ANESTHESIOLOGY

Intubation and Ventilation amid the COVID-19 Outbreak

Wuhan's Experience

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ABSTRACT

The COVID-19 outbreak has led to 80,409 diagnosed cases and 3,012 deaths in mainland China based on the data released on March 4, 2020. Approximately 3.2% of patients with COVID-19 required intubation and invasive ventilation at some point in the disease course. Providing best practices regarding intubation and ventilation for an overwhelming number of patients with COVID-19 amid an enhanced risk of cross-infection is a daunting undertaking. The authors presented the experience of caring for the critically ill patients with COVID-19 in Wuhan. It is extremely important to follow strict self-protection precautions. Timely, but not premature, intubation is crucial to counter a progressively enlarging oxygen debt despite high-flow oxygen therapy and bilevel positive airway pressure ventilation. Thorough preparation, satisfactory preoxygenation, modified rapid sequence induction, and rapid intubation using a video laryngoscope are widely used intubation strategies in Wuhan. Lung-protective ventilation, prone position ventilation, and adequate sedation and analgesia are essential components of ventilation management.

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The outbreak of the "Coronavirus Disease 2019" (COVID-19) started in December 2019 and quickly became a sweeping and unprecedented challenge to different stakeholders in mainland China.[1] Although the epidemic of COVID-19 is not yet over, it has already outpaced the previous severe acute respiratory syndrome (SARS) in 2003 and Middle East respiratory syndrome (MERS) in 2012 in nearly every respect, except for the mortality rate (table 1). As of March 4, 2019, a total of 80,409 patients were diagnosed with COVID-19, and a total of 3,012 patients among those confirmed cases died, corresponding to a mortality rate of 3.7% (http://www.nhc.gov.cn/; accessed March 5, 2020). At the writing of this article on March 5, 2020, it appears that the momentum of the epidemic in mainland China, especially that in the epicenter of Wuhan, Hubei Province, China, has slowed down. However, the disease is gaining momentum outside of China, and it could ultimately become very severe (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen; accessed March 5, 2020). The concern is whether the COVID-19 epidemic could become a once-in-a-century pandemic.[2]

It did not take more than a few days before the healthcare system and providers in the epicenter of Wuhan were stunned by the COVID-19 outbreak's scale, speed, severity, and serious threat to healthcare providers themselves. Many patients developed serious symptoms, with some of them becoming critically ill.[1] The hospitals were quickly overwhelmed, forcing the administration to lock down the city of Wuhan, reactivate the workforce a few days ahead of the most popular holiday in China, Lunar New Year, reorganize the case flow, convert noninfectious floors and hospitals into infectious ones, build two new hospitals from ground zero, and open 16 Fang Cang hospitals using the big sport, conference, exhibition, and performance buildings (fig. 1; http://wjw.wuhan.gov.cn/; accessed March 1, 2020). The most common and severe complication in patients with COVID-19 is acute hypoxemic respiratory failure or acute respiratory distress syndrome (ARDS), requiring oxygen and ventilation therapies.[3] Some of these critically ill patients required intubation and invasive ventilation.[3,4] Moreover, although elective surgeries were largely cancelled, emergency surgeries for patients with confirmed or suspected COVID-19 were permitted to proceed. Some of these surgeries were performed under general anesthesia with endotracheal intubation. Intubating and ventilating

Table 1. Demographics of Patients Infected with COVID-19, 2012 MERS, and 2002 SARS

Demographics	COVID-19*	2012 MERS†	2002 SARS†
Date started	December 2019	June 2012	November 2002
Location	Wuhan, China	Jeddah, Saudi Arabia	Guangdong, China
Confirmed patients, n	80,409	2,494	8,096
Patients admitted to the ICU	15–20%	N/A	20%‡
Patients died, n	3,012	858	744
Mortality	3.7%	37%	10%

*Demographics for COVID-19 are based on data published by the National Health Commission of the People's Republic of China (http://www.nhc.gov.cn/; accessed March 5, 2020).
†Data source.[56] ‡Data source (https://www.who.int/csr/sars/postoutbreak/en/; accessed March 5, 2020).
COVID-19, coronavirus disease 2019; ICU, intensive care unit; MERS, Middle East respiratory syndrome coronavirus; SARS, severe acute respiratory syndrome.

patients with COVID-19 who are critically ill or require emergent surgical procedures present some unique challenges to providers.

The healthcare system and providers need to be prepared in and outside of China for the COVID-19 outbreak now and for any outbreaks in the future. Preparedness is a pressing issue considering that many places and countries in the world are under-resourced, and at the time of writing this article, COVID-19 is quickly unfolding and evolving outside of mainland China. Healthcare providers, who are tasked with taking care of critically ill patients, need to perform the best practices of intubation and ventilation tailored explicitly to the victims of this sweeping COVID-19 outbreak and, at the same time, adhere to strict self-protection precautions.

Wuhan's experience needs to be highlighted and quickly communicated throughout the world. In February 2020, we conducted four webinars specifically discussing the issues related to preparedness, airway management, lung-protective ventilation, the goal of oxygenation, and extracorporeal membrane oxygenation (fig. 2). We summarize the results of these discussions, which were based on firsthand experience with treating critically ill patients in Wuhan.

Demand of Intubation and Invasive Ventilation amid the COVID-19 Outbreak

COVID-19 has a wide spectrum of clinical severity, ranging from asymptomatic to critically ill, and ultimately death.[1,5,6] A common and prominent complication of advanced

Fig. 1. Dr. Junmei Xu is working at one of the sixteen Fang Cang hospitals in Wuhan amid the COVID-19 outbreak. Dr. Xu is a senior anesthesiologist and vice president of the Second Xiangya Hospital affiliated with Xiangya Medical School, Central South University, Changsha, Hunan, China. "Xiangya Second Hospital Xu Jun Mei" is written on his back. (Photograph by Dr. Junmei Xu.)

