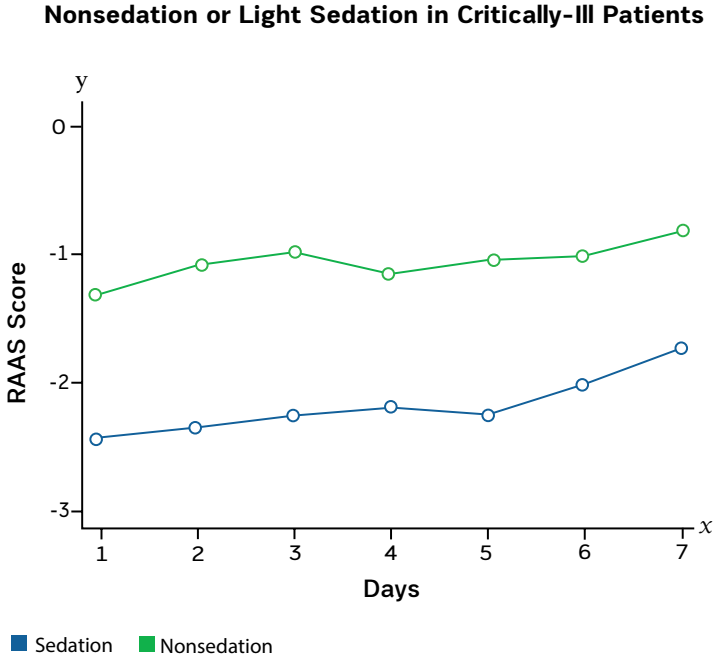


**Figure 1.** Nonsedation or Light sedation in critically-ill, mechanically ventilated patients. Adapted from Olsen et al. 2020

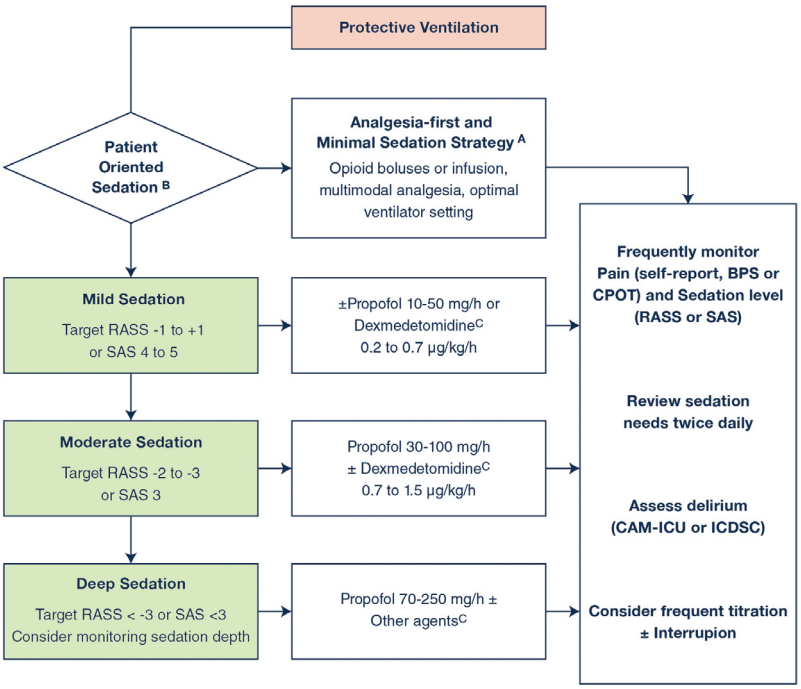


**Figure 2.** Analgesia and sedation without NMBA for protective lung ventilation strategy. Source: Chanques et al. 2020

## Which Drugs Should Be Used?

Guidelines recommend that benzodiazepines should not be used because the use of other drugs is associated with a shorter duration of mechanical ventilation, shorter duration of ICU stay, and less delirium. Benzodiazepines also have one major side effect - more self-extubation.

ARDS is one of the few indications of deep sedation. Deep sedation can be defined by a RASS score between -4 to -5 (Devlin et al. 2018). Some of these patients may need neuromuscular blocking agents (NMBA) to treat ARDS. Findings from a landmark study published in France ten years ago in the New England Journal of Medicine show that Cisatracurium, which is one of the most commonly used NMBA, is associated with better survival compared to placebo (Papazien et al. 2010). More recently, the ROSE trial published by the PETAL Clinical Trials Network in the U.S. did not produce the same results. Findings from this RCT, which enrolled 1000 patients showed that light sedation could be performed by day one in almost 30% of ARDS patients. However, none of them were COVID-19 patients (Moss et al. 2019).

With respect to the use of NMBAs in ARDS, the guidelines and recent reviews based on the RCTs suggest that NMBAs should be avoided in ARDS unless there is:

- Moderate to severe ARDS with a P/F ratio < 150 AND
- Severe dyssynchronies despite deep sedation OR
- High level of inspiratory efforts or respiratory drive
- NMBAs should be reassessed within 24 hours

Another important review published and coordinated by Chanques et al. (2020) summarises how sedation and NMBAs should be used in ARDS patients. According to this review, protective ventilation is the key in ARDS, but if protective ventilation is obtained, it is important to first target mild sedation with almost awake patients using small doses of propofol with or without dexmedetomidine. Moderate sedation should be used if mild sedation is not tolerated by increasing the dose of propofol and dexmedetomidine. Deep sedation should remain at the end of the checklist if the patient is not fully synchronised to the ventilator. Propofol should be used as the first-line drug and then other agents. It is important to keep in mind that some of these patients may need NMBAs even if they are deeply sedated.

## Is There a Difference Between COVID-19 Patients and Routine ARDS Patients?

The answer to this question is both yes and no. Yes, because there have been many patients admitted to the ICU for respiratory failure related to COVID-19 disease, generating a very high health care workers workload. Because ARDS is a very classic indication of deep sedation, and in some of these patients, light sedation is not associated with protective ventilation, many of these patients would require deep sedation. That is why during the pandemic, there have been many deeply sedated patients in ICUs. Also, COVID-19 is a droplet and airborne transmitted disease. Since there have been many patients admitted to the ICU for respiratory failure, generating a very high workload for healthcare workers, and requiring them to wear personal protective equipment, there is a temptation for deeply sedating patients to decrease the risk of incidents such as self-extubation. Because of this high use of sedation during these times and the high flow of patients in severely affected regions, there is a risk of a shortage of deep sedation drugs.

Over the last few months, there have been many reviews and expert opinions, but no comparative studies have been conducted that show that one of these drugs (benzodiazepines, dexmedetomidine, ketamine, volatile sedation, non-opioid analgesics, morphine and other opioids) would be better than the other in COVID-19 patients. Hence, for most clinicians, the strategy has been to follow local policy as well as make decisions based on the availability of drugs. Some of these drugs, such as volatile sedation, are under investigation in ARDS. There is an ongoing RCT in France where intravenous sedation drugs are compared to volatile sedation to see whether volatile sedation would be associated with better outcomes (Ammar et al. 2021; Adams et al. 2020).

## COVID-19 and the Brain

One particularity of the COVID-19 disease is that the hippocampus is one of the targets of the virus generating a local inflammatory brain response. There is also a possible brain invasion of the virus through olfactory nerves

and systemic acute brain injury related to hypoxia, inflammation, and endothelialitis. All these pathophysiological pathways lead to cognitive impairment and a high risk of ICU-associated delirium. Recovery times are not yet known, but may be prolonged. No study so far has reported the need for higher doses of sedative drugs in ARDS patients with or without COVID-19 disease.

In conclusion, severe COVID-19 patients may need deep sedation and NMBAs but the goal should always be to target light sedation once we make sure that mechanical ventilation is lung and muscle protective. ■

## Key Points

- Mechanically ventilated patients should not be deeply sedated without a specific indication and without daily attempts to lighten sedation.
- Light sedation is associated with a shorter duration of invasive mechanical ventilation and reduced tracheotomy rates.
- ARDS is one of the few indications of deep sedation and some patients may require NMBAs to treat ARDS.
- Protective ventilation is the key in ARDS; if not obtained, the first target should be mild sedation.
- Moderate sedation should be used only if mild sedation is not tolerated. Deep sedation should remain at the end of the checklist.

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# Important Questions Answered

During the question/answer session, Prof Vito Marco Ranieri discussed some important questions with Prof Salvatore Maurizio Maggiore and Prof Boris Jung regarding sedation regimen, respiratory muscle paralysis, sedation in COVID-19 patients specifically and how it is different from other regular ICU patients.

**Ranieri: What is your opinion on deep sedation using remifentanil and propofol targeting RASS -4?**

**Maggiore:** Before this pandemic, this analgosedation regimen was our standard, and that was usually the way we sedated patients. We do know that COVID-19 patients require prolonged sedation, and we also know, that, in general, the longer the sedation, the longer the patient stays in the ICU. Therefore, deep sedation increases the risk of prolonged sedation.

**Jung:** I would say that we do use remifentanil for other types of patients that are not COVID-19. We haven't used remifentanil either, exactly for the reason that Prof Maggiore mentioned because most of them would need prolonged sedation. That is why we use sufentanil in our unit.

**Ranieri: How often is respiratory muscle paralysis needed in the presence of deep sedation?**

**Jung:** I don't have any exact numbers, but we've seen around 200 COVID-19 patients in my unit. I would say that, in deeply sedated patients, at least 30 to 40% need continuous NMBAs, and around 20 to 25% would need prolonged NMBAs infusion for more than 48 hours.

**Maggiore:** I agree. We have a similar experience. The rate of patients receiving NMBAs was even higher. But this is dependent on the criteria for admission to the ICU and the severity of patients at ICU admission. All patients in our ICU were severely ill, especially in the beginning. I would say that the percentage of patients receiving NMBAs, in our case, was between 50% and 60% and the use of NMBAs was often prolonged for more than 48 hours.

**Ranieri: So in a way, both of you challenge the knowledge that you can replace the use of respiratory muscle paralysis with deep sedation, a concept that some years ago was proposed by several groups?**

**Maggiore:** The problem is not just severity but also the procedures that are undertaken in these patients. For example, for us, it is usual that during pronation, the patients are paralysed. I know that proning is performed without sedation in other instances, but considering the number of patients who were pronated during COVID-19, around 80% in our case, and the high workload for the personnel, I feel it was safer to perform this procedure when patients were paralysed.

**Jung:** We have the same experience. In our unit, 70% of patients underwent prone positioning with high use of NMBAs at the very early stage of their stay because of the high workload.

**Ranieri: Are COVID-19 patients difficult to sedate, and what is your opinion on the use of dexmedetomidine for sedation as an alternative to propofol and morphine-like agents?**

**Maggiore:** We did not find that COVID-19 patients are more difficult to sedate compared to classical ARDS. Also, we did not use dexmedetomidine in the very early phase. We usually use this drug when shifting to a light sedation strategy.

**Jung:** I agree. There are a lot of studies out there that have shown that dexmedetomidine may not be the best agent to provide deep sedation but can be an alternative for light sedation. I wouldn't say that it's propofol versus dexmedetomidine at the very early stage.

**Ranieri: Any experience with dexmedetomidine with NIV?**

**Maggiore:** Not for us because we applied non-invasive mechanical respiratory support almost exclusively outside the ICU and management of sedation in this scenario would be even more complicated.

**Ranieri: What is your experience in the use of EEG monitoring to optimise sedation and patient comfort?**

**Maggiore:** We have no experience of this. These patients received deep sedation during the very early phase,but we have not used this technique. When a patient is improving, I believe that the best strategy is to try to stop sedation as soon as possible and continue to monitor clinically the neurological status regularly.

**Jung:** In our unit, we use the BISPECTRAL index in patients who were paralysed within a target of 40 to 60. It's not a magical tool, but it can be useful.

**Ranieri: What is your opinion on the use of volatile sedation?**

**Jung:** Our team decided not to use volatile sedation during the first wave mainly because of the risk of airborne and droplet transmission to the healthcare workers. But in our usual practice otherwise, we use it quite a few times a year. We have also used it during the second wave for a patient who was really difficult to sedate and who needed a very high dose of propofol. So, we switched to volatile sedation, which worked. But overall, we chose not to use a lot of volatile sedation during COVID-19 because of the risk of infection transmission.

**Maggiore:** We are introducing this technique. Therefore, we do not have sufficient experience with this.

**Ranieri: Are there any differences between the first and second waves in terms of the need for sedation? What has been your experience?**

**Maggiore:** We have not observed any difference. In our experience, patients we have seen during the second wave are similar to the first wave, therefore there has not been much difference in terms of sedation.

**Jung:** I agree. We have also not observed any difference.

**Ranieri: Do you think that the sedation policy is strongly influenced by the level of organisation or support that we are able to provide in terms of human resources? If you have a full set of ICU with the required staff in terms of nurses and physicians, you may use a more sophisticated sedation policy. But if you are running 150 ICU beds with nurses coming from the operating theatre, or there is an intensivist recruited from the urologist floor, you may use a more basic approach for sedation. What do you think?**

**Maggiore:** I completely agree. This is also true during the management of classic ICU patients, not just COVID-19, for example, during procedures like weaning, and also for ARDS management. This is not something new, and yes, I agree.

**Jung:** We usually use a nurse driven protocol to lighten sedation as much and as early as possible. With such a high workload and the hygiene precautions it is however difficult to enter so many times in ICU rooms to adjust sedation. There is therefore a temptation of using like you said a much easier and more basic sedation protocol. However I'd really recommend to reassess the need of deep sedation at least every 4h both for the patients outcome and to optimise ICU length of stay.

**Ranieri: You discussed the ROSE Trial regarding the use of NMBAs in patients with ARDS and also compared it to the ACURASYS Study. Would you like to highlight the difference between the two trials and summarise apparently contradictory results?**

**Jung:** There are many differences between the two trials. In the ROSE trial, the PEEP level was very high compared to the ACURASYS trial. Patients could be enrolled earlier in the ROSE trial, and ventilation strategy was also different between the two trials. What I would suggest, as the authors of these studies did, is that if you start using NMBAs in ARDS patients, you may want to reassess its indication at least every day or every 24 hours to make sure that the patient really needs an NMBA because the two trials were very different from one another.

**Maggiore:** The two studies actually compared totally different things because the level of sedation was different, and the level of PEEP was higher in the ROSE trial. We have data showing that maintaining some form of spontaneous breathing with a high PEEP level may be protective for the lung. This may be one of the reasons the results of the ROSE trial are quite different as compared to the ACURASYS trial.

**Ranieri: There is a perception that COVID-19 patients are more complex than others, that the level of stress these patients are experiencing is different than the usual level of stress in regular patients admitted to the ICU. There has also been an exponential increase in workload. The patient's stress and the patient's need for sedation are probably tied to the healthcare system that has also reached the limits. Is that why these patients appear to be different? Or are these patients similar to other ICU patients with the same need in terms of sedation, mechanical ventilation, and it is the healthcare workers who are different. What do you think?**

**Maggiore:** I completely agree. We have always been aware of the limits of the system in terms of beds and equipment. However, the real issue is the personnel in terms of numbers, competencies, and workload. We have data showing that healthcare workers during the first wave of the pandemic had, in fact, a very high level of burnout. This is a fact.

**Jung:** I would not say that these patients are more difficult to care about than the usual virus associated ARDS with extra precautions taken regarding venous thrombosis. I would however say that the massive volume of patients, the risk of contamination and the high workload have made things very tough and demanding worldwide. ■

GL-ANA-02-21-00001

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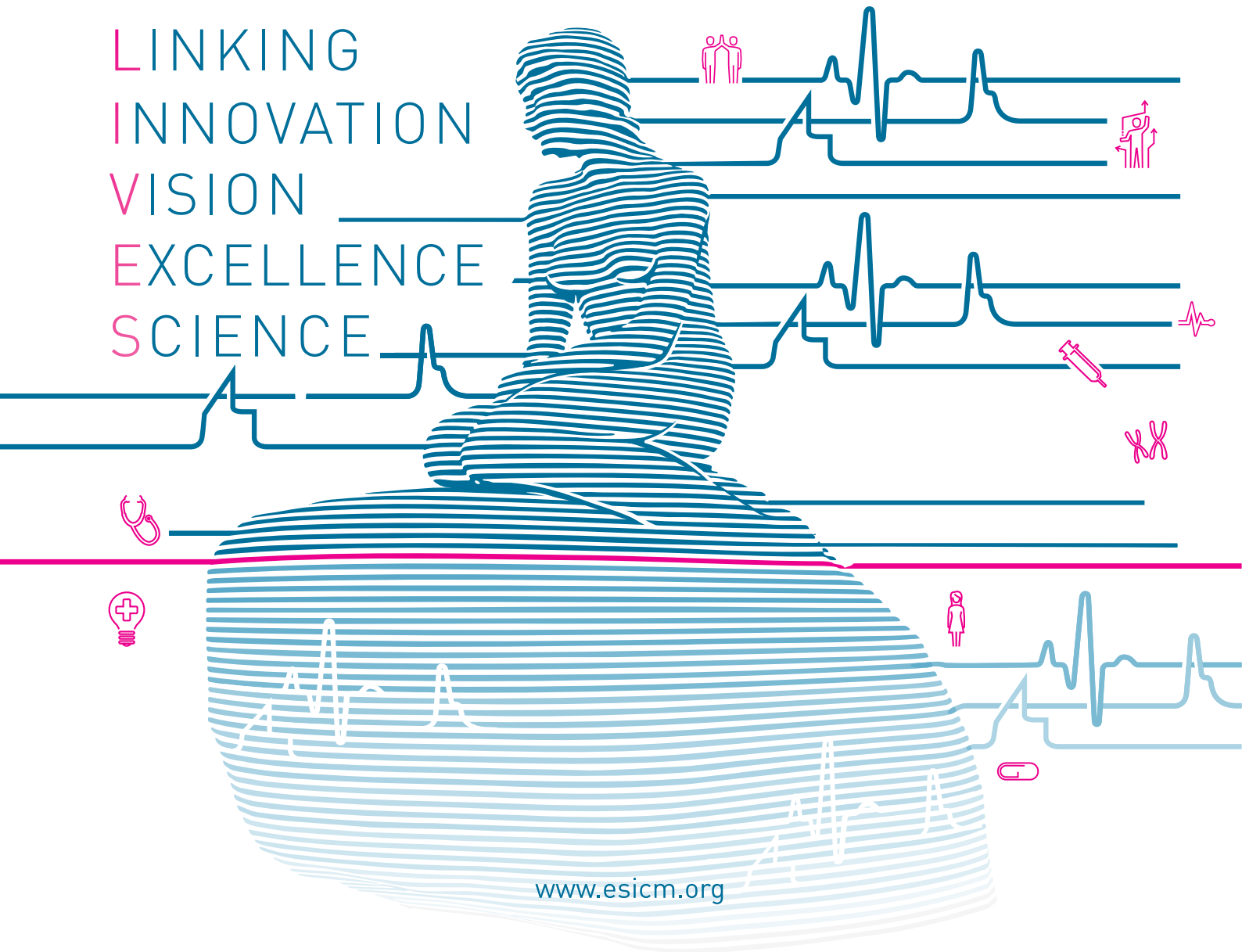

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# Twenty Lessons from 2020: With a Focus on the ICU Perspective

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2020 has been an unusual year. As we begin 2021, it is important for intensivists to look back over what has happened and see whether lessons can be learned from our combined experiences.

The year 2020 has been unusual in so many ways and as we start a new year, it is interesting and important as intensivists to look back and reflect on what has happened. Populations worldwide have experienced lockdowns, confinement and quarantine, and healthcare systems have been challenged globally by surges in the number of patients requiring hospitalisation and intensive care. Importantly, although faced by the same threat, countries vary hugely in terms of facilities available for testing, protective equipment, medical equipment and staffing, and hospital and ICU bed availability. Nevertheless, lessons can be learned from our combined experiences to help improve ICU care in all parts of the world.

**1. Informing government and policymakers about ICU occupancy and consequences is paramount**

In countries where leaders have negated the scope and impact of COVID-19, measures to limit the spread of the virus were not taken or were taken too late, resulting in higher mortality rates. Lack of awareness or lack of information may have contributed to this situation. Intensivists should be part of national outbreak management teams to inform policymakers about ICU capacity and evaluate optimal population health and safety measures, including social distancing.

**2. We could have prepared better, earlier**

Many hospitals had problems with basic supplies of protective equipment to ensure staff safety. Sufficient stocks should have been available and potential alternative supply chains already identified to be actioned before the issue became a problem.

