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CHEST

The Use of Bronchoscopy During the Coronavirus Disease 2019 Pandemic

CHEST/AABIP Guideline and Expert Panel Report

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BACKGROUND: The coronavirus disease 2019 (COVID-19) has swept the globe and is causing significant morbidity and mortality. Given that the virus is transmitted via droplets, open airway procedures such as bronchoscopy pose a significant risk to health-care workers (HCWs). The goal of this guideline was to examine the current evidence on the role of bronchoscopy during the COVID-19 pandemic and the optimal protection of patients and HCWs.

STUDY DESIGN AND METHODS: A group of approved panelists developed key clinical questions by using the Population, Intervention, Comparator, and Outcome (PICO) format that addressed specific topics on bronchoscopy related to COVID-19 infection and transmission. MEDLINE (via PubMed) was systematically searched for relevant literature and references were screened for inclusion. Validated evaluation tools were used to assess the quality of studies and to grade the level of evidence to support each recommendation. When evidence did not exist, suggestions were developed based on consensus using the modified Delphi process.

RESULTS: The systematic review and critical analysis of the literature based on six PICO questions resulted in six statements: one evidence-based graded recommendation and 5 ungraded consensus-based statements.

INTERPRETATION: The evidence on the role of bronchoscopy during the COVID-19 pandemic is sparse. To maximize protection of patients and HCWs, bronchoscopy should be used sparingly in the evaluation and management of patients with suspected or confirmed COVID-19 infections. In an area where community transmission of COVID-19 infection is present, bronchoscopy should be deferred for nonurgent indications, and if necessary to perform, HCWs should wear personal protective equipment while performing the procedure even on asymptomatic patients.

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KEY WORDS: bronchoscopy; COVID-19; personal protective equipment

ABBREVIATIONS: AABIP = American Association for Bronchology and Interventional Pulmonology; AGP = aerosol generating procedure; CDC = Centers for Disease Control and Prevention; CHEST = American College of Chest Physicians; COVID-19 = coronavirus disease 2019; GRADE = Grading of Recommendations, Assessment, Development and Evaluations; HCW = health-care worker; PAPR = powered air purifying respirator; PICO = Population, Intervention, Comparator, and Outcome; PPE = personal protective equipment; rRT-PCR = real-time reverse transcription-polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

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Summary of Recommendations

1. When patients with suspected or confirmed COVID-19 infection are undergoing bronchoscopy, we suggest that health care workers in the procedure and recovery rooms use either an N-95 respirator or a powered air purifying respirator (Ungraded Consensus-Based Statement).

Remarks:

- In addition, health care workers should wear personal protection equipment including face shield, gown and gloves.
- N-95 respirators should be discarded after bronchoscopy.

2. In patients suspected of having COVID-19 infection, we suggest that a nasopharyngeal specimen be obtained first. In the setting of severe or progressive disease requiring intubation, if additional specimen is needed to establish a diagnosis of COVID-19 or other diagnosis that will change clinical management, lower respiratory specimens from endotracheal aspirate or bronchoscopy with BAL can be performed (Ungraded Consensus-Based Statement).

Remarks: More research is needed to further compare diagnostic sensitivity for COVID-19 infection utilizing other less invasive lower respiratory specimen collection techniques such as blinded bronchial sampling, blinded protected brush and non-bronchoscopic mini-BAL.

3. When asymptomatic patients present for bronchoscopy in an area where community spread of COVID-19 is present, we suggest that health care workers in the procedure room wear N-95 respirators or powered air-purifying respirators as opposed to surgical masks (Ungraded Consensus-Based Statement).

Remarks: In addition, health care workers should wear personal protection equipment including face shield, gown and gloves.

4. Prior to performing bronchoscopy in asymptomatic patients in an area where community transmission of COVID-19 infection is present, we suggest testing for COVID-19 infection (Ungraded Consensus-Based Statement).

Remarks:

- This strategy is contingent on the availability of testing in the local setting.
- In all patients with negative results, we suggest that the procedure is performed using personal protection equipment including face shield, gown, gloves and N-95 respirators or powered air purifying respirators (PAPR).
- When test results are positive prior to bronchoscopy, we suggest postponing all non-emergent bronchoscopies.
- In patients who require emergent bronchoscopy who have positive SARS-CoV-2 test results, we suggest using personal protection equipment including face shield, gown, gloves and N-95 respirators or powered air purifying respirators (PAPR) in pre, intra, and post bronchoscopy settings as would be with every SARS-Cov-2 positive patient.