Fig. 2. Screenshot of the fourth webinar with live broadcast conducted on February 29, 2020. A total of 12 intensivists and anesthesiologists (10 people from China; 2 people from the United States) discussed the experience of using extracorporeal membrane oxygenation amid the COVID-19 outbreak. Nine of the 10 Chinese experts are currently working in Wuhan and taking care of critically ill patients with COVID-19. Most of these Chinese experts stay in hotels because they came from other provinces to Wuhan to share the workload that had overwhelmed the local teams. (Photograph by Dr. Lingzhong Meng.)

COVID-19 is acute hypoxemic respiratory insufficiency or failure requiring oxygen and ventilation therapies (fig. 3).[3,4] A recent report showed that 14% of patients developed dyspnea, tachypnea with a respiratory rate greater than or equal to 30 per minute, desaturation with peripheral oxygen saturation (Spo_2) less than or equal to 93%, poor oxygenation with a ratio of partial pressure of arterial oxygen (Pao_2) to fraction of inspired oxygen (Fio_2) less than 300 mmHg, or lung infiltrates greater than 50% within 48 h.[1] ARDS occurred in 20% of the 138 patients hospitalized and in 61% of the 36 patients admitted to the intensive care unit (ICU) in Zhongnan Hospital in Wuhan.[4] Organ dysfunction, injury, or failure, excluding the lungs, is common. Cardiac injury occurred in 23%, liver injury in 29%, and acute kidney injury in 29% of critically ill patients.[3] Neurocognitive impairments occurred in more than one third of patients with advanced COVID-19.[7]

Invasive ventilation *via* an endotracheal tube is common amid this outbreak. It was performed in 2.3% of the 1,099 patients with confirmed COVID-19 based on the patient cohort from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China,[1] in 47% of the 36 patients admitted to the ICU in Zhongnan Hospital in Wuhan,[4] and in 42% of the 52 patients admitted to the ICU in Jin Yin Tan Hospital in Wuhan.[3]

Although elective surgeries were cancelled in the epicenter of Wuhan, emergent surgeries were permitted amid this outbreak. As of February 29, 2020, a total of 105 emergent surgical procedures, including 90 cesarean sections (classified

as emergent surgery amid this outbreak; fig. 4), were performed in patients with confirmed or suspected COVID-19 in Tongji Hospital in Wuhan (data from Dr. Wan). Some of these procedures were performed under general anesthesia with endotracheal intubation. The anesthesiologists from the Department of Anesthesiology at Tongji Hospital in Wuhan performed approximately 200 nonoperating room intubations in patients with confirmed COVID-19 as of February 29, 2020. This is just a snapshot of the anesthetic practice in the epicenter of Wuhan amid this outbreak.

Currently, we do not have data detailing the total number of patients with COVID-19 who received intubation and invasive ventilation or details about the outcomes associated with and after these invasive interventions. Nonetheless, we can attempt to estimate this based on the available data. As of February 29, 2020, a total of 2,870 patients with confirmed COVID-19 have died (http://www.nhc.gov.cn/; accessed March 1, 2020). It is assumed that all of these patients died in ICUs, as most, if not all, of them should have been admitted to the ICU before their death. We estimate that, if using a mortality rate of 50% among patients who were admitted to the ICU, a total of 5,740 patients would have been admitted to the ICU ($2,870 \times 2 = 5,740$) as of February 29, 2020. One recent report showed a mortality rate of 61.5% in patients who were admitted to the ICU.[3] The other report showed a mortality rate of 49% among critically ill patients.[8] We used a mortality rate of 50% in our estimate. Based on the data reporting an invasive ventilation rate of approximately 45% in patients who were admitted to the ICU,[3,4] we estimate
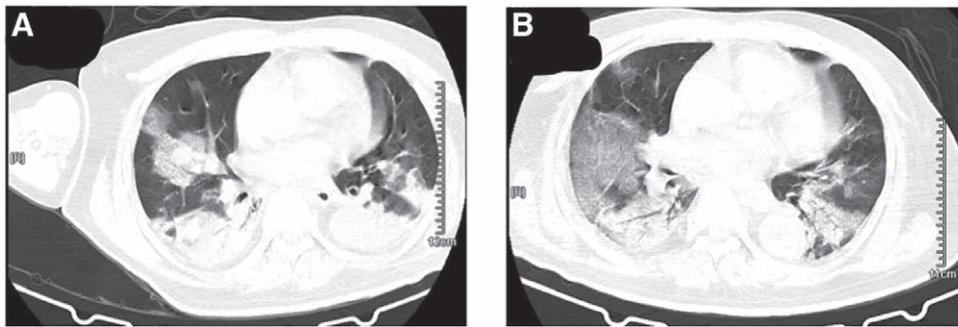
Fig. 3. A 62-yr-old male with confirmed COVID-19 required endotracheal intubation and invasive mechanical ventilation. The chest computed tomography scan suggested that, compared with that before intubation (*A*), the pulmonary disease had progressed 3 days after intubation (*B*). This progression was more likely related to the disease itself as there were no signs of ventilator-associated lung injury. (Photograph by Dr. Haibo Qiu.)

Fig. 4. A healthy newborn was delivered from a mom with confirmed COVID-19 in Tongji Hospital in Wuhan. (Photograph by Dr. Li Wan.)

that approximately 2,583 patients with COVID-19 received intubation and invasive ventilation, accounting for approximately 3.2% (2,583 of 79,824) of all confirmed COVID-19 cases, as of February 29, 2020, in mainland China.

