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## **Emergency tracheal Intubation in 202 patients with COVID-19 in Wuhan, China: lessons learned and expert recommendations**

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**Running Title:** Tracheal intubation in COVID-19 patients

## Summary

Tracheal intubation in COVID-19 patients creates a risk to physiologically compromised patients and to attending healthcare providers. Clinical information on airway management and expert recommendations in these patients are urgently needed. By analysing a two-centre retrospective observational case series from Wuhan, China, a panel of international airway management experts discussed the results and formulated consensus recommendations for the management of tracheal intubation in COVID-19 patients. Of 202 COVID-19 patients undergoing emergency tracheal intubation, most were male (n=136, 67.3%) and aged 65 yr or more (n=128, 63.4%). Most patients (n=152, 75.2%) were hypoxaemic ( $\text{SaO}_2 < 90\%$ ) before intubation. Personal protective equipment (PPE) was worn by all intubating healthcare workers. Rapid sequence induction (RSI) or modified RSI was used with an intubation success rate of 89.1% on the first attempt and 100% overall. Hypoxaemia ( $\text{SaO}_2 < 90\%$ ) was common during intubation (n=148, 73.3%). Hypotension (arterial pressure  $< 90/60$  mmHg) occurred in 36 (17.8%) patients during and 45 (22.3%) after intubation with cardiac arrest in 4 (2.0%). Pneumothorax occurred in 12 (5.9%) and death within 24 h in 21 (10.4%) patients. Up to 14 days post-procedure, there was no evidence of cross-infection in the anaesthesiologists who intubated the COVID-19 patients. Based on clinical information and expert recommendation, we propose detailed planning, strategy and methods for tracheal intubation in COVID-19 patients.

**Key Words:** airway management, ARDS, COVID-19, critical care, infection prevention and control, pneumonia, respiratory failure, tracheal intubation,

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**Editor's key points**

Data from a series of 202 COVID-19 patients undergoing tracheal intubation in two hospitals in Wuhan, China were analysed, and used to guide expert consensus recommendations from an international panel

Most patients were elderly males, and hypoxaemic before intubation

Using rapid sequence induction, first pass intubation occurred in 89%, with hypoxaemia and hypotension common during intubation

Other adverse outcomes included cardiac arrest (2%), pneumothorax (6%) and death within 24 h (10%)

Operators wore at least level 3 personal protective equipment, and none became infected

A detailed strategy and methods for tracheal intubation in COVID-19 patients is proposed

On 19 March 2020, the World Health Organization (WHO) characterized COVID-19 disease as a global pandemic, with more than 200,000 confirmed patients in more than 160 countries/territories/areas,<sup>1</sup> with an estimated 2.3% of patients need tracheal intubation.<sup>2</sup> The mortality in critically ill patients with COVID-19 ranges from 16.7% to 61.5%.<sup>3, 4</sup> Given the highly contagious nature of the causative virus SARS-CoV-2, and its transmission by droplet<sup>5-7</sup> or even aerosol infection,<sup>8, 9</sup> tracheal intubation carries a high risk to the intubator.<sup>10-12</sup> There is a lack of data on these patients regarding presenting characteristics, procedural success rates and subsequent complications. There are also few data on the risk of disease transmission to healthcare workers after tracheal intubation of acutely ill COVID-19 patients.<sup>ref</sup> These data would be useful for future planning and management for these patients and precautions for staff.<sup>11-13</sup>

We report clinical data on presenting patients' characteristics, procedural processes, complications and healthcare worker infection after tracheal intubation in COVID-19 patients. Additionally, the data were reviewed by an international panel of experts, and recommendations are made to optimise tracheal intubation success, reduce patient complications and mortality, and minimize the risk of infection of healthcare workers during tracheal intubation.

This retrospective observational case series was approved by the Huazhong Science and Technology University (TJ-C20200148 & 20200097). Written informed consent was waived as this study was a retrospective observational study without patient interventions. Data were provided by authors based in the two study hospitals and interpreted by all authors. The review panel of international experts in airway management discussed the clinical data and the problems encountered during and after intubation using two web-based teleconferences and social media. The experts provided suggestions to address problems encountered clinically, and developed a consensus agreement on a safe and adequate approach to perform tracheal intubation

in COVID-19 patients. This was used to create a simple flowchart for tracheal intubation in COVID-19 patients.