5. When bronchoscopy is indicated to diagnose, stage, or characterize a known or suspected lung cancer in an area where community transmission of COVID-19 is present, we suggest that bronchoscopy be performed in a timely and safe manner (Grade 2C).

Remarks:

- Strategies to perform bronchoscopy in a timely manner should be developed locally, taking into account local resource availability including availability of personal protective equipment, availability of COVID-19 testing and availability of downstream resources required for treatment (eg, surgery requires ICU beds and ventilators).

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- Regional availability of diagnostic and therapeutic interventions for cancer patients should be considered. In particularly resource-depleted hospitals, COVID-19 negative cancer patients should be referred to other centers, preserving resources for COVID-19 patients and facilitating safe, timely, and effective care for the cancer patient as well.
- Although efforts should be made to provide timely care, these should be balanced by the need to attend to other dimensions of quality, including safety, effectiveness, and consistency with patient values and preferences.

6. In patients with confirmed COVID-19 infection who recover and need a routine bronchoscopy, we suggest that the timing of the procedure be customized based on the indication for the procedure, the severity of the COVID-19 infection and time from symptom resolution (Ungraded Consensus-Based Statement).

Remarks: The exact time to perform bronchoscopy is still unknown. It would be reasonable to wait at least 30 days from resolution of symptoms with negative SARS-CoV-2 RNA tests from at least two consecutive nasopharyngeal swab specimens collected ≥24 hours apart. Further research is needed to better understand optimal timing of bronchoscopy performance relative to symptom resolution.

Background

The coronavirus disease 2019 (COVID-19) pandemic has manifested primarily as a severe lower respiratory tract illness with significant associated morbidity and mortality throughout the globe.[1] Transmission is generally via respiratory droplets, but airborne transmission may be possible with aerosol generating procedures (AGPs) such as bronchoscopy.[2] Therefore, bronchoscopy and other AGPs put health-care workers (HCWs) at particularly high risk of exposure and infection. Under these trying circumstances, the medical community has three overarching imperatives. The first is to ensure the protection and welfare of all patients, irrespective of their COVID-19 status. The second is to preserve the health-care workforce to sustainably meet the first responsibility, and finally, the third is to promote the health of the community at large.

Although specific data on the risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during bronchoscopy are not available, the US Centers for Disease Control and Prevention (CDC) recommends performing these AGPs in an airborne infection isolation room with an N95 respirator or higher-level respirator, eye protection, gloves, and gown.[3] These considerations and the often overwhelming demand on available human and material resources during a pandemic necessitates thoughtful and deliberate balancing of the tradeoffs that may be required to optimally fulfil the primary responsibilities of the health-care system.

In an effort to provide interim guidance to health-care practitioners, various specialty societies have issued statements germane to their particular specialties. The American Association for Bronchology and Interventional Pulmonology (AABIP)[4] recently issued a statement on the use of bronchoscopy in COVID-19. Most of these statements have relied primarily on the available CDC guidance and the consensus opinions of single specialty experts. This report provides an in-depth, multidimensional, and multidisciplinary review of the available scientific evidence and puts forward suggestions for key clinical scenarios that many practitioners are likely to face. In such a kinetic milieu, these can be expected to evolve based on an expanding evidence base, the public health burden of disease, and the availability of trained personnel or medical infrastructure. These suggestions are therefore best envisioned as a decision-making framework that continually strives for optimality among possibly competing mandates.

Methods

The primary aim of this collaborative effort between the American College of Chest Physicians (CHEST) and AABIP was to create a list of clinically relevant recommendations and suggestions for HCWs who perform bronchoscopy during the COVID-19 pandemic. We chose to base recommendations on the assumption that resources are abundant. These recommendations can then be adapted by local decision-makers based on resource availability. Using the assumption that resources (for prevention, diagnosis, and treatment) are plentiful, we aimed to answer some of the most common and important questions related to bronchoscopy during the COVID-19 pandemic.