Intubation Criteria

The decision to intubate can be obvious and require little deliberation, as for patients with cardiopulmonary arrest or a lost or jeopardized airway. It can also be a decision that lacks quality evidence for guidance and, thus, is a decision made at the discretion of the treating physician. In patients with acute hypoxemic respiratory failure due to COVID-19, it can be challenging when deciding whether to proceed with intubation and invasive ventilation. The Chinese Society of Anesthesiology Task Force on Airway Management released a fast-track publication with the recommendation to proceed with endotracheal intubation for patients showing no

improvement in respiratory distress, tachypnea (respiratory rate greater than 30 per minute), and poor oxygenation (Pao_2 to Fio_2 ratio less than 150 mmHg) after 2–h high–flow oxygen therapy or noninvasive ventilation.[9]

These criteria should be regarded as empirical as there is no robust supporting evidence. The frontline physicians taking care of critically ill patients in Wuhan suggest that intubation and invasive ventilation may have been adversely delayed in some patients. They are concerned that, amid this particular outbreak, intubation is more often used as a salvage therapy than a proactive means of supporting patients whose oxygenation is progressively declining and oxygen debt keeps increasing. The most recent report showed that, among the 22 ICU patients who were intubated, 19 (86%) of them died.[3] Although most frontline physicians believe the decision of intubation in some critically ill patients with COVID-19 had been adversely delayed, we do not know at this time if early intubation could save more lives. We do know, based on the work performed 30 yr ago by Shoemaker *et al.,* that there is a close association between the oxygen debt accumulated over 48 h and the chance of survival in patients undergoing high–risk surgery and ICU admission afterward.[10] Shoemaker *et al.*'s work highlights the importance of timely stopping an enlarging oxygen debt using effective oxygenation and ventilation therapies.

The decision-making process for nonoperating room intubation used in Wuhan is summarized in figure 5. Timely, not premature, intubation is the keyword in decision-making.

We added liberal criteria, including Spo_2 less than 93% in room air and a Pao_2 to Fio_2 ratio less than 300 mmHg, to facilitate preparedness for intubation based on the experience of taking care of critically ill patients in Wuhan. This proposal is justified as unprepared emergent intubation carries more risks, including cross-infection. It is also justified by the observation that some patients are relatively asymptomatic although they have a good degree of hypoxemia for inexplicable reasons (referred to as "silent hypoxemia" in Wuhan).[11] Silent hypoxemia may be responsible for the quick deterioration in some patients because it gives a false sense of well-being when the oxygen debt has been actually and asymptomatically increasing. This algorithm emphasizes vigilance by asking two questions for patients with respiratory distress or hypoxemia. One is whether the condition has been progressively deteriorating or if it is expected to get worse; if the answer is yes, the next question is whether 2–h high–flow oxygen therapy or noninvasive ventilation is effective.

Enhanced Risks and Protective Mandate during Intubation and Ventilation

Both patients and healthcare workers have to endure enhanced, but distinctive, risks during intubation and ventilation management amid the COVID-19 outbreak. The enhanced risks to patients will be discussed in the coming sections of this article. The enhanced risk to healthcare workers is cross–infection.

Fig. 5. Criteria for nonoperating room intubation amid the COVID-19 outbreak. Fio_2, fraction of inspired oxygen; Pao_2, partial pressure of arterial oxygen; RR, respiratory rate.
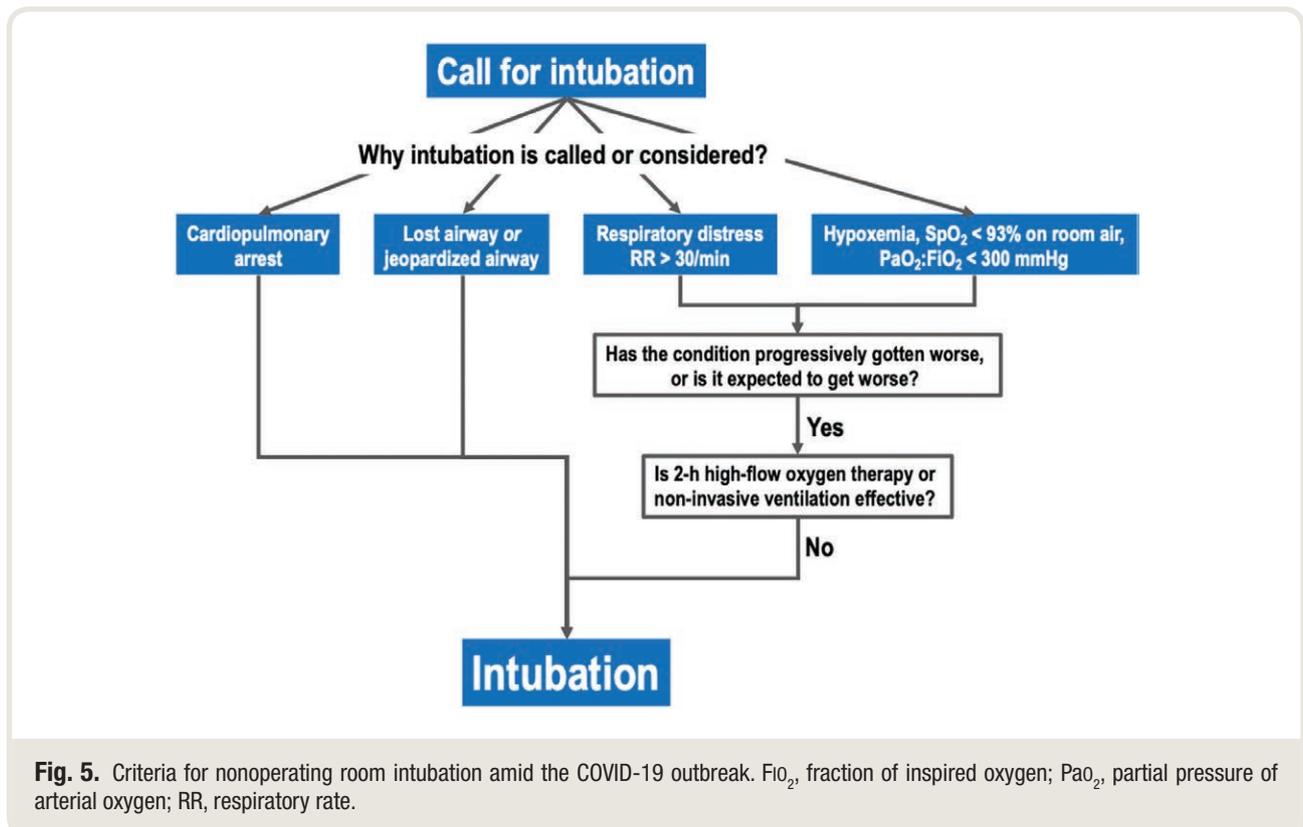
Of the 138 hospitalized patients with confirmed COVID-19 in Zhongnan Hospital in Wuhan, 40 (29%) patients were healthcare workers with hospital-associated transmission suspected as the mechanism of infection.[4] Five anesthesia providers working in Tongji Hospital in Wuhan were diagnosed with COVID-19. Two providers likely contracted the infection when taking care of patients with COVID-19 in December 2019 when the self-protection mandate had not yet been established. The other three providers likely contracted the infection from family members. All five providers have recovered. Since the establishment of the self-protection mandate in January 2020, no anesthesia providers in Tongji Hospital have contracted the infection. Dr. Shanglong Yao, a well-known anesthesiologist and former vice president of the Union Hospital in Wuhan, was diagnosed with COVID-19, with the infection likely transmitted from his daughter. Dr. Yao was hospitalized for a prolonged 4 weeks for close observation of the new-onset atrial fibrillation and poorly controlled hypertension. He eventually recovered and was discharged home (fig. 6). These are just some examples of the situations related to the healthcare providers who were infected.

