Risk of SARS-CoV-2 Transmission During Flexible Laryngoscopy: A Systematic Review.

Josh K Kay
Tulane University

Sean M. Parcel DO
Lehigh Valley Health Network, sean.parsel@lvhn.org

James J Marsh
Tulane University

Andrew J McWhorter
Louisiana State University Health Sciences Center New Orleans

Paul L Friedlander
Tulane University

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Risk of SARS-CoV-2 Transmission During Flexible Laryngoscopy
A Systematic Review

Josh K. Kay, MD; Sean M. Parsel, DO; James J. Marsh, BSPH; Andrew J. McWhorter, MD; Paul L. Friedlander, MD

IMPORTANCE Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reportedly infected otolaryngologists disproportionately in the early parts of the coronavirus disease 2019 pandemic. Recommendations from national and international health organizations suggest minimizing the use of flexible laryngoscopy as a result.

OBJECTIVE To review evidence on the risks of aerosolization and transmission of SARS-CoV-2 from patients to health care personnel during endoscopy of the upper aerodigestive tract.

EVIDENCE REVIEW A comprehensive review of literature was performed on April 19, 2020, using the PubMed/MEDLINE (1966-April 2020), Embase (1975-April 2020), and Web of Science (1900-April 2020) databases. All English-language primary research studies were included if they assessed the transmission of SARS-CoV-2 or SARS-CoV-1 during procedures in the upper aerodigestive tract. The primary outcome measure was disease transmission among health care workers. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used for accuracy of reporting.

FINDINGS The queries for SARS-CoV-2 and SARS-CoV-1 identified 6 articles for systematic review. No studies included in this review provided data for SARS-CoV-2 transmission during flexible laryngoscopy. A total of 204 of 1264 health care workers (16.1%) had procedure-specific infections of SARS-CoV-1 or SARS-CoV-2. Among those, 53 of 221 (24.0%) were exposed during intubation, 1 of 15 (6.7%) during bronchoscopy, and 1 of 1 (100%) during endoscopy-assisted intubation.

CONCLUSIONS AND RELEVANCE A substantial lack of research precludes formal conclusions about the safety of flexible laryngoscopy and transmission of SARS-CoV-2 from patients to health care workers. The use of appropriate precautionary measures and personal protective equipment appears to reduce the risk of transmission. Given the uncertainty in transmission and the known benefits of safety precautions, upper airway endoscopy may be reasonable to perform if precautionary steps are taken.

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Supplemental content

Author Affiliations: Department of Otolaryngology–Head and Neck Surgery, Tulane University, New Orleans, Louisiana (Kay, Parsel, Friedlander); Tulane University School of Medicine, New Orleans, Louisiana (Marsh); Health Sciences Center, Department of Otolaryngology–Head and Neck Surgery, Louisiana State University, New Orleans (McWhorter).

Corresponding Author: Josh K. Kay, MD, Department of Otolaryngology–Head and Neck Surgery, Tulane University, 1430 Tulane Ave, New Orleans, LA 70112 (jkay6@tulane.edu).

Occupational transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) poses a substantial risk to health care workers.[1,2] Preliminary data from the US Centers for Disease Control and Prevention show that health care professionals account for approximately 20% of cases of coronavirus disease 2019 (COVID-19) in the United States.[2] Early in the outbreak, health care workers in otolaryngology were particularly vulnerable to nosocomial infection.[3-6] This is thought to be in part owing to the nature of work in otolaryngology, which often requires frequent, prolonged exposure to and manipulation of aerodigestive tract mucosa, where viral loads are often highest.[7] In particular, the use of flexible fiberoptic laryngoscopy (FFL) is potentially an aerosol-generating procedure (AGP) that has garnered widespread caution as a high-risk procedure.[4]

Flexible fiberoptic laryngoscopy is an integral tool for ambulatory evaluation of the larynx and is commonly used in the diagnosis and management of many head and neck cancers and other upper airway conditions. Procedures are most commonly performed in offices and other low-acuity settings where precautionary measures such as negative pressure isolation rooms may not be available. Many otolaryngology clinics have taken measures to reduce or completely stop the use of FFL during the SARS-CoV-2 outbreak.[4,8] Recent recommendations from a group of 300 US laryngologists support limiting FFL to only critical cases involving airway compromise or malignant neoplasm.[9] As otolaryngologists redefine clinical care pathways amid a global pandemic, it is important to understand the science behind these recommendations.