Data were obtained from two major hospitals in Wuhan, China, where the COVID-19 outbreak originated: Tongji Hospital (4 February to 10 March, 2020) and Union Hospital (13 February to 12 March, 2020), Huazhong Science and Technology University, Wuhan, China. All patients had SARS-CoV-2 infection confirmed by reverse transcription-polymerase chain reaction (RT-PCR) testing for viral ribonucleic acid in respiratory samples, in combination with pulmonary chest computed tomography (CT) findings. Clinical and outcome data were obtained from hospital records, and were reviewed and approved by authors based in the two hospitals. Some of the basic clinical information may have been stated elsewhere in narrative form,<sup>14, 15</sup> but detailed clinical data for these patients have not been presented previously. The survey data were summarized and analysed by survey organizers at the University of Pennsylvania (Philadelphia, PA, USA).

Assessment of airway difficulty was predicted by patient history, clinical assessment of neck length and circumference, mandible size and clinician judgement. Mallampati (MP) score<sup>16</sup> was usually not evaluated due to the risks of aerosol viral spreading. Hypoxaemia was defined as oxygen saturation( $\text{SaO}_2$ )  $<90\%$  or  $\text{PaO}_2/\text{FiO}_2 < 150$  mmHg, tachypnoea with respiratory rate  $> 30$  breaths per min, arterial hypotension with blood pressure  $<90/60$  mmHg, tachycardia with heart rate  $>120$  beats per min, and unconsciousness with a negative response to purposeful physical stimulation (likely equivalent to Glasgow Coma Score<sup>17</sup>  $< 8$ ). Difficult laryngoscopy was defined as a grade III-IV Cormack and Lehane view at laryngoscopy.<sup>18</sup>

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Transmission of infection to tracheal intubators was monitored and assessed continuously by clinical symptoms and signs of COVID-19 during a 14 day quarantine in a private hotel room. Anaesthesiologists without clinical symptoms after quarantine were tested with RT-PCR in respiratory samples. Chest CT examination was performed at anaesthesiologists' request. Following confirmed negative PCR test results, anaesthesiologists were allowed to work in the hospital again for the next 14 day duty shift.

Suggestions were made by expert consensus. Given the novelty of COVID-19, there is a relative lack of specific evidence-based information. As a result, expert consensus was supplemented with evidence-based support whenever feasible.

Descriptive statistics were used to characterize the clinical features of the patients in the case series. Categorical variables are expressed as number (%) and compared by  $\chi^2$  test or Fisher's exact test between different hospitals at a two-sided significance level of 0.05. Statistical analysis was performed with PASW<sup>®</sup> Statistics 18 (SPSS Inc., Chicago, IL, USA).

Between 4 February 4 and 12 March, 2020, 202 patients with COVID-19 underwent tracheal intubation at the two study hospitals. The clinical features of these patients and data relating to peri-procedural physiology and outcomes are summarized in Tables 1 and 2.

### **Clinical characteristics and personal protection equipment preparation before tracheal intubation**

Patients were predominantly male (n=136, 67%) and aged 65 yr or greater (n=128, 63%). Forty-five (22%) patients had a predicted anatomically difficult airway and all patients were anticipated to be physiologically difficult airway due to severe hypoxaemia.<sup>19</sup>

All intubations were undertaken by two trained operators. For personal protective equipment (PPE), all intubating clinicians wore N95 respirators (Medical particulate respirator, Winner Medical Co., Shenzhen, Guangdong, China), surgical masks (covering the N95 respirator), eye protection goggles, and a protective coverall with hood and foot covers as inner layer protection (Fig. 1A). The outer layer of protection was comprised of a water-resistant full gown and either a face shield (11%, Fig 1B), a full hood either without a powered air-purifying respirator (PAPR) (64%, Fig. 1C), or with a powered air-purifying respirator (PAPR; 25%, Fig. 1D) with double pairs of gloves used in all intubations. Donning and doffing were checked by a nurse, and the two clinicians checked each other. The number of anaesthesiologists involved in the 202 intubations was 36 in Hospital A and 16 in Hospital B.

Before tracheal intubation, most patients showed gross physiologic abnormalities including hypoxaemia, tachypnoea, hypotension, tachycardia and unconsciousness (table 2). Supplemental oxygen and/or ventilation therapy was administered to all patients, most commonly by non-invasive mask ventilation (NIV, 70.8%) (Table 2).

### **Clinical characteristics during tracheal intubation**

Before induction of general anaesthesia, preoxygenation was performed for 5 min in all patients either using a face mask supplying 100% oxygen (47%) or by continuing the previous oxygen therapy (53%). Propofol was used for induction in 194 (96%) of cases with rocuronium for neuromuscular blockade in 200 (99%); other drugs used at induction are shown in table 2. Mask ventilation after induction and before intubation was undertaken in 93% of intubations. Laryngoscopy was performed with either a UEScope videolaryngoscope (TD-C model with a disposable sheath, UE Medical Devices, Inc., Taizhou, Zhejiang, China) (89.6%) or a standard Macintosh direct laryngoscope (10.4%).

