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Introduction

Orotracheal intubation is a life-saving procedure in critically ill patients with acute respiratory failure, but complications during the procedure are frequent and life-threatening situations still occur in almost 45% of the procedures (Simpson et al. 2012; Russotto et al. 2021). The vast majority of clinical evidence on intubation is mainly focused on the operating room (OR). As opposed to traditional anatomical challenges, orotracheal intubation in the intensive care unit (ICU) imposes further



What we learned during the COVID-19 pandemic that should not be forgotten

An overview of the available evidence on safe intubation practices in critically ill patients in light of new discoveries due to the coronavirus pandemic.

risks due to the high prevalence of a physiological difficult airway (Mosier 2020).

The COVID-19 pandemic brought new challenges for intubation in the ICU. Severe respiratory failure and hypoxaemia, commonly present in COVID-19 patients, impose an increased risk of cardiovascular collapse and cardiac arrest during intubation. Besides, the procedure may expose healthcare professionals to contamination and changes in usual practice aiming at staff protection may unduly increase procedure difficulty (Feldman et al. 2020). Thus, while COVID-19 imposes challenges to intensive care physicians, it also creates opportunities for improvement in relation to intubation practices in the ICU.

Our objective with this piece is to summarise the available evidence about safe intubation practices in critically ill patients in light of new discoveries due to the coronavirus pandemic.

Intubation in Critically Ill Patients – Prior Evidence

Severe adverse events occur in 1 of 22.000 cases of orotracheal intubation in the operating room. On the other hand, the incidence of life-threatening complications may be as high as 45% during intubation in the ICU (Simpson et al. 2012; Russotto et al. 2021). It must be highlighted that this high incidence of complications in the ICU cannot be attributed solely to

the lack of the anaesthesiologist. In a prospective comparison of intubation attempts for 208 patients intubated first in the OR and later in the ICU, both by anaesthesiologists, the incidence of difficult airway and complications were higher in the ICU, while first-time intubation success was lower when compared to the OR (Taboada et al. 2018). Intubation strategies – and risks – may vary among elective surgery and critically ill patients, but most of the clinical evidence is mainly focused on the OR.

The differences between airway management in the OR and ICU begins with the evaluation of the airway. Several predictors of difficult laryngoscopy, such as the 3-3-2 rule or the upper lip bite test depends on patient collaboration and may be unfeasible in the critically ill (Detsky et al. 2019). So far, the only validated airway assessment tool in ICU patients is the MACOCHA score, which still depends on the patient being able to sit for the Mallampati evaluation (De Jong et al. 2013). However, despite these limitations, assessing potential difficulties is advisable before all intubations in the ICU environment.

When it comes to efforts in preparing the scene to increase first attempt success, it is worth noting that the use of a checklist to ensure protocol adherence was not superior to standard care in a randomised controlled trial (Janz et al. 2018). Neverthe-



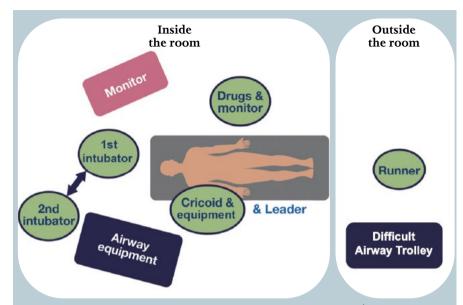
less, specific strategies during each step of the procedure can increase patient safety and must be implemented when possible.

Preparing the scene and patient positioning

Experienced staff is advisable for a safer procedure. Ideally, the presence of two airway operators with the presence of a senior physician can reduce the risk of overall complications (Schmidt et al. 2008). The leader must also plan and verbalise the primary and rescue strategies to be adopted to share their mental model with the team should any difficulties ensue during the procedure. Sedative agents, rescue devices and ventilation equipment must be checked and readily available. Two experienced operators and an easy access to a difficult airway trolley is advisable. One should not expect a bolus of fluid to be enough to manage hypotension or cardiovascular collapse. In a randomised controlled trial, routine infusion of a 500ml crystalloid solution did not prevent the occurrence of hypotension during intubation in the ICU in the absence of hypovolaemia (Janz et al. 2019). Therefore, norepinephrine must be readily available if hypotension is expected. Finally, sniff positioning must be optimal and is superior to other strategies of patient positioning during intubation in the ICU (Semler et al. 2017). Figure 1 exemplifies scene preparation before orotracheal intubation.

