Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

"Anesthesia Stat" to Intubate a Coronavirus Disease 2019 (COVID-19) Patient: Implications for the Anesthesiologist

IN DECEMBER 2019, A PNEUMONIA outbreak of unknown etiology spread through China. By February 2020, the World Health Organization formally identified the cause as coronavirus disease 2019 (COVID-19).[1] Due to its high transmissibility and rate of hospitalization, the novel virus created a pandemic.[2]

Healthcare workers around the globe are confronting this disease on many fronts. The anesthesiologist, in particular, is encountering this virus in the operating room and intensive care unit and during urgent or emergent intubations. Patients are primarily presenting with pulmonary manifestations, frequently requiring advanced oxygen support including an advanced airway.[3] Due to the highly contagious nature of COVID-19, most of the concern for medical personnel has focused on minimizing exposure during intubation. Prophylactic measures have included donning adequate personal protective equipment (PPE) and using video laryngoscopes to maintain distance from the airway.[4] Also, many anesthesiology departments have implemented dedicated intubation teams to allow for effective airway management and decrease unnecessary exposure.

Although reducing exposure of medical personnel is of obvious importance, there has been a dearth of literature discussing clinical strategies during the induction and intubation of COVID-19 patients. Importantly, optimizing the intubation process could reduce exposure by reducing time at the bedside. In this editorial, the authors briefly will review the pertinent physiology of COVID-19, understand the anesthetic implications, and provide a number of strategies to induce and intubate a COVID–positive patient efficiently and safely.

COVID-19 Pathophysiology

Coronavirus disease 2019 is caused by a coronavirus genetically related to the virus that caused the severe acute respiratory syndrome outbreak of 2003. Most patients present with respiratory symptoms ranging from nonproductive coughs with fever to shortness of breath and hypoxia in severe cases. The virus, which is contracted primarily through respiratory droplets, possesses spike proteins that bind to angiotensin-converting enzyme 2 (ACE2) receptors. These receptors are located in the lower respiratory tract and serve as the entry point for severe acute respiratory syndrome coronavirus 2.[3] Histologic analysis demonstrates diffuse lymphocytic infiltrates, hyaline membrane development, and abnormal pneumocytes.[5] These may be the result of direct cellular injury and/or activation of an immune cascade. Patients can develop hypoxic respiratory failure secondary to pneumonia, pneumonitis, or acute respiratory distress syndrome.[3]

Unfortunately, COVID-19 is not solely a pulmonary disease. Patients have presented with cardiac symptoms and an acute decrease in their ventricular function. Myocardial injury, indicated by cardiac biomarkers, has been seen in the setting of a cytokine storm or as the primary manifestation. Postulated mechanisms of a viral cardiomyopathy include myocyte apoptosis secondary to hypoxia, cytokine storm–induced myocardial injury, or direct infection from ACE2 activity.[6] Lastly, pulmonary vasoconstriction secondary to significant hypoxia and hypercarbia could exacerbate any right ventricular dysfunction.

Angiotensin-converting enzyme 2 receptors, present on cardiomyocytes, are also prevalent on endothelial cells throughout the body. Attachment to the receptor may result in downregulation of ACE2, causing unopposed angiotensin II activity. Angiotensin-converting enzyme 2 counterbalances angiotensin II by promoting anti-inflammation, antioxidation, and vasodilation. Unchecked angiotensin II could injure tissues via a proinflammatory, prothrombotic, vasoconstrictive state.[7] Tissue injury could result in endothelial dysfunction mirroring that seen in septic or distributive shock.

The autonomic nervous system is intertwined intimately in the response to sepsis. The parasympathetic system works by an efferent inflammatory reflex to attenuate the inflammatory response. On the other hand, the adrenergic sympathetic system is proinflammatory via catecholamines. However, after an initial surge, stores of catecholamines can become depleted, resulting in septic shock.[8]

The kidneys also are implicated, possibly due to tubular epithelial expression of ACE-2. Acute kidney injury (AKI) is occurring in a significant percentage of hospitalized patients

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and is associated with increased mortality. Acute kidney injury is demonstrated by elevated creatinine and blood urea nitrogen levels. The exact mechanism of renal injury is unknown, but could be due to direct viral injury, hypoxia, decreased renal perfusion, or the systemic inflammatory response.[9]

Anesthetic Management (Tables 1 and 2)

Numerous pharmacologic strategies can be implemented during induction and intubation of COVID-19 patients. Any strategy must incorporate a rapid-sequence induction to minimize exposure and avoid aspiration. Although no studies have evaluated or determined ideal agents for inducing these patients, much can be inferred from the disease's pathophysiology. Categories of pharmacologic agents include analgesics, amnestics, and paralytics.