Panelist and Content Expert Selection

CHEST and AABIP participated in the selection of panelists. Two cochairs were assigned to lead this endeavor (M. M. W. appointed by AABIP and R. A. appointed by CHEST). Cochairs in conjunction with CHEST and AABIP leadership nominated two methodologists (S. S. and D. O.) and core panelists (G. E., C. R. L., F. M., D. O., and S. S.) based on their clinical expertise in

TABLE 1] PICO Questions

Question No.	Population	Intervention	Comparator	Outcome
PICO 1	Patients with suspected or confirmed COVID-19 infections undergoing bronchoscopy	Wearing PAPR	Wearing N95 and face shield	Protection of health-care workers
PICO 2	Patients suspected of having COVID-19 infections	BAL	Nasopharyngeal oropharyngeal swabs, tracheal aspirate	Diagnosis of COVID-19 infection, protection of health-care workers
PICO 3	Asymptomatic patients presenting for bronchoscopy in an area where community person-to-person transmission has occurred	Wearing N95 masks and face shield	Wearing surgical masks and face shield	Protection of health-care workers
PICO 4	Asymptomatic patients presenting for bronchoscopy in an area where community person-to-person transmission has occurred	Testing for COVID-19 infection	No testing	Protection of health-care workers
PICO 5	Patients with high suspicion of lung cancer diagnosis	Delay of bronchoscopy by 2, 4, or 8 wk	No delay (performed within 1 wk of abnormal imaging)	Survival of lung cancer
PICO 6	Patients who have recovered from COVID-19 infection	Performing bronchoscopy 4 or 8 wk from diagnosis of COVID-19 infection	Performing bronchoscopy 14 d from diagnosis of COVID-19 infection	Protection of health-care workers, benefits to the patients

COVID-19 = coronavirus disease 2019; PAPR = powered air purifying respirator; PICO = Population, Intervention, Comparator, and Outcome.

bronchoscopy and interventional pulmonology. Advisory panel members consisted of infectious disease experts (M. P. S. and D. A. C.), critical care medicine experts (D. R. O. and C. L.), an interventional pulmonology trainee (K. G.), a pulmonary and critical care trainee (K. P.), and a respiratory therapist (D. D. G.) nominated and selected by both organizations. All panel members received individual education regarding the process and schedule, followed by conflict of interest disclosure and evaluation by cochairs.

Guideline creation schedule was developed by cochairs. Given the time-sensitive nature of the topic amid on-going COVID-19 pandemic, the schedule spanned over a period of 3 weeks and included 10 conference calls including topic and question development, literature search, literature evaluation using Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology, discussion, modified Delphi surveys, and statement development.

Question Development and Systematic Search

Cochairs and core panelists discussed and developed the primary questions in the Population, Intervention, Comparator, and Outcome (PICO) format during the first conference call. Six PICO questions were developed and assigned to each core panelist for literature review (Table 1).

To identify relevant evidence, the panel members conducted a comprehensive search using MEDLINE via PubMed followed by manual search related to each a priori developed PICO question. Search strategy, evidence table, and details of search results depicted in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram for each PICO question are available in e-Appendix 1.

Studies were excluded if they were not available in English or if they were single case reports. Expert reviews, opinions, and statements were not included, but their references were reviewed to search for additional evidence.

Study Selection and Evidence Assessment

Each panel member screened their respective search results to exclude duplicates, followed by title and abstract screen, excluding literature based on a priori established exclusion criteria. All remaining text was reviewed and direct and indirect evidence was selected and presented in evidence tables for final review and core panel discussion. With the exception of one single-center retrospective observational study related to PICO question 2,[5] and 13 studies related to PICO question 5,[6-18] no other direct evidence was identified. Evidence was graded by the methodology team using the standard GRADE quality assessment tool categorized as high, moderate, low, or very low.[19,20] With exception of PICO question 5, none of the available direct and indirect literature provided sufficient evidence for the development of recommendations. Expert opinion instead was sought to answer these PICO questions in form of suggestions in place of recommendations. Suggestions were developed based on the use of a modified Delphi process.

Method for Achieving Consensus

Search results were shared and discussed among members during a conference call with 100% participation. Evidence graded by the methodology team and summary of evidence and suggestions written by respective panel members for each PICO question were disclosed to all panel members including the advisory panel. During the conference call, suggestions were reviewed and rewritten in real time per adjustment and suggestions from the panel. This was followed by another conference call with 100% participation, soliciting additional comments and input from the advisory panel. All panel members participated in the development of suggestions to be incorporated in the initial round of the modified Delphi survey.

The modified Delphi technique is a widely accepted method for the development of consensus among experts.[21-23] To achieve consensus, a priori decision was made to conduct up to three rounds of anonymous voting or until consensus was achieved (defined a priori as consensus agreement at ≥ 80% with a minimal response rate of 80%) for each PICO question, whichever came first. To maintain complete transparency and limit bias from interaction among members, additional discussions outside of the scheduled meetings before voting were discouraged. The survey incorporated the suggestions made by all panelists and was developed and reviewed by chairs and methodologists and sent to all panel members by a CHEST-designated project coordinator. The project coordinator tallied and reported the results of the survey to the group, and all votes were anonymous. The results of the survey were discussed with all panel members including the advisory panel on the same day during a group discussion. There was 100% survey participation from the members and consensus was achieved on four PICO questions. After discussion and revision of statements, a second round of surveys was distributed, including three questions (two questions did not achieve consensus and one question required rewriting based on panel recommendation). There was 100% survey participation and agreement on all three PICO questions from the second survey.

