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Original Article

Factors affecting the risk of SARS-CoV-2 transmission to anesthesiologists performing endotracheal intubation in patients with SARS-CoV-2

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Abstract: Background: In this study, we estimated the predictive factors of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission in anesthesiologists performing endotracheal intubation in patients with confirmed SARS-CoV-2. Method: We analyzed data from a survey conducted by the Chinese Society of Anesthesiology Task Force on Airway Management on endotracheal intubation in 98 patients with SARS-CoV-2 confirmed through nucleic acid testing and chest computed tomography. The multivariate logistic model with stepwise selection was used for selecting the predictive factors significantly associated with SARS-CoV-2 infection in the corresponding anesthesiologists. Results: SARS-CoV-2 prevalence in the corresponding anesthesiologists was 20.41% after intubation in patients with SARS-CoV-2. Univariate analysis indicated that intubation for elective treatment, intubation in an operating room or isolation ward, and routine rapid induction with continuous positive-pressure ventilation (PPV) for intubation were associated with a lower SARS-CoV-2 risk in the anesthesiologists. Multivariate analysis revealed that intubation for elective treatment was associated with a significantly decreased SARS-CoV-2 risk (adjusted odds ratio [aOR] = 0.28, 95% confidence interval [CI]: 0.14-0.68, $P < 0.0001$), and coughing by patients during endotracheal intubation was associated with a significantly increased SARS-CoV-2 risk (aOR = 1.70, 95% CI: 1.39-2.97, $P = 0.0404$) in the anesthesiologists. Conclusion: Endotracheal intubation for elective treatments, intubation in an operating room or isolation ward, and routine rapid induction with continuous PPV for patients with confirmed SARS-CoV-2 are associated with a lower risk of SARS-CoV-2 transmission in practicing anesthesiologists, and coughing by patients during intubation increases the risk.

Keywords: SARS-CoV-2, anesthesiologists, intubation, predictive factors, risk

Introduction

In late 2019, a novel coronavirus was identified as the cause of an outbreak of an acute respiratory illness in Wuhan, China [1-4]. In February 2020, the World Health Organization (WHO) labeled this disease as coronavirus disease 2019 (COVID-19) and named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses [5]. On March 11 WHO declared the pandemic [6]. In suspected SARS-CoV-2 cases, infection control measures should be implemented and public health officials notified [6, 7]. The US Centers for Disease Control and Prevention (CDC) recommends standard, contact, and airborne precautions in health care settings [7]. The CDC suggests that all health care workers who enter the room of a patient with suspected or confirmed SARS-CoV-2 should wear personal protective equipment (PPE), including a gown, gloves, a respirator or medical mask, and eye or face protection, to reduce the risk of exposure [7].

Shortages in first-line health care staff may be the primary challenge of implementing surge-capacity medical plans during an epidemic [8]. Health care staff may be furloughed or isolated on accidental exposure to or contamination by SARS-CoV-2 [9-11]. SARS-CoV-2 poses a direct threat to an already overburdened medical care system and to the supporting supply chains for medications and materials [10]. Studies have analyzed the characteristics, clinical presentation, and outcomes of patients hospitalized with SARS-CoV-2 and the number of infected health care workers [12, 13]. The most common comorbidities in patients with SARS-CoV-2 are hypertension, obesity, and diabetes [13]. Among patients with SARS-CoV-2 who were discharged or died (n = 2634), 14.2% were treated in the intensive care unit, 12.2% received invasive mechanical ventilation, 3.2% were treated with kidney replacement therapy, and 21% died. Only through planning, training, and teamwork will clinicians and health care systems be best placed to deal with the many complex implications of this pandemic [12].

Health care facilities should develop tiered, proactive strategies using the best available clinical information and build on their existing surge-capacity plans to optimize resource use in the event that the current outbreak spreads and creates severe resource demands [10]. Health care systems and providers must be prepared to obtain maximal benefits from limited resources while mitigating harm to individuals, the health care system, and society [10]. Therefore, understanding the factors affecting SARS-CoV-2 transmission in first-line health care workers, such as anesthesiologists performing endotracheal intubation for patients with SARS-CoV-2, is crucial to reducing the burden on or collapse of first-line health care workers and health care facilities because of exposure to SARS-CoV-2 during aerosol-generating procedures (ie, intubation and nebulization of medication) [14]. Therefore, the current study describes the results of the survey conducted by the Chinese Society of Anesthesiology Task Force on Airway Management (CSATF-AM) to clarify the predictive factors of the infection of first-line anesthesiologists performing endotracheal intubation in patients with SARS-CoV-2.