Opioids

Opioids, such as fentanyl, hydromorphone, and morphine, are the most commonly used analgesics in anesthetic inductions. Their administration has little influence on hemodynamics, with the most common effect being bradycardia secondary to sympathetic blunting. However, at larger doses, opioids have the potential to depress myocardium, and morphine can result in hypotension from histamine release.[10] Histamine release also can cause bronchospasm, and large doses can lead to chest wall muscle rigidity, both of which could impair adequate ventilation and oxygenation.[11] Opioids are an option in inducing COVID-19 patients; however, large fentanyl doses have been associated with postinduction hypotension, possibly due to sympathetic attenuation, which could be significantly pronounced and devastating in septic patients.[12]

Benzodiazepines

Benzodiazepines, like midazolam, have even fewer cardiac side effects than opioids. Midazolam can lead to a slight reduction of systemic vascular resistance when given at high doses (0.2-0.3 mg/kg); however, these doses rarely are used in inductions.[10] In septic patients, the decrease in systemic vascular resistance could lead to dramatic hypotension.[12] Benzodiazepines should be used cautiously in patients with renal disease because they have been associated with a higher risk of AKI in intensive care unit patients.[13] Midazolam could serve as a good induction agent for COVID-19 intubations because of its fast onset of action and hemodynamic profile.

Ketamine

Ketamine, unlike other agents, is a sympathomimetic that indirectly causes sympathetic stimulation via a release of catecholamines. Epinephrine and norepinephrine release can result in elevations of blood pressure, cardiac output, and heart rate at the cost of increased myocardial oxygen demand.[10] However, ketamine can depress myocardial function directly, especially in states of catecholamine depletion and at larger doses necessary for induction of anesthesia.[10] Ketamine does have many benefits as an induction agent. Its sympathomimetic effect induces bronchodilation, which can improve lung compliance and reduce airway resistance.[11] In addition, ketamine does not suppress respiratory drive. An animal study demonstrated that ketamine attenuated renal inflammation seen with hypoxia.[13] In sepsis or septic shock, ketamine can be protective against inflammation, reduce nitric oxide production, and decrease cardiac dysfunction, all of which prevent hemodynamic instability.[12] Ketamine could be a good agent for COVID-19 patient inductions; however, the anesthesiologist must be wary of cardiac failure with induction doses, especially if there is any pre-existing history of cardiac disease or concern for viral cardiomyopathy.

Propofol

Propofol can depress sympathetic vasoconstriction and reduce calcium influx, causing profound vasodilation and depressing myocardial contraction, respectively, especially at the high doses used for induction and intubation. It suppresses the sympathetic tone more than parasympathetic activity, potentially leading to significant bradycardia.[10] Propofol also acutely depresses the respiratory drive, possibly worsening the hypoxia or hypercarbia before intubation. On the other hand, propofol can bronchodilate and decrease hypoxic pulmonary vasoconstriction.[11] Propofol, due to its antioxidant and anti-inflammatory properties, seems to be renoprotective by attenuating ischemic reperfusion injury and reducing the incidence of AKI.[13] In sepsis, however, the use of propofol can be associated with significant postinduction hypotension. Also, cardiac inotropy and lusitropy can decrease by approximately 40% in severe sepsis and should be avoided or used cautiously in COVID-19 patients.[12]

Etomidate

Etomidate does not inhibit sympathetic activity or depress myocardial contractility with induction doses. However, even a single dose can induce adrenocortical suppression.[10] Also, Thompson Bastin et al reviewed septic patients receiving etomidate for intubation and noted significant hypotension.[14] Etomidate has minimal respiratory side effects; however, coughing can occur, potentially increasing viral aerosolization.[11] Regarding the renal system, an animal study showed etomidate was less protective against tubular injury.[13] Etomidate can be considered for induction in COVID-19 patients because of its safer cardiac profile; however, hemodynamic instability due to catecholamine depletion and adrenal suppression are important considerations in these patients.[12]

Neuromuscular Blockers

Emergent airway intubation most often requires paralysis. Paralysis is specifically helpful in COVID-19 patients due to cessation of breathing and coughing, which decreases aerosolization of the virus during the procedure. Most commonly used

agents in modern practice include rocuronium, vecuronium, cisatracurium, and succinylcholine.