Results

1. When patients with suspected or confirmed COVID-19 infection are undergoing bronchoscopy, we suggest that health care workers in the procedure and recovery rooms use either an N-95 respirator or a powered air purifying respirator (Ungraded Consensus-Based Statement).

Remarks:

- In addition, health care workers should wear personal protection equipment including face shield, gown and gloves.
- N-95 respirators should be discarded after bronchoscopy.

COVID-19 is caused by SARS-CoV-2 and currently understood to be transmitted from person-to-person via droplets, contact, and fomites, largely based on prior epidemiologic data from the previous coronavirus outbreaks.[24] Accordingly, the World Health Organization and the CDC have made recommendations for HCWs and individuals to maintain a 1-m (3-ft) or 2-m (6-ft) distance, respectively, from patients suspected of being infected.[25,26] Routinely performed AGPs such as bronchoscopy have however been associated with infection of HCWs despite droplet and contact precautions, prompting the CDC and many scientific societies to recommend airborne precautions in these circumstances.[4,25,27] Although data specific to SARS-CoV-2 are lacking, a systematic review reported ORs for transmission of SARS-CoV-2 to HCWs of 6.6 (95% CI, 2.3-18.9), 4.2 (95% CI, 1.5-11.5), and 1.9 (95% CI, 0.2-14.2) for endotracheal intubation, tracheostomy, and bronchoscopy, respectively; however, the association with bronchoscopy did not reach statistical significance.[28] One study demonstrated that SARS-CoV-2 could remain aerosolized for up to 3 h in experimental conditions.[29] The CDC currently recommends the use of either powered air purifying respirators (PAPRs) with contact precautions or N95 respirators based enhanced respiratory and contact precautions (including eye protection) as comparable strategies for protection of HCWs during AGPs such as bronchoscopy.[30]

Our systematic review did not identify any study directly comparing these two interventions, either in the context of SARS-CoV-2 or other pathogens associated with a risk of aerosolization during bronchoscopy. A theoretical benefit of PAPRs over N95 respirators is a higher assigned protection factor, as defined by the minimum factor by which exposure is reduced, which ranges from 25 to 1,000 for PAPRs vs 10 for N95 respirators (higher number representing higher filtration efficiency).[31] Accordingly, during the 2009 influenza pandemic, the CDC, Occupational Safety and Health Administration, and Institute of Medicine suggested the use of PAPRs over other precautions during AGPs.[32] In addition, PAPRs do not require prior fit testing (which even when performed appropriately does not guarantee consistent face seal), are more comfortable, are reusable (a potential benefit in times of scarce resources), and do not require an additional face shield.[32] N95 respirators, conversely, do not afford protection unless a tight seal is maintained throughout the procedure and may be uncomfortable because of resistance of airflow and CO_2 rebreathing.[33,34] The reusability of PAPRs may however carry significant risks of contamination if donning and doffing and decontamination procedures are not strictly followed. Errors in don and doff procedures may be more common with PAPRs, exposing HCWs and patients to possible contamination.[35] Other potential downsides of PAPRs include availability, upfront investment, storage issues, maintenance (high-efficiency particulate filter and battery), training issues, and possibly movement limitations which may interfere with highly technical procedures.[32] Although the higher assigned protection factor of PAPRs provides increased protections, these practical considerations do not allow firm conclusions favoring one intervention over the other.

One major characteristic of the COVID-19 pandemic has been the shortage of personal protective equipment (PPE) for HCWs, specifically regarding face masks and N95 respirators. The CDC suggested that the extended N95 respirator use (same N95 respirator used for consecutive patients) and reuse (N95 respirator donned and doffed multiple times) for 8 h (continuous or intermittent) may be acceptable under specific conditions provided (1) the respirator is not damaged, hard to breathe through, or contaminated; (2) the respirator is discarded after close interaction with patients under contact precautions or after AGPs; and (3) appropriate handwashing is performed before and after touching or adjusting the respirator. We agree with these recommendations and suggest that N95 respirator be discarded after bronchoscopy.