Patients and methods

Database

In February 2020, CSATF-AM administered questionnaires to anesthesiologists on endotracheal intubation in patients with SARS-CoV-2 each time they performed the intubation in patients with confirmed SARS-CoV-2. The questionnaires were designed to collect the basic information of every eligible patient-including age, sex, physical characteristics (eg, incisor distance and thyromental distance), medical tests (eg, chest computed tomography [CT] and nucleic acid test results), and medical services received-and that of the corresponding anesthesiologist-including contamination status as well as routine blood test, chest CT, and nucleic acid test results. To protect privacy, the personal information of patients and anesthesiologists was encrypted in the database and anonymous identification numbers were provided. The study protocols were approved by the Institutional Review Board, Clinical Committee of Henan Provincial People's Hospital, Zhengzhou University (IRB No. 57, 2020).

Patients and anesthesiologists

All patients with suspected SARS-CoV-2 underwent three nucleic acid tests and chest CT. At least one positive nucleic acid test result along with chest CT abnormality was used to confirm the diagnosis of SARS-CoV-2. The survey was sent before the procedure and prepared for each patient contemporarily with the procedure. Therefore, this was a prospective survey study. CSATF-AM distributed the questionnaires in the associated anesthesiology departments in hospitals that had patients with SARS-CoV-2. Anesthesiologists received the questionnaires before performing endotracheal intubation and completed them after the procedure. All CSATF-AM-registered anesthesiologists have performed ≥ 500 intubations or worked for ≥ 5 years after specialization; thus, they were all similarly skilled in performing intubation. Of 118 suspected patients, 98 were confirmed to have SARS-CoV-2. Similarly, of the 98 corresponding anesthesiologists, 20 who had posi-

Table 1A. Questionnaire for anesthesiologists performing endotracheal intubation in patients with SARS-CoV-2: information related to the patient

Q1: Patient sex and age
Q2: Does the patient have a fever? (Response: Yes or No)
Q3: Does the patient have a history of exposure to patients with SARS-CoV-2? (Response: (a) Direct contact with patients with SARS-CoV-2, (b) Direct contact with a person who was in a highly affected area, (c) Indirect contact with a person who was in a highly affected area, or (d) No history of contact)
Q4: Does the patient have a history of difficult airway intubation? (Response: Yes, No, or Not evaluated)
Q5: Patient incisor distance (Response: < 3 cm, ≥ 3 cm, and Not evaluated)
Q6: Patient thyromental distance (Response: < 6 cm, ≥ 6 cm, and Not evaluated)
Q7: Patient head and neck mobility (Response: Normal, Limited, and Not evaluated)
Q8: Patient neck thickness (Response: Normal, Stubby, and Not evaluated)
Q9: Patient Mallampati score (Response: I, II, III, IV, and Not evaluated)
Q10: Summary of negative results on any of the three nucleic acid tests

Table 1B. Questionnaire for anesthesiologists performing endotracheal intubation patients with SARS-CoV-2: information related to the procedure

M1: Reason for performing endotracheal intubation (Response: (a) General anesthesia, (b) Elective treatment, or (c) Emergency)
M2: Location of performing endotracheal intubation (Response: (a) Operating room, (b) Isolation ward, (c) Emergency department, (d) Intensive care unit, or (e) Respiratory care ward)
M3: Protective measures taken (Response: (a) Tertiary protection, (b) Secondary protection, or (c) Primary protection)
M4: Preparation before performing endotracheal intubation (choose one or more answers). (Response: (a) Difficult airway cart, (b) Difficult airway box, (c) Simple respirator, (d) Respirator or anesthesia machine, and/or (e) Filter or artificial nose)
M5: Endotracheal intubation method (Response: (a) Routine rapid induction with continuous positive-pressure ventilation, (b) Rapid sequence induction, (c) Retention of spontaneous breathing, or (d) Other)
M6: Was positive-pressure mask ventilation employed before intubation? (Response: Yes or No)
M7: Was disposable intubation equipment used? (Response: Yes or No)
M8: Intubation equipment used (Response: (a) Video laryngoscopy intubation, (b) Ordinary laryngoscopy intubation, (c) Video tube intubation, (d) Visual intubation soft scope, or (e) Other)
M9: Number of operators (Response: (a) One anesthetist, (b) Two anesthesiologists, (c) One anesthetist and one doctor, or (d) Other)
M10: Did the patient cough during intubation? (Response: Yes or No)
M11: Number of attempts at intubation (Response: (a) Success the first time, (b) Success the second time, (c) Success the third time, or (d) failure)

tive results in at least one nucleic acid test and demonstrated chest CT abnormality after they performed endotracheal intubation, were included in the infected anesthesiologist group, whereas the remaining 78 tested negative in all tests and had no chest CT abnormality and were included in the noninfected anesthesiologist group.