**3. Better training and intensivist support should be available for non-ICU staff**

Plans to convert beds from other wards into temporary ICUs were often in place, but many of the nurses and doctors who volunteered to care for patients on these units had little experience of intensive care and there were few strategies in place to rapidly train these staff members in the necessary basics of ICU care. A pyramid approach should be in place such that ICU doctors supervise non-ICU doctors and ICU nurses supervise non-ICU nurses.

**4. COVID-19 is a form of viral sepsis**

COVID-19 is a condition in which a viral infection causes organ failure associated with a dysregulated host response, i.e., COVID-19 is sepsis. This highlights that, although most commonly associated with bacterial infection, sepsis can also be caused by viruses, fungi, or parasites. The realisation that patients with COVID-19 have sepsis has important implications for the ways in which we treat them.

**5. Pharmacological management should be individualised and considered in terms of the dual phases of viral replication and inadequate host response**

As in other areas of critical care, one size fits all treatment strategies are inadequate in COVID-19 and treatments should rather be personalised. It is important to understand the mode of action of proposed therapies for COVID-19 and use them appropriately. For example, anti-viral drugs, in particular the use of remdesivir, have given disappointing results in critically ill patients in whom the key phase of viral replication is less important than the dysregulated host response. These patients may rather benefit from immunomodulatory agents. The administration of dexamethasone is about the only treatment that has shown effectiveness in severely ill patients. Biomarkers may help to identify the

right treatment for the right patient at the right time. However, further research is necessary to identify which biomarkers are optimal.

**6. COVID-19 is a thrombotic coagulopathy**
As our understanding of the pathophysiology of COVID-19 improved, we realised that it is associated with a thrombotic coagulopathy state with high rates of venous thromboembolism and arterial thrombosis. As such, we have moved towards increasing the level of anticoagulant therapy to patients with severe COVID-19.

**7. Acute respiratory failure is not always ARDS**
COVID-19 respiratory failure was initially widely considered as ARDS in all patients and treated as such. There have been discussions about type 1 and type 2 respiratory failure in severe COVID-19, but the type 1 may just represent an earlier stage of the disease. ARDS associated with COVID-19 is not very different from other forms. Discussions about pulmonary compliance were largely superfluous, because we need to individualise patient management rather than use the same settings for everyone.

**8. The type of respiratory support will vary for different patients and at different stages of the disease**
There is no need to intubate the trachea when non-invasive support is sufficient. Continuous positive airway pressure (CPAP) can be adequate in some patients and different systems with, for example, helmets etc., have been successfully implemented. This approach helps save mechanical ventilators for those patients who cannot be managed non-invasively. We have also appreciated that proning in COVID-19 patients receiving mechanical ventilation is important, despite the high workload required for this technique, as it at least improves oxygenation. We learned it might also be of value in some patients receiving non-invasive ventilation.

**9. COVID-19 can present with severe cardiovascular syndromes**
The presenting symptoms of COVID-19 need not be respiratory. In addition to an increased risk of myocardial infarction, COVID-19 can present with life-threatening arrhythmias. Although rare, myocarditis with heart failure and severe cardiogenic shock can occur. Following the first wave, a novel multiple inflammatory syndrome was identified, typically occurring several weeks after initial infection. Mostly children seem to be affected, but (young) adults can also develop this syndrome, which responds well to corticosteroids. It seems likely that cardiovascular complications in COVID-19 have hitherto been underreported and we need to be aware of novel syndromic presentations of COVID-19.

> "as in other areas of critical care, one size fits all treatment strategies are inadequate in COVID-19 and treatments should rather be personalised"

**10. Tissue perfusion should be optimised**
The importance of tissue perfusion in COVID-19 patients has sometimes been overlooked. Although shock is usually relatively mild in patients with COVID-19, it can contribute to the development of multiple organ failure. The pathophysiology can involve the four phenotypes: hypovolaemic, cardiogenic (myocardial injury, right heart failure due to increased afterload), obstructive (pulmonary embolism), and distributive (exaggerated host response). Indeed, early in the pandemic, diuretics were often prescribed on the basis of severe lung oedema, but resultant secondary hypovolaemia may have impaired tissue perfusion. Maintenance of an optimal fluid status is of paramount importance in all patients, including those with COVID-19.

**11. Clinical trials could have been better organised**
With the rush to try and identify any treatment that was effective against SARS-CoV-2, multiple small, single-centre clinical trials were started on a multitude of different potential therapeutic interventions. These effectively limited enrolment of patients into other larger studies, and often struggled to include enough patients, therefore, preventing useful conclusions being drawn from their results. Larger, more carefully considered international trials, such as the Recovery, Solidarity and Remap-CAP platforms, would have provided more valuable data.

**12. The hydroxychloroquine story caused considerable harm**
The initial data in favour of hydroxychloroquine use were not very convincing, and yet because everyone was eager to have an effective treatment, because of the considerable media coverage, and because the drug was promoted by several world leaders, many patients and their relatives wanted to be treated with it. In addition to the fact that it did not work, this demand prevented the inclusion of many patients in clinical trials as they could not be randomised. Importantly, pandemics should not be used as an excuse to condone reduced standards of scientific research.

**13. There is a need to determine futility, especially when resources are limited**
If resources are exceeded, selecting which patients should be admitted to the ICU or to receive organ support should not be

based on a lottery or a 'first come, first served' basis as was done in some centres. We should not admit patients to the ICU or submit them to organ support interventions if they are going to die regardless of our efforts. This is not only a futile and unkind action for the patient and his/her family, but increases costs for society as a whole, limiting the availability of these resources for those who could truly benefit. The high mortality rates with such an approach also have a negative impact on the morale of the personnel. Criteria for ICU admission and use of life-support therapies should be established and used on all ICUs at all times, not just during a pandemic, to ensure that only patients who will benefit are included.

**14. Families are important and good communication is key**

Families have sometimes been kept away from their loved ones for safety reasons, creating anxiety and loneliness for them and the patient. Taking time to explain how the patient is, is vitally important, although can be difficult, especially on a hectic ICU. Providing some form of regular contact via video link should be considered a minimum for both patient and family.

**15. Good teamwork and support are crucial**

Regular team debriefings are important to provide positive feedback and to acknowledge the input from each team member. It is also important to provide reassurance that when resources are stretched, it may not be possible to treat patients to the high standards normally demanded, and that doing everything we can has to be enough.

**16. Psychological support for the personnel is essential**

Adequate, early psychological support is essential and must be available for all medical and paramedical teams because the risk of burnout is real and staff wellbeing crucial for continued efficient functioning. Psychological support should be actively encouraged and not, as is still often the case, seen as a sign of weakness. In the initial surge of COVID-19 cases, the importance of this support was often overlooked.

**17. Follow-up clinics should be implemented.**

Increasingly, long-term sequelae of COVID-19 are being recognised, potentially involving multiple organs. As such, follow-up services and rehabilitation programmes should be provided to detect and manage such problems.

**18. Telemedicine has many advantages in a pandemic**

We have all become much more familiar with telemedicine over the last year. Online meetings with colleagues to discuss the very latest treatments and data, online training programmes for staff, online consultations and monitoring of patients at home, and video links so that relatives can see and talk to (where possible) their loved one in hospital, are just some examples of how telemedicine has been embraced and become an important communication tool in the hospital setting.

**19. Limiting the impact on non-COVID patients is important**

The negative impact of this pandemic on non-COVID patients will not be fully apparent for some months or even years. Many hospitals had to cancel routine procedures to be able to provide enough beds for their COVID-19 patients, and people were often afraid to attend hospitals or their general practitioner for fear of adding undue burden to the system or for fear of catching the disease. Patients whose treatments or follow-ups have been cancelled or postponed, patients with life-modifying diseases who have not been diagnosed, individuals with impaired mental health as a result of lockdown, fear and/or loneliness - these are just some examples of how COVID-19 has impacted even those who have not been infected.

**20. We need to learn from our mistakes and be better prepared for similar pandemics in the future**

The scope of COVID-19 caught us all by surprise. Yet, given that viral mutation is part of nature, novel viral pandemics are to be expected in the future. Reflection on the past year is needed to develop plans for improved preparation, at all organisational levels. ■

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# Evidence-Based Management of Atrial Fibrillation

## The 2020 ESC Guidelines and the addition of Landiolol

An overview of the updated guidelines for the diagnosis and management of atrial fibrillation, developed in association with the European Association for Cardio-Thoracic Surgery.

The European Society of Cardiology (ESC) provides a range of scientific and educational activities, such as the production and continuous updating of clinical practice guidelines for the diagnosis and treatment of cardiovascular diseases. In 2020, the ESC published new updated guidelines for the diagnosis and management of atrial fibrillation (AF), developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS) (Hindricks et al. 2020).

Rate control is an integral part of AF management and is often sufficient to improve AF-related symptoms. In these guidelines, beta-blockers are recommended as first-choice drugs to control heart rate in AF patients with left ventricular ejection fraction (LVEF) ≥40% or LVEF<40% (Class I, LoE*B) (Hindricks et al. 2020). **For the first time landiolol is included in these important guidelines. Landiolol is included as the only agent with a specific dose recommendation in patients with cardiac dysfunction (dosages of 1 µg/kg/min up to 10 µg/kg/min)** (Hindricks et al. 2020). On the other hand, intravenous amiodarone may be considered in patients with haemodynamic instability or severely depressed LVEF, for acute control of heart rate nevertheless with a lower Class of Recommendation (Class IIb, LoE B) (Hindricks et al. 2020).

Landiolol is a new ultra-short acting (T1/2=4min), intravenous, most β1 selective blocker, for the treatment of supraventricular tachyarrhythmias such as AF, atrial flutter (AFl) and non-compensatory sinus tachycardia (SmPC Rapibloc®). **Landiolol is a new kind of β-blocker, a pure S-enantiomer molecule which offers rate control with minimal negative impact on blood pressure** (Balic et al. 2018). Furthermore, landiolol has low volume distribution of 0.3 l/kg – 0.4 l/kg (SmPC Rapibloc®). This is very important because landiolol will not be stored in the tissues (DiPiro et al. 2010), thus avoiding possible toxicities (Abialbon 2019). Compared to esmolol, in experimental models, **landiolol showed very high cardioselectivity (β1/β2-selectivity = 33:1 vs. 255:1)** (Shibata et al. 2012). This translates to eightfold higher cardioselectivity for landiolol over esmolol. **Landiolol due to the highest cardioselectivity offers minimal impact on respiratory function** (Balic et al. 2018) **and unveils β2-receptor-mediated coronary hyperaemia** (Maman et al. 2017). In an experimental study, landiolol appeared to have a minimal effect on the refractory period of the action potential of a cardiomyocyte, in contrast to esmolol which dose-dependently shortened the refractory period. This is because landiolol does not affect Na+ and Ca2+ ion currents, resulting in a minimal affected cardiac contractility **(less inotropic effect)** (Shibata et al. 2012). **Landiolol also has a favourable safety profile for patients with renal and hepatic comorbidities,** due to inactive metabolites and hydrolysis by plasma esterases (Yokayama 2016).

**Further statements from ESC guidelines** (Hindricks et al. 2020):

- **Amiodarone** can be useful as a last resort when heart rate cannot be controlled.
- **Some antiarrhythmic drugs** (AADs) also have rate-limiting properties (e.g., amiodarone, dronedarone, sotalol) but generally they should be used only for rhythm control.
- **Intravenous administration of amiodarone** may lead to a further decrease in blood pressure in haemodynamic instable patients.
- **The "rhythm control strategy"** refers to attempts to restore and maintain sinus rhythm, and may engage a combination of treatment approaches, along with an adequate rate control.

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# Is Videolaryngoscopy the New Gold Standard for Intubation Following the COVID-19 Crisis?

## Videolaryngoscopy for critically ill patients

Videolaryngoscopy may be the new gold standard for tracheal intubation following the COVID-19 pandemic onset.

## Introduction

Patients admitted to Intensive Care Units (ICU) often require respiratory support. Orotracheal intubation is one of the most frequent procedures performed in ICU (Lascarrou et al. 2017; Roux et al. 2014; Martin et al. 2020).When performed in critically ill patients, intubation is a challenging issue as it may be associated with life-threatening complications in up to one third of cases (Jaber et al. 2006; De Jong et al. 2013b). Severe hypoxaemia occurring during intubation procedure can result in cardiac arrest (Mort 2004; De Jong et al. 2018), cerebral anoxia, and death (Cook et al. 2010). Difficult intubation is known to be associated with life-threatening complications (De Jong et al. 2013b; De Jong et al. 2014a; Jaber et al. 2006; Jaber et al. 2010; Martin et al. 2011; Driver et al. 2018).The failure of first-attempt intubation appears a major factor for developing life-threatening complications related to intubation (De Jong et al. 2020).

In this setting, the place of videolaryngoscopy for intubation procedure in critically ill patients remains debated in the past years (Jaber et al. 2019; Mosier et al. 2020). However, the recent COVID-19 pandemic highlighted the potential usefulness of videolaryngoscopy to reduce intubation provider contamination (El-Boghdadly et al. 2020; Cook et al. 2020; Patwa et al. 2020). Is videolaryngoscopy the new gold standard for intubation during and after the COVID-19 crisis?

## What are the Videolaryngoscopes?

Videolaryngoscopes were first proposed to improve airway management through improved glottis visualisation, aiming to reduce incidence of difficult intubation in the operating room. Then, their use was extended to airway management in other settings. These devices contain a miniaturised camera aimed at the tip of the blade to indirectly visualise the glottis.

Videolaryngoscopes differ in design, blade type and technical configuration. Three main categories of videolaryngoscopes exist according to the type of blade. First, the Macintosh blade-shaped optical laryngoscopes have Macintosh blades combined with video technology. The glottis can be seen either directly or via a video screen. Second, the anatomically shaped blades without a tube guide have anatomically shaped, giving a view of the glottis without the need to flex or extend the neck, providing only an indirect view of the glottis, with the need to use a preshaped stylet into the tracheal tube. Third, the anatomically shaped blade with a tube guide do not necessitate a preshaped stylet.

Despite the better visualisation of the glottis, the main challenge when using videolaryngoscopes remains to insert the tube into the trachea. In other terms, achieving a 100% percentage of glottis opening (POGO) view (corresponding to a Cormack-Lehane grade 1 in direct laryngoscopy) during videolaryngoscopy does not guarantee successful intubation, as the tube has to pass a sharp angle to enter the larynx. **Table 1** presents ten tips to improve first-attempt intubation success using videolaryngoscopes.

## What are the Data in Literature?

In the ICU setting in the 2010's, it has been suggested that videolaryngoscopes could

| | |
|---|---|
| 1 | Training of the operator in simulation centre. |
| 2 | Training of the operator in patients: at least 10 intubation performed in patients using the videolaryngoscopes |
| 3 | Use of a predefined airway management algorithm |
| 4 | Careful assessment of the difficulty of intubation before intubation, using the MACOCHA score for example |
| 5 | Choice of a single videolaryngoscopy device |
| 6 | Adequate preoxygenation for limiting hypoxaemia and rush during the procedure |
| 7 | Careful suctioning of secretions |
| 8 | Rapid sequence induction with the use of neuromuscular blockers |
| 9 | Use of a stylet or bougie for unchannelled videolaryngoscopes |
| 10 | Allow less good visualisation of the glottis to allow easier catheterisation of the trachea |

**Table 1.** Ten tips to improve first-attempt intubation success using videolaryngoscopes

help to reduce difficult intubation rate (Kory et al. 2013; Lakticova et al. 2013). In a before-after study reporting a quality improvement process using a videolaryngoscope in an airway management algorithm (De Jong et al. 2013a), the systematic use of a combo videolaryngoscope for intubation significantly reduced the incidence of difficult intubation and/or difficult laryngoscopy (De Jong et al. 2013a). In the multivariate analysis, the "standard laryngoscopy" group was an independent risk factor for difficult intubation and/or difficult laryngoscopy. In addition, in the subgroup of patients with difficult intubation predicted by the MACOCHA score (De Jong et al. 2013b), the incidence of difficult intubation was much higher in the "standard laryngoscopy" group (47%) than in the "combo videolaryngoscope" group (0%).

These results were confirmed in 2014 by a systematic review and meta-analysis establishing that use of videolaryngoscopes for intubation in ICU could reduce the rate of difficult intubation (De Jong et al. 2014b). Videolaryngoscopy improved difficult intubation, first-attempt success, Cormack 3/4 grades, oesophageal intubation, and did not modify severe hypoxaemia, severe cardiovascular collapse, and airway injury, when compared with direct laryngoscopy. However, in 2016, Lascarrou et al. (2017) showed in a large multicentre randomised controlled trial that videolaryngoscopy compared with direct laryngoscopy did not improve first-pass orotracheal intubation rates and was associated with higher rates of severe life-threatening complications.

Several meta-analyses (Arulkumaran et al. 2018; Zhao et al. 2017; Huang et al. 2017) were then published, with conflicting results regarding the superiority of the videolaryngoscopes over direct laryngoscopy for intubation in critically ill patients. The disparities between included trials were however considerable, with high heterogeneity.

A prospective observational study that compares the use of direct laryngoscopy with a conventional Macintosh blade to the

**1. Insertion of the videolaryngoscope into the mouth**

The operator is holding the tracheal tube with stylet in the other hand and starts to insert it.

**2. Insertion of the tracheal tube in front of the glottis.**

The operator does not enter the trachea with the stylet to avoid tracheal injuries.

**3. Withdrawal of the stylet**

The operator is pushing the tracheal tube throughout the glottis during this procedure.

**4. Insertion of the tracheal tube without stylet into the trachea**

The operator checks the good positioning of the tracheal tube.

**Figure 1.** Intubation using a videolaryngoscope and an endotracheal tube + stylet

C-MAC® videolaryngoscope (Karl-Storz) (Dey et al. 2020), among operators that had performed, at least, 50 intubations in clinical simulation with the videolaryngoscope, was recently performed. In the videolaryngoscope group, there was a higher first-attempt intubation rate than in the conventional Macintosh blade group.

## What May Explain the Discrepancies in Literature?

One of the most important point is the use of a stylet to preshape the endotracheal tube, described in **Figure 1**. In the study of Lascarrou et al.( 2017), it was used in less than 20% of cases. Using a preshaped endotracheal tube with a stylet may have potential advantages over conventional endotracheal tube and can help to increase success of intubation using videolaryngoscopy (Apfelbaum et al. 2013; Jaber et al. 2020; Sorbello and Hodzovic 2020).

The expertise of operators is also very important when assessing the results of published observational and randomised studies. In the study of Lascarrou et al. (2017), it is worth noting that more than 80% of the operators were non-expert. The experience required to attain 90% probability of optimal performance with videolaryngoscopes has been evaluated (Cortellazzi et al. 2015). At least 75 attempts with videolaryngoscopes were required to achieve that level of proficiency (Cortellazzi et al. 2015).

A team recently implemented the McGrath MAC videolaryngoscope (Medtronic) as part of a quality improvement initiative (Amalric et al. 2020). They positioned the videolaryngoscope as the first-line laryngoscope for every intubation in critically ill patients to reinforce skill training. In the multivariate analysis, the absence of dedicated videolaryngoscopy expertise, junior status, and the presence of coma were independent risk factors of first-attempt failure. They reported for the first time in the critically ill that specific videolaryngoscopy skill training, assessed by the number of previous videolaryngoscopies performed, was an independent factor of first-attempt intubation success. There was an increase of the first-attempt procedure success rate according to the operators' level of expertise. Having performed more than 15 videolaryngoscopies was associated with a first-pass success rate of 87%.

That is why training and education are essential, through clinical simulation and practice with cadaveric specimens, to secure the implementation of these new techniques in critically ill patients.

## What were the Expert Positions Before the COVID-19 Pandemic?

The clinical practice guidelines for the management of the critically ill patient's difficult airway published by the Difficult Airway Society (DAS) in 2018 (Higgs et al. 2018) suggest the use of videolaryngoscopes in the presence of a difficult airway or as a rescue strategy when the

direct laryngoscope has failed. Similarly, the expert guidelines on intubation and extubation in intensive care from the Société Francaised'Anesthésie et de Réanimation (SFAR) and the Société de Réanimation de Langue Francaise (SRLF) published in 2017 (Quintard et al. 2017) have included the videolaryngoscope in the algorithm for the airway management as the first option in the intubation of patients who score ≥ 3 in the MACOCHA score (De Jong et al. 2013b), and as the rescue strategy when intubation with the direct laryngoscopy fails.