It was estimated that, as of February 11, 2020, a total of 1,716 health workers had confirmed COVID-19 and five had died (0.3%) in mainland China.[12] The total number of cases of healthcare worker infections could be much more than this estimate. It was an observation that most of these infections occurred at the early stage of this outbreak when the self-protection mandate had not been established and reinforced. The mechanisms of transmission responsible for these infections are unknown; some cases may be nosocomial infections while the remainder may not be work related. We also do not know how many nosocomial infections are attributable to the intubation process or ventilation management.

The lesson we learned from the 2003 SARS outbreak is that, compared with healthcare workers who do not perform intubation or ventilation management, those who perform these tasks have a higher risk of contracting the infection. A systematic review showed that compared with healthcare workers who did not perform aerosol-generating procedures, those who performed tracheal intubation had an increased risk of contracting the 2003 SARS (odds ratio, 6.6), as were those who performed noninvasive ventilation (odds ratio, 3.1), tracheotomy (odds ratio, 4.2), and manual ventilation before intubation (odds ratio, 2.8).[13] A separate study found that the protection guidelines failed to thoroughly prevent the transmission of 2003 SARS to healthcare workers and that 9% of the interviewed healthcare workers who had intubated patients contracted SARS.[14] However, the cause-effect relationship between

Fig. 6. Dr. Shanglong Yao was hospitalized after diagnosis of COVID-19. Dr. Yao is a senior anesthesiologist and former vice president of the Union Hospital affiliated with Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China. (Photograph by Dr. Shanglong Yao.)

infection and intubation in these healthcare workers who contracted SARS was unknown.[14]

Despite the enhanced risk to healthcare workers, the potential harm of withholding intubation may outweigh the potential risk of cross-infection in patients who would benefit from invasive ventilation support.[15] Whenever intubation and invasive ventilation are needed, they should be timely and effectively provided. The healthcare workers who are involved in caring for patients with known or suspected COVID-19 should strictly adhere to the self-protection mandate (table 2).

The self-protection mandate for healthcare workers was quickly established and reinforced throughout different hospitals in Wuhan after the recognition of human-to-human transmission of COVID-19 toward the end of January 2020. Extensive and efficient education and training were provided to all healthcare workers. At the same time, personal protective equipment that was most needed was delivered to Wuhan and the rest of the country where the epidemic was quickly evolving. The contact and airborne precautions, with components of personal protective equipment, are presented in table 2. The different levels of precautions were scaled per the settings of patient care in Wuhan and the rest of China (table 3). Full precaution (level III) is mandatory for any care that involves direct patient contact, including intubation and ventilation management.

In China, it is mandatory to strictly follow the personal protective equipment donning process for high-risk exposure in the following order: disposable hair cover, fit-tested N95 respirator or equivalent, fluid-resistant gown, two layers of gloves, goggle and face shield, and fluid-resistant shoe covers.[9] Before entering an isolation area, an experienced nurse or assistant is responsible for checking the donning process (fig. 7). It is crucial to make sure the personal protective equipment is donned in the manner that will not interfere with procedures. It is also mandatory to strictly follow the personal protective equipment doffing process after high-risk exposure in the following order: hand hygiene, face shield and goggle removal, fluid-resistant gown removal, outer glove removal, shoe cover removal, inner glove removal, hand hygiene, N95 respirator or equivalent removal, and hair cover removal.[9] The doffing process should also be supervised, but not facilitated, to reduce the chance of contamination. It is mandatory to report any inadvertent contamination of the skin or mucosa to the hospital infection control office to assess the need for quarantine. A shower and the use of oral, nasal, and external auditory canal disinfectants are recommended after the removal of personal protective equipment.

Intubation and Extubation

Patients with confirmed or suspected COVID-19 should be regarded as having an augmented risk of presenting potentially difficult and complicated intubation for the following reasons. First, when a patient requires intubation for acute hypoxemic respiratory failure, they have minimal to no respiratory reserve, and their compensatory mechanisms have already been exhausted. It is common to see a patient who starts with a dangerously low SpO_2 quickly decline after loss of spontaneous breathing, followed by a slow recovery with manual facemask ventilation. Second, due to strict infection control and the urgency of intubation, a careful airway evaluation is frequently not possible. Third, the personal protective equipment mandated by the level III scaled precaution makes the performance of the procedure clumsy, which may easily compromise the intubation process.