2. In patients suspected of having COVID-19 infection, we suggest that a nasopharyngeal specimen be obtained first. In the setting of severe or progressive disease requiring intubation, if additional specimen is needed to establish a diagnosis of COVID-19 or other diagnoses that will change clinical management, lower respiratory specimens from endotracheal aspirate or bronchoscopy with BAL can be performed (Ungraded Consensus-Based Statement).

Remarks: More research is needed to further compare diagnostic sensitivity for COVID-19 infection utilizing other less invasive lower respiratory specimen collection techniques such as blinded bronchial sampling, blinded protected brush and non-bronchoscopic mini-BAL.

The optimal test to detect COVID-19 infection centers around a balance of the availability of the test, timeliness of result, diagnostic yield, and invasiveness of sampling, while minimizing the risk of disease transmission to HCWs. To generate guidance for best practice in the diagnostic assessment for COVID-19 infection, it is reasonable to use available data from prior recommendations on similar infections such as Middle East respiratory syndrome coronavirus and influenza A (H1N1) coupled with known assessment of the risk of AGPs.[28,36] Data was published on 1,070 specimens from 205 patients with COVID-19 infections, described as having a spectrum of severity of symptoms from mild fever, dry cough, and fatigue to more severe respiratory symptoms, who underwent a variety of specimen collections from different sites; however, the severity of illness was not distinguished relative to the sites sampled and the number of some sampled sites was small. The specimen sites were described and confirmed with real-time reverse transcription-polymerase chain reaction (rRT-PCR) testing for COVID-19 infections, identifying positive rates in 14 of 15 (93%) of BAL specimens, 72 of 104 (72%) of sputum samples, five of eight (63%) of nasal swabs, six of 13 (46%) of bronchoscopic brush samples, 126 of 398 (32%) of pharyngeal swabs, 44 of 153 (29%) of feces samples, three of 307 (1%) of blood samples, and zero of 72 (0%) of urine samples.[5] Given sample size, the true sensitivity for each site is not fully known in this setting.[5] The World Health Organization[37] online guidelines for COVID-19 suggest that endotracheal aspirate or bronchoscopy with BAL be considered if a single upper respiratory specimen is negative and there is clinical concern because of severe or progressive disease.

When reviewing the literature for comparisons of various techniques for respiratory specimens and distinguishing upper and lower respiratory tract specimens, there are limited data assessing diagnostic yield in bacterial pathogens and none specifically for viruses or SAR-CoV-2. The literature on ventilator-associated pneumonia described multiple sampling methods to detect pathogens including endotracheal aspirate, blinded bronchial sampling, blinded protected brush, nonbronchoscopic mini-BAL, and bronchoscopic BAL.[38-40] When these particular sampling modalities were reviewed and compared with endotracheal aspirates in that setting, the data did not suggest superiority of a specific technique performed nonbronchoscopically and cited high variability and inconsistency in standardization of technique.

Beyond actual specimen collection, it will be important to follow safety procedures for transport and processing of the specimens in the laboratory setting. Lower respiratory specimen testing and handling for COVID-19 is different than upper respiratory specimen testing and may require expert laboratory facilities and therefore longer turnaround times.[41]

We determined that because bronchoscopy is an AGP, minimizing risk of transmission of infection to HCWs should be considered and less invasive modalities of establishing the diagnosis of COVID-19 should be used first. The role of lower respiratory specimens via endotracheal aspirate or bronchoscopy can be considered in the setting of severe progressive disease after negative upper respiratory specimens or when considering an alternative diagnosis which may lead to a change in clinical management.

3. When asymptomatic patients present for bronchoscopy in an area where community spread of COVID-19 is present, we suggest that health care workers in the procedure room wear N-95 respirators or powered air-purifying respirators (PAPR) as opposed to surgical masks (Ungraded Consensus-Based Statement).

Remarks: In addition, health care workers should wear personal protection equipment including face shield, gown and gloves.

In a major pandemic like the one we are experiencing with COVID-19, a guiding principle of health-care delivery is full protection of HCWs to preserve the workforce able to care for sick patients. The SARS-CoV-2 virus presents a major challenge because people can carry the virus but remain asymptomatic, and therefore, can transmit the infection to fellow humans and HCWs while seemingly appearing healthy.[42,43]

A mathematical model, that simulated the spatiotemporal dynamics of COVID-19 infections among 375 Chinese cities prior to travel restrictions, showed that undocumented infections were the infection source for 79% of documented infections.[44] A small study of 24 asymptomatic infected patients from China found that the median communicable period, defined as the interval from the first day of positive nucleic acid tests to the first day of continuous negative tests, was 9.5 days (up to 21 days).[45]

Another study evaluated 468 COVID-19 transmission events that were reported in mainland China outside of Hubei Province and estimated presymptomatic transmission of the infection at 12.6%.[46]

Asymptomatic communication of infection becomes a major concern when community transmission is confirmed in a geographic area. This is particularly concerning to HCWs performing open airway procedure such as bronchoscopy in such a community.