## What are the Expert Positions During the COVID-19 Pandemic?

The COVID-19 pandemic has further highlighted the place of videolaryngoscopy during intubation in ICU, in order to limit the contamination of the intubating provider. International guidelines recommend using video laryngoscopy where available to increase the distance between the patient and intubating provider, and to perform intubation by the most experienced operator (Cook et al. 2020; Patwa et al. 2020). If using a bougie or a stylet, the operator is advised to be careful when removing it so as not to spray secretions on the intubating team (Cook et al. 2020).

## What About the Future of Videolaryngoscopy in the ICU?

Future trials will better define the role of videolaryngoscopy in ICU, especially with respect to appropriate use of airway adjuncts as stylets. First pass intubation success rate alone has demonstrated to be an accurate primary outcome, strongly associated with the occurrence of complications during intubation procedure (De Jong et al. 2020). The expertise of operator will be a major confounding factor to take into account when designing future randomised clinical trials.

## Conclusion

Videolaryngoscopy in critically ill patients should be widely used, after appropriate formation and training of intubator providers. Further studies are still needed before being able to perform recommendations to implement videolaryngoscopy for first-attempt intubation of ICU patients.

## Conflict of interest

Dr De Jong reports receiving consulting fees from Medtronic. Pr. Jaber reports receiving consulting fees from Drager, Medtronic, Baxter, Fresenius-Xenios, and Fisher & Paykel. Dr Aarab has no conflict of interest. ■

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# A French Hospital's Journey Through the Pandemic

During the COVID-19 pandemic, Foch Hospital in Suresnes, France adapted its medical strategy to manage high patient flow, limited resources and staff shortages to ensure efficient patient care. Here is an overview of how the hospital rose up to the challenge.

How should we treat patients infected with a virus we know hardly anything about? This was the very first challenge that hospitals in Europe had to solve when COVID-19 patients started to flood in early March.

Foch Hospital in Suresnes, France – one of the largest private healthcare institutions of public utility in the Paris region – is no stranger to this challenge.

In the absence of scientific studies and reliable information about COVID-19, they had to improve at first, and as they learnt a little bit more about it, they adapted their medical strategy day after day, constantly sharing information between the various departments to ensure consistent and optimum care for patients.

"Every day was bringing new challenges", shares Dr Charles Cerf, Head of the Intensive Care department. "We connected with intensivist colleagues from other institutions to share experience", That is how for example they quickly decided to replace assisted ventilation with high-flow oxygen therapy. "This critically helped rationalise the use of resuscitation ventilators and to only use intubation if non-invasive therapy failed", he adds.

Even more than beds or intensive care materials, experienced nurses and doctors started lacking very quickly. The hospital had no choice but to redeploy staff from other departments to the intensive care: first anaesthesia teams, as well as surgical staff and recovery room staff, followed by nurses, doctors and care teams with little or no training to intensive care.

"This was a tremendous source of stress for the staff, who had to urgently acquire new skills and remain mobilised for an indefinite time", comments Floriane de Dadelsen, Deputy Director.

> **"the hospital had no choice but to redeploy staff from other departments to the intensive care: first anaesthesia teams, as well as surgical staff and recovery room staff, followed by nurses, doctors and care teams with little or no training to intensive care"**

At the pick of the pandemic in early April, fatigue had already set in for several of them, without the slightest drop in the number of patients being treated. At the request of the Regional Health Agency (ARS), the hospital had already stopped all scheduled procedures in order to be able to accommodate as many COVID-19 patients as possible and to relieve emergencies for public hospitals.

The distribution of patients between public and private institutions managed by the ARS was shown to be quite effective; however the provision of heavy equipment and consumables to satisfy the high demand was often complicated.

"Accurately predicting the volume of materials when we had no idea of the exact number of patients we would have to accommodate, and building stocks as the ARS controls the delivery of equipment and medicines to ensure equal distribution among health institutions was just impossible", adds Ms. Dadelsen.

The biomedical team was on the front line in early May to manage a return to a somewhat normal: restore the hospital to what it was, treat diseases other than COVID-19 whilst prioritising the most urgent cases, enable nursing staff to go on holiday with the hope, in the meantime, that the number of patients would not rise again.

Several months after the first wave, the team reflected on the lessons learned from the management of the health crisis.

Numerous positive points made them proud: the sharing of teams which enabled an efficient level of care to be maintained; the faultless mobilisation of support activities for the hospital - biomedical team, logistics, pharmacists - who struggled to overcome the shortage of materials and medicines; the flexibility and reactivity


of all staff who had to adapt day after day to a perpetually changing working environment; the cohesion of governing authorities and efficiency of management which enabled an unprecedented and stressful situation to be managed over time.

However, certain problems remained: the challenge to deploy telemetry and remote monitoring tools due to the ineffective Wi-Fi network; the lack of budgetary resources to renew its pool of heavy equipment; and for months mobilising all hospital resources for COVID-19, to the detriment of other diseases, and chronic diseases, in particular.

Though the hospital is now better prepared today for a massive influx of patients, this crisis has demonstrated the need to rethink certain aspects of healthcare crisis management: stronger collaboration between healthcare institutions, stock management of materials and consumables, partnerships with manufacturers to implement financing solutions to lease or renew equipment without putting a strain on the hospital's investment capacities.

So many logistical and financial challenges which require loser cooperation amongst all those involved - public authorities, care institutions and companies – and at all levels.

The management of the crisis in figures:

• An accommodation capacity multiplied by 3.4 in mid-April with 48 resuscitation beds as opposed to 14 in normal circumstances, 8 intensive care unit beds as opposed to 8 continuous care in normal circumstances and 113 hospital beds.

• €1.2 million mobilised in on-call staff and additional hours (according to Foch internal data). ■

## Key Points

- Foch Hospital in Suresnes, France is one of the largest private healthcare institutions of public utility in the Paris region.
- During the COVID-19 crisis, the hospital has adapted its medical strategy and has improved information sharing between departments to ensure optimum care.
- The hospital team learned several lessons: sharing of teams to improve efficiency of care, mobilisation of support activities for the hospital, overcoming shortage of materials and medicines, managing changes in staff working environment, and cohesion of governing authorities.

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# Prioritisation: A Physicians' Problem?

## An opinion

In light of harsh criticism regarding physicians' prioritising scarce resources during the COVID-19 pandemic, the question arises: is prioritising truly a physicians' problem?

- The COVID-19 pandemic has led to pronounced discrepancies between the need for medical care and the ability of many health care systems to provide it.
- Subsequently, treating teams needed and still need to take prioritisation decisions as to the allocation of scarce resources. Such decisions have to be based on the best medical knowledge and on ethical values and principles.
- Specifically, one core ethical value, giving priority to patients with the best odds of success, has been harshly challenged by both medical ethicists and non-medical stakeholders due to misconceptions, naiveté or their own interests. Therefore, physicians might understandably, but inappropriately refrain from making prioritisation decisions altogether.

## Introduction

In many parts of the world, the COVID-19 pandemic has led to pronounced regional, national and even supranational discrepancies between the need for medical care and the ability of the respective health care systems to provide it. Specifically, the strength and effectiveness of critical care teams have been hampered (1) by the lack of equipment, mostly during the first wave of the pandemic; (2) by the lasting uncertainty as to adequate and comprehensive treatment regimes for patients suffering from COVID-19 worldwide; and (3) by an increasing incidence and prevalence of infections amongst nurses and physicians as well as their facing considerable psychological sequelae, regarding the enormous occupational and private burdens (Ranney et al. 2020; Grasselli et al. 2020; Stasi et al. 2020; Azoulay et al. 2020). The often unmet demands for equipment and additional personnel apt to work in intensive care units (ICUs) have forced and still force treating teams to make prioritisation decisions as to the allocation of such scarce resources. There is remarkably uniform agreement within the medical community that such decisions must be based both on the best knowledge available regarding the respective medical aspects and on ethical values and principles (Marckmann et al. 2020; Jöbges and Biller-Andorno 2020; Emanuel et al. 2020). However, the process of prioritisation – and especially the criterion of "best odds of success of treatment" – has met considerable and sometimes hurtful criticism, amongst others from ethicists, authorities, interest groups and self-appointed experts. Therefore, the general question amongst physicians might understandably arise: "Is prioritisation really our problem?"

## Distributive Justice: Allocating Scarce Resources During the Pandemic

During the COVID-19 pandemic, medical societies in several countries have published recommendations regarding the allocation of scarce critical care resources. Overall, they build on using the best medical evidence available and on adhering to distinct ethical values (White and Lo 2020b; Marckmann et al. 2020; Jöbges and Biller-Andorno 2020; White and Lo 2020a; Truog et al. 2020; Emanuel et al. 2020; Beauchamp and Childress 2019).

With regards to the fair distribution of both treatments and vaccines, three core ethical values appear undisputed: treating patients equally; maximising the benefits achievable under the circumstances prevailing; and giving priority to patients with the best odds of success (White and Lo 2020b; Michalsen 2020; Jöbges and Andorno 2020).

Each patient deserves a fair chance of receiving medical care. However, the odds of success when applying a treatment – i.e. a scarce resource in this context – or the achievable benefit of a vaccine will not be distributed equally amongst all those in need. Therefore, those with higher odds of success – as defined by transparent and reasoned medical and ethical criteria in advance – will receive priority. Medical determinants with a negative impact on the prognosis need to be described and integrated into the decision-making

process as transparent as possible regarding the best medical evidence available at that time (Marckmann et al. 2020; White and Lo 2020a; Emanuel et al. 2020). Clearly, chronological age alone, social value, religion, disabilities, or wealth must not determine a person's chance to benefit from scarce resources. Especially, none of these characteristics should convey a disadvantage upon an individual or a sub-population – but no undue advantage either.

## Watchfulness, Criticism and Professionalism

As to the allocation of scarce resources in clinical practice, there are two primary points in time for prioritisation decisions: (1) *ex ante*, i.e. before scarce resources must be allotted – that is the decision to start or withhold intensive care (life-sustaining) treatments, and
(2) *ex post*, i.e. once scarce resource allotment has already been implemented – that is the decision to continue or withdraw such treatments.

For the same patient, withholding and withdrawing are mostly assessed as equally justified, and they are based on indication, the individual's will – and availability of the resource needed. Furthermore, limiting life-sustaining treatments and changing the goal of therapy from cure to comfort care is common in ICUs worldwide, regardless the cause of the illness or injury (Sprung et al. 2019). Yet, the crucial question arose during the COVID-19 pandemic whether it is justified that one patient be removed from a specific critical care treatment modality for the sake of another patient who has a higher likelihood of successful through this treatment modality. As of yet, there is no concordance with regards to this difficult question (Dufner 2020; Marckmann et al. 2020; Jöbges and Biller-Andorno 2020; Peterson et al. 2020; White and Lo 2020a; Truog et al. 2020; Emanuel et al. 2020).

No matter at what point in the course of the pandemic prioritisation decisions need to be made, they are complex and challenging. They might bear grave consequences for individual patients and their families as well as for the health care teams caring for them (Azoulay et al. 2020; Michalsen 2020; Moss et al. 2016). Furthermore, such decisions might impact on health equity and social coherence. Undoubtedly, there has been inequity regarding health care systems and health care delivery worldwide – even in affluent countries. A pandemic appears to mirror and epitomise this, as it is, quoting Rudolf Virchow, "a social phenomenon that has some medical aspects". Forseeably so, prioritisation has become a concerning socio-political issue, raising fears about unfair treatment of patients, discrimination against certain subpopulations, for instance people with disabilities, unlawful medical conduct, and even conspiracies (Lopez et al. 2021; White and Lo 2020b; Dufner 2020; Ferrara et al. 2020). Not only the populations at large worldwide, but also scientists, physicians and nurses, elected officials, and authorities – to name but a few stakeholders – are vastly challenged by the complexity, perpetuation, and continuously massive impact of the crisis as to many realms of what used to be "the normal life". Crises often lead to seclusion, angst, and zest for simple solutions amongst those affected (U.S. Department of Health and Human Services 2019; Webster and Kruglanski 1994).

> **the crucial question arose during the COVID-19 pandemic whether it is justified that one patient be removed from a specific critical care treatment modality for the sake of another patient who has a higher likelihood of successful through this treatment modality**

Subsequently, watchful ethicists have brought forth alternative prioritisation models that seek to adjust for factors that would structurally decrease the odds of successful treatment in "vulnerable populations".

Moreover, though, individuals, subpopulations, and institutions have criticised the often burdensome decision-making process regarding prioritisation and sought to overtrump it by pure authorative power, media alert, or legal action.

For example, in some countries experts' advice was openly dismissed and social distancing rules were implemented very hesitantly, if at all. In other countries, the governments were very reluctant to acknowledge any need for prioritisation despite high SARS-CoV-2-related infection and hospital occupancy rates. Both positions raised considerable concerns as to the authorities' transparency of decision-making as well as their acting in the best interest of the public at large.

The press and social media worldwide sometimes elaborated thoroughly and compendiously on prioritisation, but sometimes appeared to be very critical, if not specious about it (National Health Service 2020; Arbuthnott et al. 2020; Pergande 2020; Spanke 2020; Ferrara et al. 2020; Baker and Fink 2020). At least in democratic societies, scientists and political decision-makers have to stand scrutiny regarding their findings, assessments and rulings. General mistrust and misguided angst, however, that an "uncontrollable elite" would attack the people's civil rights using pandemic-related public health measures has rather spurred conspiracy theories and led to unfounded counterattacks (Ferrara et al. 2020).

Finally, advocates of persons with disabilities have brought the German prioritisation recommendations (Marckmann et al. 2020) to the attention of the German Supreme Court on the grounds of discrimination against this subpopulation (Wortmann 2020). The ruling is pending. The twin

public health-oriented responsibility of physicians, to care both for their individual patients and the population at large, is clearly acknowledged (White and Bo 2020b; Dufner 2020). The overarching question, though, is whether in a crisis scenario health care teams should be compelled to integrate long-standing structural health inequities into urgent prioritisation decisions. This would convert alleged or true discrimination against members of distinct subpopulations into their unfair advantage – compared to non-members of these subpopulations – in an individual prioritisation situation.

Despite thoughtful deliberations by ethicists on one side and scheming by self-proclaimed experts on the other, the patients' needs can remain quite limitless during the pandemic. As resources were and are limited, though, they still needed and need to be allocated fairly, consistently, and reliably. Weighing patients' individual prognoses and assessing their odds of success with the aim to determine who will likely benefit from the scarce resource(s) if applied, does require expertise, reasoning and time of medical professionals. Yet, they are the only ones able to fulfil this task on a factual level.

## Conclusion

During the COVID-19 pandemic, many critical care resources have become or may still become scarce. Subsequently, the treating teams needed and need to selectively allot the resources available by making prioritisation decisions based on the odds of success. It is of utmost importance these inevitable decisions not be taken as discretionary decisions, but taken thoroughly, consistently, proportionately, and transparently as to rules based on medical assessment and ethical values.

Watchful clinical ethicists have drawn attention to the twin responsibility of physicians to care both for their individual patients and for heath equity within the population at large. Whether the latter is truly a mission to be accomplished during acute prioritisation challenges remains to be debated.

There have also been and will be criticism and fraudious attempts to circumvent medically reasoned decisions, often spurred by ignorance, presumptuousness, and scouting for personal advantages. Additionally, legal stipulations may direct the allocation of resources and may even overrule medical judgement for each and every prioritisation decision.

Nevertheless, physicians still have to make prioritisation decisions and decide according to their knowledge, skill and expertise. To refrain from prioritising appears unprofessional – if not unethical.

## Conflict of interest

None. ■

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# Nutrition Management of COVID-19 Patients in the ICU and Post-ICU

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This article is a summary of a webinar series where three nutritional experts discussed a practical approach on how to feed and how to provide high-quality nutritional therapy to critically ill patients during hospitalisation. Prof Elizabeth De Waele, Dr Arthur Van Zanten and Prof Paul Wischmeyer in the webinar series discuss nutrition support for COVID-19 ICU patients and strategies for the nutrition management of COVID-19 patients post-ICU.

Patients with coronavirus disease may suffer from pneumosepsis. It is a dysregulated host response to pneumonia. There is often also the accompanying complication of multiple organ dysfunction syndrome (failure of the cardiovascular system, the hepatic system, the renal system, the neurological system, the respiratory system, and the haematological system). The GI tract and nutrition are also issues that must be considered to prevent further loss of lean mass and declining immune function.

Many COVID-19 patients survive ICU stay. But many of these survivors are debilitated and may have to learn how to walk again. Swallowing is very difficult after prolonged intubation, as patients have progressive loss of body weight and even more loss of lean body mass. They suffer from concentration disturbances, decline of cognitive functions and anxiety, depression and post-traumatic stress disorder, also called the Post-Intensive Care Syndrome. All these factors do not help nutritional intake during the recovery phase. That is why it is essential to have prolonged nutrition therapy combined with exercise rehabilitation throughout every phase of critical illness and recovery.

Optimising nutrition therapy in COVID-19 patients both in the ICU and post-ICU is extremely important. It is known that in general, patients often do not receive their full nutritional requirements whilst in the ICU (Bendavid 2019). Evidence shows that patients are consistently underfed at ward level often not exceeding more than 50% of their needs, particularly those only on oral intake (Peterson et al. 2010; Chapple et al. 2010; Wittholz et al. 2020; Ridley et al. 2019). COVID-19 patients can also be obese, suffer from hypertension, diabetes, COPD and other premorbid diseases. While acute illness can be severe and requires admission to the ICU, that is not where this journey ends. Clinicians have to manage the nutritional care needs of the patient both in the ICU and during the recovery phase even beyond hospital discharge ensuring this coordinated care is continued and carried out.

## Practical Tips for Nutrition Therapy in Critically Ill COVID-19 Patients

Here are some practical questions and tips on how to manage nutrition issues when providing care to COVID-19 patients in the ICU:

- *When to start enteral nutrition in patients with vasopressors?* Enteral nutrition can begin when haemodynamic stability is achieved. There is no need to wait until vasopressors have been stopped. When mean arterial pressure is stable, and when $ScvO_2$ and lactate levels are acceptable, early enteral nutrition can begin (Reignier et al. 2018).
- *There was initial concern at the start of the pandemic about feeding prone ventilated patients with enteral nutrition. Is this justified?* Most COVID-19 patients are able to tolerate enteral feeding with nasogastric tube placement whilst in prone position. Clinical evidence does not support withholding enteral nutrition in this state (Reintam et al. 2018). Therefore, healthcare providers can successfully feed COVID-19 ICU patients with enteral nutrition even in prone position.
- *What to do in cases with persistently high Gastric Residual Volumes (GRV)?* Some units don't measure GRVs at all as it is an aerosol generating procedure. However in those that do, use of prokinetics is recommended, although if you choose to use hydroxychloroquine it is important to monitor for QTC prolongation. If high GRVs persist, the next step, would be to introduce jejunal feeding if this is currently

carried out in the hospital or unit or consider parenteral nutrition (PN)

• *Permissive underfeeding, and how long?* Early enteral nutrition is important to preserve gut function. Permissive underfeeding is not superior in sepsis patients compared to full feeding. Heyland et al. (2010) also showed that no feeding is inferior to trophic feeding. Guidelines suggest that there is a slow build of enteral feeding in the first 1-3 days and that the aim is to get to nutritional targets by day 4 (de Koning et al. 2019).

• *What about energy target?* In critically ill mechanically ventilated patients, energy expenditure (EE) should be determined by using indirect calorimetry. If indirect calorimetry is used, isocaloric nutrition rather than hypocaloric nutrition can be progressively implemented after the early phase of acute illness (after Day 1-3). Hypocaloric nutrition should be administered in the early phase of acute illness (<70% of requirements). Caloric delivery should be increased up to 80-100% after day 3. If predictive equations are used to estimate the energy need, hypocaloric nutrition should be preferred over isocaloric nutrition for the first week of ICU stay (Singer et al. 2019).

• *Very high protein products, and why?* Many COVID-19 patients are obese, and this requires a high protein, low-calorie strategy to prevent overfeeding. In a general ICU population, to prevent overfeeding calories, which studies show can be detrimental, the volume provided does not often meet protein needs on a per kg bodyweight basis unless higher protein feeds are given. To meet the guideline recommendation of 1.3 g/kg/day of proteins, high protein feeds are recommended for use and enteral protein supplements can also be used when this is not sufficient (Zanten et al. 2018). Many clinicians report finding it difficult to achieve protein requirements without the use of high protein enteral feeds.