Methods

Systematic Review

A comprehensive review of literature was performed on April 19, 2020, from the PubMed/MEDLINE (1966 to April 2020), Embase

(1975 to April 2020), and Web of Science (1900 to April 2020) databases. The search included all available dates of each database. The primary objective was to determine the incidence of SARS-CoV-2 transmission through AGPs of the upper aerodigestive tract. Secondary objectives were to determine the risk associated with performing these invasive procedures and assess the benefit of personal protective equipment (PPE). Search criteria included all occurrences in the title or abstract of the terms *SARS-CoV-2* or *COVID-19* and *laryngoscopy* or *intubation* or *bronchoscopy* or *esophagoscopy* or *nasal endoscopy* or *sinus surgery* and *aerosol* or *disease transmission* or *nosocomial* or *health care worker*. Given the paucity of studies on COVID-19, the search was expanded to include SARS-CoV-1 by altering the search criteria and specifying date of publication prior to October 2019. Specific electronic search criteria can be found in eTable 1 in the Supplement. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline was used to ensure adequate reporting of this systematic review.

Inclusion criteria for the literature search were defined using the Population, Intervention, Comparator, Outcome, and Study Design approach. The population included was male and female health care workers of all ages. The intervention was endoscopic procedures of the upper aerodigestive tract. The comparator was transmission of SARS-CoV-1 or SARS-CoV-2 in the absence of invasive procedures. The outcome was transmission of SARS-CoV-1 or SARS-CoV-2. The study design included case reports, case series, case-control and cohort studies, and randomized clinical trials. Conference proceedings and unpublished studies were included if they provided sufficient information including demographics and outcomes.

Two investigators (J.K.K. and J.J.M.) independently performed eligibility assessment of data in a standardized manner. Both reviewers were blinded to the other's assessment. A third investigator (S.M.P.) reviewed all included studies and assessed for interrater agreement. Duplicate records were removed. The abstract of each citation was then screened for relevance to the assessment of viral transmission from AGPs. Irrelevant citations were excluded. The full texts of the remaining citations were obtained, along with additional records from the reference lists of the published articles. The full-text articles were reviewed, and noneligible studies were excluded. Studies not reported in English and those that did not directly assess effects of aerosolization of SARS-CoV-2 particles during endoscopy of the upper aerodigestive tract were excluded. Studies meeting eligibility criteria were included for qualitative and quantitative synthesis.

Data Extraction

All included studies were coded, and data were extracted and compiled in a spreadsheet. Data gathered from full-text articles included population demographics, study design, date of publication, type of intervention (laryngoscopy, bronchoscopy, esophagoscopy, or nasal endoscopy), use of PPE, and rates of viral transmission or rates of infections among health care workers. The principal summary measure was prevalence of procedure-based infections of health care workers. The secondary assessment measure was risk of infection associated with use of PPE.

Risk of Bias and Assessment of Quality

The risk of bias was assessed at the study level by examining each study design, authors' stated purpose for the study, and source of data collection for all included studies. This was performed independently by 2 investigators (J.K.K. and J.J.M.), and any discrepancies were reviewed by a third investigator (S.M.P.). Investigators were blinded to the others' assessments. The risk of bias for observational studies was assessed using the Newcastle-Ottawa Quality Assessment Scale for cross-sectional studies, cohort studies, and case-control studies. This instrument comprises 8 points that assess the selection, comparability, and exposure described in the studies. Points are awarded for adequacy of reporting within the study, which are then added to form a final quality score. The minimum score is 0 and the maximum score is 9. For purposes of this study, high quality was defined by scores between 7 and 9, moderate quality was defined by scores between 4 and 6, and poor quality was defined by scores less than 4.

Key Points

Question What is the evidence for minimizing the use of flexible laryngoscopy during the coronavirus disease 2019 pandemic?

Findings This systematic review found a paucity of data regarding the risks of severe acute respiratory syndrome coronavirus 2 aerosolization and transmission during endoscopic procedures of the aerodigestive tract. Aggregate data suggested a decreased risk in endoscopic procedures compared with other aerosol-generating procedures such as intubation; use of proper personal protective equipment also diminished the risk for nosocomial transmission during upper airway procedures.

Meaning Although more clinical and basic science research is needed to formalize conclusions, flexible laryngoscopy can likely be performed safely during the coronavirus disease 2019 pandemic with appropriate precautionary measures.