Questionnaire

Information on patients with confirmed SARS-CoV-2 was collected using 10 questions (**Table 1A**), and the medical information during intubation was collected using 11 questions (**Table 1B**).

Statistical analysis

All analyses were performed using R® for Windows. Statistical significance was set at $P < 0.05$. Fisher's exact test of independence (for a total sample size of < 1000) was performed to compare patients' basic characteristics and endotracheal intubation information between the noninfected and infected anesthesiologist groups. A multivariate logistic model with stepwise selection was used to select all variables with significant effects on SARS-CoV-2 in anesthesiologists. Univariate and multivariate logistic regression analyses were performed to calculate the odds ratio (OR) and corresponding 95% confidence interval (CI) for SARS-CoV-2 risk in the anesthesiologists.

Results

SARS-CoV-2 prevalence in the anesthesiologists who performed intubation in patients with confirmed SARS-CoV-2 was 20.41% (**Table 2**). Moreover, the distribution of patient and anesthesiologist baseline characteristics and Q1-Q10 responses did not significantly differ between the noninfected and infected anesthesiologist groups (**Table 2**). **Table 3** presents the differences in procedures used during endotracheal intubation between noninfected and infected anesthesiologist groups. Reason for performing endotracheal intubation, M1 (P = 0.0276), location of performing endotracheal intubation, M2 (P = 0.0193), endotracheal intubation method, M5 (P = 0.0092), and the patient cough during intubation, M10 (P = 0.0161) were significantly associated with infection in the participating anesthesiologists. **Table 4** presents the estimated coefficients of multivariate logistic regression for all variables in **Table 2** (M1-M11). Because of the collinearity between these variables, only a few variables were significant in this model (Supplementary Tables 1 and 2). Therefore, we used a stepwise selection method for variable selection and found intubation for elective treatment and coughing by the patient during intubation to be significant variables (**Table 4**).

The results of univariate and multivariate logistic regression for assessing SARS-CoV-2 risk in anesthesiologists are presented in **Table 5**. Univariate logistic regression demonstrated that endotracheal intubation for elective treatment, in the operating room, in isolation wards, and by using routine rapid induction with continuous positive-pressure ventilation (PPV) were associated with a relatively low SARS-CoV-2 risk (crude ORs = 0.13 [P < 0.0001], 0.10 [P = 0.0281], 0.19 [P = 0.0001], and 0.20 [P < 0.0001], respectively). By contrast, presence of multiple anesthesiologists and coughing by the patient during intubation were associated with a relatively high SARS-CoV-2 risk (crude ORs = 1.39 [P = 0.0170] and 3.00 [P = 0.0227], respectively). After multivariate analysis, only endotracheal intubation for elective treatment remained associated with a relatively low SARS-CoV-2 risk (adjusted OR = 0.28, 95% CI: 0.14-0.68) and only coughing by the patient during intubation associated with a relatively high SARS-CoV-2 risk (adjusted OR = 1.70, 95% CI = 1.39-2.97).

Discussion

Limiting transmission is an essential component of care in patients with suspected or confirmed SARS-CoV-2. In a report on 138 patients with SARS-CoV-2 in China, 43% were estimated to have acquired the infection in a hospital setting [15]. Airborne precautions are necessary during aerosol-generating procedures, such as tracheal intubation [6]. Because airborne infections are possible, the use of isolation room (ie, a single-patient negative-pressure room) is recommended. Patients should at least be asked to wear masks and be placed in a private room with the door closed, and any personnel entering this room should wear the appropriate PPE [6, 7]. Patients with suspected or confirmed SARS-CoV-2 who require hospitalization should be cared for in a facility that can provide an isolation room. However, no study has investigated risk factors for SARS-CoV-2 infection and its transmission rate in anesthesiologists performing endotracheal intubation in patients with SARS-CoV-2 or indicated the intubation equipment and location, protective measures, and procedures that can provide sufficient safety to them. Whether patients with SARS-CoV-2 with fever have a higher transmission rate to anesthesiologists performing intubation in them remains unclear. All SARS-CoV-2 guidelines have been designed on the basis of experiences with other airborne transmission diseases, such as tuberculosis, varicella, measles, smallpox, Middle East respiratory syndrome, SARS, and Ebola. Therefore, the current survey estimated the SARS-CoV-2 transmission risk factors associated with various endotracheal intubation equipment, protective measures, and methods to identify the optimal protective measures when performing intubation in patients with SARS-CoV-2.