• *Hydrolysed vs. Polymeric feeds:* Both the ASPEN guidelines and the Canadian Critical Care Nutrition Practice Guidelines do not recommend the use of hydrolysed protein feeds. This is because there is no evidence to support use of hydrolysed feeds for routine use in ICU patients. Whole protein enteral feeds are recommended in all the nutritional guidelines.

• *Monitoring for refeeding hypophosphataemia:* Lower caloric intake is associated with better 6-month survival in refeeding syndrome but not in patients without RFS. As per ESPEN guidelines, in patients with refeeding hypophosphataemia, electrolytes should be measured 2-3 times a day and supplemented if needed, and energy supply should be restricted for 48 hours and then gradually increased (Singer et al. 2019).

• *Ramping up proteins & calories:* In critically ill COVID-19 patients, during the phase of critical illness, a minimum of 1.3g/kg protein equivalents should be delivered per day progressively as per ESPEN guidelines (Singer et al. 2019).

• *When to use parenteral nutrition (PN)?* As per ESPEN guidelines (Singer et al. 2019), in patients who do not tolerate full dose EN during the first week in the ICU, the safety and benefits of initiating PN should be weighed on a case by case basis, and PN should not be started until all strategies to maximise EN tolerance have been attempted.

• *What to do in renal failure patients and during continuous veno-venous haemofiltration (CVVH)?* Use normal protein dose, and start CVVH on normal renal criteria. Increase protein dose to compensate for the loss of amino acids into the ultrafiltrate. Only when dialysis is resource-limited, consider lowering the protein dose, but preferably not below 1.0g/kg bodyweight (Zhu et al. 2018).

• *Glucose control:* ESPEN Guidelines (Singer et al. 2019) recommend that blood glucose should be measured initially after ICU admission or after commencement of artificial nutrition support and at least every 4 hours for the first two days. Insulin should be administered when glucose levels exceed 10 mmol/L.

• *Special feeds* (immunonutrition, fish oil): Special feeds are not recommended for use in COVID-19 patients.

• *Extubation phase:* Consider interrupting gastric feeding before extubation a few hours before or empty the stomach (GRV). Many COVID-19 patients demonstrate post-extubation stridor and need to be re-intubated. Give prophylactic steroids. Keep in mind that extubation is not the end of medical nutrition therapy. Many patients remain dysphagic and are unable to meet targets. It is important that patients are able to demonstrate they can eat sufficiently before the feeding tube is removed.

## Nutritional Considerations in COVID-19 Patients During the Post-ICU Phase

It is becoming evident that general ICU patients on discharge to ward level are still being underfed (Peterson et al. 2010; Ridley et al. 2019, Wittholz et al. 2020). The Nutrition Day data shows that it takes, on average, nearly two weeks for patients on ICU to meet their full nutritional needs (Bendavid 2017). It is often at the point of ICU discharge that nasogastric tubes are routinely removed. A few studies have shown that patients do not improve their nutritional intake beyond 50% of their needs with oral intake alone and that this persists in the post-ICU phase (Peterson et al. 2010; Wittholz et al. 2020; Ridley et al. 2019). At a point where critically ill patients may best be able to utilise the nutritional substrates for anabolic processes, is also the phase where continued underfeeding appears to persist. Growing evidence shows that post-ICU patients are not meeting their nutritional requirements.

What does the future look like for an ICU COVID-19 survivor? We don't know because we don't have the data. This is a

new disease. Healthcare practitioners need to learn from this experience to be able to tailor their approach to this new patient population. However, we do know that patients who suffer from acute respiratory distress syndrome are still not back at baseline even after five years (Herridge et al. 2003). We see the same issues with COVID-19 patients. They have longer than average length of ICU stays and ventilation, and they also appear to lose lean body mass. It is important to invest in nutrition in post-ICU patients. Clinical evidence clearly shows that higher daily protein delivery during hospitalisation is associated with decreased mortality following hospital discharge (Weijs et al. 2019). COVID-19 patients have muscle weakness, debility and loss of function. They are still in need of calories, proteins, vitamins and trace elements (Wittholz et al. 2019). It's not that they don't want to eat, but they may face multiple issues and complications that prevent them from being able to meet their nutritional needs. This is something that needs to change because recovery for these patients is long and slow. They do not appear to resume a normal oral intake whilst in hospital, and become even more vulnerable during the post-ICU phase (Moisey et al. 2020).

Here are some practical recommendations for post-ICU nutrition:

- Use ESPEN guidelines for the nutritional management of individuals with SARS-CoV-2 infection (Wischmeyer et al. 2017; Arends et al. 2017; Weimann et al. 2017; Vokert et al. 2019; NICE guidelines 2017). Avoid premature removal of feeding tubes until patients have demonstrated ability to meet most of their requirements. If a patient is eating <50% of needs for >3 days, enteral nutrition should be commenced.
- Focus on practical issues. If they cannot eat enough, proactively provide oral nutritional supplements. To rebuild muscle mass and function, patients will need ongoing nutrition support, likely oral nutritional supplements and those with leucine and Vitamin D.
- Utilise a crisis situation to learn and apply new protocols, improve decision-making, use telemedicine etc.
- Follow-up on survivors and monitor their nutritional information, including their intake, body weight and muscle mass.
- Provide patients relevant and practical nutritional related information at discharge. This is to ensure patients and carers are aware of what is required and why, and especially to support compliance to eating sufficiently at meals or additional nutrition support measures such as oral nutritional supplements or enteral nutrition.
- Use home enteral nutrition programmes. Only when proactive feeding strategies are used (longer EN, overnight EN or oral nutritional supplements), are patients likely to meet their nutritional needs (van Zanten et al. 2019). ■

This article is based on two-part COVID-19 Webinar Series hosted by Nutricia. To watch the complete webinars please visit: https://nutricia.wavecast.io/critical-care-and-tube-feeding

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# How the Pandemic Changed Telemedicine

An overview of the large-scale transition to telemedicine at Mayo Clinic during the COVID-19 pandemic and how it happened in a matter of days and represented one of the most rapid transformations of healthcare in history.

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## Impact of the Pandemic on Society

The 2019 Coronavirus Disease (COVID-19) pandemic has affected nearly all aspects of society, from family interactions to social activities to workplace structures. Travel restrictions and financial losses have fundamentally altered routine day-to-day undertakings for numerous businesses and millions of people. Standard practices have been altered in most large-scale enterprises, including healthcare.

## Telemedicine is a Natural Fit for Remote Work

The use of telemedicine has accelerated at an unprecedented pace during the COVID-19 pandemic, primarily due to concerns regarding the safety of patients and their healthcare providers. In the larger society, where travel restrictions and policies to reduce person-to-person contact have been implemented to limit disease transmission, many activities have moved to an online environment, including standard office work and schooling. In healthcare, telemedicine has been adopted during the COVID-19 pandemic to promote "contactless" care.

At Mayo Clinic, the sudden and unanticipated disruption of the health care delivery model at the onset of the COVID-19 pandemic resulted in a rapid acceptance of telemedicine by providers and patients (Temesgen et al. 2020). The large-scale transition to telemedicine happened in a matter of days and represented one of the most rapid transformations of healthcare in history.

## Status of Telemedicine Leading up to the Pandemic

Prior to the COVID-19 pandemic, telemedicine solutions had been used as components of disaster responses for over 30 years. For example, the US National Aeronautics and Space Administration (NASA), which had a long history of remote biologic monitoring, utilised telemedicine technologies to assist in relief efforts following earthquakes in Mexico City in 1985 and Armenia in 1988 (Nicogossian and Doarn 2011). In the years that followed, international initiatives were launched to leverage telemedicine in disaster preparedness. In 2017, the North Atlantic Treaty Organization (NATO) established a Multinational Telemedicine System (MnTS) for use in disaster management, which allows for medical specialists to engage in disaster response across national borders (Doarn et al. 2018). In 2020, with decades of foundational experience, COVID-19 enabled design of a National Emergency Tele-Critical Care Network (NETCCN). As conceived, NETCCN would assist health care providers, wherever they are located, by obtaining real-time patient and supplies data, and by extending the reach of critical care specialists to areas of acute need (Scott et al. 2020).

## Technological Enablers of Change and Barriers for Widespread Adoption

The American Telemedicine Association defines telemedicine (which is often used interchangeably with the term telehealth) as "the use of medical information, exchanged from one site to another via electronic communications, to improve patients' health status". While this is a broad definition that could encompass phone calls or asynchronous uses of technology, the feature that truly distinguishes telemedicine from other remote health services is the presence of a real-time audiovisual communication tool that connects providers and patients across locations (Herasevich and Subramanian 2019). A second defining feature of telemedicine is the use of an electronic medical record (EMR) that offers remote providers access to patients' clinical data. Tele-ICU comprises a subset of telemedicine, which may additionally include real-time remote access to monitoring tools and the ability to place orders remotely using Computerized Provider Order Entry (CPOE).

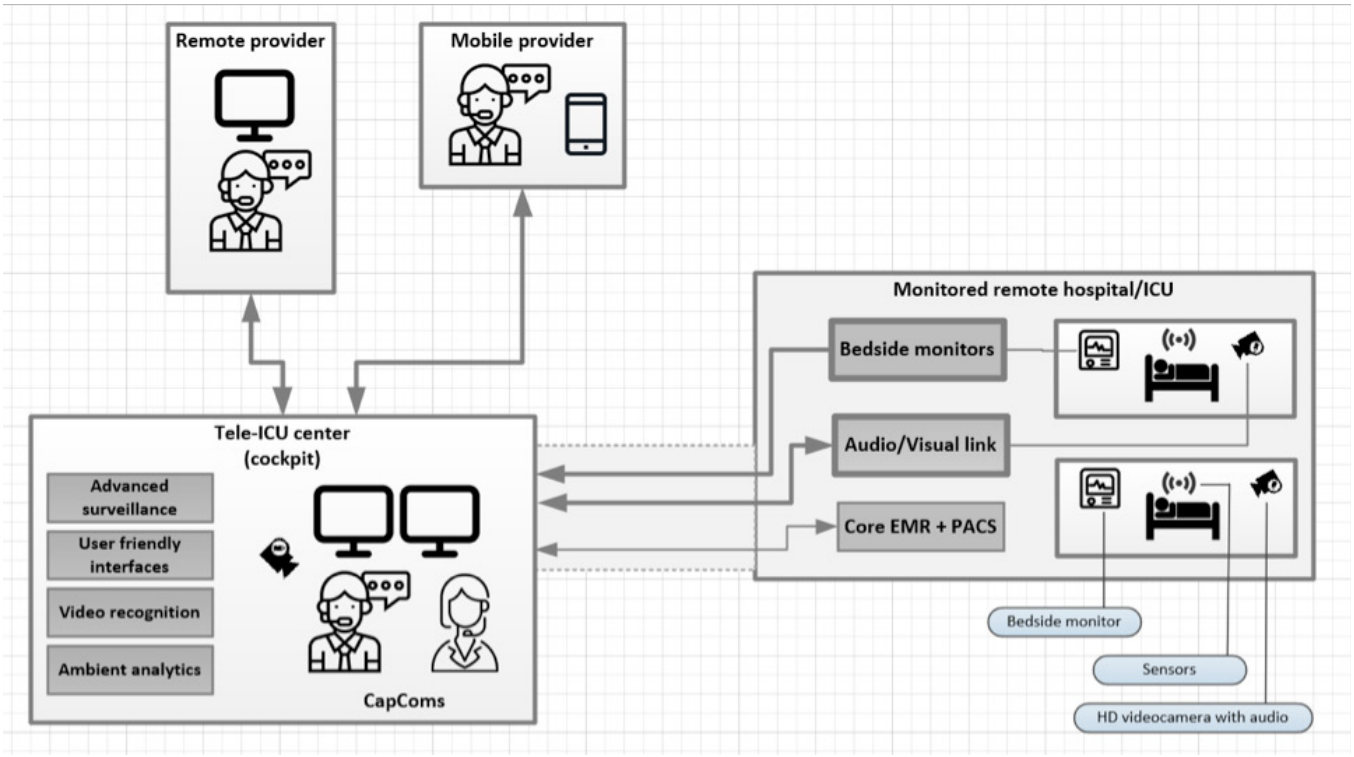


**Figure 1.** Structure of advanced Tele-ICU centre

Advances in Tele-ICU have been intimately linked to advances in technology. The first use of a two-way audiovisual link in critical care was reported in 1977 (Grundy et al. 1977). However, it was not until 1997 that a practical use of telemedicine in ICU care was established, when a group of Johns Hopkins intensivists began monitoring a 10-bed surgical ICU in a hospital in Northern Virginia, relying in part on a telephone access system to transmit data from bedside monitors. As the remote hospital had no EMR, chart-based patient data such as clinical notes and bedside flow sheets needed to be scanned and transmitted digitally. The system evolved, and ultimately led to the creation of the company VISICU in 1998 (Rosenfeld et al. 2000). The first modern Tele-ICU system was installed by VISICU in 2000 at Sentara Healthcare in Norfolk, Virginia. Tele-ICU practices expanded notably in 2005-2010, with expansion facilitated by improvements in network speed and bandwidth. During this early phase of Tele-ICU development, systems from VISICU and iMD Soft dominated the commercial market. These early systems used traditional models of administrative and technical structure, whereby, for example, networking programmes would utilise a single central hub to provide Tele-ICU for a remote location or a point-to-point programme within the same healthcare system. Technologically-current Tele-ICU systems use real-time/synchronous audio-visual links between remote clinicians and patients.

Presently, there are no practical barriers in terms of network speed or quality to establishing a Tele-ICU. Nonetheless, adoption of Tele-ICU in the years prior to the COVID-19 pandemic was relatively slow. Barriers to widespread adoption were as follows:

**1) Cost.** Start-up costs for a Tele-ICU command centre may be up to $5 million, when considering expenses related to construction, installation, and training. Thereafter, yearly operating expenditures may be up to $2 million.

**2) Regulatory requirements.** A Tele-ICU system must be HIPAA compliant. Popular consumer-level video conferencing tools do not generally meet the requirements. While nearly every EMR vendor now offers a secure audio/video communication package, these simple, widely-available tools do not meet Tele-ICU regulatory requirements for active patient-monitoring (APM) systems. The US Food and Drug Administration (FDA) has guidance regarding differentiating APM from medical device data systems (MDDS). Devices (including software devices) used for APM must be FDA class II certified (Code of Federal Regulations 21; Medical Devices Data System FDA). Currently, FDA class II certified APM for Tele-ICU include only Philips VISICU, InTouch Health Remote, and iMD Soft Meta Vision ICU (Herasevich and Subramanian 2019).

**3) Medical Licensing.** Licensing is cited as one of the most significant barriers to telemedicine in the U.S. Currently, each U.S. state grants its medical licenses independently, and – outside of the context

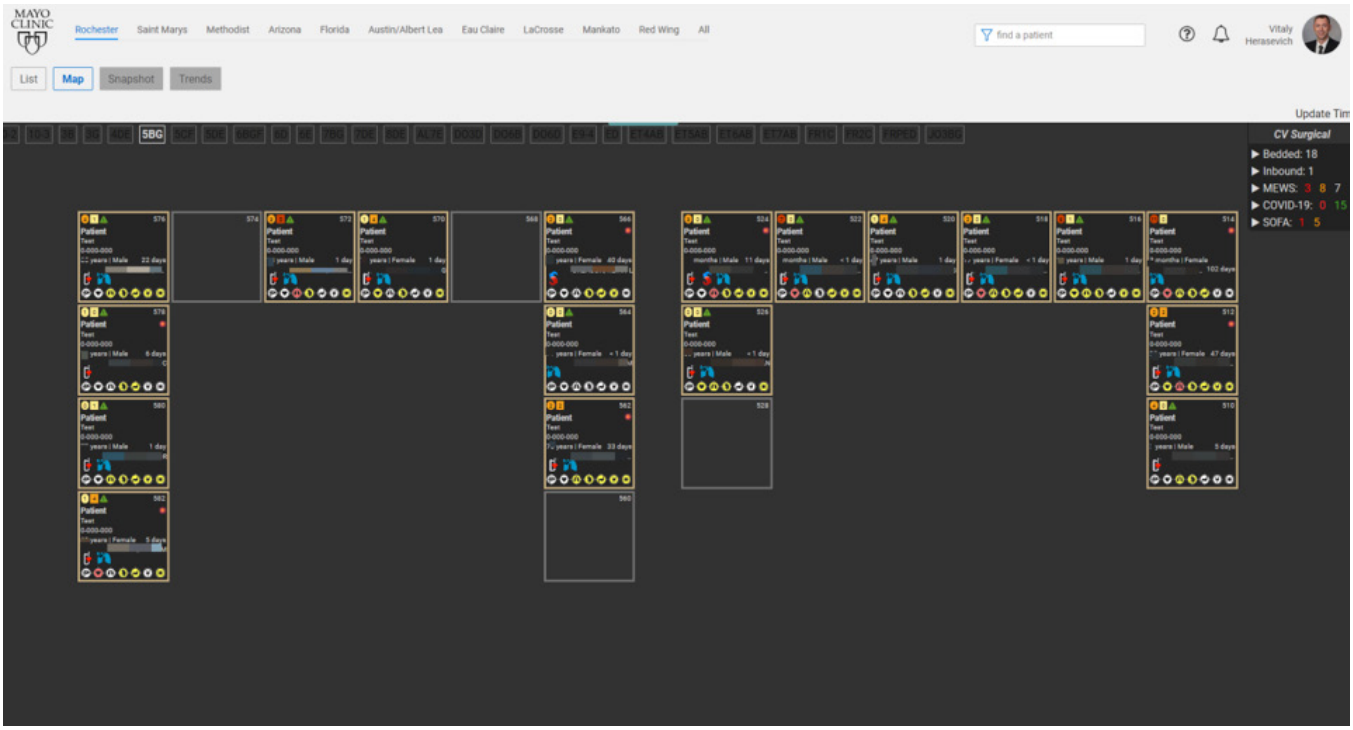


**Figure 2.** Acute Care Multi-patient viewer (AMP). A remote situational awareness tool to prioritise patient care efficiently and to predict risk escalation across locations in real time. By permission of Mayo Foundation for Medical Education and Research. All rights reserved.

of temporary, emergency changes made during the COVID-19 pandemic – each state mandates that an individual who provides medical treatment to a patient located in their state holds a medical license issued from their state. Therefore, establishing multi-state Tele-ICU services requires that every provider in the practice secures medical licenses in all of the states included in their Tele-ICU practice. While an interstate medical licensure compact exists to help expedite multi-state licensure for qualified physicians (https://www.imlcc.org), the licensure process is generally considered to be cumbersome.

## Rapid Deployment

Telemedicine transformed healthcare delivery in response to two distinct features of the US COVID-19 pandemic: (1) the demand for stay-at-home outpatient care, and (2) the surge of inpatient hospital admission (Wosik et al. 2020). Beginning in March 2020, there emerged an urgent need for telehealth solutions to manage the problem of large cohorts of outpatients who were unable to travel for routine appointments, in order to evaluate new symptoms and to manage long-term care needs. At Mayo Clinic, more than 6500 providers performed outpatient video telemedicine consults from the onset of the pandemic through July 15, 2020, a 2000% increase from the 300 providers who had performed telemedicine consults pre-pandemic (Demaerschalk et al. 2021). This rapid increase serves as proof that the existing telemedicine systems are scalable, and that there are no major technological barriers to expansion. Separately, in response to regional surges in inpatient hospital admissions of critically-ill patients with COVID-19, the Mayo Clinic Enhanced ICU (which provides tele-ICU care) was able to establish new telemedicine ICU consultative services in hospitals in New York, Wisconsin, and Florida within days, facilitated in part due to licensing waivers.