Intubation time was generally  $\leq 3$  min (92.6%). The first time and overall intubation success rates were 89% and 100%, respectively (Table 2). During intubation, hypoxaemia occurred in 73% and hypotension in 18% (Table 2). There were three (1.5%) cases of unexpected difficult laryngoscopy. Eleven intubators reported vision hampered by fogging of their mask, all from the centre where a full hood without PAPR was used despite routine use of anti-fog treatment.

### **Clinical characteristics after tracheal intubation**

Hypoxaemia, which was often prolonged, occurred in 16% and hypotension in 22% (Table 2). Pneumothorax was identified in 5.9%. There were four cardiac arrests

during intubation only at Hospital B; all four patients were successfully resuscitated.

Prone position ventilation was used in 40% of patients within 24 h after tracheal intubation. All-cause mortality within 24 h after tracheal intubation was 10.4%.

### **Overall clinical features and outcome**

This study summarizes patient, physiological and outcome data around the time of tracheal intubation in 202 COVID-19 patients. The investigating authors and a group of international experts identified the problems encountered, their possible causes and made recommendations for prevention. Previous publications have made recommendations regarding airway management in COVID-19 patients.<sup>20-22a</sup> This study bases management recommendations for COVID-19 patients on relevant clinical data.

The high rate of first-pass and overall intubation success in a group of patients who are likely to present both physiological and logistical difficulties is notable. Intubation occurred promptly in all cases. There was worsening of already deranged physiology with four cases of cardiac arrest, all successfully resuscitated. Pneumothorax after intubation and early mortality were notable major adverse outcomes, There was no evidence of disease transmission to intubating medical personnel.

### **Personnel for tracheal intubation**

All personnel for tracheal intubations were anaesthesiologists. It is likely that the high rates of success and speed reflect clinician experience. Tracheal intubation has been reported in 12 COVID-19 patients by pulmonologists in another hospital in China.<sup>23</sup> We suggest that the intubation team should consist of at least two personnel to minimise risks of healthcare worker infection.<sup>11, 12</sup> A third person may standby as an additional

assistant if needed. The most skilled airway manager should perform tracheal intubation with a second operator assisting. The airway plan, including back-up techniques, should be agreed upon before starting the procedure. Where tracheal intubation is undertaken by a non-anaesthesiologist, these individuals should be previously well-trained before attempting airway management in a COVID-19 patient, and whenever feasible an anaesthesiologist and/or ENT surgeon should be immediately available to assist in the event of unexpected difficulty in airway management.<sup>12</sup>

### **Personal protective equipment (PPE) preparation and outcome**

PAPRs were the PPE of choice in both hospitals. However, availability may be limited to some hospitals during a worldwide pandemic,<sup>24</sup> and no PAPR was available in 137 cases from Hospital A. When face shields or full hoods without PAPR were substituted, there were no instances of infection of operators. To estimate the confidence interval of the transmission rate from this "zero numerator" data, we used the "rule of three" statistical method.<sup>25</sup> With no events in a series of 202 cases the upper 95% confidence limit of the transmission rate is unlikely to be > 1.5%. A larger series is necessary to give greater confidence. Recent narrative publications are also reassuring that with similar PPE to that described here the risk of disease transmission to health care workers is very low.<sup>14, 15</sup> There remains uncertainty and variable practice regarding PPE globally, and some recommend lower levels of PPE (e.g. either face-shield or eye goggles rather than both).<sup>26-28</sup> Outcome data on the association between level of PPE and coronavirus transmission from the current epidemic are lacking and require further investigation. During the SARS epidemic, besides non-compliance with appropriate

precautions and a lack of trained and monitored practices in the use of PPE, the recommended practices themselves were considered to have contributed to healthcare worker infection. Since it had become so complicated, errors were likely unavoidable opportunities for transmission through contamination during donning or doffing of PPE.<sup>29</sup>

There is uncertainty whether an N-95/FFP3 respirator should be worn if a PAPR is used. Intubators from the two hospitals in this study chose to wear N-95/FFP3 to protect them from self-contamination during the doffing of PPE. The PPE may have had an impact on the logistical ease of intubation, despite using anti-fogging measures: 80% of operators from Hospital A complained of fogging of their eye goggles when using a full hood without PAPR, which impaired technical efficiency during tracheal intubation. Measures to prevent fogging in eye goggles (e.g. liquid soap, iodophor) should be used to prevent interference with vision during airway management if PAPR devices are unavailable.