We sought to determine whether HCWs should don N95 respirators or surgical masks during bronchoscopy performed on asymptomatic patients and found only one study related to COVID-19 infections. Wang et al[47] retrospectively evaluated the infection rate among HCWs in a Chinese hospital in two different groups: the first group was comprised of staff at high-risk units (respiratory, infectious disease, and ICU wards) who wore N95 respirators and cleaned hands frequently, whereas the second group included staff in other less-risky wards who did not wear surgical masks and washed their hands occasionally. Despite a higher exposure to patients with COVID-19 infection, none of the 278 staff (56 doctors and 222 nurses) in the N95 respirator group became infected, whereas 10 of 213 staff (77 doctors and 136 nurses) from the no-mask group were confirmed as infected. The study did not speculate as to whether the protection of HCWs in the N95 respirator group was solely because of wearing the mask or aided by the frequent handwashing strategy.

A meta-analysis conducted in 2020 showed that the use of N95 respirators compared with surgical masks was not associated with a lower rate of transmission of influenza.[48] Another recent systematic review and meta-analysis found low certainty evidence suggesting that surgical masks and N95 respirators offer similar protection against viral respiratory infection during nonaerosol generating care. However, the study recommended use of N95 respirators for high-risk AGPs such as bronchoscopy.[49]

The panel reached consensus favoring wearing N95 respirators vs surgical masks based on the weak evidence that originated from China supporting the superior protection of N95 respirators over surgical masks against COVID-19 infections and the serious consequences of exposing HCWs to asymptomatic patients carrying the COVID-19 infection.

4. Prior to performing bronchoscopy in asymptomatic patients in an area where community transmission of COVID-19 infection is present, we suggest testing for COVID-19 infection (Ungraded Consensus-Based Statement).

Remarks:

- This strategy is contingent on the availability of testing in the local setting.
- In all patient with negative results, we suggest that the procedure be performed using personal protection equipment including face shield, gown, gloves and N-95 respirators or powered air purifying respirators (PAPR).
- When test results are positive prior to bronchoscopy, we suggest postponing all non-emergent bronchoscopies.
- In patients who require emergent bronchoscopy with either a known positive SARS-CoV-2 test results or unknown infection status due to inability to test emergently, we suggest using personal protection equipment including face shield, gown, gloves and

N-95 respirators or powered air purifying respirators (PAPR) in pre, intra, and post bronchoscopy settings as would be with every SARS-CoV-2 positive patient.

Our comprehensive literature search showed no direct evidence comparing COVID-19 testing vs no testing prior to bronchoscopy in any population, including asymptomatic patients. Examination of the existing indirect evidence shows that effect estimates of asymptomatic disease proportion in the population and infection transmission rates are limited by population heterogeneity, small sample size, selection bias because most asymptomatic patients may never seek medical attention to undergo testing, and lack of adjustment for other covariates; all of this results in significant imprecision in effect estimates.

The diagnosis of SARS-CoV-2 is based on viral RNA detection using rRT-PCR tests. Multiple molecular assays are available and new assays are being developed around the world.[50,51] Debates about the efficiency, sensitivity, and availability of the tests have been ongoing, both within and outside the United States. The Food and Drug Administration has granted emergency use authorization to > 20 commercial COVID-19 diagnostic tests and assays. Different rRT-PCR tests' sensitivities are reported in the literature ranging from 59% to 97%.[52,53]

Interpretation of negative test results becomes even harder in an asymptomatic patient without suspicion of disease. Numerous potential preanalytical and analytical deficiencies exist in the diagnosis of COVID-19 infection ranging from inadequate procedures for specimen collection and handling, sample contamination, inadequately validated assays, and misinterpretation of expression profiles as noted by Lippi et al.[41] Ongoing refinement of molecular targets and validation of rRT-PCR assays are underway.