Nondepolarizing muscle blockers can cause some cardiovascular effects secondary to histamine release; however, this does not occur with the use of rocuronium, vecuronium, and cisatracurium.[10] On the other hand, the depolarizing muscle relaxant succinylcholine can have more exaggerated cardiovascular effects compared with nondepolarizing agents. Malignant arrhythmias can occur secondary to muscarinic interaction at the sinus node or from hyperkalemia release at extrajunctional receptors.[10] Succinylcholine, which also causes histamine release, can induce bronchoconstriction.[11] The nondepolarizing muscle blocker used is based on practitioner preference and should account for potential side effects.

Equipment

Any discussion of equipment must be focused on reducing viral exposure. Equipment can be divided into provider- specific and procedure- specific. Provider equipment primarily encompasses PPE, which, at a minimum, must include an N95 mask, face/eye protection, cap or hat, 2 sets of gloves, and a gown. Shoe covers can be used if available. The face/eye protection can be a shield or goggles but should be checked for any smears or streaks to avoid visual disturbances. All PPE must be donned properly in an area outside the patient room and partially doffed inside patient or anteroom with the exception of the N95 mask and 1 set of gloves.

Procedural equipment should keep the intubation process simple, straightforward, and easy to replicate. Video laryngoscope is ideal to maintain distance from the airway and also reduce potential airway difficulty. If available, a handheld video laryngoscope also may be considered due to its smaller size and ease of handling compared to traditional video laryngoscopes. Also, handheld laryngoscopes may be easier to clean and can be used as a traditional Macintosh blade if needed. An endotracheal tube (ETT) should be loaded with a stylet and syringe for cuff inflation. A smaller, backup ETT should be readily available for unanticipated airway difficulties. Induction medications should be drawn up and connected to stopcocks, with an extension to facilitate injection easily to a proximal port of the IV. All preparations should be done prior to entering the room to shorten exposure time. Any superfluous equipment should be kept outside the COVID-19 patient room to avoid unnecessary contamination or waste. Drapes or clear boxes with access for intubation can be used at the head of the bed to minimize exposure. Any additional strategy to minimize exposure should be tested and understood properly by the anesthesiologist, because some of these tricks potentially could interfere with the intubation and increase the time in the room.

In addition to procedural equipment, additional preparations are needed for an emergent COVID intubation. The team that will enter (ie, anesthesiologist, nurse, respiratory therapist) should be determined outside the room. Also, when possible, the ventilator should be set up and ready in the room before the anesthesiologist entering the room. An Ambu bag with mask and a viral filter inserted distally and functioning suction line and intravenous line should be checked and readily available.

Recommendations

Many anesthesiology departments have deployed dedicated intubation teams, separate from the operating room/call teams, to allow for expedited airway management while decreasing unnecessary exposure. Using the same personnel on these shifts allows teams to develop familiarity with one another and develop a rhythm when dealing with the novel challenges that are presented by intubation of patients with COVID. Most of these teams function in a buddy system, with an attending anesthesiologist plus a certified registered nurse anesthetist or resident, and are scheduled in shifts (8-hour or 12-hour) to allow for the highest skilled individuals for airway management while preventing exhaustion.

When called to intubate these patients emergently, the anesthesiologist must appreciate the pathophysiology of this virus and the effect it can have on multiple organ systems. Before entering the COVID-19 patient's room, a review of the chart or a discussion with the primary team should include past medical history, current hemodynamic state, pertinent labs and findings, current medication regimens, and the need to intubate over other strategies to improve oxygenation and ventilation.