Because of the high risk of disease transmission during tracheal intubation<sup>11</sup> we suggest that highly protective levels of PPE are worn (Figure 1). The zero rate of transmission to intubating healthcare workers in our study suggests maximal airborne and droplet precautions are useful in preventing transmission of infection. The risk of virus exposure due to self-contamination is high during the removal of PPE. Therefore, educational training for proper donning and doffing of PPE as well as monitoring for compliance is crucial.<sup>30</sup> Each intubator should receive individualized training and practice on donning and doffing of PPE by an institution-approved instructor until he or she is qualified to use PPE properly. Special attention should be paid to prevention of self-contamination during doffing of PPE. Intubators should be trained in PPE use by

instructors and, if conditions permit, simulation before they undertake tracheal intubation in COVID-19 patients.

### **Induction drugs**

Drug choices differed between the two hospitals (Table 2). Propofol was used in almost all patients, often combined with other sedative agents. Considering the high incidence of hypotension during tracheal intubation, propofol may have been overused due to its ease of availability. Midazolam and etomidate were used in only a small portion of patients. Ketamine was not used at all [note: was it available at both hospitals?]. A single low dose of etomidate is not considered to impair adrenal or immune function significantly.<sup>31, 32</sup> Midazolam causes less interference with cardiovascular function and has the benefit of a strong amnesic effect. Ketamine, which can stimulate the cardiovascular function through its sympathomimetic effects, was not used due to its low availability in China. Neuromuscular blocking agents were used in all 202 patients.

Propofol use should be minimized if other induction agents with lower risks of hypotension are available. A combination of etomidate (0.2-0.6 mg kg<sup>-1</sup>) or ketamine (1-2 mg kg<sup>-1</sup>) with low dose midazolam is recommended. There should be immediate availability and appropriate use of prophylactic cardiovascular stimulating agents at the time of tracheal intubation to minimise hypotension. Rocuronium (e.g. 1.2 mg kg<sup>-1</sup>) is the recommended neuromuscular blocking agent due to its rapid onset of action and favourable side effect profile compared to succinylcholine. The longer duration of

rocuronium reduces the risk of coughing compared to succinylcholine if intubation attempts are prolonged.

### **Intubation technique**

The modified RSI with mask ventilation before intubation, in combination with videolaryngoscopy, achieved high first pass and overall intubation success rates. Although not evaluated in comparative trials, a technique based on RSI for tracheal intubation provides the following advantages in patients with COVID-19: 1) minimises the risks of pulmonary aspiration of gastric contents; 2) enables rapid intubation to optimise oxygenation and ventilation to correct hypoxaemia; and 3) minimises the duration of healthcare worker exposure to patients, which in turn reduces overall exposure to SARS-CoV-2 virus. Videolaryngoscopy can extend the distance between the operator's head and the patient's mouth.<sup>33</sup> Videolaryngoscopy improves the view at laryngoscopy, improves success when intubation is difficult and facilitates help from the assistant.<sup>34</sup> Awake flexible fiberoptic bronchoscopy was not used in this study. Its use should be minimised, to reduce healthcare worker exposure to viral aerosolization.<sup>11</sup>

Flexible fiberoptic bronchoscopy has been reported in patients with COVID-19 both in 12 awake patients<sup>23</sup> and in 58 patients under general anaesthesia.<sup>35</sup> During flexible bronchoscopic intubation with general anaesthesia there was less hypoxaemia when HFNO was used compared to mask pre-oxygenation (3.6% vs 26.7%, respectively). The same group has also reported using supraglottic jet oxygenation and ventilation (SJOV) to maintain oxygenation and ventilation during fiberoptic intubation in

paralyzed non-COVID-19 patients.<sup>36</sup> Compared to HFNO, SJOV may provide not only oxygenation but also efficient ventilation in apnoeic patients.<sup>37</sup>

*Recommendations: Based on the clinical characteristics and expert experience and opinion, we recommend head-elevated positioning before intubation to optimise intubation conditions.<sup>38, 39</sup> We recommend videolaryngoscopy over direct laryngoscopy. In case of difficulty, a second generation supraglottic airway should be available. A difficult airway cart, including emergency front of neck airway equipment, should be immediately available. Despite the above reports, awake fiberoptic bronchoscopy in paralyzed patients is not recommended as a primary intubation technique, and should be reserved for patients with a high risk or known difficult airway. A flow chart to assist future practice on tracheal intubation in COVID-19 patients is shown in figure 2.*