Although direct evidence regarding the utility of COVID-19 testing prior to bronchoscopy does not exist, review of the existing literature supports the presence of patients with asymptomatic COVID-19 in the community. Some but not all asymptomatic patients may be identified through testing. However, a proportion of these asymptomatic patients may have false-negative results. During a pandemic crisis and when dealing with highly contagious infections, there are numerous factors that play a role in every response. The decision to use a test relies on more than just test sensitivity and specificity. Some of the other factors that play a significant role are the magnitude of harm that comes from lack of infection detection, potential actionable items once infection is identified, and overall loss and cost to the public at large, should an infected individual go unrecognized. In the case of COVID-19 infection, a major consideration is the prevalence of asymptomatic disease. When asymptomatic disease is rare, the need for extensive workup and testing may be unnecessary, and harm may outweigh the benefit.

If a patient with asymptomatic COVID-19 who is in need of urgent bronchoscopy is tested positive, postponing the bronchoscopy may protect HCWs who would have come in contact with the patient. This in turn can reduce the chance of infection transmission to vulnerable patients by asymptomatic HCWs during the incubation period. Additionally, patients who would come in contact with a patient with asymptomatic COVID-19 during the postbronchoscopy recovery period are spared. Inevitably, some asymptomatic patients may be missed on a false-negative test and undergo bronchoscopy. However, given all elective and semielective bronchoscopies are avoided, and some asymptomatic patients are detected on testing, the number of infected individuals who would not be detected can be significantly diminished, decreasing the frequency of harm. This highlights the importance of testing as a tool for risk reduction and not risk elimination.

Assuming an ideal scenario with abundant availability of resources, performing tests prior to every bronchoscopy in an asymptomatic patient in the era of COVID-19 pandemic mitigates risks to HCWs and patients. We fully realize that test availability may be limited even for symptomatic patients and therefore this strategy may not be feasible in highly endemic areas. An equally important approach in these settings is to limit the number of bronchoscopy procedures performed and postpone most of them unless absolutely necessary. Table 2 provides general guidance to bronchoscopists on procedure urgency.

Acknowledging the possibility of false negative results, necessary respiratory protection and appropriate PPE should be used to prevent transmission of disease during bronchoscopy, on asymptomatic patients who were not detected on testing.

5. **When bronchoscopy is indicated to diagnose, stage, or characterize a known or suspected lung cancer in an area where community transmission of COVID-19 is present, we suggest that bronchoscopy be performed in a timely and safe manner** (Grade 2C).

Remarks:

- Strategies to perform bronchoscopy in timely manner should be developed locally, taking into account local resource availability, including availability of personal protective equipment, availability of COVID-19 testing, and availability of downstream resources required for treatment (eg, surgery requires ICU beds and ventilators).
- Regional availability of diagnostic and therapeutic interventions for cancer patients should be considered. In particularly resource-depleted hospitals, COVID-19 negative cancer patients should be referred to other centers, preserving resources for COVID-19 patients and facilitating safe, timely, and effective care for the cancer patient as well.
- Although efforts should be made to provide timely care, these should be balanced by the need to attend to other dimensions of quality, including safety, effectiveness, and consistency with patient values and preferences.

The Institute of Medicine has identified timeliness as one of the six dimensions of health-care quality. For lung cancer, delays in care may lead to missed opportunities for cure or palliation and emotional distress. The CHEST Evidence-Based Guidelines and the British Thoracic Society and the National Cancer Network all address timeliness of care to varying degrees, but they vary somewhat in the details and definitions of what constitutes timely care. Bronchoscopy is an integral part of lung cancer care because it is often required for diagnosis and staging, which in turn determines treatment. Timeliness of bronchoscopic diagnosis impacts everything that occurs downstream from it. Indeed, guideline consistent care with bronchoscopic endobronchial ultrasound for staging and diagnosis as the first test in patients with T1-3, N1-3, M0 disease has been shown to decreases complications, decrease number of tests required, and decrease time to treatment.[54]

However, in the context of the COVID-19 epidemic, there is a compelling need to consider the efficient allocation of constrained resources. Balancing the need to deliver high-quality cancer care and the public health and resource allocation needs associated with the COVID-19 pandemic requires careful consideration of where resources can be deployed for the most benefit. In the context of the COVID-19 pandemic, the question is whether it is reasonable to forego or delay bronchoscopy of patients with known or suspected lung cancer, and if so for how long?