Results

Systematic Review

The initial database query for SARS-CoV-2–specific studies identified 69 citations (43 from PubMed/MEDLINE, 22 from Embase, and 4 from Web of Science). After application of exclusion criteria and removal of duplicates, only 1 citation was eligible for full-text review. Given the paucity of information and the similarities between transmission of SARS-CoV-2 and SARS-CoV-1, the search was expanded to include SARS-CoV-1.[10] This search returned an additional 95 citations (59 from PubMed/MEDLINE, 9 from Embase, and 27 from Web of Science). After removal of duplicates and application of exclusion criteria, 5 citations were added for full-text review, for a total of 6 citations, including 3 case-control studies, 2 retrospective cohort studies, and 1 case series (**Table 1**).[11-16] The PRISMA flow diagram of included and excluded studies can be found in the **Figure**. The overall methodological quality of the studies (eTable 2 in the Supplement) was moderate, with a median Newcastle-Ottawa Quality Assessment Scale score of 5.5 (interquartile range, 4.3-8.0).

Risk of SARS-CoV-2 Transmission

One case-control study examined the transmission and infectivity of SARS-CoV-2 in health care workers.[11] This study assessed hospital activities among 121 health care workers with moderate-risk to

Table 1. Description of Nosocomial Infections Among Exposed Health Care Workers

Source	Population	Study design	Nosocomial infections				
			All health care workers, No./ No. (%)[a]	Bronchoscopy		Intubation[b]	
				Frequency, No./ No. (%)	Effect size (95% CI)	Frequency, No./ No. (%)	Effect size (95% CI)
SARS-CoV-2							
Heinzerling et al,[11] 2020 (US)	121 Exposed health care workers	Case-control	3/121 (2.5)	0/3	NR	1/3 (33.3)	NR
SARS-CoV-1							
Raboud et al,[12] 2010 (Canada)	697 Exposed health care workers	Cohort	26/624 (4.2)	0/10	RR, 1.10 (0.07-16.92)	12/144 (8.3)	RR, 2.85 (1.35-6.04)
Ofner-Agostini et al,[13] 2006 (Canada)	17 Infected health care workers	Case series	17[c]	NR	NR	7[c]	NR
Caputo et al,[14] 2006 (Canada)	59 Intubation-exposed health care workers	Case-control	3/33 (9.1)	NR	NR	4/34 (11.8)	NR
Pei et al,[15] 2006 (China)	443 Exposed health care workers	Case-control	147/443 (33.2)	NR	NR	28/37 (75.7)	OR, 30.79 (7.91-119.84)
Loeb et al,[16] 2004 (Canada)	43 Exposed health care workers	Cohort	8/43 (18.6)	1/2 (50.0)	RR, 2.14 (0.46-9.90)	3/4 (75.0)	RR, 4.20 (1.58-11.4)
Total	NA	NA	204/1264 (16.1)	1/15 (6.7)	NA	53/221 (24.0)	NA

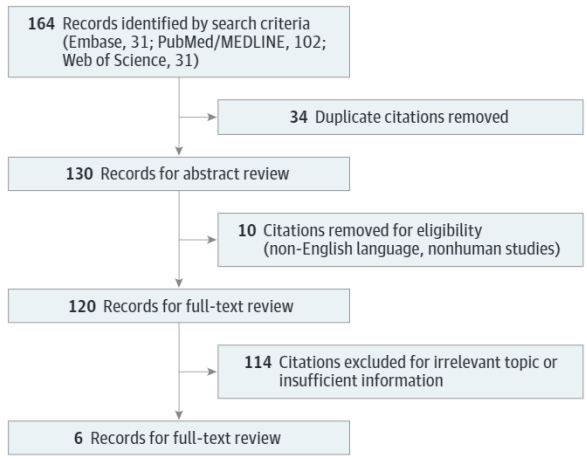
Abbreviations: NA, not applicable; NR, not reported; OR, odds ratio; RR, relative risk; SARS-CoV, severe acute respiratory syndrome coronavirus.

[a] Total infection rates of all health care workers described in the study.

[b] Includes all intubations (endoscopic-assisted intubation and direct visualization).

[c] Case series of infected health care workers; all 17 were infected. The total population number was not reported, and the infection rate was not determined.

Figure. Flow Diagram of the Systematic Search Showing Application of Inclusion and Exclusion Criteria



A total of 6 articles were included in the final systematic review.

high-risk exposures, including 3 confirmed cases of COVID-19. Two of the 3 individuals (66.7%) with confirmed cases of COVID-19 were participating in AGPs, such as intubation without a face mask, a respirator, eye protection, or a gown. The third infected health care worker reported inconsistent use of a face mask with moderate-risk exposures. None of 3 health care workers exposed to bronchoscopy were infected.