### **Peri-procedural hypoxaemia and its prevention**

Most patients were hypoxaemic before tracheal intubation, suggesting a severe intrapulmonary shunt.<sup>40</sup> The shortage of available hospital beds during the COVID-19 pandemic may have led to delays in the decision to intubate. Some patients were profoundly hypoxaemic without signs of respiratory distress. This 'silent hypoxia',<sup>41</sup> may be putatively attributed to altered central nervous system sensation and regulation of responses to hypoxaemia.<sup>42</sup> This may also result in delayed recognition of the severity of respiratory failure and thus delayed tracheal intubation. Undertaking tracheal intubation before the patient is severely hypoxaemic has been recommended to reduce mortality in these patients.<sup>11, 12</sup> However robust evidence that this approach reduces mortality is lacking.

More than 80% of patients in this study received noninvasive ventilation (NIV) before tracheal intubation. Although previous studies have suggested effective use of NIV in SARS-infected patients,<sup>43</sup> such practice has been shown to delay tracheal intubation and decrease hospital survival in community-acquired acute pneumonia.<sup>44</sup> Further, NIV may increase the intubation rate in patients with COVID-19.<sup>45</sup> Based on recent studies in patients with COVID-19, prolonged NIV (>2 h) is not recommended before definitive tracheal intubation and ventilatory support.<sup>13, 14, 46</sup> High-flow nasal cannula oxygen (HFNO) is used increasingly to treat acute respiratory failure before invasive ventilation,<sup>47-49</sup> and has been used in COVID-19 patients.<sup>3</sup> This approach reduces intubation rate in acute respiratory failure.<sup>48, 50</sup> It is still controversial whether HFNO increases virus aerosol spreading. One study using HFNO at 60 L min<sup>-1</sup> in patients with bacterial pneumonia did not show an increase in bacterial spread in an ICU setting, which is also supported by a limited systematic review.<sup>51, 52</sup> Overall, HFNO is likely to have a low risk of aerosol generation.

Hypoxaemia worsened after induction of anaesthesia with 18% of patients developing hypoxaemia during tracheal intubation despite mask ventilation, likely due to severe lung injury. After induction of anaesthesia but before intubation, oxygenation can be supplemented by HFNO, SJOV, low flow nasal oxygen (LFNO, i.e. oxygen flow <5 L min<sup>-1</sup>) or continuous positive airway pressure (CPAP). When choosing a technique, the aim should be to maximise oxygenation/ventilation while minimising aerosol generation. Most techniques can generate aerosol, and there is a lack of evidence to guide recommendations specific to this setting. In this series, no patients continued HFNO therapy during tracheal intubation. The provision of oxygen during the apnoeic period of

intubation attempt(s) is especially important in obese patients and/or those with a known or predicted difficult airway. Periprocedural hypoxaemia is a significant risk.<sup>53</sup> Most protocols for airway management for patients with COVID-19 now consider HFNO a relative contraindication.<sup>20-22</sup> After intubation, hypoxaemia was readily corrected and persisted in only 1 in 6 patients.

*Recommendations: Based on the clinical information and expert opinion, we suggest that where possible, tracheal intubation should be performed earlier in the phase of the illness to avoid undertaking the procedure in the presence of severe hypoxaemia, which may help reduce overall mortality in COVID-19 patients.<sup>11, 12</sup> Given the lack of evidence regarding the safety of HFNO or LFNO during tracheal intubation, their use should be based on the benefit/risk ratio in individual patients. In the absence of clear evidence, high-level PPE precautions should be used when HFNO is used during intubation.*

### **Hypotension and cardiac arrest during and after tracheal intubation**

Hypotension occurred in 18% of patients during and 28% of patients after tracheal intubation. Four patients developed cardiac arrest. These data are consistent with estimates of peri-intubation hypotension incidence reported previously,<sup>54, 55</sup> and cardiac arrest of 2-3% in the critically ill, with the latter associated with increased mortality.<sup>56, 57</sup> Predictors of cardiac arrest in the critically ill at the time of tracheal intubation include both hypotension and hypoxaemia before intubation (OR 3.4 and 4.0, respectively).<sup>57</sup> As with hypoxaemia, tracheal intubation earlier in the course of the disease may reduce the risk of cardiovascular collapse. All cases of cardiac arrest

occurred in hospital B. In hospital A, prophylactic use of cardiovascular stimulating agents was administered at the time of intubation.