Full-genome sequencing and phylogenic analysis indicated that SARS-CoV-2 is a betacoronavirus in the same subgenus as SARS-CoV but in

Table 2. Baseline characteristics of patients with SARS-CoV-2 receiving endotracheal intubation described by the anesthesiologists performing intubation

Characteristics	Noninfected anesthesiologists N = 78 (%)	Infected anesthesiologists N = 20 (%)	*P* Value
Age, mean (SD)	59.26 (15.14)	61.46 (8.81)	0.4000
Sex			0.5545
Male	61 (78.21)	14 (70)	
Female	17 (21.79)	6 (30)	
Patients with fever			0.7673
Yes	68 (87.18)	17 (85)	
No	9 (11.54)	3 (15)	
Unclear	1 (1.28)	0 (0)	
Patient exposure to SARS-CoV-2			0.5882
Direct with SARS-CoV-2	36 (46.15)	8 (40)	
Direct with affected areas	31 (39.74)	7 (35)	
Indirect with affected areas	8 (10.26)	4 (20)	
No	3 (3.85)	1 (5)	
Patients with a history of difficult airway for intubation			0.4902
Yes	7 (8.97)	0 (0)	
No	58 (74.36)	17 (85)	
Not evaluated	13 (16.67)	3 (15)	
Incisors distance in patients			0.3015
< 3 cm	5 (6.41)	3 (15)	
≥ 3 cm	64 (82.05)	14 (70)	
Not evaluated	9 (11.54)	3 (15)	
Thyromental distance in patients			0.4052
< 6 cm	21 (26.92)	3 (15)	
> 6 cm	44 (56.41)	15 (75)	
Not evaluated	13 (16.67)	2 (10)	
Head and neck mobility in patients			0.5252
Normal	63 (80.77)	15 (75)	
Limited	6 (7.69)	3 (15)	
Not evaluated	9 (11.54)	2 (10)	
Thickness of neck in patients			1.000
Normal	55 (70.51)	14 (70)	
Stubby	22 (28.21)	6 (30)	
Not evaluated	1 (1.28)	0 (0)	
Mallampati Scoring in patients			0.8321
I	9 (11.54)	2 (10)	
II	32 (41.03)	11 (55)	
III	4 (5.13)	1 (5)	
IV	1 (1.28)	0 (0)	
Not evaluated	32 (41.03)	6 (30)	
False negative of SARS-CoV-2 test in patients			0.5169
Yes	13 (16.67)	5 (25)	
No	65 (83.33)	15 (75)	

SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; SD, standard deviation.

Table 3. Procedures performed by anesthesiologist during endotracheal intubation in patients with confirmed SARS-CoV-2

Procedures	Noninfected anesthesiologists N = 78 (%)	Infected anesthesiologists N = 20 (%)	*P* Value
Reasons for performing endotracheal intubation			0.0276
Intubation for general anesthesia	12 (15.38)	4 (20)	
Intubation for elective treatment	39 (50)	6 (30)	
Intubation for emergency	27 (34.62)	10 (50)	
Intubation location			0.0193
Operating room	10 (12.82)	1 (5)	
Isolation ward	39 (50)	7 (35)	
Emergency department	0 (0)	2 (10)	
ICU	29 (37.18)	9 (45)	
Respiratory care ward	0 (0)	1 (5)	
Protective measures			1.0000
Tertiary protection	61 (78.21)	16 (80)	
Secondary protection	14 (17.95)	4 (20)	
Primary protection	3 (3.85)	0 (0)	
Prepare before performing endotracheal intubation			
Difficult airway cart			0.4997
Yes	11 (14.1)	4 (20)	
No	67 (85.9)	16 (80)	
Difficult airway box			0.4227
Yes	55 (70.51)	12 (60)	
No	23 (29.49)	8 (40)	
Simple respirator			0.3166
Yes	49 (62.82)	10 (50)	
No	29 (37.18)	10 (50)	
Respirator or anesthesia machine			0.3295
Yes	66 (84.62)	15 (75)	
No	12 (15.38)	5 (25)	
Filter or artificial nose			0.8066
Yes	38 (48.72)	9 (45)	
No	40 (51.28)	11 (55)	
Endotracheal intubation methods			0.0092
Routine rapid induction with continuous PPV	56 (71.79)	11 (55)	
Rapid sequence induction without PPV	21 (26.92)	5 (25)	
Retain spontaneous breathing	0 (0)	3 (15)	
Other	1 (1.28)	1 (5)	
Positive-pressure ventilation			0.7842
Yes	57 (73.08)	14 (70)	
No	21 (26.92)	6 (30)	
Disposable intubation tools			1
Yes	68 (87.18)	18 (90)	
No	10 (12.82)	2 (10)	
Tools used in intubation			0.2254
Video laryngoscopy intubation	75 (96.15)	18 (90)	
Ordinary laryngoscopy intubation	3 (3.85)	1 (5)	
Video tube intubation	0 (0)	0 (0)	