After ensuring intubation is required, the anesthesiologist should determine appropriate preinduction monitoring. Coronavirus disease 2019 has worse outcomes in patients with comorbidities such as hypertension and heart failure, and these patients are more likely to require mechanical ventilation. Beyond basic monitoring (ie, pulse oximetry, noninvasive blood pressure, electrocardiography, and capnography), patients with significant cardiovascular disease, virus-induced cardiomyopathy, or hypotension secondary to distributive shock may need an arterial line, central line, or defibrillator pads. Induction and intubation can cause significant hemodynamic instability, and these additional monitors could contribute to a more stable procedure and allow for quickly initiating vasopressor infusions and assisting in advanced life support care, if needed.

In addition to monitoring, the anesthesiologist should check with the primary team and nursing about sedation plans after the intubation. No intubation should be attempted without confirming that a functioning IV is available and suction with a Yankauer is prepared. Lastly, clinicians must confirm with respiratory therapy about a connected Ambu bag with a viral filter in line and a configured ventilator. All these steps streamline the process and minimize time in the room and should be completed prior to entering the patient room.

Upon entering the COVID-19 patient room, after securing appropriate personal and procedural equipment, the anesthesiologist should move quickly to the head of the bed while assessing the patient's current oxygenation and airway. Most, if not all, of these patients will have advanced oxygen delivery, such as a nonrebreather mask, high-flow nasal cannula, or bilevel positive airway pressure. The anesthesiologist should not remove the patient's current therapy in favor of Ambu bag to avoid increased aerosolization. The World Health Organization has suggested using any mode to preoxygenate for 5 minutes.[3] If airway concerns are elicited on quick assessment, a fellow anesthesia provider (ie, buddy) should enter to provide assistance. If the brief

Table 1
Summary of Intubation Recommendations for COVID Patients

	Preprocedural	Intraprocedural	Postprocedural
Patient	Obtain patient history. Discussion with team about patient status and need for intubation.	• Assess airway. • Observe current oxygen delivery method. • Do not exchange for Ambu bag to reduce aerosolization.	• Confirm hemodynamic and respiratory stability.
Provider	Use buddy system to monitor appropriate PPE donning.	• Optimize efficiency to reduce exposure time.	• Use buddy system to monitor appropriate PPE doffing.
Procedure	Set up equipment prior to entering. Confirm ventilator setup with RT. Confirm sedation and room equipment with the team/nursing.	• Use video laryngoscopy to maintain distance and optimize first attempt. • Instruct help to reduce time.	• Discard single-use equipment. • Sterilize equipment after exiting room.

Abbreviations: COVID, coronavirus disease; PPE, personal protective equipment; RT, respiratory therapist.

airway exam does not raise any alarms, the colleague should wait outside and act as a runner in case additional resources are necessary. Assuming a straightforward airway, medications may be injected by the anesthesiologist via the extension tubing. The respiratory therapist should remain near the ventilator and patient head in case cricoid pressure or any assistance is necessary.[4] Table 1 summarizes the authors' recommendations when approaching a COVID-19 positive intubation.

In the authors' experience at an institution in New York City with a census high in COVID patients, the ideal anesthetic was one that facilitated quick intubation and reduced intervention post-intubation. By the time patients require intubation, many had progressed to the septic phase of COVID-19. The authors noted the need for significantly decreased anesthetic to intubate these patients successfully while maintaining hemodynamic stability. Rapid-sequence strategies using benzodiazepines with rocuronium resulted in a smooth and hemodynamically stable intubation. Midazolam doses commonly used were between 4 and 6 mg, approximately 0.05 mg/kg, and rocuronium doses of 1.2 mg/kg. Analgesia was not a concern, as most patients had no tachycardic response to intubation. Propofol and etomidate usage was noted to have greater hemodynamic instability, possibly due to catecholamine depletion consistent with severe sepsis. Rocuronium was preferred over succinylcholine, because COVID-19 patients have long ventilatory courses and ventilator synchrony improves oxygenation and ventilation. Succinylcholine also was avoided, because many patients had AKI and elevated potassium levels. Cisatracurium is a theoretically ideal agent in renal injury patients, but, as the timeline to consider extubation is a long one, the use of cisatracurium may not be warranted. As the most common hemodynamic derangement was hypotension, phenylephrine commonly was administered, with induction in doses of 100 to 200 μg. If additional hemodynamic support was anticipated, proper monitoring and access was established prior to airway management. If additional hemodynamic support is required, norepinephrine, a first-line agent in septic shock, is recommended.[12] Table 2