Risk of SARS-CoV-1 Transmission

Five studies were identified assessing the risk of occupational transmission of SARS-CoV-1 during procedures of the upper aerodigestive tract.[12-16] These consisted of 2 retrospective cohort studies, 2 retrospective case-control studies, and 1 case series. All 5 of the studies provided data for procedure-specific risk during intubation, 2 of the 5 studies provided data for bronchoscopy, and 1 of the 5 studies provided data for endoscopic-assisted intubation. None of the studies included procedure-specific data on FFL. Among the studies included, 1143 health care workers were exposed to SARS-CoV-1 and 201 (17.6%) were infected.

Several of the studies provided data on procedure-specific odds ratios and relative risk (Table 1). The risk of infection after intubation was significant in 1 study, with more than a 30-fold increase in risk (odds ratio, 30.79 [95% CI, 7.91-119.84]).[15] Similarly, other studies reported increased relative risks, ranging from 2.85 to 4.20.[12,16] The relative risk for bronchoscopy was reported in 2 studies and was not clinically significant (2.14 [95% CI, 0.46-9.90] and 1.10 [95% CI, 0.07-16.92]).[16]

Combined Risk of Transmission

Of the 6 studies included in this review, all assessed for the risk of intubation, 1 for the risk of flexible bronchoscopy, 1 for the risk of flexible endoscopy-assisted intubation, 0 for the risk of esophagoscopy, and 0 for the risk of FFL (Table 1).[11-16] The systematic search yielded a total of 1264 health care workers for inclusion. Of these, 204 (16.1%) were infected with either SARS-CoV-2 or SARS-CoV-1 and 55 of 237 (23.2%) were infected during any type of aerodigestive tract procedure. The procedure-specific infections included 53 of 221 (24.0%) exposed during intubation, 1 of 15 (6.7%) during bronchoscopy, and 1 of 1 (100%) during flexible endoscopy–assisted intubation. No exposures to SARS-CoV-2 or SARS-CoV-1 were reported during FFL. The outcome of transmission was confirmed using serologic testing in 4 studies, real-time polymerase chain reaction in 1 study, and structured interviewing in 1 study.

Table 2. Risk of Nosocomial Infection and Use of Personal Protective Equipment

Source	Surgical mask		Respirator		Gown		Gloves		Eye protection	
	Infection rate, No./ No. (%)	Effect size (95% CI)	Infection rate, No./ No. (%)	Effect size (95% CI)	Infection rate, No./ No. (%)	Effect size (95% CI)	Infection rate, No./ No. (%)	Effect size (95% CI)	Infection rate, No./ No. (%)	Effect size (95% CI)
Raboud et al,[12] 2010	5/30 (16.7)	RR, 4.88 (1.98-12.05)	0/28	RR, 0.41 (0.03-6.49)	20/561 (3.6)	NR	23/578 (4.0)	NR	13/464 (2.8)	NR
Ofner-Agostini et al,[13] 2006	NR	NR	14[a]	NR	14[a]	NR	15[a]	NR	4[a]	NR
Caputo et al,[14] 2006	1/2 (50.0)	NR	2/51 (3.9)	NR	NR	NR	0/29	NR	1/15 (6.7)	NR
Pei et al,[15] 2006	75/230 (32.6)	OR, 0.48 (0.24-0.95)	NR	NR	87/283 (30.7)	OR, 0.23 (0.12-0.42)	95/365 (26.0)	OR, 0.11 (0.04-0.27)	24/120 (20.0)	OR, 0.45 (0.27-0.75)
Loeb et al,[16] 2004	1/4 (25.0)	RR, 0.45 (0.07-2.71)	2/16 (12.5)	RR, 0.22 (0.05-0.93)	3/20 (15.0)	RR, 0.36 (0.10-1.24)	4/22 (18.2)	RR, 0.45 (0.14-1.46)	NR	NR
Total	82/266 (30.8)	NA	4/95 (4.2)	NA	124/864 (14.4)	NA	122/994 (12.3)	NA	38/599 (6.3)	NA

Abbreviations: NA, not applicable; NR, not reported; OR, odds ratio; RR, relative risk.

[a] Case series of infected health care workers; all 17 were infected. The total population number was not reported, and infection rate was not determined.