Pre-oxygenation

Pre-oxygenation before intubation aims at prolonging the period of safe apnoea after sedation and neuromuscular blockade. Offering 100% oxygen for 3 to 5 minutes reduces the risk of desaturation in comparison to standard of care. Strategies for proper pre-oxygenation includes the use of noninvasive ventilation, high-flow nasal canula, bag-valve-mask ventilation with 15 L/min oxygen and nonrebreather mask with a flush-rate oxygen delivery



During orotracheal intubation, there are some roles that each team member can have (and sometimes more than one role at a time): (a) the 1st intubator, (b) drug administrator (drugs), (c) an observer of the patient's clinical state (monitor), (d) cricoid force applier or BURP manoeuvre (cricoid), (e) airway equipment assistant (equipment), (f) a runner to call for help or provide additional equipment if necessary, (g) a 2nd intubator (if possible/available), (h) a team leader/coordinator (leader), and (i) a manual in-line stabiliser (MILS). Usually, at least 4 members are necessary: the 1st intubator (physician), someone for drugs & monitor (the nurse), someone for cricoid & equipment (a respiratory therapist or a physician) and a runner (in the context of the risk of aerosol generating usually outside of the room with advanced devices available in a difficult airway trolley). A 2nd intubator (physician) can or cannot be present. Ideally, at least two physicians proficient in airway management should be present during the procedure with one of them assuming the leader role (avoid this role for the 1st intubator).

 $\textbf{Figure 1. Scene preparation before Orotracheal intubation. Adapted from Higgs et al.\ 2018.}$

(>40 L/min). A randomised controlled trial suggested that bag-valve mask ventilation before first intubation attempt improved patient oxygenation without an increased risk for aspiration of gastric content. Although not definitive, these results suggest that ventilation before intubation is not harmful as previously reported and may be interesting in severely hypoxaemic patients (Casey et al. 2019). On the other hand, apnoeic oxygenation during intubation with nasal catheter or high-flow nasal canula seems ineffective and should not be routinely performed (Vourc'h et al. 2015; Bailard et al. 2006; Simon et al. 2016; Semler et al. 2016).

Sedation strategies and use of neuromuscular blockade

There is not enough evidence to support the use of a specific sedation strategy over

another during intubation in the ICU. In an observational cohort in 34 institutions, etomidate, propofol, midazolam and ketamine were the most used drugs by intensivists (Groth et al. 2018). The patient baseline condition is usually determinant in the choice of sedation strategy. Propofol and midazolam are more commonly used in a situation of haemodynamic stability, while etomidate and ketamine are preferred in a clinical scenario of shock (Mendes et al. 2020).

The use of neuromuscular blockade during intubation in the ICU is still a matter of debate. While several randomised controlled trials support the use of neuromuscular blockade and rapid sequence induction in the OR (Lundstrøm et al. 2018), the evidence in the ICU is based solely on observational studies (Li et al. 1999; Mosier et al. 2015; Wilcox et al.



2012). Potential risks of eliminating patient effort and respiratory drive with the use of NMB includes the risk of a rapid fall in patient oxygenation and a high risk of cardiovascular collapse in a do-not-intubate, do-not-ventilate scenario.

However, despite the lack of randomised trials and potential risks, available evidence suggests that the use of neuromuscular blockade can increase first attempt success and reduce overall complications during intubation in the ICU. So far, the use of NMB in the ICU may vary from 20 to 90% of intubations in different cohorts (Simpson et al. 2012; Yamanaka et al. 2010; Doig et al. 2009). In a recent survey regarding practices of airway management in the ICU, physicians reported the use of NMB in the minority of cases (Mendes et al. 2020).