*Recommendations: Where possible, tracheal intubation should be performed earlier in the phase of the illness to avoid increased risk of cardiovascular collapse during anaesthesia and intubation. Despite a lack of a clear evidence, we recommend consideration of the following measures to minimise hypotension: 1) a 250 ml crystalloid bolus i.v. if not contraindicated (heart failure, kidney failure with volume overload or similar); 2) reduction in the use or dose of propofol as an induction agent; and 3) prophylactic use of cardiovascular stimulating agents (e.g. phenylephrine, epinephrine, or norepinephrine).*

### **Prevention of pneumothorax after tracheal intubation**

Pneumothorax developed after tracheal intubation in 5.9% of patients, which is higher than in previous reports (~ 2%).<sup>3</sup> The lungs of late-stage COVID-19 patients are severely damaged similar to ARDS,<sup>6,7</sup> predisposing to the development of pneumothorax. Ventilatory manoeuvres that generate high airway pressures around the time of intubation (coughing during NIV or CPAP, application of large tidal volumes, recruitment manoeuvres) may lead to increased risk of pneumothorax. Early prone ventilation is likely to improve lung compliance and has been observed anecdotally to benefit COVID-19 patients, and is recommended in those with severe ARDS.<sup>20, 58</sup> Prone ventilation was used more commonly in hospital A than in hospital B, and both pneumothorax rate and mortality were lower in the former. Whether these are related is

speculative. A high percentage of patients used NIV before tracheal intubation, which has been associated with a high risk of pneumothorax (up to 15%) in SARS patients.<sup>43</sup>

*Recommendations: Early intubation is expected to reduce the risk of pneumothorax. Noninvasive ventilation before intubation should be used with great caution. Large volume ventilation and recruitment manoeuvres to correct hypoxaemia immediately after tracheal intubation should be avoided. A protective ventilation strategy with small tidal volumes (e.g. 6 ml kg<sup>-1</sup> ideal body weight) maintaining lower airway pressures is recommended. Early prone ventilation should be considered, especially where peak pressure or driving pressure is high. Methods to identify or exclude pneumothorax (e.g. chest radiography, point of care ultrasound) should be available immediately after tracheal intubation to enable prompt diagnosis.*

### **Mortality for critically ill patients with COVID-19**

The 24-h mortality following tracheal intubation was 10.4%. Others have reported 28-day mortality of up to 61% in critically ill patients with COVID-19.<sup>3, 4</sup> The 24-h mortality may be related to events at tracheal intubation, but our observational data do not allow further analysis of this. Cardiac arrest at the time of tracheal intubation of the critically ill is associated with a 3.9-fold increase in the risk of 28-day mortality. High rates of mortality in critically ill patients with COVID-19 are predominantly due to the severity and speed of the illness associated with SARS-CoV-2 and the lack of effective antiviral treatment. Limited medical resources during a pandemic when the healthcare system is overloaded likely contribute to delays in tracheal intubation and mechanical ventilation. Provision of sufficient critical care facilities and services to enable timely

tracheal intubation and invasive ventilation might logically improve survival but is unproven and is a major challenge during an epidemic surge. Research should explore whether optimal airway management at the time of intubation in critically ill patients with COVID-19 improves overall outcome.

Clinical data were obtained from only two hospitals and include relatively small patient numbers without comparators or controls. The expert opinion and recommendations were necessarily undertaken in a short timeframe. Nevertheless, we believe this article provides valuable information and discussion to meet current and ongoing global needs.

### **Conclusions**

Amongst 202 COVID-19 patients requiring urgent intubation, the majority were male and elderly. Hypoxaemia was almost universal, and hypotension was common. A technique based on RSI and videolaryngoscopy enabled prompt tracheal intubation and was universally successful. Cardiac arrest occurred in 2%, and pneumothorax and early mortality were both observed. Despite differing approaches to PPE, there was no intubation-related healthcare worker COVID-19 infection. Based on the clinical information, analysis and expert opinion, we provide a flow chart to facilitate tracheal intubation of adult COVID-19 patients (Fig. 2), and to improve safety of both patients and healthcare workers.

### **Authors' contributions**

Data generation and collection: WY, FG, HZ, LX, WM, AL, TW, LW, WX, SY, XC

Data analysis and interpretation, conception, writing and final approval of manuscript:

All authors

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**Declaration of interests**

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## Appendix

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**22a High-flow nasal-oxygenation-assisted fiberoptic tracheal intubation in critically ill patients with COVID-19 pneumonia: a prospective randomised controlled trial**

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**Table 1.** Clinical characteristics of patients infected with COVID-19 from two hospitals in Wuhan, China. Data shown as *n* (%). Proportions were analysed using  $\chi^2$  test or Fisher's exact test. RSI, rapid sequence induction intubation technique.