Use of PPE

All 6 of the clinical studies included data on the use of PPE by health care workers during exposures. Data for use of surgical masks, gowns, eye protection, and respirators (N95, powered air purifying respirator, or equivalent) were present in 5 of the 6 studies (**Table 2**).[12-16] Only 3 of the 6 studies included data on risks without masks. None of the studies included data specifically using negative pressure isolation. Data on PPE from a case series of only infected health care workers were excluded from quantitative analysis.

A total of 370 of 2818 health care workers (13.1%) were infected while using some type of PPE. Data represented the number of infections among exposed health care workers who reported consistent use of various types of PPE. Infections were highest among health care workers reporting the use of a surgical mask (82 of 266 [30.8%]), gown (124 of 864 [14.4%]), or gloves (122 of 994 [12.3%]). Fewer hospital-acquired infections were reported among health care workers who used eye protection (38 of 599 [6.3%]) or respirators (4 of 95 [4.2%]). Only 1 study evaluated procedure-specific risk and PPE use.[14] This study interviewed 33 health care workers who performed intubation on patients with SARS-CoV-1 and found frequencies of SARS infection with the use of N95 or equivalent respirators (2 of 33 [6.1%]) and eye protection (2 of 44 [4.5%]) compared with those not wearing PPE (7 of 35 [20.0%]) or surgical masks alone (1 of 2 [50.0%]).

Discussion

This systematic review demonstrates a limited amount of evidence about the transmission of SARS-CoV-2 during FFL and other endoscopic procedures of the upper aerodigestive tract. To our knowledge, to date, no study has provided specific data on the risk of SARS-CoV-2 transmission during FFL. The 1 study analyzing SARS-CoV-2 transmission among health care workers found no instances of transmission during bronchoscopy in 3 exposed health care workers.[11]

Because of the limited results from the systematic search specific to SARS-CoV-2 transmission and endoscopy of the aerodigestive tract, we expanded the search criteria to include SARS-CoV-1. Both viruses are similar in aerosol stability, and the current guidelines regarding AGP-associated transmission originally arose from SARS-CoV-1.[10] With the additional 5 studies included, 23.2% of health care workers exposed during AGP contracted SARS-CoV-1 or SARS-CoV-2; however, the risk of infection during endoscopy alone appears lower in the limited data provided (1 of 15 [6.7%]). Even with the expanded criteria, there were no data regarding procedure-specific risk during FFL for either virus.

In the absence of dedicated data on FFL aerosolization, it is often included with other upper endoscopy procedures, although important differences exist. Current guidelines from the Centers for Disease Control and Prevention and the World Health Organization on AGPs do not specifically mention laryngoscopy (**Box**).[17,18] Moreover, much of the current guidance in the literature regarding endoscopic procedures relies on epidemiologic data for bronchoscopy.[17-20] In light of this fact, the World Health Organization highlights a significant research gap in defining risk for aerosolization during endoscopic procedures for pandemic-prone acute respiratory infections.[20] The organization provides recommendations based on several systematic reviews; however, in the case of bronchoscopy, there are only 3 studies cited evaluating the procedure-specific risk of transmission for airborne diseases, which include 2 studies cited in this systematic review.[12,15] The third study is an epidemiologic study suggesting an increased rate of tuberculosis infection in pulmonary fellows compared with other health care workers.[19] Recently published consensus from a group of laryngologists echoes the recommendations from the American Academy of Bronchology and Interventional Pulmonology, which suggest limiting endoscopic procedures to critical cases in negative pressure rooms.[9]

Unlike bronchoscopy, FFL is often performed in low-acuity, outpatient settings and is rarely performed concomitantly with other AGPs. In all studies reviewed, data for bronchoscopy are provided in combination with the risk of intubation and cardiopulmonary resuscitation. Equating the risk for these 2 procedures is based entirely on expert opinion in the absence of strong clinical or basic sci-

Box. List of Centers for Disease Control and Prevention and World Health Organization Aerosol-Generating Procedures

Centers for Disease Control and Prevention[17]
- Tracheal intubation and extubation
- Noninvasive ventilation
- Manual ventilation before intubation
- Bronchoscopy
- Administration of high-flow oxygen or nebulized medications
- Tracheotomy
- Cardiopulmonary resuscitation
- Upper endoscopy