Auxiliary devices and airway manipulation

Two recently published randomised controlled trials evaluated the use of auxiliary devices to increase first-attempt intubation success in the intensive care unit. The Styleto trial has shown that the routine use of a tracheal tube plus a stylet during intubation is superior to the tracheal tube alone to achieve first-attempt intubation success. Although this trial was not powered to evaluate possible differences among serious adverse events between groups, the use of a stylet did not increase traumatic injuries related to tracheal intubation in the ICU (Jaber et al. 2021). Similarly, a randomised trial evaluated the use of a bougie versus tracheal tube and stylet on first-attempt emergency intubation success. The rate of success was higher in the bougie group with similar rates of procedure related complications (Driver et al. 2018). Nevertheless, we believe adequate training about the caveats of using these devices is strongly advisable to avoid as much as possible preventable (and eventually fatal) complications associated

with these devices, such as tracheal tears and posterior wall injuries, specially by inexperienced physicians.

When it comes to airway manipulation during intubation the most readily available strategy for dealing with difficult laryngoscopy is posterior displacement of the larynx by backward pression. The Sellick manoeuvre is largely adopted during intubation but it was originally described to "control regurgitation until intubation with a cuffed endotracheal tube was completed" and should not be the first strategy (Sellick 1961). On the contrary, the displacement of the larynx backward, upward and rightward with the so called BURP manoeuvre can improve vocal chords visualisation and may be adopted to improve intubation success (Takahata et al. 1997).

Direct laryngoscopy X Video laryngoscopy

Video laryngoscopy (VL) has emerged as a new standard of care or best practice during intubation in the ICU. It is supposed to provide a better view of the vocal cords even when difficulty is expected due to anatomical reasons. It does not demand a perfect alignment of the structures and can magnify the image, facilitating the intubation process. It also allows concurrent visualisation by a second operator that can immediately aid in airway management. However, it is more expensive and less available than direct laryngoscopy (DL). More important, previous knowledge of the intubation with DL is not directly transferrable to VL and variable learning curves can be expected.

In a small single center randomised trial, the use of VL improved first attempt success during urgent endotracheal intubation (Silverberg et al. 2015). However, in a larger trial published, VL compared with DL did not improve first attempt success rate and, unexpectedly, was associated with higher rates of severe life-threatening complica-

tions. The reasons for intubation failure varied among both strategies. In the DL group, the inability of glottis visualisation was the main reason for intubation failure. On the other hand, in the VL group, glottis visualisation was not possible in only 22% of the cases and failure of tracheal intubation was the most reported reason despite proper vocal cord visualisation. It is possible that the absence of previous training and proper skill may have contributed to the trial results (Lascarrou et al. 2017).

Confirmation of intubation

The use of waveform capnography to confirm intubation is mandatory and should not be considered as an optional auxiliary device. Lung auscultation and visualisation of chest wall movement are not reliable signs and cannot be used as single strategy to check intubation success, especially in the absence of neuromuscular blockade (Whitaker and Benson 2016; Linko et al. 1983).

The Need to Recognise and Anticipate the Physiologically Difficult Airway: A Life-Threatening Situation

As previously discussed, the occurrence of severe complications is much higher in the ICU setting than in the operating room. Cardiac arrest may occur in up to 4% of the patients and haemodynamic instability along with hypoxia are the most common reasons for this event (Russotto et al. 2021; Heffner et al. 2013). Moreover, life threatening situations may occur even with first attempt success in patients with severely deranged physiology and pre-intubation status is important to identify patients at increased risk for complications (Heffner et al. 2013). In a large retrospective cohort of intubation in critically ill patients, arterial hypotension prior to intubation, hypoxia prior to



intubation, absence of pre-oxygenation, age and obesity were independently associated with cardiac arrest and death (De Jong et al. 2018). Three of these may be modifiable risk factors in case of proper recognition before initiating the procedure.