<b>Patient characteristics</b>	<b>Total (<i>n</i> = 202)</b>	<b>Hospital A (<i>n</i> = 137)</b>	<b>Hospital B (<i>n</i> = 65)</b>	<b><i>P</i>-value</b>
Gender				
Female	66 (32.7%)	43 (31.4%)	23 (35.4%)	0.571
Male	136 (67.3%)	94 (68.6%)	42 (64.6%)	
Age $\geq$ 65 yr	128 (63.4%)	90 (65.7%)	38 (58.5%)	0.319
Difficult airway history	0 (0%)	0 (0%)	0 (0%)	-
Suspected difficult airway	45 (22.3%)	41 (29.9%)	4 (6.2%)	<0.001
Unanticipated difficult airway	3 (1.5%)	3 (2.2%)	0 (0%)	0.553
Modified RSI	202 (100%)	137 (100%)	65 (100%)	-
Awake intubation	0 (0%)	0 (0%)	0 (0%)	-

**Table 2.** Airway management of patients infected with COVID-19 from two hospitals in Wuhan, China. Data shown as *n* (%). Proportions were analysed using  $\chi^2$  test or Fisher's exact test.

Characteristics	Total ( <i>n</i> = 202)	Hospital A ( <i>n</i> = 137)	Hospital B ( <i>n</i> = 65)	<i>P</i> -value
<b>BEFORE INTUBATION</b>				
<b>Physical status during oxygen therapy</b>				
SaO <sub>2</sub> < 90%	152 (75.2%)	106 (77.4%)	46 (70.8%)	0.310
PaO <sub>2</sub> /FiO <sub>2</sub> < 150 mmHg	194 (96.0%)	130 (94.9%)	64 (98.5%)	0.407
Respiratory rate > 30 breaths per min	109 (54%)	69 (50.4%)	40 (61.5%)	0.137
BP < 90/60 mmHg	16 (7.9%)	14 (10.2%)	2 (3.1%)	0.079
HR > 120 beats per min	49 (24.3%)	27 (19.7%)	22 (33.8%)	0.029
Unconsciousness	26 (12.9%)	14 (10.2%)	12 (18.5%)	0.102
<b>Oxygen therapy technique</b>				
Regular nasal cannula	8 (4.0%)	6 (4.4%)	2 (3.1%)	0.954
Mask with reservoir bag	21 (10.4%)	14 (10.2%)	7 (10.8%)	0.905
High Flow Nasal Cannula (HFNO)	28 (13.9%)	16 (11.7%)	12 (18.5%)	0.192
Noninvasive Ventilation (NIV)	143 (70.8%)	101 (73.7%)	42 (64.6%)	0.184
<b>Operators personal protective equipment</b>				
Respirator (N95 or equivalent, inside)	202 (100%)	137 (100%)	65 (100%)	-
Surgical mask (outside)	202 (100%)	137 (100%)	65 (100%)	-
Goggles	202 (100%)	137 (100%)	65 (100%)	-
Face shield	22 (10.9%)	7 (5.1%)	15 (23.1%)	<0.001
Full hood without a PAPR	130 (64.4%)	130 (94.9%)	0 (0%)	<0.001
PAPR	50 (24.8%)	0 (0%)	50 (76.9%)	<0.001
Intubation hampered by mask fog	11 (5.4%)	11 (8.0%)	0 (0%)	0.044
Anti-fog treatment	197 (97.5%)	132 (96.4%)	65 (100%)	0.282
Anti-fog method	/	liquid soap	Iodophor	-
Necessary individuals	/	2	2	-
Operator infection	0 (0%)	0 (0%)	0 (0%)	-
<b>INTUBATION</b>				
<b>Induction</b>				