Visual intubation soft scope	0 (0)	0 (0)	
Other	0 (0)	1 (5)	
Numbers of operators			0.4416
One anesthesiologist	17 (21.79)	4 (20)	
Multiple anesthesiologists (≥ 2)	23 (29.49)	9 (45)	
One anesthesiologist and other doctors (≥ 2)	37 (47.44)	7 (35)	
Other	1 (1.28)	0 (0)	
Patients with cough during intubation			0.0160
Yes	11 (11.22)	7 (35)	
No	67 (88.78)	14 (65)	
How many intubation attempts			0.3682
Success the first time	77 (98.72)	19 (95)	
Success the second time	1 (1.28)	1 (5)	
Success the third time	0 (0)	0 (0)	
Failure	0 (0)	0 (0)	

PPV, positive-pressure ventilation; ICU, intensive care unit.

Table 4. Multivariate logistic model with stepwise selection for SARS-CoV-2 risk in the anesthesiologists performing endotracheal intubation in patients with confirmed SARS-CoV-2

	Coefficient	SE	Z	*P*
Endotracheal intubation for elective treatment	-1.41	0.68	-2.06	0.0390
Coughing by patients during intubation	3.39	1.29	2.62	0.0088

SE, standard error; Z, Z-test.

Table 5. Univariate and multivariate logistic regression for SARS-CoV-2 risk in anesthesiologists performing endotracheal intubation in patients with confirmed SARS-CoV-2

		Value	95% CI	*P*
Intubation for elective treatment	Crude OR	0.13	0.05-0.30	< 0.0001
	Adjusted OR*	0.28	0.14-0.68	0.0194
Endotracheal intubation in operating room	Crude OR	0.10	0.01-0.52	0.0281
	Adjusted OR*	0.12	0.01-0.95	0.0787
Endotracheal intubation in isolation ward	Crude OR	0.19	0.08-0.40	0.0001
	Adjusted OR*	0.58	0.15-2.09	0.4048
Routine rapid induction for intubation	Crude OR	0.20	0.10-0.37	< 0.0001
	Adjusted OR*	0.36	0.08-1.51	0.1577
Number of operators: Multiple anesthesiologists	Crude OR	1.39	1.07-1.82	0.0170
	Adjusted OR*	3.04	0.74-4.12	0.2297
Patients with cough during intubation	Crude OR	3.00	1.79-4.90	0.0227
	Adjusted OR*	1.70	1.39-2.97	0.0404

*All the aforementioned variables were used in the multivariate analysis. OR, odds ratio; CI, confidence interval.

a different clade. Nevertheless, the structure of its receptor-binding gene region is very similar to that of SARS-CoV; thus, SARS-CoV-2 uses the same receptor as SARS-CoV, that is, the angiotensin-converting enzyme 2 (ACE2), for cell entry [16]. For health care workers with potential exposure to SARS-CoV-2, the US CDC and WHO have provided guidelines for work restriction and monitoring [6, 7]. These guidelines are based on experiences of health care workers with SARS, given that SARS demonstrated airborne transmission [17] and transmission to health care workers was a common feature of most SARS outbreaks [18, 19]. The approach depends on exposure duration, patient symptoms, and facemask use (for anesthesiologists), PPE type used by the health care workers, and the aerosol-generating procedure used [6, 7]. However, SARS and SARS-CoV-2 have differences in transmissibility, infectious period, infectious situation, community spread, and clinical spectrum [20]. Therefore, the prevention policies for SARS-CoV-2 cannot be identical to those used for SARS, particularly in health care workers; the SARS-CoV-2 pandemic has required the use of more health facilities than SARS. Moreover, transmissibility appears to be higher for SARS-CoV-2 than for SARS [20], and health care workers must be protected so that they can care for more patients with SARS-CoV-2 [20].

In our study, SARS-CoV-2 transmissibility in the anesthesiologists was 20.41% after performing intubation in patients with confirmed SARS-CoV-2. However, this rate was only 4.16%-13.04% for SARS [21, 22]. Therefore, understanding the significant predictive factors of high SARS-CoV-2 transmissibility in first-line health care workers, such as anesthesiologists who perform intubation in patients with SARS-CoV-2, is vital for public health and policy development.