High-risk situations other than hypotension and hypoxaemia may also behave as physiologically difficult airway. Pulmonary hypertension or right ventricular dysfunction, severe acidosis, intracranial hypertension and the full stomach scenario may all

impose a greater risk of complications, even in the absence of traditional anatomic predictors of difficult airway (Mosier 2020). **Table 1** highlights physiologically difficult situations and possible strategies to overcome them.

Respiratory failure

- Pre-oxygenation with positive pressure ventilation
- Routine bag-valve-mask ventilation after induction and before laryngoscopy in the absence of a high risk of aspiration
- Consider apnoeic oxygenation if high risk of aspiration

Haemodynamic instability

- Prepare push dose vasopressors
- Prepare a norepinephrine infusion should hypotension be anticipated
- Ensure fluid replacement if hypovolaemia is likely, but don't rely on routine fluid boluses to correct or avoid hypotension

Metabolic acidosis

- Administer sodium bicarbonate before intubation
- Ensure adequate minute-ventilation after intubation (at least 2X100 mL/Kg of predicted body weight)

Acute brain injury and intracranial hypertension

- Avoid even short-term desaturation and hypotension episodes
- Avoid severe hypertension during the procedure
- Avoid long intubation attempts that risk acute hypercapnia

Abdominal distension / Vomiting / Upper gastrointestinal bleeding / Full stomach

- Have a rigid aspirator readily available
- · Consider awake intubation or avoid neuromuscular blockade
- Place a nasogastric tube in case of suspected bowel obstruction or ileum
- Avoid videolaringoscopy unless judged extremely necessary

Pulmonary hypertension / Right ventricular dysfunction

- Avoid hypercapnia and low minute ventilation
- Avoid hyperinflation and start with low PEEP (5 8 cmH, O)
- Start norepinephrine pre-emptively and avoid (even short term) hypotension episodes

Table 1. Physiologically difficult situations and preventive strategies



Intubation in COVID-19 patients poses as a major challenge when it comes to physiologically difficult airway. Hypoxaemia is common and safe apnoea time may be as short as 60 seconds in lungs with a poor compliance (Mosier 2020). Moreover, the combination of severe hypoxaemia due to pneumonia and hypercapnia due to increased dead space ventilation further increases the risk of acute cor pulmonale and right ventricular dysfunction (Mekontso et al. 2016).

Intubation of the COVID-19 Respiratory Failure

Given that COVID-19 is a disease transmitted predominantly by droplets, intubation and airway management are procedures with high level of exposure of healthcare workers and increased risk of contracting the illness. Some proposed changes in usual practice due to the COVID-19 pandemic affected all steps of intubation, from preparation to checking proper tube position. Therefore, protective measures are important but may increase the risk of severe complications and it is necessary to balance the risks and benefits of each of these measures.

What has changed that increased the procedure risk

To reduce staff exposition, guidelines and recommendations suggested to limit the number of people inside the room (Cook et al. 2020; Orser 2020). However, previous publications also suggested that two operators can reduce complications during the procedure. Therefore, a reduced number of people is adequate but the presence of two airway operators is still advisable (Jaber et al. 2006). Also, initial recommendations suggested changes in patient preoxygenation to reduce staff exposure to aerosol. Non-invasive ventilation and high flow nasal canula were contraindicated by some (Cook et al. 2020). Moreover,

low flow non-rebreathing mask, which is incapable of providing 100% oxygen, was suggested as a possible alternative. Although the concern with aerosolisation is understandable, poor preoxygenation can reduce the safe apnoea time and decrease first attempt success. Desperate rescue manoeuvres due to severe desaturation is probably more problematic than the use of proper preoxygenation, eventually leading to cardiac arrest and a crash scenario where any concerns about staff safety are forgotten. Another common reason for crashing after intubation is to forget about the necessary trade-off of increasing respiratory rates when using low tidal volume ventilation for acute hypoxaemic respiratory failure. This has been a frequent observation in our practice, especially with physicians inexperienced with a physiologically difficult airway. Finally, the use of bag mask ventilation and even the use of certain supraglottic devices were discouraged during intubation in COVID-19 patients. However, emergent surgical access of a failed first attempt is probably more difficult and riskier for the patient and staff than traditional algorithms in "do-not-intubate" situations (AMIB 2020).