Table 2. Contact and Airborne Precautions amid the COVID-19 Epidemic*

Components	Explanations
Patient placement	Use airborne infection isolation rooms or dedicated operating rooms for patients with confirmed or suspected COVID-19.
Traffic control	Limit the number of healthcare personnel present during the procedure to only those essential for patient care and procedural support. Room doors should be kept closed except when entering or leaving the room, and entry and exit should be minimized.
Equipment	Dedicated medical equipment should be used for patient care. All nondedicated, nondisposable medical equipment used for patient care should be cleaned and disinfected.
Engineering controls	Closed suctioning systems for airway suctioning.
Hand hygiene	Use alcohol-based hand sanitizer. If hands are visibly soiled, use soap and water before using alcohol-based hand sanitizer.
Gloves	Perform hand hygiene, then put on clean, nonsterile gloves. Change gloves if they become torn or heavily contaminated.
Gowns	A clean, nonsterile, long-sleeved, and waterproof gown. Isolation gowns are defined as a gown intended to protect healthcare patients and personnel from the transfer of microorganisms, body fluids, and particulate material, whereas protective gowns refer to impervious gowns with a high level of protection.[57]
Medical mask	Surgical or procedure masks that are flat or pleated (some are like cups); they are affixed to the head with straps.
Respiratory protection	A particulate respirator that is at least as protective as a U.S. National Institute for Occupational Safety and Health–certified N95, European Union standard FFP2, or equivalent.
Eye protection	Goggles or a disposable face shield that covers the front and sides of the face.
Head covering	Different from the conventional surgical hat. It covers the entire head, neck and shoulders.

*Based on the recommendations by the Centers for Disease Control and Prevention (https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control.html; accessed March 5, 2020) and World Health Organization (https://apps.who.int/iris/handle/10665/330674; accessed March 5, 2020) with modifications.
FFP2, medium efficiency filtering face piece.

Table 3. Scaled Protection for Healthcare Workers amid the COVID-19 Epidemic*

Scale	Routine	Level I	Level II	Level III
Setting	Clinics, regular floors	Fever clinics, floors for infectious diseases	Noncontact care for patients with confirmed or suspected COVID-19	Direct contacts with patients with confirmed or suspected COVID-19
Medical mask	+	+	−	−
Respiratory protection	−	−	+	+
Eye protection	−	−	±	+
Hand hygiene	+	+	+	+
Gloves	±	+	+	+
Scrubs	+	+	+	+
Isolation gown	−	+	±!	−
Protective clothing	−	−	±!	+
Disposable hair cover	−	+	+	+
Head covering	−	−	−	+
Shoe cover	−	−	+	+

*Based on the regulations established in Tongji Hospital in Wuhan with modifications.

+, mandatory; −, not needed; ±, decision made according to the work scenario; ±!, choice between isolation gown or protective clothing is decided based on the local resources for level III–scaled protection.

Fourth, strict infection and traffic control restrict backup supplies and helpers from being readily available when they are needed. Fifth, the psychological pressure related to concerns of cross-infection challenges the providers, which may make an otherwise easy intubation complicated.

Preparedness minimizes the chance of cross-infection and improves the chance of smooth intubation. The proposed approach to prepare for intubation for patients with confirmed or suspected COVID-19 is summarized in table 4. We recommend using the acronym OH–MS. MAID—Oxygen, Helper, Monitor, Suction, Machine,

Airway supplies, Intravenous access, and Drugs—to facilitate the preparation process for intubation. In Wuhan, all portable supplies, needed or potentially needed, are packed in one package. One-time use disposable supplies are preferred. Equipment that has to be reused is dedicated for patients with confirmed or suspected COVID-19. No glitch or imperfection is minor when there is an associated risk. Preparedness is even more crucial amid the COVID-19 outbreak, as the chance of contamination may be readily enhanced during the process of a complicated intubation when all attention is devoted to saving a patient's life. An

Fig. 7. The level III–scaled protection in Wuhan. (*A*) A nurse is checking and facilitating the donning process for a healthcare worker. (*B*) An anesthesiologist is fully equipped before entering an isolation room. (*C*) An anesthesiologist is wearing a head cover that is connected to a positive pressure ventilation system, which makes the full-coverage level III–scaled protection much more tolerable. (Photograph by Dr. Li Wan.)

Table 4. Intubation Preparation for Patients with Confirmed or Suspected COVID-19 (Acronym: OH–MS. MAID)

Components	Action	Backup Plan
O: Oxygen	Ensure an adequate supply of oxygen is available	Ensure a separate, full oxygen tank is available in the room
H: Helpers	Identify and ensure helpers are readily available	Clearly understand how to obtain the needed help
M: Monitor	Ensure pulse oximetry, electrocardiography, and noninvasive blood pressure monitors are functional	Ensure backup monitors are readily available, at least outside of the room
S: Suction	Ensure suction is functional and readily available	Ensure a separate (may be portable) suction is available
M: Machine	Ensure an anesthesia machine or an ICU ventilator is functional and ready to go	Ensure a bag-mask system (*e.g.*, Ambu bag) capable of positive-pressure ventilation is readily available
A: Airway supplies	Ensure the video laryngoscope (*e.g.*, GlideScope) is functional and have a direct laryngoscope as a backup	Have a difficult airway cart in the room if a difficult airway is anticipated; otherwise, it should be readily available but outside of the room
I: Intravenous access	Flush and ensure functional intravenous access	Have the supplies readily available in case a new access site is needed
D: Drugs	Have all drugs for sedation, anesthesia induction and muscle relaxation and different vasoactive drugs prepared	Have a drug tray based on the same standards for OR and ICU settings

ICU, intensive care unit; OR, operating room.

experienced practitioner, instead of students or junior personnel, should be assigned to this job. A careful and efficient airway evaluation, whenever possible, should be performed ahead of intubation.

Equipment that is used for more than one patient should be cleaned and disinfected before and after each use. The mixture of ethanol and chlorhexidine is recommended as the disinfecting solution for the breathing circuit in China. Two single-use filters (PALL BB50T Breathing Circuit Filter, Pall Corp., USA), placed in the inhalation and exhalation breathing circuits, are used for infection control in Wuhan. This breathing circuit filter appears capable of preventing the spread of influenza A (H1N1) virus from intubated patients,[16] and thus is implicated to be equally capable of preventing the spread of the 2019 novel coronavirus.