Table 2
Summary of Pharmacologic Considerations in COVID-19 Intubations

Drug	Considerations Advantages	Disadvantages
Opioids - Fentanyl - Morphine	- Minimal effect on hemodynamics	- Sympathetic blunting (↓HR and BP with large doses) - Histamine release (morphine) - Chest wall rigidity (with large doses)
Midazolam	- Minimal reduction in SVR	- Hypotension (with large doses) - Worsen AKI
Ketamine	- Increases cardiac output - Anti-inflammatory - Bronchodilator	- Direct myocardial depressant (with induction doses)
Propofol	- Anti-inflammatory	- Hypotension - Vasodilation
Etomidate	- Minimal effects on hemodynamics	- Coughing (aerosolization) - Adrenocortical suppression - Hypotension (in catecholamine depletion, sepsis)
NMBs - Rocuronium - Vecuronium - Cisatracurium	- Minimal effects on hemodynamics - No effects in renal disease (cisatracurium)	- Delayed metabolism in renal disease (rocuronium, vecuronium)
Succinylcholine	- Short acting	- Malignant arrhythmias - Bronchoconstriction (histamine release)

Abbreviations: AKI, acute kidney injury; BP, blood pressure; COVID-19, coronavirus disease 2019; HR, heart rate; NMBs, nondepolarizing muscle blockers; SVR, systemic vascular resistance.

summarizes pharmacologic considerations for intubating COVID-19 patients.

During laryngoscopy and intubation, COVID-19 patients desaturate very quickly. These patients have little- to- no reserve even with optimal preoxygenation, but that must not distract the anesthesiologist from establishing an advanced airway. Also, desaturation commonly persisted immediately after intubation. Early on in the pandemic, practitioners were fooled by the persistent desaturation and convinced to replace the ETT. Rather than removal and replacement, confirmation through visualization from a video laryngoscope, end-tidal carbon dioxide, along with bilateral chest rise should be used to confirm ETT placement. The patient can be bag ventilated for a 3 to 4 breaths to allow for this. When connecting the ventilator circuit, placement of the viral filter proximal and ensuring the ETT cuff is inflated are advised to avoid aerosolization.

In many circumstances, the anesthesiologist will be required to manage the airway in a cardiac/respiratory arrest. These situations may become chaotic and stressful, especially in a COVID patient, and efficient securing of the airway and reducing exposure remain critical. It is imperative that the anesthesiologist remain vigilant and calm and quickly survey the room for the necessary equipment. In addition to recommendations discussed, the anesthesiologist must limit mask ventilation and immediately secure the airway. Most importantly, the code team must cease chest compressions during laryngoscopy and intubation and only should continue once the ETT placement and cuff inflation are confirmed to reduce aerosolization and exposure to the anesthesiologist and any other member of the team assisting with the airway. The ventilator should be connected immediately, ensuring in-line viral filters.

After completion of the intubation and before doffing the PPE, the next steps include discarding and sterilization. Any single-use items, including syringes, stylets, and blades, should be discarded prior to exiting the room. Equipment such as the video laryngoscope should be disinfected and sterilized after exiting the room but in a designated area where doffing will occur to avoid viral spread and contamination.[15]

Conclusion

Illness resulting from COVID-19 not uncommonly requires urgent intubation. From a logistical perspective, vigilance is of utmost importance to guarantee proper PPE and protection from the virus. This can be ensured by a buddy system to watch appropriate donning and doffing of PPE. A buddy system also can help to acquire additional medications or equipment and alternate intubations to avoid fatigue.

Because COVID-19 is a novel disease, information will continue to emerge and departmental discussions should continue to update best practices. As New York City has encountered a disproportionate number of cases within the United States, the authors feel uniquely qualified to help disseminate what has been found to be the safest and most efficient ways to take care of these patients.

Conflict of Interest

H.V. Bhatt is an anesthesiology consultant for Neochord, LLC.

Samit Ghia, MD
Michael Lazar, MD
Jonathan Epstein, MD
Himani V. Bhatt, DO, MPA, FASE, FASA
Department of Anesthesiology, Critical Care and Perioperative Medicine, Icahn School of Medicine at Mount Sinai, New York, NY

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