## Going Forward

Looking ahead to a post-pandemic future, it seems safe to predict that virtual care will remain a part of the US healthcare landscape. The experience during the COVID-19 pandemic has established telemedicine as a reliable and useful mode of healthcare delivery. It is now clear that telemedicine solutions can serve to increase access to care, both for inpatients and for outpatients. It is also clear, based on the experience with COVID-19 itself, that remote patient monitoring can facilitate safe treatment at home for conditions that previously required hospitalisation. Given these benefits, it is likely that state and federal regulations and policies pertinent to telemedicine will undergo changes, with the intention of reducing barriers to establishing telemedicine practices. Already, bipartisan legislation has been introduced to the US Congress ("The Protecting Access to Post-COVID-19 Telehealth Act of 2021") which proposes to eliminate most geographic and originating site restrictions on the use of telehealth in Medicare, extend Centers for Medicare and Medicaid Service reimbursements for telemedicine beyond the COVID-

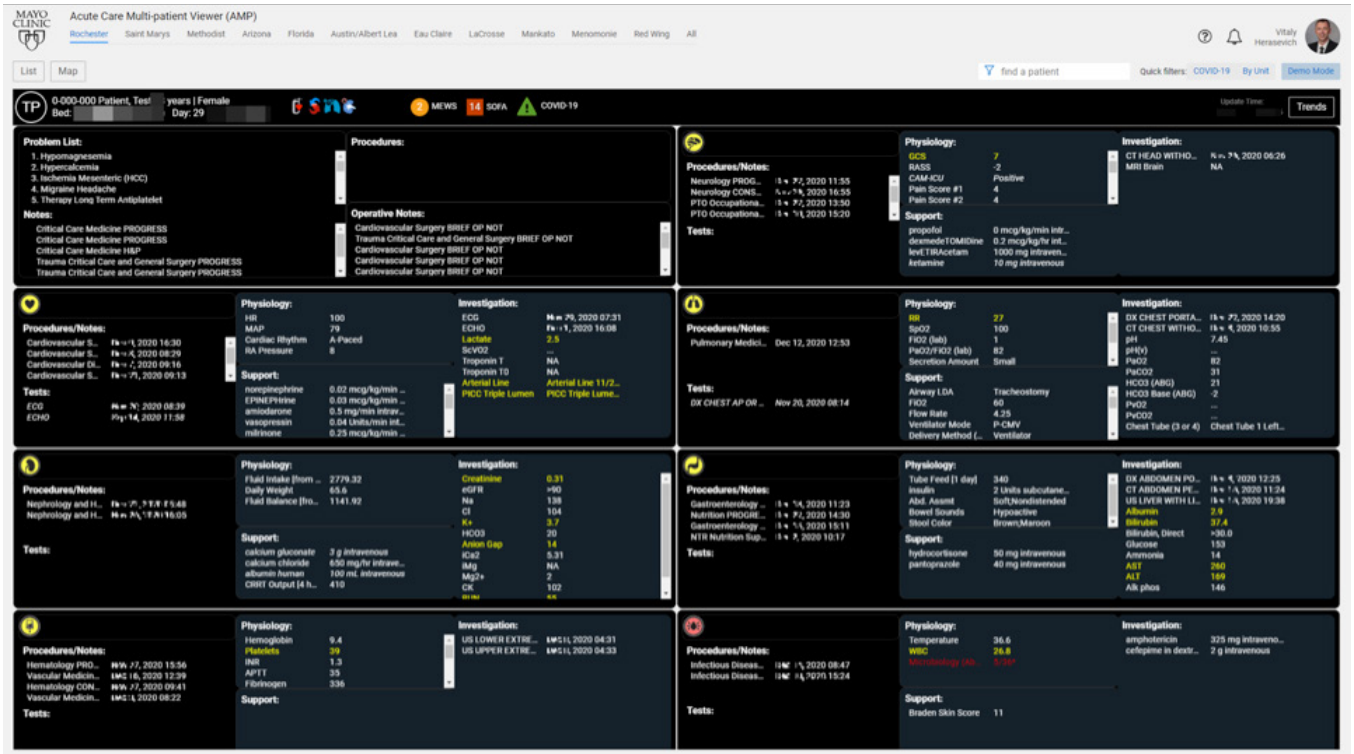


**Figure 3.** Acute Care Multi-patient viewer (AMP). A single patient viewer for remote ICU, driven by rules that extract and present high impact clinical data in a user-friendly format. By permission of Mayo Foundation for Medical Education and Research. All rights reserved.

19 public health emergency, and make permanent the disaster waiver authority to expand telehealth in Medicare during future emergencies and disasters.

At this point it is evident that telemedicine in general, and Tele-ICU in particular, have great opportunities to incorporate a new generation of tools that will allow for marked improvements in remote care. What will be the functional utility of such state of the art systems and how will they exhibit the true value of telemedicine? First, they will integrate real-time clinical analytics for the purpose of clinical surveillance. Embedding smart algorithms that utilise machine learning into telemedicine systems will allow for predictive and prescriptive analytics among large populations of patients. Such analytics have the potential to foster more accurate and timely care in the management of patients, and to enhance safety when monitoring large numbers of patients. Second, the Tele-ICU Command Centre will transform from a site of co-located physicians and nurses to a multifunctional cockpit operation involving various functions, services and teams in one physical location (**Figure 1**). Third, real-time ambient intelligence will be at the centre of digital technologies. Fourth, future systems will integrate hospitals around best care protocols.

An example of technology designed for the next generation of Tele-ICU is Acute care MultiPatient viewer (AMP). This is an advanced Clinical Control Tower system, which includes central alert screening capabilities. AMP can use machine learning models to generate alerts, which are managed by a designated capsule communicator or "CapCom," analogous to NASA's ground-based astronaut who maintains contact with crew members in their spacecraft. AMP also has advanced visualisation for situational awareness and standard communication channels (**Figure 2**). Video recognition, sound processing and sensor analytics embedded in the workflow will further enhance the system (Davoudi et al. 2019).

Remote clinicians dealing with large numbers of patients at once require smart tools that enable clinical decision-making without scrolling through the full EMR. High impact data should be extracted by rules and presented in user-friendly formats to minimise cognitive load and errors (**Figure 3**) (Ahmed et al. 2011). Actionable, predictive, real-time clinical analytics enable proactive and efficient patient care.

After all, telemedicine provides opportunities to harness technology to develop better ways to provide care, rather than simply new ways to do the job. Tele-ICU care will mature from a tool to support regional staffing shortages to a viable clinical service that could apply to a wide range of clinical needs.

## Conflict of Interest

None. ■

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# How To Ventilate COVID-19 Patients?

## TwinStream® ICU with p-BLV® (Pulsatile Bilevel Ventilation)

The Austrian critical care ventilator TwinStream® ICU was designed with the explicit purpose of saving critically respiratory-distressed patients. In particular those patients with severe lung diseases (e.g. ARDS) who can no longer be supported with conventional ventilation.

Its unique p-BLV® mode has become an established value in many Intensive Care Units in Austrian and German hospitals. And when severe multi-trauma patients are admitted the TwinStream® ICU often proves to be an effective last resort.

Since the start of the pandemic the TwinStream® ICU has become an invaluable asset in the fight against COVID-19. Prof. Dr. Thomas Uhlig, Clinic director and head of the ICU at the Lüdenscheid Clinic, Germany, explains:

### Why is the TwinStream® ICU such an important asset in the fight against COVID-19?

"We ventilate all COVID-19 patients which require intubation with the TwinStream® ICU first, until we see a clear improvement of the oxygenation, because p-BLV® is much more efficient at recruiting lung volumes than other ventilation methods.

Hypercapnia is another problem we are faced with after non-invasive ventilation. With p-BLV® we can kill two birds with one stone. Its combination of high-frequency ventilation (improved oxygenation) and low-frequency ventilation (efficient $CO_2$ elimination) makes it our most effective ventilation method for this type of patients".

### How long are COVID-19 patients usually ventilated by the TwinStream® ICU?

"As soon as the $PaO_2/FiO_2$ ratio and airway pressures are again within a tolerable range, a conventional ventilator can take over. But if there is an acute deterioration, we ventilate with the TwinStream® ICU again. Our average patient is ventilated for around 14 days, of which on average around 5-7 days with the TwinStream® ICU".

### How old are the COVID-19 patients which you have ventilated so far?

"Since April we have ventilated COVID-19 patients between the ages of 20 and 85".

### Conflict of Interest

Prof. Dr. Uhlig declares no conflict of interest and has not received any funding or equipment from Carl Reiner GmbH. ■

# Rethinking Critical Care - Use and Challenges of Artificial Intelligence

## Why digitalisation of intensive care medicine means less rather than more data

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Intensive Care Medicine is generating an amount of data that is hardly analysable by humans. Digitalising and using artificial intelligence has to focus on providing less rather than more data.

### Introduction – AI in Intensive Care Medicine: Ghost or Glimmer of Hope?

Whether it's flying robots buzzing around the patient's bed or glowing beams that miraculously heal people in seconds: we are currently a long way from such science fiction scenarios in medicine - Good thing.

But the use of artificial intelligence (AI) in medicine is not a mysterium, and it certainly must not become one. After all, AI is not an autonomously acting black box over which we no longer have any influence and whose actions we humans can no longer comprehend. What many people are currently forgetting: every AI-based algorithm is always based on human intelligence. Everything that an AI does is developed and implemented by us humans. Only with highly complex deep learning do algorithms begin to independently recognise new patterns in the data sets and thus develop something like an apparent intelligence (Peine 2020). The machines therefore still have a long way to go before they have a life or even a will of their own.

No other area in a hospital is more influenced by the omnipresence of high-tech devices, then today's intensive care units. Compared to other medical specialties there might be no other field where critically ill patients are such depended from organ support by machines and where their vitals are so frequently and continuously monitored. Thus, critically ill patients often generate data volumes that – in all dimensions - are not analysable by human brains (Johnson 2016).

Up to ten devices surround each patient bed in order to monitor all relevant parameters. This is actually quite a comfortable situation for us - if it weren't for the enormous volumes of data that have to be sifted through, documented and evaluated by far too few specialists at the same time. If we don't take countermeasures now, the system will inevitably collapse.

Patient data on an intensive care unit (ICU) are recorded in different resolutions or time intervals, depending on the urgency and implication **(Table 1)**. Digital, electronic health records (EHR) are thus inconceivable in modern ICU treatment. At the same time, EHRs are creating predetermined value for the use of big data, often linking all further incoming source systems like radiological, microbiological or laboratory findings, medication or other examination. EHRs bundle all relevant data and are particular sources for big data analysis. Nowadays, we aggregate over 1,000 data points per patient in a single hour on the wards (Cleophas 2015). If a physician cares for between 14 and 20 patients daily, there are between 14,000 and 20,000 data points that he or she would have to look at. This is a volume of work that almost no one can keep an overview of - this inevitably results in errors that can cost lives. This density of data will not decrease in the future. In fact, it is increasing by 30% per year, which intensive care physicians have to evaluate additionally. Like in an airplane cockpit, doctors try to keep the flood of

| Data | Example | Time interval |
|---|---|---|
| Vitals | • ECG,<br>• bloodpressure,<br>• oxygen saturation,<br>• body temperature,<br>• respiratory rate | seconds |
| Parameters of mechanical ventilation (MV) | • oxygen concentration,<br>• ventilatory mode,<br>• ventilarory pressures,<br>• respiratory mechanics | seconds – minutes |
| medication | • catecholamines<br>• analgosedation<br>• antihypertensive therapy<br>• anti-infective therapy<br>• anticoagulation | minutes – hours |
| Scores | • Glasgow ComaScale<br>• SAPS II<br>• SOFA<br>• TISS-10 | 24h |
| Diagnosis during course of treatment | • Secondary surgery<br>• secondary complications (i.e., infections, sepsis, organ failure, haemorrhage) | 24h |

**Table 1.** Examples of EHR data and their frequency

data under control - sometimes with up to six screens simultaneously, on which new data appear every second. As a result, we have to spend an incredible amount of time preparing and interpreting this mass of data and recording it in accordance with general documentation requirements. The time that has to be invested in this could be used far more sensibly.

To give you a better idea, consider the following comparison: if you're traveling at 200 km/h on a busy highway, you'll certainly be pleased with the numerous assistance systems that work for the driver in her or his own car. Even if these systems - apart from autonomous driving - are active and support the person behind the wheel, for example in keeping in lane, he or she still has the steering wheel in his or her own hands and can intervene at any time. So it's not about replacing the driver, but about cooperative assistance. With cars that are traveling so fast that the human eye can no longer perceive some things, we gladly accept this assistance. So why are there still many reservations from the medical field?

## Availability of Intensive Care Datasets

In particular, the publication of two medical databases, the Medical Information Mart for Intensive Care III database (MIMIC-III) (Johnson 2016), consisting of data from 61,532 ICU patients from Beth Israel Deaconess Medical Center (USA), and the eICU Collaborative Research Database v2.0 (eICU) (Pollard 2018), consisting of data from 200,859 ICU patients from over 300 ICUs in the USA, has led to a democratisation of research in the field of big data in intensive care medicine. Recently, a European equivalent, the "Amsterdam UMCdb," with associated data from 20,181 ICU patients has also been published. With this retrospective data, scientists can now train AI systems without access to proprietary hospital data and any associated data privacy concerns.

## Explainability and Transparency are Crucial

The complexity of algorithms means that a profound and detailed knowledge is needed to really understand them. That, in turn, would be the normal prerequisite for gaining acceptance for a new technology or product in medicine: Explain, Understand, Deploy. So how can it be ensured at all that a system actually fulfills the ethical principles for AI, such as being non-discriminatory, beneficial, autonomous and fair, if it cannot even be explained which factors and processing procedures underlie the result of an AI system?

Explainability therefore means both understandability and accountability. When medical decisions are supplemented and, in some cases, even overridden by AI-based algorithms, human experts should still have the possibility and ability to understand and explain the process of machine decision-making, at least upon request. An essential criterion of explainable artificial intelligence - especially in medicine - therefore remains causality as well as the measurement of the quality of explainability. Based on these premises, the challenge is to provide insight into why neural networks and other machine learning algorithms make their decisions (Wachter 2017) and how models that can be interpreted by humans can be developed and optimised (Stewart 2018). The aim has to be to generate adequate explanations for the decisions made (FDA 2020). The European Commission has also recently taken a position on this topic in a white paper (European Commission 2021).

**Figure 1.** Improving ARDS detection with an app

## Intensive Care Units: What to do Now?

To cut to the chase: if we want to maintain our high-quality care in critical care, we need to act now! Critical care needs a work environment where medical staff is not spending 50% of their work time in front of a computer. Meaningful mechanisms and powerful tools are needed - coupled with algorithms that help ensure we can focus on the essential data. In the future, we will need support systems that are technologically mature and help us provide evidence-based therapy at every moment. Telemedicine solutions bring specialist expertise to our patients' bedsides - both in the big city and in the countryside.

## Clinical Decision Support Systems (CDSS)

Evidently, sepsis/septic shock and the acute respiratory distress syndrome are the most relevant fatal entities in the ICU (SepNet Critical Care Trials Group 2016; Phua 2009), with mortality rates up to 50%. Both syndromes have in common that early diagnosis and adequate, guideline-adhered treatment is urgently demanded. However, particularly regarding early diagnosis, ICU physicians are often confronted with patients being transferred from home to ambulatory care to the ED and finally to the ICU. This is often time consuming and may aggravate patients` outcome due to delayed treatment.

Besides, in ARDS, nearly 40% of the cases are not even diagnosed by physicians, which suggests procedural and infrastructural deficits (Bellani 2016). Digital use and the approach of pre-processing data from EHRs respectively, could be a meaningful solution (Peine 2021). As kind of a medical decision support, a mobile device could draw attention to the relevant diagnosis of ARDS by providing diagnostic data and treatment recommendations from the EHR to a smartphone app (or other mobile devices). The use case 'Algorithmic Surveillance of ICU patients with acute respiratory distress syndrome' (ASIC) follows this strategy within a quality improvement project and is an integral part of the 'Smart Medical Information Technology for Healthcare' (SMITH) project (Winter 2018). It is the aim of this project to improve ARDS detection and guideline adherence in the treatment of mechanically ventilated ARDS-patients by implementing an application software (app) provided on a mobile device and consecutively improve outcome in this patient population **(Figure 1)**. The data used by the ASIC app is obtained from the local EHR. Further, the ASIC app operates system-independently on different devices; however, it is primarily intended to be used on a mobile device (e.g. tablet, smartphone). All in all, this app use is only one clinical example for upcoming, diverse clinical considerations, giving physicians the opportunity to

-timely keep vital data under control
-make adequate diagnosis
-adhere to guidelines.

Moreover, app use can be a relevant interlink to bundle data from the EHR and to transfer them for the purpose of AI research. Ideally, an intersectoral infrastructure will lead to interoperability for comparing big data on a higher level and for building data bases in analogy to MIMIC-III.

## Conflict of Interest

LM, AP, and GM are co-founders of Clinomic GmbH. LM and AP are chief executive officers of Clinomic GmbH. GM received restricted research grants and consultancy fees from BBraun Melsungen, Biotest, Adrenomed, and Sphingotec GmbH outside of the submitted work. LM rand AP received consultancy fees from Sphingotec GmbH. JB received consultancy fees from Bayer and Biotest. ■

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# Prone Position in Awake, Non-Intubated Patients with ARDS: From Physiology to the Bedside

Prone position (PP) in awake, non-intubated patients with respiratory failure is a physiology-based ventilatory strategy that improves oxygenation and may decrease the need for intubation and invasive mechanical ventilation (IMV).

## Introduction

During the pandemic caused by the SARS-CoV-2 virus, which produces coronavirus disease 2019 (COVID-19), prone positioning (PP) has been proposed for awake, non-intubated patients hospitalised for pneumonia and respiratory failure. This therapy is not new and has been described for two decades (Valter 2003), but has become popular around the world over the past year as a result of the large number of patients with acute respiratory failure, as part of an attempt to improve oxygenation and prevent the need for intubation and IMV given the lack of mechanical ventilators and free beds in intensive care units (ICUs) in many hospitals. Observational and some prospective clinical studies have been carried out with a limited number of patients and significant improvement has been observed, with an increase in arterial partial pressure of oxygen ($PaO_2$), decrease in respiratory rate (RR) and decrease in respiratory failure; yet there remains some debate on the benefits of PP in awake patients in terms of achieving a significant decrease in intubation.

## Pathophysiologic Considerations for ARDS and Prone Position

Acute respiratory distress syndrome (ARDS) is characterised by progressive inflammation of the alveolar-capillary unit with the infiltration of inflammatory cells and formation of hyaline membranes, significantly affecting gas exchange. It can be triggered by direct lung injury, such as by viral pneumonia (e.g., the SARS-CoV-2 or influenza viruses), or by serious systemic diseases (e.g., sepsis, burns, multiple trauma). The local and/or systemic inflammatory response generates an endothelial lesion at the pulmonary capillaries, increased permeability of the alveolar-capillary membrane, interstitial oedema, alveolar oedema, diapedesis and activation of lymphocytes, neutrophils and macrophages in the lungs, which generate a greater amount of inflammatory cytokines including metabolites derived from arachidonic acid and interleukins, activating the complement system and reacting with proteases and free radicals, in turn damaging the endothelium and activating the tissue factor pathway, leading to a prothrombotic state.

Multiple mechanisms of hypoxaemia are involved in ARDS: decreased oxygen diffusion, hypoventilation, increased shunting, and ventilation/perfusion (V/Q) mismatch. Clinically, ARDS manifests as dyspnoea, tachypnoea, and increased load on respiratory muscles; arterial gas studies show a decrease in $PaO_2$, a decrease in peripheral arterial oxygen saturation

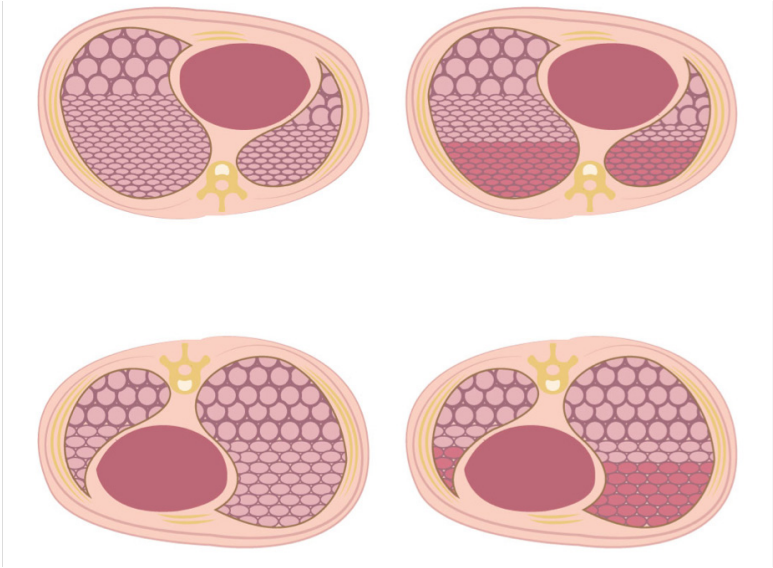

**Figure 1.** Recruitment of lungs with prone position

**Figure 2.** Awake prone position

($SpO_2$), and an increase in partial pressure of carbon dioxide ($PaCO_2$). In ventilatory mechanics there is a decrease in static lung compliance (Cst).