Table 1 demonstrates that no significant factors were associated with patients with confirmed SARS-CoV-2 and the infected anesthesiologists performing intubation in them. No association was noted between patient symptoms and signs, such as fever and other clinical characteristics, and SARS-CoV-2 transmissibility in the anesthesiologists. Confirmed SARS-CoV-2 with fever, false-negative nuclear acid test results, history of exposure to other patients with SARS-CoV-2, difficult airway for intubation, narrow incisor distance, narrow thyromental distance, limited head and neck mobility, and stubby neck were not associated with the transmissibility of SARS-CoV-2 infection in the anesthesiologists. Patients with SARS-CoV-2 typically first experience a viral-type illness with symptoms ranging from a mild upper respiratory tract infection (eg, pharyngitis and rhinorrhea) to a lower respiratory tract infection (eg, cough and fever), influenza-like symptoms (eg, fever, chills, headache, and myalgias), or gastroenteritis (eg, nausea, vomiting, and diarrhea) [7, 23]. Nevertheless, older adults with infection may lack fever or localized infection-specific symptoms or signs [24]. For example, rather than high fever, productive cough, and pleuritic chest pain, pneumonia in older adults may present as a low-grade fever (37.22°C) and increased oxygen requirement like dyspnea [24]. Pneumonia in some patients may also be associated with nonspecific symptoms such as increased confusion, falls, and anorexia. These nonspecific symptoms are common in older adults and do not have high positive predictive value for infection [24]. Therefore, the endpoint of our study (transmission risk of intubation for patients with SARS-CoV-2) was different from that of Wang Y et al., who demonstrated that symptomatic febrile patients are exposed to higher viral loads. Moreover, higher viral load was not proportional to high risk of transmission during intubation [25].

The incidence of SARS-CoV-2 was lower with elective intubation than with intubation for emergency procedures probably because during the emergency situations, the anesthesiologists might not have been able to adequately follow the standard protective measures [26, 27]. Furthermore, oxygen saturation is relatively low in patients with SARS-CoV-2 with unplanned intubation; these patients may present with conditions such as pressure-assisted ventilation-induced cough reflex during intubation, leading to droplet diffusion and aerosol formation and thus increasing airborne SARS-CoV-2 transmission [26-28]. Performing intubation in an isolation ward or operating room is safer and reduces SARS-CoV-2 prevalence compared with that in an emergency room, intensive care unit, and respiratory care ward [26], because isolation wards or operating rooms in China are equipped with anesthesiologists and medical personnel with training in standard protection and sufficient preparation for protection against airborne transmission [26]. Anesthesiologists have a better understanding of patient condition when intubating in an isolation ward or operating room; moreover, in these areas, elective rather than emergency intubation is performed, and before intubation, adequate anesthesia is administered [26]. In these areas, enhanced PPE for droplet or airborne infection and a sufficient amount of muscle relaxant are used before intubation, particularly in patients with SARS-CoV-2. All these measures are generally effective in preventing patients from coughing, droplet spread, and other infectious events [26]. Moreover, for sputum removal, a closed sputum suction device is used, which is difficult to use during emergency intubation [26]. In the current study, on univariate logistic regression, routine rapid induction with continuous PPV for intubation in patients with SARS-CoV-2 was found to reduce SARS-CoV-2 transmission to anesthesiologists (**Table 4**). Routine rapid induction with continuous PPV for anesthesia-induced tracheal intubation is routinely used for patients with SARS-CoV-2 [26]. After patients are anesthetized, they are given muscle relaxants and maintained under continuous PPV, which reduces hypoxia and the resultant coughing, thereby allowing anesthesiologists to perform intubation safely. Our results (**Table 5**) indicated that reduction in coughing by patients during intubation was essential. Another risk factor for SARS-CoV-2 transmission on univariate analysis was the presence of two or more anesthesiologists during intubation (**Table 4**), probably because the presence of more than one anesthesiologist indicates difficult or emergency intubation. However, because this factor corresponded with emergency and difficult intubation and other clinical factors, it became nonsignificant on multivariate analysis (**Table 4**). Multivariate analysis revealed that only two factors were associated with risk of SARS-CoV-2 infection in anesthesiologists performing intubation: elective intubation as a protective factor and patient coughing during intubation as a high-risk factor.

Endotracheal intubation in patients with SARS-CoV-2 entails a risk to both the physiologically compromised patient and the attending health care providers [29]. On the basis of a two-center retrospective observational case series from Wuhan, China, a panel of international airway management experts formulated recommendations for the management of tracheal intubation in patients with SARS-CoV-2 [29]. PPE was recommended to be worn by all intubating health care 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. However, these clinical recommendations were not based on a multivariate logistic model with stepwise selection considering all the variables with significant effects on the SARS-CoV-2 in anesthesiologists. Sorbello et al. also presented recommendations based on clinical experiences of managing patients throughout Italy and described key elements of clinical management, including safe oxygen therapy; airway management; PPE; and nontechnical aspects of caring for patients diagnosed with SARS-CoV-2 [12]. Only through planning, training, and team work will clinicians and health care systems be best placed to deal with the many complex implications of this new pandemic [12]. These recommendations and key elements from the United Kingdom consensus [30] and the study by Sorbello et al. were similar to our finding that elective intubation was associated with a relatively low SARS-CoV-2 transmission risk (**Table 5**). Other single-center Italian study supported Sorbello et al.'s findings [31]. Most recommendations support the need to minimize the team size and administer full-dose RSI [12, 29-31]. Our results based on a multivariate logistic model with stepwise selection were consistent with these recommendations. However, 19 patients experienced coughing during intubation in our study, possibly indicating inadequate dose of neuromuscular blocking agents. The full dose RSI is strongly recommended. The China consensus should be improved as soon as possible and decrease the human error and highlight the importance of checklists.