In Wuhan, most of the patients were on either high-flow oxygen therapy or bilevel positive airway pressure ventilation when the intubation was called. If the patient is on high-flow oxygen therapy, consider using a bag valve mask or a tightly fitting facemask connected to the already prepared ventilator for preoxygenation. If the patient is on a bilevel positive airway pressure machine, continue bilevel positive airway pressure ventilation for preoxygenation (Supplemental Digital Content, http://links.lww.com/ALN/C348). Increase oxygen flow and use 100% F_{IO_2} to maximize oxygenation. Make sure the airway is patent. It is well advised to apply an oral or nasal airway at the first sign of difficult masking. Consider manual positive pressure ventilation using a bag valve mask if preoxygenation fails to improve oxygenation.

It was shown that noninvasive ventilation applied for 3 min before tracheal intubation resulted in better oxygenation than a nonrebreather bag valve mask.[17] However, a multicenter randomized trial based on the evaluation of 100% F_{IO_2} administered with noninvasive ventilation *versus* that with a facemask for 3 min before tracheal intubation failed to demonstrate any benefits of using noninvasive ventilation

as a preoxygenation method to reduce organ dysfunction in hypoxemic, critically ill patients.[18] Clearly, there is a gap between improved oxygenation and unchanged outcomes. Although the aerosol-generating potential of noninvasive ventilation is a potential concern to some providers,[19] the bilevel positive airway pressure machine is widely used amid this outbreak for patients with acute hypoxemic respiratory failure in Wuhan and the rest of China. We would not recommend using bilevel positive airway pressure for preoxygenation in patients who are not on bilevel positive airway pressure ventilation; however, bilevel positive airway pressure ventilation should be continued if it is already in use.

After satisfactory preoxygenation, modified rapid sequence induction is the recommended technique for anesthesia induction.[9] Midazolam 1 to 2 mg may be considered for extremely anxious patients. Intravenous lidocaine, 1.5 mg/kg or more, is effective in suppressing coughing during endotracheal intubation.[20] Use a small dose of etomidate (0.2 to 0.3 mg/kg) for patients with hemodynamic instability or propofol (1 to 1.5 mg/kg) for patients with stable hemodynamics for induction.[9] Some providers may opt to avoid etomidate due to concerns of adrenal suppression. Rocuronium 1 mg/kg or succinylcholine 1 mg/kg is administered immediately after loss of consciousness. Fentanyl 50 to 100 mcg, sufentanil 10 to 20 mcg, or remifentanil 2.5 mcg/kg[21] may be used to suppress laryngeal reflexes and optimize the intubation condition. Because opioids have the potential to cause coughing,[22] some providers prefer to give opioids after the accomplishment of satisfactory muscle relaxation. The choice and dose of anesthetics should be determined on a case-by-case basis, with the patient's hemodynamic stability, severity of illness, and mental status taken into consideration. Vasoactive drugs should be readily available to treat extreme cardiovascular reactions. Ventilation through a patent airway and using a small tidal volume should be continued throughout the induction process until the patient is intubated. The goal

is to have the patient intubated within 60 s after administration of muscle relaxants.[9] The rationale behind modified rapid sequence induction in China is to shorten the period of potentially ineffective ventilation, from the moment of losing consciousness to the moment of successful endotracheal intubation, in critically ill patients with minimal to no oxygen reserve due to COVID-19.

The approach of using modified rapid sequence induction in this patient population may be criticized, as some providers may prefer to proceed with slow and controlled induction if there is no immediate aspiration risk. They may argue that maximizing oxygen reserve, immediately after anesthetic induction but before endotracheal intubation, is warranted in patients with acute hypoxemic respiratory failure. They may also argue that immediately administering muscle relaxants after anesthesia induction, without testing the effectiveness of bag valve mask ventilation, is not well advised. We recognize this potential difference in approaches and leave it open for further discussion.

Patient coughing during intubation can generate aerosols and should be avoided. Gentle airway manipulation is warranted. It is prudent to use video laryngoscopy rather than direct laryngoscopy for intubation because the former increases the distance between the healthcare worker's face and the patient's face, which may minimize the risk of contamination (fig. 8). Videoscopes also allow assistants to visualize the airway so that they can better facilitate the procedure. In Wuhan, chest auscultation after intubation is not recommended, unless absolutely needed, due to concerns of contamination. Capnography, fogging inside of the endotracheal tube, chest movement, SpO_2, the color of the patient's skin and mucous membrane, and vigilance are used to differentiate between a failed and successful intubation.

The same precautions should be considered during extubation. Measures to prevent patient agitation, coughing, and bucking should be applied. Appropriate levels of sedation, such as dexmedetomidine $(0.4\ mcg \cdot kg^{-1} \cdot h^{-1})$[23] or remifentanil (1 to 4 ng/ml target organ concentration)[24] infusion, should be considered. Intravenous lidocaine (1 to 1.5 mg/kg) is effective for cough reduction.[25,26] Alfentanil (15 mcg/kg) is also effective in decreasing coughing and agitation during anesthesia emergence.[27]

Ventilation Management

Mechanical ventilation, though vital in supporting respiratory function in patients with acute hypoxemic respiratory failure or ARDS, may promote lung damage, a phenomenon known as ventilator-induced lung injury.[28] Currently, we lack any guidelines or evidence to help us manage invasive mechanical ventilation in critically ill patients with COVID-19. It is well advised to adopt the guidelines established for patients with ARDS,[29,30] with appropriate modifications based on the firsthand patient care experience in Wuhan (table 5). This is justified as 67% of the ICU patients developed ARDS based on the recent report.[3]