There are large areas of alveolar collapse, predominantly in the gravity-dependent lung regions (posteriorbasal segment) that are richest in capillaries, and therefore changes in body position result in changes in ventilatory mechanics and gas exchange. The supine position does not benefit ventilatory mechanics due to the weight of the heart, the anterior chest wall and the abdomen, which falls on the gravity-dependent pulmonary areas, decreasing Cst and functional residual capacity (FRC), predisposing to the formation of atelectasis and shunts and contributing to hypoxaemia and alveolar hypoventilation (Bower 2020). On the other hand, in the prone position (PP), the weight of the heart, anterior wall of the rib cage and abdomen falls on the bed, releasing the pressure exerted on the dependent alveoli and causing a rapid improvement in ventilation. In most cases, due to the increase in FRC and tidal volume, a decrease in shunting and atelectatic areas is also observed **(Figure 1)**.

The improvement in ventilatory mechanics is not the only advantage observed in non-intubated patients in the PP. In ARDS there is a capillary derecruitment due to microthrombosis and collapse of the pulmonary vasculature due to hypoxaemia-mediated redistribution, which decreases perfusion. This occurs predominantly in areas with poor ventilation, heavily impacting gas exchange. PP favours more homogeneous ventilation, which improves oxygenation and favours capillary recruitment, benefitting V/Q significantly.

## Evidence on Prone Position in Non-Intubated Patients with ARDS

PP has been shown to decrease mortality in patients with ARDS receiving IMV (Guerin 2017); however, there is still no solid evidence that this occurs in non-intubated patients. Some studies conducted in the last two decades have shown improvement in oxygenation in patients with hypoxaemic respiratory failure placed in PP, but research on this topic grew exponentially last year during the COVID-19 pandemic.

The prone position (PP) in awake, non-intubated patients with acute hypoxaemic respiratory failure results in better oxygenation, demonstrated by an increase in $PaO_2$ and $SpO_2$ and the $PaO_2/FiO_2$ ratio, while pH increases due to a decrease in the level of $PaCO_2$, and a decrease in RR and work of breathing is also observed **(Figure 2)**. PP is not associated with haemodynamic deterioration (Scaravilli 2015). In addition, PP combined with non-invasive ventilation (NIV) or a high-flow nasal cannula (HFNC) in patients with moderate to severe acute respiratory distress syndrome (ARDS) has

| | |
|---|---|
| **Pre-prone checklist** | Look for indications and contraindications for prone positioning (PP)<br>Check oxygen therapy/NIV/HFNC is secure with adequate length on the tubing<br>Haemodynamic & pulse oximetry monitoring |
| **Indications** | Acute hypoxaemic respiratory failure<br>Alert and conscious patient |
| **Contraindications** | Immediate need for intubation<br>Haemodynamic instability<br>$PaO_2/FiO_2$ less than 100 mmHg on NIV/HFNC<br>Agitation or altered mental status or seizures<br>Unstable spine/thoracic surgery |
| **Assist the patient** | Explain procedure and benefits and assist with position change before placing in PP<br>Continue pulse oximetry, haemodynamic & respiratory rate (RR) monitoring<br>Help the patient into the PP, using pillows if necessary, to support the chest<br>Reverse Trendelenburg position may aid comfort |
| **Post-prone monitoring** | Check for desaturation or patient intolerance<br>Serial measurement of ROX index ($SaO_2/FiO_2$/RR)<br>Any fall in ROX index should prompt escalation of care<br>If desaturation: Check oxygen tubing for disconnection<br>If patient intolerance: Change position<br>If patient is able to tolerate PP with $SpO_2$ 92-96%, advise patient to remain in the prone position for 2-4 h<br>Monitor for desaturation 15 min after each position change |
| **When to stop PP?** | In any case of respiratory distress<br>ROX index < 2.85 at 2 h and < 3.47 at 6 h may suggest poor response and should prompt escalation of care<br>In case of sustained improvement in $SpO_2$ to more than 93% in room air 2h after stopping PP |

**Table 1.** Recommendations for awake prone positioning. PP: prone positioning, RR: respiratory rate, NIV: non-invasive ventilation, HFNC: high-flow nasal canula, ROX: respiratory rate.

been shown to be safe and effective and may prevent intubation (Ding 2020; Perez-Nieto 2020). One further advantage of PP without intubation is that it allows the patient to interact with family during hospitalisation, favouring humanisation in healthcare (Slessarev 2020).

Due to the COVID-19 pandemic and the high global demand for respiratory support, the PP in awake non-intubated patients has become popular in China, and clinical interest has increased rapidly in the Americas and Europe. An early strategy combining the PP together with non-invasive ventilation (NIV) or a high-flow nasal cannula (HFNC) has been reported to be associated with reduced intubation and mortality (Sun 2020) and improved oxygenation compared to patients who were not administered this therapy (Caputo 2020; Thompson 2020; Jagan 2020), and therefore may be beneficial; however, one prospective observational cohort study found no benefit in terms of reducing the intubation rate (Ferrando 2020).

## Practical Considerations for Prone Position in Non-Intubated Patients with Respiratory Failure

Due to the great demand for medical attention due to COVID-19, it is appropriate to encourage all patients with respiratory failure, with $SpO_2$<92-94% and RR> 22-28 breaths per minute, to practise the prone position because it is a free, low-risk manoeuvre that requires minimal assistance to perform. The safety and efficacy of PP has been demonstrated in non-intubated patients and so can

be performed safely in all areas of care, including the emergency room, ICUs, and other hospital care units **(Table 1)**.

Patients receiving supplemental oxygen through nasal cannulas (HFNCs or LFNCs), oxygen masks, and NIV can safely self-pronate depending on their tolerance and comfort. It should be considered that some more vulnerable groups of patients (the elderly, obese, etc.) may require help to properly position themselves in the PP. Patients must be aware of the procedure, awake, cooperative, and able to communicate on their own and mobilise with minimal assistance. The recommended duration of PP in non-intubated patients is not clear, but based on the patient's tolerance, can be set at a minimum of 2 hours every 12 hours or up to 16 hours a day, and alternative lateral and semi-prone positions can be tried if the patient cannot bend fully (Sodhi 2020).

Proposed contraindications to initiating PP in non-intubated patients include patients requiring immediate intubation, airway compromise, respiratory fatigue, patient non-cooperation, neurological deterioration, haemodynamic instability, arrhythmias, spinal instability, pelvic instability, chest trauma, recent abdominal surgery and pregnancy in the 2nd and 3rd trimesters. Some of these contraindications could be relative, but the risk of complications must be taken into account.

All non-intubated patients in the PP should be continuously monitored for treatment failure and the need for greater respiratory support, including IMV or admission to the ICU. Close monitoring of $SpO_2$, vital signs (mainly RR), and dyspnoea is recommended, as well as the use of the ROX index to determine the need to intubate patients (Sryma 2020). An RR> 26 breaths per minute sustained for more than 30 minutes and a work of breathing (WOB) scale score> 5 points are associated with the need for intubation (Apigo 2020).

There is no consensus on when to stop PP therapy, but we can recommend that when the patient is in the supine position and presents a $SaO_2$> 92 to 94%, with RR <22 to 28 breaths per minute and relief of dyspnoea, PP may be discontinued.

In conclusion, PP in awake, non-intubated patients with respiratory failure is a physiology-based ventilatory strategy that improves oxygenation and may decrease the need for intubation. As a minimal risk intervention requiring minimal assistance, it is now a globally accepted therapy to improve oxygenation in patients with respiratory failure, including from COVID-19 (Sodhi 2020). Randomised controlled studies are required to confirm the current theoretical benefits of this therapy.

## Conflict of Interest

No authors declare any conflict of interest. ■

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# Cardiorespiratory Compromise in the Perioperative Environment - Prediction, Quality, Analytics and AI

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Perioperative cardiorespiratory compromise is common and goes largely undetected. Predictive cardiorespiratory indices can help in early detection of harmful deviations and guide preemptive treatment. Using continuous cardiorespiratory monitoring coupled with these tools, we now know which patients are likely to decompensate both within and outside the operating room. There is a tremendous opportunity for artificial intelligence-based solutions to integrate these streams of continuous monitoring data with clinical records and design the next generation of quality and patient safety improvement measures.

## Introduction

Despite major advances in perioperative care, postoperative complications are relatively common and a leading cause of death (Bartels et al. 2013). In fact the thirty days after non-cardiac surgery is still one of the leading causes of mortality in the United States (Carlberg et al. 2004). Perioperative physicians rely on continuous vital signs data to make important clinical decisions during a patient's journey from the operating room, to the post-anaesthesia care unit, the general care floor and the intensive care unit. Physiologic monitoring data in combination with patient specific information in electronic health records can help build useful risk prediction tools. Not all patients may benefit from advanced continuous monitoring, and identifying high risk patient using predictive algorithms will allow patient specific recommendations. Also, clinical care information can help build and monitor quality metrics dashboards. The authors envision a not too distant future where these streams of data when used in context of natural language processing and free text from clinical notes, laboratory values and imaging studies, will develop dynamic prediction tools to improve perioperative patient safety. For example, perioperative intelligence (Maheshwari et al. 2019) can help advance perioperative medicine by focused application of artificial intelligence technologies in three key areas; identification of at-risk patients, early detection of complications, and timely and effective treatment.

## Hypotension Prediction in the Perioperative Environment

Perioperative hypotension is strongly associated with myocardial injury after non-cardiac surgery (MINS) (Sessler et al. 2018). Identifying high risk patients can help target appropriate preventive and therapeutic measures. For example, routine screening for troponins in high risk patients can help detect MINS, in turn ensuring timely management including close monitoring, optimisation of haemodynamic status, and cardiology consultations as necessary (Devereaux and Sessler 2015). Patient baseline state, like age and comorbid conditions, can predict who will suffer from cardiorespiratory compromise. Revised Cardiac Risk Index (RCRI) (Lee et al. 1999) and American College of Surgeon's National Surgical Quality Improvement Program

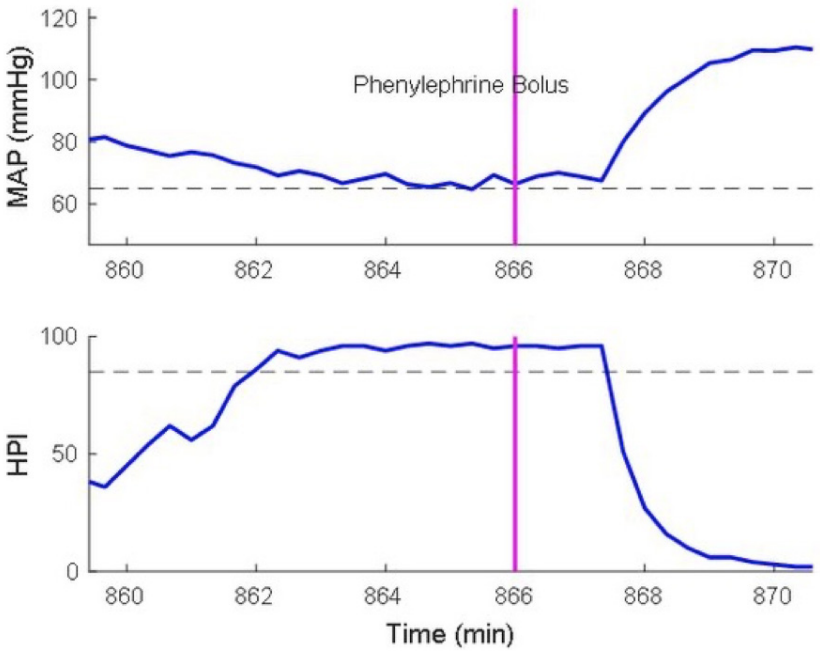


**Figure 1.** Relationship between hypotension prediction index and mean arterial pressure. Source: Maheshwari et al. 2020a

(ACS NSQIP) (Bilimoria et al. 2013) are commonly used risk indices to calculate postoperative cardiac complications. When used in the right environment these risk prediction tools, can influence the decision for preoperative cardiac testing, surgical timing, and subsequent intraoperative and postoperative care.

Hypotension avoidance is a key to modern anaesthesia practice; however, not all hypotension can be avoided. Predicting hypotension in advance and instituting corrective actions proactively can help avoid it. For example, simple algorithms based on heart rate variability can help predict hypotension and bradycardia after induction of anaesthesia (Hanss et al. 2008). More complex machine learning based algorithm like Hypotension Prediction Index (HPI) (Hatib et al. 2018) which utilises arterial pressure waveform information can predict hypotension up to 15 minutes in advance. The HPI algorithm prediction performance seems optimal based on few retrospective and prospective studies (Davies et al. 2020; Maheshwari et al. 2020a) **(Figure 1)**.

Two randomised trials have evaluated HPI performance in high risk patients. Winjeberge et al. (2020) randomised 60 patients undergoing moderate to high risk noncardiac surgery who required continuous invasive arterial pressure monitoring, half with HPI guidance and half without HPI guidance, and found 400% hypotension reduction with HPI guidance. Whereas, Maheshwari et al. (2020b), in a similar trial, randomised 214 patients and found no difference in hypotension among groups (http://youtu.be/2WGKrpiQA3s). Time between alert and hypotensive event, rate of baseline hypotension and treatment protocol compliance can explain some of the difference and needs to be studied further. In the critical care setting, hypotension is very common and prolonged, complicated in aetiology and pathogenesis, but hypotension prediction may help in timely treatment. For example, using Medical Information Mart for Intensive Care dataset (MIMIC III) database, Cherifa et al. (2020) used a Super Learner (SL) algorithm which is an ensemble machine-learning algorithm to predict an acute hypotensive episode 10 minutes in advance. Hypotension prediction in dynamic critical care setting is crucial for timely treatment. Algorithms which can help guide appropriate treatment and which result in better patient outcomes are needed. In addition, any hypotension prediction index in the ICU should be tested in a prospective trial and have an efferent arm (intervention arm) that is well defined.

Thus, evaluation of prediction system in real life clinical scenarios is critical. Not only do we need to confirm the prediction performance of a particular algorithm, that is, does it really predict a particular outcome, but equally important is how the intended use of an algorithm changes an outcome of interest in routine clinical care. The latter part is difficult and is currently lacking for most machine learning based algorithms used in perioperative care. We need to test these algorithms just like any other drug or device and show consistent outcomes improvement.

## Respiratory Depression and Perioperative Pulmonary Complications Prediction

Postoperative respiratory complications are common (Miskovic and Lumb 2017). Alteration in respiratory drive, respiratory volumes and atelectasis can persist for up to six weeks after major surgery. Standardized Endpoints for Perioperative Medicine (StEP) Collaborative (Abbott et al. 2018) identified four important pulmonary outcomes; atelectasis detected on computed tomography or chest radiograph, pneumonia using U.S. Centers for Disease Control criteria, Acute Respiratory Distress Syndrome using Berlin consensus definition, pulmonary aspiration with clear clinical history and radiological evidence. We currently don't have robust algorithms to predict or help prevent pulmonary complication and this will remain an area of research interest.

In addition, patients can have respiratory depression events and stories of tragic harm suffered by patients who arrested on the

**Multivariable Model Predictors**

| Clinical Characteristic | Estimate | OR (95% CI) | Pr > \|t\| | Points if Clinical Characteristic = 'Yes' |
|---|---|---|---|---|
| Age (≥60 - <70) | 0.8077 | 2.243 | <0.0001 | 8 |
| Age (≥70 - <80) | 1.2323 | 3.429 | <0.0001 | 12 |
| Age (≥80) | 1.5647 | 4.781 | <0.0001 | 16 |
| Sex (M) | 0.7550 | 2.128 | <0.0001 | 8 |
| Opioid Naïve | 0.2912 | 1.338 | 0.0782 | 3 |
| Sleep Disorders | 0.4755 | 1.609 | 0.0175 | 5 |
| Chronic Heart Failure | 0.7494 | 2.116 | 0.0668 | 7 |
| | | | | Sum = PRODIGY Score |

**PRODIGY Score Distribution**

| | Low-Risk | Intermediate-Risk | High-Risk | *p* value |
|---|---|---|---|---|
| PRODIGY Score | <8 points | ≥8 & <15 points | ≥15 points | |
| % Pts with RD in Risk Category | 24% | 42% | 65% | <0.0001 |
| Sensitivity | — | 0.86 | 0.52 | |
| Specificity | — | 0.39 | 0.77 | |
| OR (p value) | $OR_{IL}$ = 2.34; p<0.001<br>$OR_{HL}$ = 6.07; p<0.001 | ORHI = 2.6; p<0.001 | | |

**Table 1.** The PRODIGY risk score and distribution across risk categories. Cells highlighted in green depict an example patient with a high risk of 15 points

general care floor of the hospital (hospital ward code blue), are common. Sudden respiratory arrests are almost never truly sudden, and deterioration in vital signs happens for 4-6 hours before the index event (Saugel et al. 2020; Khanna et al. 2019). Slow deteriorations are usually missed because most monitoring on the hospital general care ward is intermittent every 4-6 hours, the world over (Weinger 2007). Large datasets with national resuscitation registries repeatedly show that unrecognised deterioration on the ward is common, and associated with persistent harm (Anderson et al. 2019). Prior work using continuous portable respiratory monitoring devices has shown that postoperative hypoxaemia is common, persistent and prolonged and goes undetected in up to 90% of patients (Sun et al. 2015). In addition, simple bedside tools such as the STOP-BANG score, or the type of opioids used do not effectively predict amount and duration of hypoxaemia (Khanna et al. 2016; Belcher et al. 2016). Hypoventilation and apnoea events are at least as common, if not more than hypoxaemic events (Khanna et al. 2020a; Overdyk et al. 2007). Portable, light-weight, accurate and well validated monitoring systems are needed not just for respiratory depression monitoring but also for assessment of continuous blood pressure on hospital ward patients (Saugel et al. 2020). One challenge is the burden of alarms that essentially convert a general hospital ward to a critical care unit, and the lack of effective intervention, that leads to increased burden for nursing staff and lack of proven benefit from large trials. Future technical advancements of 'surveillance monitoring' systems, will need an integrated EMR streaming, and an effective economic model that justifies large scale use across hospitals.