What has changed that improved patient safety

On the other hand, some recommendations during intubation in COVID-19 should come to stay as the new standard of practice in the ICU. The presence of a runner outside the room with an easy access to rescue devices is advisable and can accelerate the process of accessing an urgent or crashed airway. Moreover, COVID-19 has brought the best experienced airway manager to the patient room. In any intubation, even if a less experienced operator is primarily managing the airway, a senior staff must be present to ensure a low rate of complications (Cook et

al. 2020). Despite initial recommendations, recent trials evaluating the use of noninvasive ventilation and high flow nasal canula in COVID-19 patients have facilitated personnel acceptance of using these resources during intubation (Grieco et al. 2021). Adequate preoxygenation with available devices, especially positive pressure ventilation, must remain as the gold standard in preparation for intubation. The routine use of neuromuscular blockade to reduce cough and aerosol dispersion brought the experience of the operating room into the ICU. Although not tested in a randomised trial, available evidence suggests that this strategy can increase first attempt success (Li et al. 1999; Mosier et al. 2015; Wilcox et al. 2012). Fnally, some have suggested a faster escalation to senior physicians and between devices (such as the adoption of the Vortex approach) instead of repeat attempts (3 or more) with the same operator and/or device. With adequate preparedness and sharing of the mental model of the most experienced physician, sharp decision-making during airway management is a desired consequence to improve procedural safety.

Current Approach to Airway Management - Suggested Do's and Don'ts

In **Table 2**, we suggest current do's and don'ts on airway management for critically ill patients, COVID-19 or not, based on current literature, and the authors' previous and acquired experience during the pandemic.

Conclusion

The COVID-19 pandemic brought several challenges to airway management practices in the ICU. The fear of staff contamination changed the usual practice with positive and negative effects to staff and patient safety. Now, after the experience with COVID-19 patients, it is important to filter which



DO	DON'T
Share the mental model and back-up plans of the most experienced operator beforehand	Repeat three attempts with the same device or less experienced operators
Evaluate for a difficult airway	Adopt a one-size-fits-all approach
Aim for first attempt success (with higher order devices in the primary strategy if necessary)	Always use direct laryngoscopy as the primary strategy
Include at least two operators, with at least one more experienced	Operate the airway without a second knowledgeable operator
Fastly escalate between devices should any unanticipated difficulties arise	Avoid bag valve mask ventilation should it be necessary (even in COVID-19)
Anticipate and prepare for physiological difficulties	Proceed to a surgical airway without considering suitable alternatives
Position the patient in a sniffing position attentive to ear-to-sternal notch alignment	Routinely use ramped patient positioning unless necessary to improve ear-to-sternal notch alignment
Pre-oxygenate with positive pressure ventilation in respiratory failure	Rely solely on apnoeic oxygenation to avoid desaturation
Check positioning with capnography	Check positioning solely with auscultation or chest expansion
Prepare a norepinephrine infusion beforehand	Rely on fluid boluses to avoid hypotension or haemo- dynamic collapse
Use neuromuscular blockers more liberally	Avoid neuromuscular blockers without a clear justification
Aim for an adequate post-intubation minute-ventilation to avoid severe hypercapnic acidosis and cardiac arrest	Start mechanical ventilation with low tidal volumes (≤ 6 mL/kg) without a higher respiratory rate (≥ 25–30 ipm) from outstart.

Table 2. What to do and not to do in airway management of the critically ill



recommendations should be left aside and which ones must stay for good. As with other expert recommendations based on few observations that have led to suggestions of non-evidence informed approaches to the management of known syndromes in critically ill patients, we believe that airway management strategies should also have

been maintained to current standards, actually taking them to higher standards if necessary. While protecting healthcare workers is a top priority (and should be done with proper protective equipment), lowering airway management standards for staff protection is both unacceptable and unadvisable. The main lesson we learned in

airway management during the pandemic is to keep the highest possible standards informed by the best available evidence to avoid potentially catastrophic and lethal complications.

Conflict of Interest

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