The ARDS lung-protective ventilation guidelines emphasize: (1) a tidal volume less than or equal to 6 ml/kg predicted body weight; (2) a respiratory rate less than or equal to 35 breaths/min; (3) a plateau airway pressure less than or equal to 30 cm H_2O; and (4) a positive end-expiratory pressure (PEEP) greater than or equal to 5 cm H_2O.[31,32] The tidal volume can be started at 8 ml/kg and then lowered with an ultimate goal of 6 ml/kg. Some clinicians believe that, as long as the plateau pressure can be maintained at less than or equal to 30 cm H_2O, it may be safe to ventilate the patient with tidal volumes greater than 6 ml/kg predicted body weight.[33] The precise tidal volume for an individual patient should be adjusted according to the patient's plateau pressure, selected PEEP, thoracoabdominal compliance, and breathing effort.[29] It is advantageous to have a driving
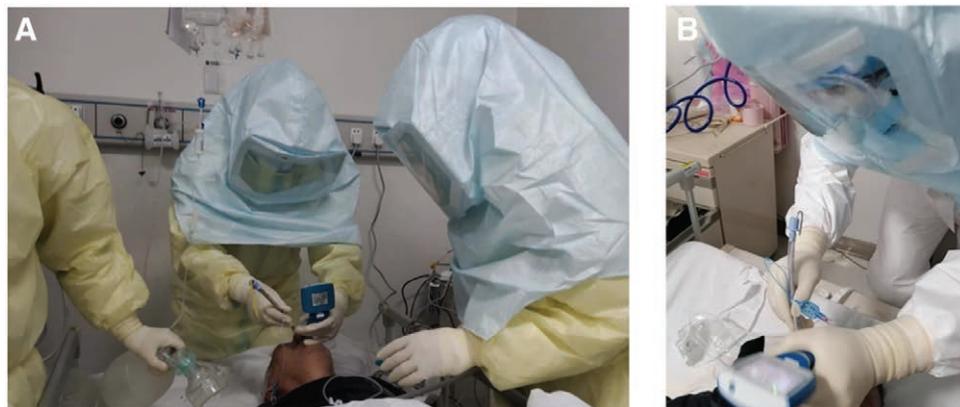
Fig. 8. Anesthesiologists performing endotracheal intubation in patients with COVID-19. (*A*) Three anesthesiologists wearing level III–scaled protection were performing endotracheal intubation. (*B*) Only one anesthesiologist was performing endotracheal intubation. (Photograph by Dr. Li Wan.)

pressure (plateau pressure minus PEEP) below 12 to 15 cm H_2O *via* tidal volume and PEEP adjustments in patients who are not spontaneously breathing.[34]

In Wuhan, patients with acute hypoxemic respiratory failure due to COVID-19 have a poor tolerance to high PEEP, likely as the result of the direct and severe lung damage by the virus and inflammatory reactions. The plateau pressure reaches 40 to 50 cm H_2O when the PEEP is set at 18 cm H_2O, Fio_2 at 100%, and the tidal volume at 6 ml/kg according to the Fio_2 and PEEP table.[32] The widely used practice in Wuhan, after lung recruitment maneuvers, is to set PEEP at 20 cm H_2O and titrate down in a decrement of 2 to 3 cm H_2O each time until the goals of oxygenation, plateau pressure, and compliance are all achieved. The commonly used PEEP in this patient population is less than 10 cm H_2O.

No mode of ventilation has been suggested to be superior to others.[35] There is literature suggesting that high-frequency oscillatory ventilation may be an option for viral-induced lung injury.[36] However, it may be best to avoid high-frequency oscillatory ventilation in patients with COVID-19 due to concerns of aerosol generation.[19,37,38] High-frequency oscillatory ventilation has not been used amid this outbreak in Wuhan. Pressure–regulated volume control ventilation, although increasingly popular in the perioperative arena, has not gained momentum in ICUs due to the lack of evidence for its outcome benefits. In patients with acute lung injury or ARDS, the tidal volume can markedly exceed the lung-protective ventilation target during pressure-regulated volume control ventilation,[39] which is not desirable. Pressure-regulated volume control is not the preferred mode of ventilation in Wuhan.

Ventilation in the prone position improves lung mechanics and gas exchange and is currently recommended by the guidelines.[29,30] The prone position, if planned, should not be a desperate final attempt but should be considered in the early stages of the disease,[40] as the evidence suggests that the early application of prolonged ventilation in the prone position decreases 28- and 90-day mortality in patients with severe ARDS.[41] Prone position ventilation is currently widely used for critically ill patients in Wuhan (fig. 9). Lung recruitment maneuvers, *via* transient elevations in airway pressure applied during mechanical ventilation, can open collapsed alveoli and thus increase the number of alveoli available for gas exchange. Lung recruitment maneuvers do not significantly reduce mortality but may improve oxygenation and shorten the length of hospital stay in ARDS patients.[42] Overall, recruitment maneuvers are not supported by high-quality evidence,[43] and caution should be exercised when using it because it can be irritating, incite coughing, and generate aerosols.

Adjunct therapies can be considered. Many patients with acute hypoxemic respiratory failure due to COVID-19 have breathing overdrive. Appropriate sedation and analgesia, such as dexmedetomidine, propofol and remifentanil infusion, are warranted. The outcome evidence related to the use of muscle relaxants has been controversial.[44,45] A recent meta-analysis concluded that muscle relaxants improve oxygenation after 48 h, but do not reduce mortality in moderate and severe ARDS patients.[46] Nonetheless, muscle relaxation should be considered in cases of breathing overdrive, patient–ventilator dyssynchrony, and inability to achieve the targeted tidal volume and plateau pressure. It is appropriate to be conservative with intravenous fluids in patients with severe lung injury if there are no signs of tissue hypoperfusion.[29] Conservative fluid therapy is the strategy used in Wuhan. It is important to avoid corticosteroid treatment, given that this treatment has been shown to increase mortality and hospital-acquired infections in patients with severe influenza.[47–49] However, the most recent study suggested that early dexamethasone administration may reduce overall mortality and mechanical ventilation duration in ARDS patients.[50] Corticosteroid treatment is currently used in selected patients with severe inflammatory lung injury in Wuhan. Disconnecting the patient from the ventilator results in loss of PEEP and atelectasis, and it should be avoided. In-line catheters for airway suctioning

Fig. 9. Prone position ventilation for critically ill patients with COVID-19. (*A*) An intubated patient turned prone; (*B*) an intubated patient with extracorporeal membrane oxygenation support turned prone. (Photograph by Drs. Haibo Qiu and Chun Pan.)