Currently, surveillance sensor products provide continuous data, with easy access to trends, and patterns, though blood pressure monitoring remains scarce. While universal continuous monitoring is an ambitious goal, we need to target monitoring and intervention to high risk patients. The PRODIGY is by far the largest prospective observational study of continuous, (alarms silenced and monitors blinded) oximetry and capnography, thus generating a sizeable data of vital sign parameters and corresponding outcome data in both surgical and medical patients (Khanna et al. 2020b). Using nearly 1500 patients across three continents over one year, continuous oximetry and capnography data was recorded in adults receiving opioids for pain management and nursing on the hospital general care ward. Monitors were covered and alarms silenced, while providers followed the usual, 4-6 hrs intervals vital signs checks. The recorded waveform data was analysed by an independent clinical event committee and artefacts were removed. Predictors of opioid induced respiratory depression were used in multivariate regression analysis to build a 5-factor risk prediction tool called the PRODIGY score **(Table 1)**. There is much to be learnt from the work surrounding PRODIGY. First, there were many more monitor detected respiratory depression episodes than we could ever imagine (46% of the total cohort), which would have gone unnoticed by traditional monitoring. Second, these episodes were not benign, and even

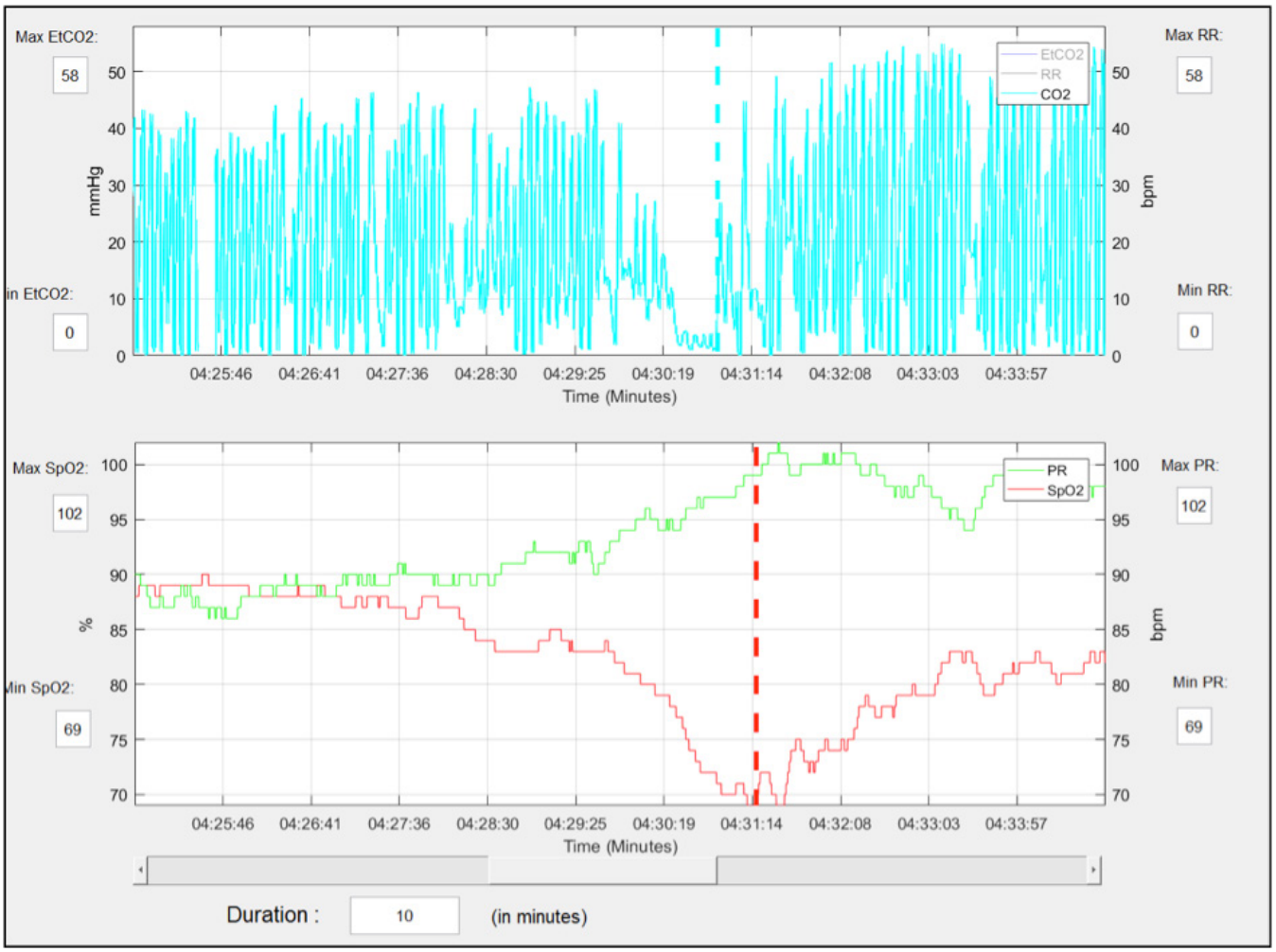


**Figure 2.** Data from the PRODIGY trial showing continuously monitored capnography and oximetry data showing a significant apnoea hypoxaemia episode (blue and red dashed areas)

though clinical events were few, patients with these episodes, had a mean length of hospital stay 3 days more than those who did not, and furthermore this translated into an exponential increase in hospital costs. Third, and most important, risk prediction using continuous monitoring offers the ability to trend oximetry and capnography data over time **(Figures 2 & 3)**. Providing this data to clinicians would allow for pattern recognition and likely early intervention to correct cardiorespiratory compromise events. Artificial intelligence based learning and interpretation can provide critical insights, for example in sepsis detection (Yuan et al. 2020). Minimising false alarms is key for widespread clinical adoption.

## Quality and Safety – Using AI to Build Connections

Machine learning (ML) and Artificial Intelligence (AI) have great potential to improve the quality and delivery of safe medical care in the perioperative period. Variability in clinical practice is one of the most significant drivers of perioperative complications (Lundberg et al. 2018). Universal adaptation of electronic medical records has allowed the acquisition of an enormous volume of clinical data; however, it put providers in a position of frequently not being able to process all available information in a timely and efficient manner. As such, important information may be missed delaying the right treatment or choosing the management plan, which is suboptimal. In the operating room, recovery room, or intensive care units, an inflow of patient data from monitors and clinical information available in medical records can be challenging to process and respond to. In particular, recognition of complex patterns in medical records along with continuous stream of monitoring data leading to undesirable outcome has been challenging to clinical providers. On the other hand, the advantage of ML and AI relies on their ability to sift through a massive amount of data, detect patterns and similarities, and provide decision support based on best and most successful scenarios learned from the analysis of similar cohorts in the past. Additionally, ML improves its predictive capabilties as more data becomes available

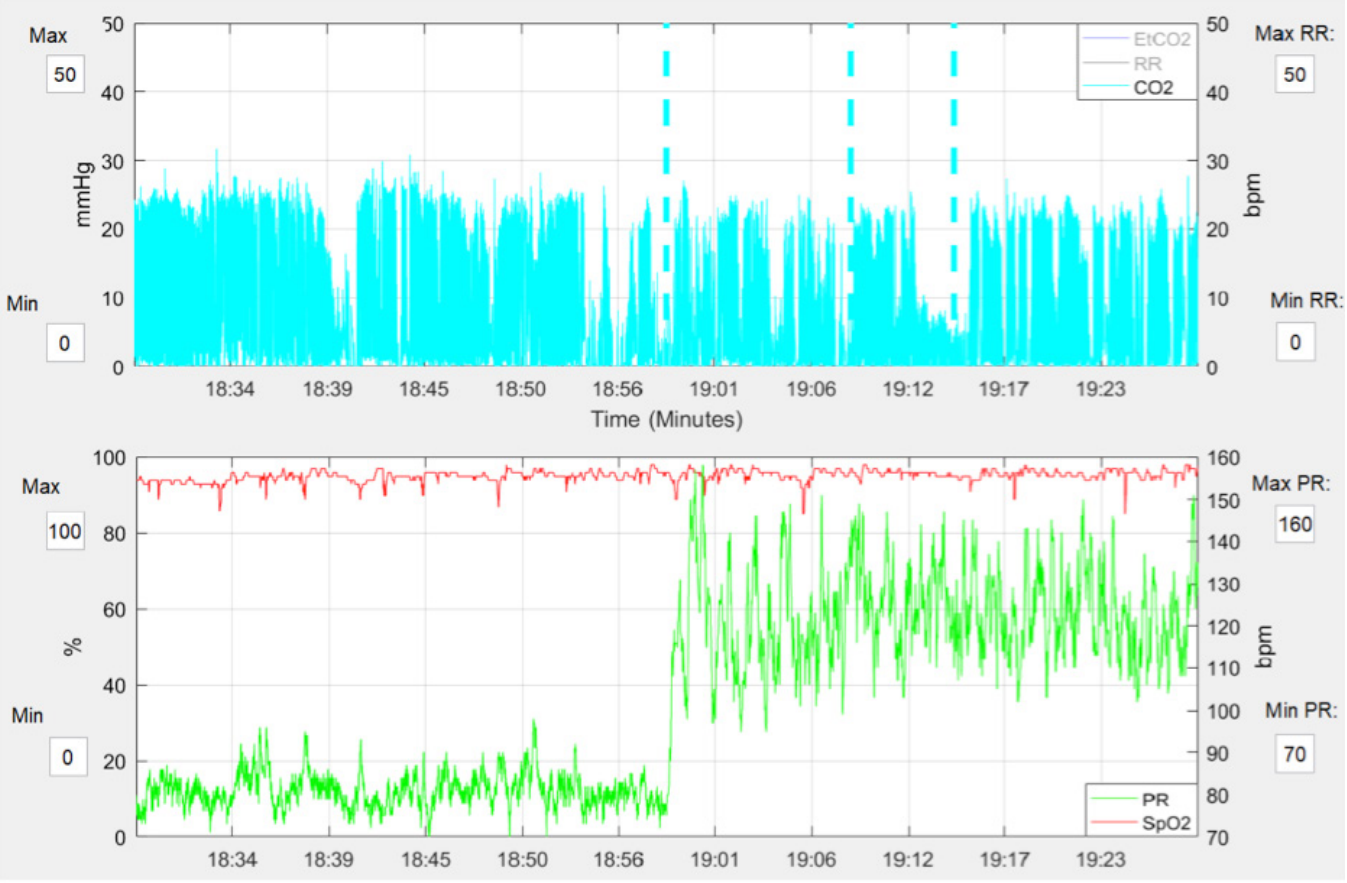


**Figure 3.** Data from the PRODIGY trial showing continuously monitored capnography and oximetry data showing a probable occult atrial fibrillation episode detected by a combination of changes in vital signs. Source: Weingarten et al. 2020.

and can update the models in real-time, making prediction or treatment suggestions clinically relevant and actionable. A comparison of population subsets based on outcomes further identifies the similarities and differences in patient characteristics, nuances of the procedures, and provided treatments. This insight can help provide compliance feedback with best practices to providers in near real-time when corrective intervention is still possible and potentially can change the clinical outcome trajectory. Avoidance of intraoperative hypoxia and arterial hypotension (described above) can be used as an example where ML and AI can significantly enhance providers' ability to deliver quality and safe patient care. Lundberg et al. developed an ML-based system to predict intraoperative hypoxia (Lundberg et al. 2018). The system was trained on minute-by-minute data from the electronic medical records of over fifty thousand surgeries. Providing anaesthesiologists with explainable hypoxaemia risks score and factors contributing to future hypoxia could allow intervention to modifiable risk factors before hypoxia occurred. Most importantly, the explanations identified by the algorithm for hypoxia predictions were broadly consistent with the literature and with prior knowledge from anaesthesiologists.

There are many examples of how AI and ML can help detect potentially harmful conditions during the perioperative period and help providers devise appropriate clinical responses. Wise implementation of these systems may improve the quality and safety of perioperative medical care. Instead of providing "reactive" intervention when cardiorespiratory complications already occur, AI may enable the ability to be "proactive" and avoid some of the complications altogether.

## How Will AI Help in the Future?

Artificial intelligence is a computational science which attempts to replicate the complex task of information management similar to human brain. Machine learning, deep learning, natural language processing are various components of artificial intelligence which take data as input, process it through a learning model and provide a desirable output, commonly a prediction. Unlike prediction models or scores built on static retrospective data analysis, artificial intelligence gives us the ability to continuously collect data and improve these models without having to necessarily build new ones. Research and applica-

tions in various healthcare areas where cardiopulmonary deterioration needs to be monitored has been growing by leaps and bounds (Maheshwari et al. 2020b).

Data collection using various devices of the kinds described previously is the first step in developing any kind of intervention. Artificial intelligence holds the promise of detecting artefacts and outliers in the data while providing right data to right clinicians in real time for timely intervention (Ruskin and Hueske-Kraus 2015).

Development and implementation of AI models which can be deployed on monitoring devices themselves is a significant leap forward compared to retrospective data analysis. Complex indices or scores have been created using feature engineering, a process leveraged in AI to manage various variables and generate meaningful information. For example, scores such as hypotension prediction index, previously mentioned, in its development used millions of such pulse contour waveform features to predict hypotension (Hatib et al. 2018). In this regard, new scores such as the post-intubation hypotension prediction index and the post intubation hypoxaemia prediction index could also easily be built better with an AI model (Smischney et al. 2020a; Smischney et al. 2020b). The ability of AI to use multiple forms of data is also a unique characteristic which provides ability to not only use numerical data but also waveform data, text data amongst others.

Limitations of AI such as explainability, generalisability and bias for application across different clinical sites are getting addressed through newer and evolving techniques. Multi-site validation of various algorithms is also improving with more and more prospective randomised controlled studies being undertaken. With the recent advances in artificial intelligence including advancing research in healthcare, introduction of 5G telecommunication technology and application of internet of things (IOT) devices in healthcare, cardiopulmonary deterioration is likely to be detected and intervened upon earlier amongst perioperative patients.

## Conclusion

The only way of preventing perioperative patient harm is continuous and better patient monitoring with an emphasis on early detection and prevention using effective therapeutic interventions. Tools such as HPI and PRODIGY need to be developed, and more importantly rigorously tested in appropriate clinical scenarios. Artificial intelligence applications to improve patient care and outcomes will need leadership, skilled personnel and right data handling infrastructure.

## Conflict of Interest

AKK consults for Edwards Lifesciences, Medtronic, Philips North America, and Zoll Medical. AKK is on the clinical advisory board for Retia Medical and is a founding member for BrainX LLC, a collaborative platform for research and development of AI products in healthcare. PM is the founder of BrainXLLC, BrainX LLC and JC and KM are founding members. KM is a consultant for Edwards Lifesciences. AKK is also funded with a Clinical and Translational Science Institute (CTSI) NIH/NCTAS KL2 TR001421 award for a trial on continuous postoperative haemodynamic and saturation monitoring. ■

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# Mouth Care Challenges and the Use of the COVID-19 Oral Grading System

## Identifying Risk Factors for Extubation in Patients with COVID-19

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This paper describes the experiences of the Speech and Language Therapy (SLT) service at Nightingale Hospital, adapting to changing demands, which included upper airway challenges associated with extubation and oral management in patients with COVID-19.

## Background

The London Nightingale Hospital was set up in response to the COVID-19 pandemic to provide critical care for patients requiring intubation and ventilation. Its workforce comprised of redeployed medical, nursing and allied health clinicians, including Speech and Language Therapists (SLT), from a range of settings.

## Clinical Situation

Speech and Language Therapists (SLTs) provide assessment and management of patients with speech, voice or swallowing difficulties post-extubation, with or without tracheostomy. In this setting of predominantly intubated patients, SLTs utilised their expertise to focus on oral care practices and delivery of oral care training. Reports of trauma and swelling to the lips and tongue, as well as challenges with dryness, secretions and mouth opening led to the development of the COVID Oral Grading System (COGS). Swelling, mucosa, trauma, infection and jaw mobility were scored on an individualised scale and repeated daily. The COGS helped identify the presence and severity of oral deficits observed in COVID-19.

## Discussion

The COGS enabled systematic, structured assessment and monitoring of the oral cavity and upper airway of patients with COVID-19. Common deficits such as tongue swelling, and unmanaged oral secretions were identified as risk factors for complications peri and post-extubation. The systematic assessment tool was useful to measure outcomes of mouth care regimes and inform aspects of pre-extubation decision-making. It also provided a template for clinicians to increase their knowledge and understanding of this patient group to disseminate and share.

## Background and Clinical Context

### *The London Nightingale Hospital*

The London Nightingale Hospital was established in April 2020 within a purpose-built conference facility in East London, rapidly set up in response to the COVID-19 pandemic. Its primary objective was to support London's NHS critical care network with additional capacity of up to 4,000 beds providing care for intubated and ventilated patients during the first wave of the pandemic.

The hospital workforce was comprised of medical, nursing, and allied health clinicians from a broad range of clinical backgrounds, who were deployed to the Nightingale at short notice. This workforce was agile and adaptable, took on new clinical roles as well as a central role in leadership and guideline development. The organisational culture encouraged sharing and dissemination of skills across professional groups. Clinical decision-making was collaborative within a flat and supportive hierarchy.

To establish robust clinical governance and standardise practice, Standard Operating Procedures (SOPs) were put in place for every aspect of care, which were reviewed weekly. This included a criteria checklist for extubation which outlined markers for ventilation and airway clearance as well as a guide to mouth care, cleaning and decontamination.

### *Admissions to NHS Nightingale London*

Patients admitted to the Nightingale Hospital had a primary diagnosis of COVID-19

| Minimum standard: | Tools |
|---|---|
| **ORAL ASSESSMENT**<br>Four hourly mouth checks<br>Look for coating, ulcers or blood in mouth | Pen torch<br>Visual mouthcare chart |
| **ORAL HYGIENE**<br>Twice daily tooth brushing:<br>Clean teeth gently using a toothbrush and small amount of toothpaste, wet toothbrush to wipe away paste and suction any residue | Toothbrush and toothpaste<br>Water<br>Suction (or suction toothbrush) |
| **ORAL MOISTURISATION**<br>Moisten the mouth and lips at regular intervals, using a water-based gel | Mouthcare applicator or sponge<br>Artificial saliva gel |
| **ORAL DECONTAMINATION**<br>If chlorhexidine gel is prescribed, this should be used 4 times a day at a separate time to teeth cleaning. Apply gel onto a sponge and wipe across the tongue, cheeks and palate. AVOID putting this on the teeth and DO NOT suction or wash away. | Corsodyl gel 1% Chlorhexidine<br>Mouthcare applicator |

**Table 1.** Mouthcare Standard Operating Procedure

and single organ failure (i.e. lungs), that required ongoing intubation and ventilation. These patients were received from their admitting NHS hospital after a 48 hour period of cardiovascular stability. The anticipated patient pathway was to provide respiratory interventions during the acute phase of illness to optimise recovery. Once patients demonstrated improved respiratory function, they were identified for ventilator weaning with subsequent sedation hold and preparation for extubation. At that time, ventilatory needs for patients with COVID-19 were expected to be for only a few weeks before resolution of symptoms allowed extubation. For some, a short period of rehabilitation was expected prior to returning to the local hospital. This planned patient flow would allow for increased capacity of care to meet the anticipated need at that time. The Nightingale Hospital was not set-up to manage additional complications such as the need for ECMO or tracheostomy, so those patients had to be repatriated to their local hospital for ongoing care.

***Allied Health Profession Roles***

A team of allied health professionals formed an essential part of the rehabilitation team at NHS Nightingale. Physiotherapists were involved in proning and respiratory management; Occupational Therapists supported positioning, self-care and cognitive management; Dietitians ensured nutritional needs were optimised and Speech and Language Therapists (SLTs) managed mouthcare, swallowing and communication issues, especially post-extubation (Brodsky et al. 2018; McRae et al. 2019).

Although SLTs are seldom involved in the care of sedated and intubated patients, their advanced understanding of upper airway anatomy, bulbar function, and oral secretion management helped to establish a valuable role in patients with COVID-19 in critical care. A planned extubation was typically led by an intensive-care consultant, an operating department practitioner (ODP) and/or an anaesthetist who have combined skills in upper airway anatomy, intubation and ventilation. Assumptions are made about normal upper airway patency in the absence of contrary evidence. Patients who are intubated for respiratory support, are expected to be extubated without complication following recovery from the acute episode.

## Invasive Ventilation in COVID-19

The primary aim of intubation in the COVID-19 patient was to enhance transpulmonary pressure, open collapsed alveoli, improve oxygen debt and provide the opportunity for lungs to heal (Meng et al. 2020). The requirement for invasive intubation not only exposes the patient to procedure-related trauma but also enhanced risk of cross-infection to the healthcare team from potential aerosolisation. For these reasons, careful attention needs directing to pre-extubation assessments to minimise the risk of further trauma and cross-infection caused by multiple intubations.

## The Challenges of Extubation

Extubation decisions can often be relatively straightforward once the initial cause of respiratory failure has resolved

| | Scale | Focus |
|---|---|---|
| Swelling | **0 → 3** | Status of lip and tongue swelling |
| Mucosa | **-3 → +3** | Level of oral dryness or excessive secretions |
| Trauma | **0 →3** | Level of trauma to oral cavity to include lips, tongue and palate |
| Infection | **0 → 2** | Evidence of infection or coating inside the oral cavity |
| Jaw mobility | **0 → 2** | Degree of jaw opening or movement |

**Table 2.** Summary of COVID Oral Grading System (COGS)

and consciousness has returned to normal (Rotheray et al., 2012). In patients who require extended periods of intubation (four days or more), attention should be paid to risk of laryngeal trauma which may compromise the upper airway enough to necessitate re-intubation (Wittekamp et al. 2009; Esteller et al. 2005; Thomas et al. 1995; Whited 1983; Whited 1984; Kasantos et al.1983). Laryngeal oedema is reported in up to 55% of patients following tracheal extubation (Zhou et al. 2011; Brodsky et al. 2018). In neurological populations, additional attention needs to be paid to the upper airway where muscle activity, oral secretion load, cognition and arousal levels may impact the success of an extubation (Nguyen et al. 2006; Coplin et al. 2000).

For patients with COVID-19 who required intubation for ventilatory needs it was unknown whether they would experience any focal laryngeal impairments. They often required excessively prolonged intubation due to the risks of aerosolisation and cross-infection to healthcare practitioners through placement of surgical tracheostomy. Consensus guidelines were developed to guide the safe extubation of patients with COVID-19 and reduce the risks of failed extubation and re-intubation (Cook et al. 2000).