We noted that anesthesiologists performing intubation in patients with SARS-CoV-2 had a significantly increased SARS-CoV-2 risk when patients coughed during intubation (**Table 5**). On the basis of the SARS-related experiences, the health care procedures with high potential of generating droplets and aerosols thereby increasing SARS risk were manipulation of the airway (ie, performing endotracheal intubation or suctioning) and administration of aerosolized medications [32, 33]. Therefore, CSATF-AM recommended administration of muscle relaxants to patients with SARS-CoV-2 before intubation [26]. In airways that are difficult to intubate, muscle relaxant use minimizes choking or coughing [34, 35]. Performing intubation without muscle relaxants typically causes patients to cough [26]. Moreover, anesthesiologists should begin the intubation only after the onset of the effect of the muscle relaxant to minimize coughing by patients [26]. Muscle relaxants such as succinylcholine and rocuronium bromide that have a rapid onset of action are recommended by CSATF-AM for patients with SARS-CoV-2 [26]. CSATF-AM strongly recommends using positive-pressure headgear when intubating patients with SARS-CoV-2 to prevent the airborne transmission through patients coughing during intubation [26]. Our finding that coughing by patients with SARS-CoV-2 during intubation is a risk factor for SARS-CoV-2 infection in the anesthesiologists validates the recommendations of CSATF-AM [26].

This is the first study demonstrating the factors predicting the risk of SARS-CoV-2 transmission to anesthesiologists performing intubation in patients with SARS-CoV-2. Moreover, all CSATF-AM-registered anesthesiologists have performed ≥ 500 intubations or worked for ≥ 5 years after specialization; thus, they were all similarly skilled in performing intubation. However, the SARS-CoV-2 prevalence was found to be high (20.41%)-higher than that reported for patients with SARS [21, 22]. Our results could provide valuable information regarding SARS-CoV-2 transmission during intubation. Moreover, the high SARS-CoV-2 transmissibility during intubation in patients with SARS-CoV-2 demonstrates the importance of implementing protective procedures during intubation for SARS-CoV-2 cases. Performing elective rather than emergency intubation, intubation in isolation ward or operating room, and routine rapid induction for intubation with continuous PPV are strongly recommended. Moreover, using an adequate dose of muscle relaxants and performing intubation after drug effect onset could minimize or prevent patient coughing during intubation. We hope that these measures will reduce SARS-CoV-2 risk in anesthesiologists and thus prevent increasing the burden on the health care systems. These findings may serve a valuable reference to anesthesiologists performing intubation in patients with any airborne transmission diseases in the future.

The limitations of our study are as follows: First, the major limitations of using questionnaires could not be avoided. Nevertheless, only CSATF-AM-registered experienced anesthesiologists answered the questionnaires. Moreover, the interval between SARS-CoV-2 outbreak and the survey was very close (< 1 month). Thus, the recall bias, understanding, interpretation bias, or unconscientious responses in the questionnaires might be low. Second, SARS-CoV-2 severity in the anesthesiologists after performing intubation in patients with SARS-CoV-2 was unclear. In several cases, anesthesiologists with severe SARS-CoV-2 symptoms could not respond to the questionnaires. Therefore, underestimation of the prevalence and loss of some crucial events may have occurred. Third, SARS-CoV-2 prevalence in the participating anesthesiologists after the intubation of patients with confirmed SARS-CoV-2 was 20.41%. These findings might be because inadequate protective measures or endotracheal intubation methods in anesthesiologists meeting the initial outbreak of SARS-CoV-2 in February 2020 (**Table 3**). Moreover, the anesthesiologists might have a history of exposure to other SARS-CoV-2 cases outside the health care systems, which could not be evaluated in this survey, indicating a potential for overestimation of SARS-CoV-2 prevalence. Fourth, the sample size was too small to analyze all variables in the regression model. Fifth, a mixed formula (records for patients and survey for anesthesiologists) would have been more precise and less at risk of bias. However, the some of the patients with SARS-CoV-2 receiving intubation might be too severely ill to answer the questionnaires. Moreover, patients who could answer the questionnaires might be associated with recovery from SARS-CoV-2 or other severe underlying diseases, leading to a risk of selection bias from relatively healthy SARS-CoV-2 patients. Thus, we did not access the patients' records. Sixth, PPE was not standardized for all anesthesiologists in February in China. No official records exist on which standard PPE should be worn by anesthesiologists performing endotracheal intubation for patients with SARS-CoV-2. Therefore, we wished to determine the predictors of the risk SARS-CoV-2 transmission for anesthesiologists performing endotracheal intubation in patients with SARS-CoV-2. Sometimes, for emergency intubation, protective measures taken need to be categorized into tertiary, secondary, or primary protection (**Table 1**). Tertiary protection might be difficult for anesthesiologists performing unplanned intubations. Therefore, three levels of PPE were considered for the multivariate logistic model with stepwise selection by selecting all the variables with significant effects on the SARS-CoV-2 in anesthesiologists.