World Health Organization[18]
- Intubation or extubation and related procedures (eg, manual ventilation and open suctioning)
- Cardiopulmonary resuscitation
- Bronchoscopy
- Surgery and postmortem procedures involving high-speed devices
- Some dental procedures (eg, drilling)
- Noninvasive ventilation (eg, bilevel positive airway pressure and continuous positive airway pressure ventilation)
- High-frequency oscillation ventilation
- Induction of sputum

ence data. This is not to suggest that concerns for aerosolization and transmission are unsupported in theory. Other procedures of the aerodigestive tract have demonstrated risk to health care workers. Aggregated data from this review revealed infections in up to 24% of health care workers during intubation procedures. Several of the studies show an increased likelihood of SARS-CoV-1 infection during intubation, which is consistent with the data provided by the World Health Organization report on pandemic-prone upper respiratory tract viruses (pooled odds ratio, 6.6 [95% CI, 2.3-18.9]).[12,15,16,19]

Although the evidence behind avoiding or limiting FFL is poor, there are theoretical risks for SARS-CoV-2 transmission during the procedure. Transmission of the virus is thought to occur primarily through large respiratory droplets and direct contact; however, newer evidence suggests that aerosolization can play an important role.[10,21,22] Data suggest that viral stability in smaller aerosol particles may persist for up to 3 hours and as far as 4 m from the source.[10,22] These findings are supported by the SARS-CoV-1 data, which show higher overall rates of infection in health care workers using PPE precautions for respiratory droplets alone (eg, surgical mask). To compound the issue, many patients shed viral particles for days before showing symptoms and some patients remain asymptomatic throughout infection, and false-negative rates for real-time polymerase chain reaction tests are significant.[23,24]

Aerosols are formed at the interface of airflow and the fluid-lined aerodigestive tract mucosa. The size of the respiratory particulate formed is inversely proportional to the energy of the mechanism (eg, airflow) forming the particle. That is, the theoretical risks of aerosolization during low-energy procedures such as FFL are lower than during high-energy mechanisms such as high-speed drilling or sneezing.[25] This finding is supported by a recent cadaveric study that found no detectable aerosol production during cold instrumentation of the nose.[26]

Other factors may be associated with increased risk of transmission with FFL. Many otolaryngology clinics use atomized anesthetic with decongestants prior to laryngoscopic examination, which could increase the risk for aerosolization arising from the nasal cavities, where viral load is often the highest.[7] This generation of a plume of small virus-laden particles may increase the risk of transmission.[27] This process is not required to complete FFL, and alternate methods have been described without the use of pressurized gas or atomization.[4] Alternatively, FFL could cause irritation of the pharynx or larynx, causing excessive coughing or sneezing and, thus, more aerosolization.[28] One study showed high-density aerosol particles extending up to 66 cm during simulated sneezes on cadavers.[26] Although there are no reasonable measures that can ensure avoidance of coughing or sneezing, the importance of proper local anesthetization was highlighted early in the pandemic by otolaryngologists as a precautionary measure to reduce risk during FFL.[3]

Limitations

There are several limitations to this study. We excluded articles not written in English or without full text available. Exclusion of these articles could result in publication bias; however, only 9 of 164 articles (5.5%) were excluded for language other than English. Although both SARS-CoV-1 and SARS-CoV-2 initially caused a higher disease burden in Asia, 5 of the 6 studies included in this review focus on outbreaks in North America and, thus, may not reflect the true nature of transmission risk. Overall, the quality of evidence included in this review is moderate; consequently, higher-powered and rigorously designed studies would be beneficial before forming conclusions about the use of FFL during the COVID-19 outbreak. In addition, there is a heterogeneity of reporting styles between studies that makes comparison of variables such as use of PPE difficult to define.

Conclusions

As the COVID-19 pandemic continues to evolve, otolaryngologists will be faced with adapting clinical care to address the inherent risk of performing upper aerodigestive tract procedures that may produce aerosolized particles. Despite the theoretical risks, this review found that there are limited data regarding the risk for aerosolization and transmission of SARS-CoV-2 during FFL. The current recommendations for minimizing FFL are based on underpowered retrospective studies of separate endoscopic procedures. Although FFL may increase the risk for aerosol generation, it can likely be performed safely with proper precautionary measures.

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Concept and design: Kay, Parsel, McWhorter, Friedlander.
Acquisition, analysis, or interpretation of data: Kay, Parsel, Marsh.
Drafting of the manuscript: Kay, Parsel, Marsh, Friedlander.
Critical revision of the manuscript for important intellectual content: Kay, Parsel, Marsh, McWhorter.

Statistical analysis: Kay, Marsh.
Supervision: Parsel, Friedlander.

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