Table 5. Goals, Setups, and Adjunct Therapies of Mechanical Ventilation for Critically Ill Patients with COVID-19

Components	Recommendation	Additional Information
Physiologic goals		
Pao_2	55–80 mmHg[32]*	The lower limit is much lower than the normal range
Spo_2	88–95%[32]*	The lower limit is lower than the normal range
pH	7.30–7.45*	The lower limit is mildly acidotic
$Paco_2$	Permissive hypercapnia	For patients without intracranial hypertension and adjust per the pH goal
Ventilation mode		
Preferred mode	No recommendation[35]	Insufficient data to make a recommendation[35]
High-frequency oscillatory ventilation	Not recommended[29]	Potential to generate aerosols[19]; no evidence of benefits[29]
Ventilator setup		
Tidal volume	≤ 6 ml/kg predicted body weight[29,31]	Adjust per pH and plateau pressure goals
Respiratory rate	≤ 35 breaths/min	Adjust per pH and plateau pressure goals
Airway pressure	Plateau pressure ≤ 30 cm H_2O[29,31]	Maintain > 25 cm H_2O to open alveoli
PEEP	Higher PEEP over lower PEEP[29]	Adjust per Pao_2 and Spo_2 goals[32]
Fio_2	0.3–1.0	Adjust per Pao_2 and Spo_2 goals[32]
Patient position		
Prone position	Recommended[29]	Conflicting data regarding the benefits[29,41,58] vs. no benefits[59,60]
Semirecumbent position (≥ 30º)	Recommended[29,61]	To reduce the risk of aspiration and ventilator-associated pneumonia[29,61]
Adjunct therapies		
Sedation and analgesia	Recommended	For anxious patients, patients with ventilation overdrive and patients with patient–ventilator dyssynchrony
Muscle relaxation	No recommendation	Benefits[44] vs. no benefits[45]; case-by-case decision making
Systematic corticosteroid	Not recommended[47,49]	Associated with increased mortality and hospital-acquired infections[47,49]
β-2 agonists	Not recommended[29]	For patients without bronchospasm[29]
Conservative fluid strategy	Recommended[29]	For patients who do not have evidence of tissue hypoperfusion[29]
Recruitment maneuvers	Recommended[29]	Perform cautiously; avoid patient coughing
PA catheter	Not recommended[29]	No evidence of benefits
ECMO	No recommendation	Evidence based on observational study[51] and case report[62]; selectively use
Weaning		
Spontaneous breathing trial	Recommended[29]	For patients who are ready for weaning[29]
Weaning protocol	Recommended[29]	For patients who can tolerate weaning

*Data sources (http://www.ardsnet.org/files/ventilator_protocol_2008-07.pdf; accessed March 5, 2020).

ECMO, extracorporeal membrane oxygenation; Fio_2, inspired oxygen fraction; PA, pulmonary artery; $Paco_2$, arterial blood carbon dioxide partial pressure; Pao_2, arterial blood oxygen partial pressure; PEEP, positive end-expiratory pressure; Spo_2, pulse oxygen saturation.

and endotracheal tube clamping are recommended before disconnecting breathing circuits.

Extracorporeal membrane oxygenation was successfully used in patients with severe influenza[51] and may play an important role in select patients. A recent review concluded that the potential of extracorporeal membrane oxygenation in reducing mortality in patients with ARDS due to H1N1 infection was apparent and that extracorporeal membrane oxygenation should be used as a salvage option in severely hypoxemic ARDS patients.[52] The Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR) trial showed that there is a potential role for extracorporeal membrane oxygenation–based management protocols in patients with severe but potentially reversible respiratory failure, and these protocols may improve survival without causing severe disabilities.[53] The ECMO to Rescue Lung Injury in Severe ARDS (EOLIA) trial showed that extra-corporeal membrane oxygenation was not able to sig-nificantly reduce 60-day mortality in patients with very severe ARDS;[54] however, the *post hoc* Bayesian analysis sug-gested a potential mortality benefit under a broad set of assumptions.[55] Extracorporeal membrane oxygenation has been used in some critically ill patients with COVID-19 in Wuhan. More than 40 extracorporeal membrane oxy-genation cases (combined) have been treated in Zhongnan Hospital, Jin Yin Tan Hospital, and Lung Hospital in Wuhan. The outcomes of these patients remain to be analyzed.

Summary

The COVID-19 outbreak is a sweeping and unprecedented challenge in China. Its impacts are currently rapidly unfold-ing outside of China. As of March 4, 2020, COVID-19 was confirmed in 80,409 patients and led to 3,012 deaths in mainland China. Approximately 3.2% of patients with COVID-19 received intubation and invasive ventilation support. How to provide the best practices of intubation and ventilation amid this mass medical emergency is a real but unprecedented question. In this article, we summarize the firsthand experience pertinent to intubation and ven-tilation management from the physicians who are taking care of the critically ill patients with COVID-19 in Wuhan. In patients with acute refractory hypoxemic respiratory failure, timely, but not premature, intubation and invasive

ventilation support may be superior to high-flow oxygen therapy and bilevel positive airway pressure ventilation in boosting transpulmonary pressure, opening collapsed alveoli, improving oxygenation, decreasing oxygen debt, and offering a better chance for the lungs to heal. The invasive nature of intubation and ventilation exposes patients to an augmented risk of procedure-related mishaps. At the same time, these procedures present healthcare providers with an enhanced risk of cross-infection; thus, strict self-protection precautions are mandatory.

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Competing Interests

The authors declare no competing interests.

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