Conclusions

SARS-CoV-2 transmissibility in anesthesiologists during intubation in patients with confirmed SARS-CoV-2 was 20.41%. Performing intubation for elective treatment rather than emergency treatment and preventing coughing by patients during intubation are the most crucial factors to reduce SARS-CoV-2 transmission.

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Disclosure of conflict of interest

None.

Abbreviations

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; PPV, positive-pressure ventilation; OR, odds ratio; CI, confidence intervals; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; CSATF-AM, Chinese Society of Anesthesiology Task Force on Airway Management; CT, computed tomography; MERS, Middle East Respiratory Syndrome; SARS, Severe Acute Respiratory Syndrome; ACE2, angiotensin-converting enzyme 2; AIC, Akaike's Information Criteria; ICU, intensive care unit; PPE, personal protective equipment.

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Supplementary Table 1. Regression coefficients for the full model of endotracheal intubation and predictive factors of SARS-CoV-2 in anesthesiologists performing endotracheal intubation in patients with confirmed SARS-CoV-2

	Coefficient	SE	Z	*P*
Reason for performing intubation				
Intubation for general anesthesia	1.34	1.15	1.17	0.2436
Intubation for elective treatment	-1.49	0.87	-1.71	0.0473
Intubation in the operating room	-23.37	7566.41	0.00	0.9975
Intubation in the isolation ward	-20.08	7566.41	0.00	0.9979
Intubation in the ICU	-20.46	7566.41	0.00	0.9978
Protective measures taken				
Secondary protection	18.26	6127.58	0.00	09976
Difficult airway cart	0.13	1.08	0.12	0.9026
Difficult airway box	-0.36	0.79	-0.45	0.6510
Simple respirator	-1.29	1.00	-1.30	0.1952
Respirator or anesthesia machine	0.81	1.04	0.78	0.4331
Filter or artificial nose	0.38	1.06	0.36	0.7189
Intubation method				
Routine rapid induction	-16.80	9724.07	0.00	0.9986
Adopted positive-pressure ventilation before intubation	15.94	9724.07	0.00	0.9987
Disposable intubation tools	1894	3355.82	0.01	09955
Ordinary laryngoscopy intubation	1.51	1.57	0.96	0.3375
Number of operators				
One anesthetist	-1.61	1.07	-1.50	0.1342
Two anesthesiologists	1.94	0.95	-2.03	0.0426
Coughing by patients during intubation	13.09	35.82	0.01	0.0945
Intubation success at first time	17.93	6453.52	0.00	0.9978

SE, standard error; Z, Z-test; ICU, intensive care unit.

Supplementary Table 2. Multivariate logistic model with stepwise selection for results in Supplemental Table 1 based on Akaike's information criteria and predictive factors of SARS-CoV-2 in anesthesiologists performing endotracheal intubation in patients with confirmed SARS-CoV-2

	Coefficient	SE	Z	*P*
Endotracheal intubation for elective treatment	-1.29	0.74	-1.74	0.0810
Endotracheal intubation in operating room	-21.26	4595.81	0.00	0.9963
Endotracheal intubation in isolation ward	-19.34	4595.81	0.00	0.9966
Endotracheal intubation in ICU	-19.40	4595.81	0.00	0.9966
Protective measures with simple respirator	-1.04	0.71	-1.48	0.1395
Intubation method with disposable intubation tools	17.36	1892..2	0.01	0.9927
Number of operators: multiple anesthesiologists	20.71	1892..2	0.01	0.9913
Coughing by patients during intubation	1.43	0.70	2.04	0.0409

SE, standard error; Z, Z-test; ICU, intensive care unit.