In this paper we describe the experiences of the SLT service at Nightingale Hospital, adapting to changing demands, which included upper airway challenges associated with extubation and oral management in this patient group.

## Mouthcare Challenges in Intubated Patients With COVID-19

As a new SLT service delivering to a novel patient group who were predominantly intubated, the SLTs utilised their skills to support oral care practices and delivery of oral care training. Staff had limited experience and confidence in mouthcare delivery and the use of specific products, such as chlorhexidine, so a new Standard Operating Procedure split the mouthcare tasks into separate components to address oral assessment, hygiene, moisturisation and decontamination **(Table 1)**.

Reports of trauma to lips and tongue were identified in those patients with COVID-19 who required regular proning whilst intubated. This had an impact on the level and approach to oral care. In response, the SLT team developed a clinical tool to assess oral presentations, which helped to identify daily trends, deliver tailored management and training. This also helped to contribute to multidisciplinary discussions about upper airway structural issues and their potential risk for extubation.

The COVID Oral Grading System (COGS) drew on themes identified by SLT and healthcare staff around the status of oral mucosa and limited mouth opening. A summary is provided in **Table 2**. Its principles are based on existing published assessment tools, specifically the Yale Residue Scale (Neubauer et al. 2015) which uses image-based assessment and The Modified Barium Swallow Impairment Profile (Martin-Harris et al. 2008) which recognises the imprecision that arises from scoring all assessment components on the same size scale. Existing tools such as the oral rehabilitation therapy outcome measure scale (Enderby and John 2015) was not considered to have face validity in this patient population.

The COGS aimed to identify the presence and severity of characteristics observed in patients with COVID-19 including swelling, mucosa, trauma, infection and jaw mobility. Swelling, trauma and infection are scored on a 4-point scale. Mucosa is scored on a 7-point scale with negative scores to represent dryness and positive to represent excessive wetness or secretions. Jaw mobility

| Oral presentations | Possible clinical implication |
|---|---|
| Swelling of the tongue and lips | • Poor oral and/or oropharyngeal airway patency post-extubation<br>• Greater re-intubation complexity<br>• Oro-pharyngeal dysphagia |
| Unmanaged oral secretions (saliva) | • Pooled oral secretions in pharynx sitting above cuff<br>• Absent or ineffective swallow<br>• Aspiration risk during and post-extubation |
| Dry oral mucosa | • Systemic dryness<br>• Increased risk of oral infection<br>• Increased risk of trauma |
| Infection | • Increased risk of ventilator acquired pneumonia (VAP)<br>• Increased requirement for polypharmacy |
| Trauma of the lips and tongue caused by presence of endotracheal tube (ETT)<br>Trauma of the tongue due to biting | • Development of infection<br>• Aspiration of fresh blood<br>• Implications on speech and swallowing post-extubation |
| Jaw clamping | • Inability to conduct oral hygiene<br>• Difficulty in voiding oral or oro-pharyngeal secretions before or after extubation |

**Table 3.** Oral presentations and potential clinical implications of the COVID-19 patient cohort

is measured on a 3-point scale to improve clinical relevance and inter-rater reliability. The COGS was administered to five patients to assess for redundancy and sufficiency in the themes presented. No additional themes were identified, and clinicians felt all existing themes held clinical value and could be used to support treatment plans and decision-making.

## The COVID Oral Grading System (COGS)

The COGS was used by the SLTs on a daily basis with all patients to help identify specific impairments of the tongue and oral mucosa, and provide direction towards treatment needs. In those patients receiving treatment, an improvement in oral grading scores was identified after 2-3 days. Using the tool helped to highlight potential implications for patients who were being considered for extubation in the proceeding days. Patients with worse scores (greater than or equal to 2) on swelling or mucosa were discussed with the multidisciplinary team with recommendations to manage clinical risk peri and post-extubation.

### Demographic Data

The patient group consisted of 54 patients. 9 (17%) were female. Median age was 61 years, range 35-78 years. 76% of the population were from a non-white background. All were able to live without assistance prior to admission. This cohort arrived at The Nightingale Hospital after an average of 3.9 days intubated (range 1-15 days). 72% of patients were proned for up to 16 hours per day for a period of their Nightingale admission. **Table 3** shows the range of oral presentations identified in this cohort, presented alongside potential clinical implications.

Upper airway swelling (COGS swelling scale ≥ 2) and an excess of oropharyngeal secretions (COGS mucosa scale ≥ 2) were considered the most relevant to those under consideration for extubation. A swelling score ≥ 2 would lead to recommendations and prompts for the treating team to include:

- Implementation of measures to assess for laryngeal/pharyngeal swelling whilst the tube is still in place (e.g. cuff leak test).
- Preparation of post-extubation equipment to augment the upper airway if required (for example, facial CPAP to provide continuous positive airway pressure and/or re-intubation equipment).
- Consideration of interventions to reduce swelling prior to extubation (for example, prescription of dexamethasone or increase in reflux medications).
- Optimisation of patient positioning to minimise tongue contact to posterior pharyngeal wall.
- Awaiting improved consciousness level to optimise the chance of the patient augmenting their own airway and adjusting posturally.

## SWELLING

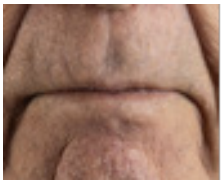
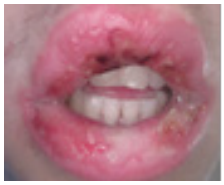
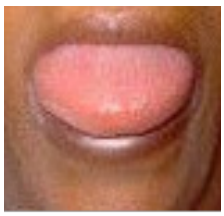
| | Score | Description | Considerations |
|---|---|---|---|
|  | **0** | No evidence of lip or tongue swelling. | • Continue routine mouth care and moisturisation. |
|  | **1** | Some evidence of tongue or lip swelling – not enough to cause oral airflow issues. | • Continue routine mouth care and moisturisation.<br>• Consider cause of swelling & possible interventions. |
|  | **2** | Marked evidence of lip or tongue swelling with concern for oral airflow. | • Continue routine mouth care and moisturisation.<br>• Consider cause of swelling & possible interventions.<br>• Alert ITU/anaesthetic team if patient is being considered for extubation. |
|  | **3** | Severe evidence of tongue or lip swelling with extreme concern for oral airflow. | • Continue routine mouth care and moisturisation.<br>• Consider cause of swelling & possible interventions.<br>• Alert ITU/anaesthetic team if patient is being considered for extubation – support tracheostomy rather than extubation. |
| | **U** | Unable to score | |

**Image Credit:** 1-2 iStock; 3 Mouthcare Matters; 4 Michelle Lunn

A mucosa scale of ≥ 3 would result in one or several of the recommendations below:

• Speech and Language Therapy and Physiotherapy to assess swallow and cough response prior to extubation to establish likelihood of patients being able to manage their own secretions post-extubation. Measuring of secretions voided from above-cuff suction port hour to hour to understand possible load of oral secretions resting in the pharynx.

• Voiding secretions from mouth, oropharynx and above-cuff suction port immediately prior to extubation.

• Ensuring upright positioning of the patient during extubation to minimise risk of aspiration and optimise cough attempts.

• Physiotherapy presence at the extubation to provide pre, peri and post suction and post-extubation cough augmentation if needed.

• Ensure optimal consciousness level to give the best possible chance of the patient managing their own secretions.

Pre-extubation, during the sedation hold, the SLT was also able to provide simple assessment of communication and cognition (including attention and responsiveness to instruction) and put recommendations in place for the team to use post-extubation to optimise likelihood of the patient following medical instructions. Those unable to follow the instructions required for post-extubation treatment (such as the instruction to open the mouth and cough) would be identified as potentially at risk of airway difficulties post-extubation. Patients who were clamping the mouth closed were also identified as being a post-extubation airway as well as mouth-care risk.

The mucosa, trauma and infection scales were considered the most relevant to those requiring ongoing invasive ventilation. Those with very dry oral mucosa were provided with moisturising gels and assessed for any

## MUCOSA

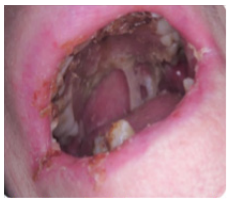
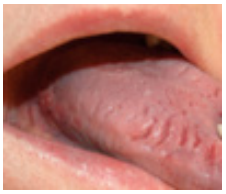
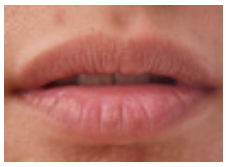
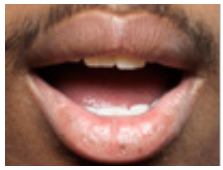
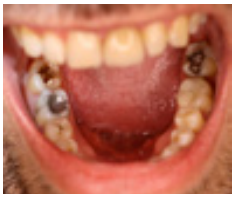
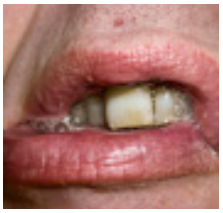
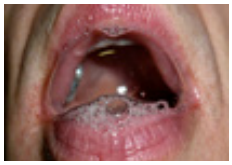
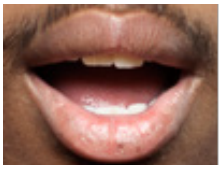
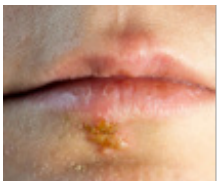
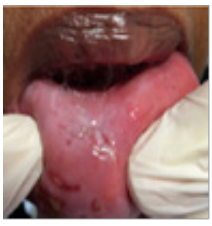
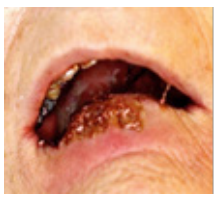
| | Score | Description | Considerations |
|---|---|---|---|
|  | **-3** | Extremely dry with cracked mucosa and solid secretions that need soaking | • Check overall hydration and fluid balance.<br>• Check not over-using Corsodyl or other drying agents.<br>• Definite need for oral soaking and then gels. |
|  | **-2** | Partially dry but some cracking and perhaps some thick, sticky secretions | • Check overall hydration and fluid balance.<br>• Check not over-using Corsodyl or other drying agents.<br>• Definite need for oral gels. |
|  | **-1** | Slightly dry but quickly recoverable with moisture balm | • Vaseline or gel at lips. |
|  | **0** | Normal mucosal appearance, neither dry nor wet | • Continue usual mouth care. |
|  | **1** | Slightly wet mouth with small amounts of loose secretions fully contained in the mouth when upright or semi-supine. | • Continue usual mouth care.<br>• Gentle oral suction or swabbing. |
|  | **2** | Partially wet mouth with moderate amounts of loose secretions mostly contained in the mouth when semi-supine | • Continue usual mouth care.<br>• Gentle oral suction or swabbing – remember to suction into lingual sulci.<br>• Consider posture & positioning as well as above cuff clearance via suction port. |
|  | **3** | Extremely wet mouth and tongue with notable loss of loose secretions at the lips | • Continue usual mouth care.<br>• Gentle oral suction including sulci.<br>• Consider posture & positioning as well as above cuff clearance via suction port (especially in those due to extubation). |

**Image Credit:** 1-2 Mouthcare Matters; 3-4 iStock; 5 Robert Adds; 6-7 ©James Friedman

## TRAUMA

| | Score | Description | Considerations |
|---|---|---|---|
|  | **0** | No evidence of trauma to the oral cavity | • Continue usual mouth care |
|  | **1** | Slight trauma to the oral cavity | • Continue usual mouth care<br>• Medical review for prescription of Corsodyl / Chlorhexidine<br>• Investigate and try to treat cause of trauma |
|  | **2** | Notable trauma to the oral cavity | • Continue usual mouth care<br>• Medical review for prescription of Corsodyl / Chlorhexidine<br>• Caution when suctioning (avoid over-suctioning)<br>• Investigate and try to treat cause of trauma |
|  | **3** | Substantial trauma to the oral cavity | • Continue usual mouth care<br>• Medical review for prescription of Corsodyl / Chlorhexidine<br>• Investigate and try to treat cause of trauma |

**Identify site of trauma:** - Lips (commissure/main body, left/right, upper/lower) - Tongue (anterior/posterior, lateral/blade) - Palate (soft/hard)

**Image Credit:** 1-2 iStock; 3-4 Mouthcare Matters

treatable causes of dryness such as over-use of decontamination gels (e.g. chlorhexidine) and negative fluid balance. Trauma was more common than infection in our cohort, most associated with pressure sores from endotracheal tube (ETT) ties at the lips with some inner cheek and tongue biting. Infection was difficult to score in a number of patients due to restrictions in accessing the oral cavity either due to tongue swelling, jaw movement and ETT presence.

## Discussion

### *Clinical Presentations and Implications for Patient Management*

Our experience at the Nightingale Hospital has highlighted unique challenges in managing the oral and upper airway of patients with COVID-19. Oral swelling was a consistent issue that has been described in only one previous case study reporting complications in the management of a ventilated patient with acute respiratory distress syndrome (ARDS) due to tongue swelling, thought to be a reactive response to anti-viral drug treatment (Scott et al. 2010). Laryngeal oedema has been reported in up to 55% of patients following tracheal extubation (Zhou et al. 2011), however this could not be evaluated directly with our patient group due to restrictions for nasendoscopy use. Observed swelling of tongue and lips was strong evidence of widespread oedema. An anaphylactic response to research trials of tocilizumab targeting cytokine release syndrome could be relevant in this population but unlikely to be the only cause (Park et al. 2020). Swelling response to sedative drugs as well as prolonged inactivity of the tongue could be additional causative factors as well as a direct result of the multi-organ inflammatory response to the virus itself (Roberts et al. 2020). Other considerations include impaired venous drainage from high levels of positive pressure ventilation required in this population as well as fluid overload. Facial oedema as a direct result of proning (Messerole et al. 2002) should also be considered though poor resolution of swelling on return to supine is suggestive

## INFECTION

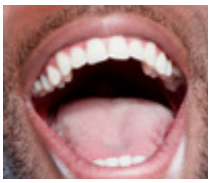
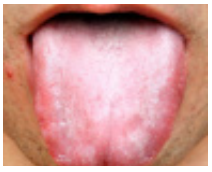
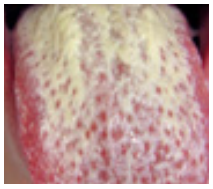
| | Score | Description | Considerations |
|---|---|---|---|
|  | **0** | No evidence of infection or coating within the oral cavity or lips | • Continue with mouth care |
|  | **1** | Evidence of oral coating that may be suggestive of infection | • Gentle oral brushing<br>• Continue with mouth care<br>• Consider prescription of topical treatment eg: Nystatin |
|  | **2** | Definite coating and/ or evidence of infection within the oral cavity | • Gentle oral brushing<br>• Continue with mouth care<br>• Consider prescription of systemic treatment eg: Fluconazole |
| | **U** | Unable to score | |

**Image Credit:** 1-2 iStock; 3 Mouthcare Matters

## JAW MOVEMENT

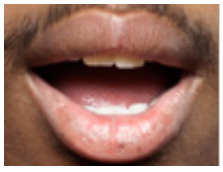
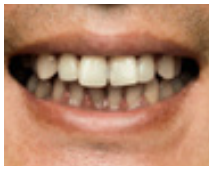
| | Score | Description | Considerations |
|---|---|---|---|
|  | **0** | Soft jaw with easy opening and access to mouth and/ or able to manipulate jaw open by several millimetres | Consider interventions to maintain range of jaw movement. |
|  | **1** | Jaw movement restricted. Requires manipulation to open a few millimetres. Difficulty accessing mouth. | Be mindful of ET tube placement whilst manipulating the jaw. Consider assistance to stabilise ET tube. |
|  | **2** | Complete restriction of the jaw with no movement on manipulation. Unable to access mouth. | Consider risk of trauma to oral cavity from jaw clenching. |

**Image Credit:** 1-3 iStock

of other aetiologies. This clinical presentation was similar to that reported in facial lymphoedema, following head and neck cancer management. Swelling responses to localised trauma from prolonged intubation as well as over-use of oral decontamination products such as chlorhexidine were also identified as possible irritants and contributors which required specialist input from the tissue viability nurses for dressing and advice of ETT fixation.

***Use of the COVID Oral Grading System***

The COGS has proven a useful clinical tool for assessment of patient need as well as a training tool for staff new to working in the COVID-19 critical care environment. The mucosa scale has been useful to alert staff to oral secretion load of a patient prior to extubation as well as oral care needs to treat dryness by moisturisation and hydration. The system has also supported healthcare staff to consider risk of avoidable trauma from suction equipment and pre-emptively manage risk of ventilator acquired infection with oral care and decontamination. Prescription of routine chlorhexidine for decontamination should however be appraised carefully considering emerging evidence to suggest failure to prevent ventilator acquired pneumonia and perhaps contribute to excess mortality in certain patient groups (Klompas et al. 2014; Price et al. 2014).

When used alongside a sedation scale such as the Richmond Agitation-Sedation Scale (Sessler et al. 2002) and simple communication assessment, the COGS can contribute to a holistic pre-extubation checklist in this complex patient group.

***Implications & Recommendations for Practice***

In this patient group we have been required to look beyond the reason for intubation in order to manage the decision to extubate to minimise risk of trauma and avoidable aerosolisation risks associated with re-intubation. Whilst the post-extubation challenges seen in other patient groups still apply, we should also take into account the challenges that are unique to the COVID group which are brought about by the virus itself as well as necessary management of long periods of ventilation and sedation, post-ITU syndromes and central nervous system. We have highlighted the added value of a systematic oral assessment, such as the COGS, which can be used as part of the pre-extubation decision-making process. Further development of this clinical tool may help manage risk of secondary complications in COVID-19 and cross-contamination to the health care team.

## Conflict of Interest

None. ■

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# AGENDA

For a full listing of events visit https://iii.hm/icuevents2021

## MARCH

**2** ISICEM e-Day - ARDS
Virtual meeting
https://iii.hm/17cz

**19-20** 2020 World Critical Care and Anesthesiology Conference
Virtual meeting
https://iii.hm/17d0

## APRIL

**8-10** 17th Emirates Critical Care Conference
16th World Federation of Critical Care Nurses (WFCCN) World Congress
Hybrid meeting
https://iii.hm/17d1

**13** ISICEM e-DAY – ECMO
Virtual Meeting
https://iii.hm/17d2

**14-16** EURONEURO 2021
Virtual meeting
https://iii.hm/17d3

## MAY

**5-7** EuroELSO 2021
Virtual meeting
https://iii.hm/17d4

**31 MAY-4 JUN** Blood Diseases in the ICU - Advanced Training Course
Saint-Louis Hospital, Paris, France
https://iii.hm/17d5

## JUNE

**1** ISICEM e-DAY – Hemodynamic Monitoring
Virtual Meeting
https://iii.hm/17d6

**3-5** LIVES Forum 2021 - Septic shock: From the bug to organ failure
Dublin, Ireland
https://iii.hm/17d7

**9-11** Reanimation 2021
Paris, France
https://iii.hm/17d8

**15-18** ESPNIC 2021
Virtual Meeting
https://iii.hm/17d9

**23-26** ESRA 2021
Thessaloniki, Greece
https://iii.hm/17da

## JULY

**7-9** 8th ERAS World Congress
New Orleans, USA
https://iii.hm/17db

**9-12** ECCMID 2021
Vienna, Austria
https://iii.hm/17dc

**17-21** International Society on Thrombosis and Haemostasis (ISTH) 2021
Hybrid meeting
https://iii.hm/17dd

## AUGUST

**31 AUG-3 SEPT** 40th ISICEM
Brussels, Belgium
https://iii.hm/17de


ICU
MANAGEMENT & PRACTICE





**ICU MANAGEMENT AND PRACTICE IS PUBLISHED BY**
MindByte Communications Ltd
9, Vassili Michailidi CY-3026 Limassol, Cyprus
Email — office@icu-management.org
Website — icu-management.org

**SUBSCRIPTION RATES**
One year — 55 Euros + 5% VAT if applicable
Two years — 90 Euros + 5% VAT if applicable
Note: For a free digital subscription please contact Samna Ghani, editorial@icu-management.org

**PRODUCTION, PRINTING AND DISTRIBUTION**
Printed in Hungary by ABEL Printing
Total classic and digital distribution: 21,500
ISSN = 1377-7564


icu-management.org ICU_Management