Bolus of i.v. fluid	0 (0%)	0 (0%)	0 (0%)	-
Prophylactic vasopressor	41 (20.3%)	41 (29.9%)	0 (0%)	<0.001
Pre-oxygenate with 100% FiO <sub>2</sub> for 5 min	202 (100%)	137 (100%)	65 (100%)	-
Pre-oxygenate via prior oxygen therapy	107 (53.0%)	92 (67.2%)	15 (23.1%)	<0.001
Pre-oxygenate via face mask	95 (47.0%)	45 (32.8%)	50 (76.9%)	<0.001
Propofol	194 (96.0%)	135 (98.5%)	59 (90.8%)	0.024
Etomidate	6 (3.0%)	5 (3.6%)	1 (1.5%)	0.702
Midazolam	27 (13.4%)	27 (19.7%)	0 (0%)	<0.001
Sufentanil	99 (49%)	94 (68.6%)	5 (7.7%)	<0.001
Fentanyl	60 (29.7%)	6 (4.4%)	54 (83.1%)	<0.001
Rocuronium	200 (99.0%)	137 (100%)	63 (96.9%)	0.102
Mask ventilation after induction	188 (93.1%)	123 (89.8%)	65 (100%)	0.018
<b>Intubation device at first attempt</b>				
Macintosh laryngoscope	21 (10.4%)	21 (15.3%)	0 (0%)	0.001
Videolaryngoscope with disposable blade	181 (89.6%)	116 (84.7%)	65 (100%)	0.001
<b>Results of intubation</b>				
Successful intubation at the first attempt	180 (89.1%)	116 (84.7%)	64 (98.5%)	0.003
Total successful intubation	202 (100%)	137 (100%)	65 (100%)	-
Duration of intubation ≤ 3 min	187 (92.6%)	123 (89.8%)	64 (98.5%)	0.040
Duration of intubation > 3 min	12 (5.9%)	11 (8%)	1 (1.5%)	0.108
Duration of intubation > 5 min	3 (1.5%)	3 (2.2%)	0 (0%)	0.553
<b>Adverse events during intubation</b>				
Hypoxaemia (SaO <sub>2</sub> <90%)	175 (73.3%)	110 (80.3%)	38 (58.5%)	0.001
Hypotension (BP < 90/60 mmHg)	36 (17.8%)	14 (10.2%)	22 (33.8%)	<0.001
<b>AFTER INTUBATION</b>				
<b>Physical status</b>				
Hypoxaemia (SaO <sub>2</sub> <90%)	36 (17.8%)	16 (11.7%)	20 (30.8%)	0.001
Hypotension (BP < 90/60 mmHg)	18 (27.7%)	27 (19.7%)	18 (27.7%)	0.203
Cardiac arrest	4 (2.0%)	0 (0%)	4 (6.2%)	0.017
<b>Ventilation &amp; adverse events</b>				
Prone ventilation	67 (33.2%)	55 (40.1%)	12 (18.5%)	0.002
Pneumothorax	12 (5.9%)	6 (4.4%)	6 (9.2%)	0.296
All-cause mortality within 24 h	21 (10.4%)	11 (8.0%)	10 (15.4%)	0.110

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**Figure Legends**

Fig 1. Two layers of personal protective equipment (PPE). A. Inner layer; B. Outer layer with a face shield; C. Outer layer with a hood without a powered air-purifying respirator (PAPR); D. Outer layer with a hood PAPR.

Fig 2. Flowchart of recommended tracheal intubation procedure in patients with COVID-19. A suggested strategy based on clinical data for tracheal intubation in 202 patients with COVID-19 from Wuhan, China, and on recommendations from a group of international experts in airway management. PPE, personal protection equipment;  $FiO_2$ , fraction of inspired oxygen; HEPA, High-efficiency particulate air; HFNO, high flow nasal oxygen;  $EtCO_2$ , end-tidal carbon dioxide.



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## Tracheal Intubation in Adult Patients with COVID-19

### BEFORE INTUBATION

#### Personnel

1. Experienced provider & one assistant (PPE trained)
2. Learn medical & airway history
3. Intubation strategy & backup plan

#### Hand Hygiene & Donning PPE

1. Highest level PPE available
2. Minimum PPE:  
Eye protection, fit-tested respirator (e.g. N95 or FFP3), fluid-resistant gown, gloves

### INTUBATION

#### Preparation

1. Consider bolus of 250 ml, if not contraindicated
2. Pre-oxygenate 100% FiO<sub>2</sub>, 5 min

#### Modified Rapid Sequence Induction (RSI)

1. Prophylactic vasopressor
2. Etomidate / ketamine, ± midazolam  
minimize propofol as supplement, if used
3. Rocuronium (1.2 mg/kg)

#### Oxygenation & Intubation

1. ± Small tidal volume mask ventilation (with a HEPA filter) ;  
± Continuous prior oxygen therapy / continuous HFNO, only if experienced personnel with sufficient precautions
2. Videolaryngoscope, initial attempt
3. Supraglottic airway device as backup
4. Emergency front-of-neck airway

### AFTER INTUBATION

#### Confirmation of Placement & Ventilation

1. Bilateral chest rise & EtCO<sub>2</sub>
2. Ultrasound, if needed
3. Avoid high airway pressure (↓pneumothorax)

#### Doffing PPE & Hand Hygiene

1. Doff the PPE, avoid self-contamination
2. Hand hygiene between procedures ± bath
3. Disinfect / discard equipments as per local institutional procedures