The answer to this question is highly context dependent and will of course vary depending on the presentation of the patient. In addition, optimal diagnostic and staging strategies are contingent on the benefits and harms of the available treatments.[55] The availability of different

TABLE 2] Urgency of Bronchoscopy Procedures

Emergent Bronchoscopy	Urgent Bronchoscopy	Nonurgent Bronchoscopy
Severe or moderate symptomatic tracheal or bronchial stenosis	Lung mass suspicious of cancer	Mild tracheal or bronchial stenosis
Symptomatic central airway obstruction (endotracheal or endobronchial mass or mucus plug)	Mediastinal or hilar adenopathy suspicious of cancer	Clearance of mucus
Massive hemoptysis	Whole lung lavage	High suspicion of sarcoidosis with no immediate need to start therapy
Migrated stent	Foreign object aspiration	Chronic interstitial lung disease
	Mild to moderate hemoptysis	Detection of chronic infection mycobacterial
	Suspected pulmonary infection in patients who are immunocompromised	Bronchoscopic lung volume reduction
		Bronchial thermoplasty
		Chronic cough
		Tracheobronchomalacia evaluation

treatment modalities during the COVID-19 pandemic also needs to be considered because some treatment alternatives, such as lobectomy for cure, may consume resources that are particularly scarce (eg, ventilators).

A complete quantitative analysis of every possible scenario according to resources availability and stage of disease is beyond the scope of this guideline. We instead focus on a more general question: What is the impact of delays in care on lung cancer survival? The goal is to summarize the available evidence to arrive at a more nuanced understanding of how timeliness of care impacts lung cancer outcomes. This information can in turn be used to inform decision-making at the local level as to how best to allocate available health-care resources.

To summarize the evidence of the impact of timeliness of care on lung cancer outcomes, we used the third edition of the CHEST evidence-based lung cancer guidelines.[56] A supplemental literature review identified 13 additional references.[6-18] The methodology of the studies, the definitions used, and the evidence quality precluded arriving at a point estimate of the effect of time delay on outcomes. Issues included varying definitions of when cancer was first identified (eg, symptoms vs imaging vs tissue diagnosis), which interval was relevant (eg, symptoms to treatment vs diagnosis to treatment), heterogeneity in populations (eg, surgically treated vs all patients with lung cancer), differences in histology (eg, all types vs non-small cell lung cancer), intractable problems because of residual confounding within groups, confounding by indication (eg, sicker patients seen more rapidly), selection bias, and failure to adjust for lead time bias (eg, measuring survival from time of treatment rather than time of presentation). We therefore have provided evidence tables with the new studies identified, with additional methodology comments (e-Appendix 2, 3).[6-18,57-61]

The available evidence is often conflicting regarding the relationship between timeliness of care and outcome.[7,13,17] Paradoxically, multiple studies reported that more timely care was associated with worse outcomes.[6,7,9,12,13] Two studies found evidence that the impact of timeliness of care on survival varies based on lung cancer stage.[6,8] Timely care was associated with improved survival in local and stage II disease. Conversely, in patients with metastatic disease, timely care was associated with decreased survival. These findings explain the paradoxical and contradictory results of earlier studies. In early stage disease, medical emergencies are less common, and there is likely to be less confounding by indication. In late stage disease, confounding by indication plays a role (e-Appendix 2). On balance, the available data suggest that although we cannot precisely quantify the impact of delays in care, it is probable that delays have a greater impact early in the disease process.[6,12,17] More timely care is likely to have the greatest benefit in patients with stage IA2, IA3, IB, IIA, and IIB disease.

When resources for cancer care are constrained because of COVID-19, the first step is to take an inventory of what treatments and diagnostic modalities are available for cancer care. In hospitals most burdened by COVID-19, surgery will not be an option; therefore, collaboration with outside centers and referral may be best. Inventory should not be just at the local hospital level, but rather hospitals should share information regarding availability of resources regionally, such as ICU beds, ventilators, and types of services still available for cancer care. If there is no availability because of the absence of resources at one hospital, then referral to outside centers is warranted. In areas with the highest rates of COVID-19, referral of COVID-19-negative patients with cancer to other centers will be a good strategy. This requires coordination between centers, hence the emphasis on taking inventory at both the hospital and regional level. Cancer centers that are physically separate from general hospitals with separate teams would be able to serve this purpose well. This has some appeal because it would keep vulnerable patients with cancer out of hospitals with a high rate of COVID-19, freeing up resources for patients with COVID-19. It would also create a sort of reverse quarantine, where care for COVID-19-negative patients with cancer would be delivered.

Finally, although there is limited evidence of the benefit of timeliness of care, there is evidence that guideline consistent care leads to better outcomes.[13,54,62] In a study of 1,924 elderly patients, Nadpara et al[13] found no association between survival outcomes and timeliness of care but did find an association with guideline consistent care. Hence, the emphasis should still be on appropriate evidence-based guideline consistent care. Regional information sharing and collaboration between centers with appropriate referral to optimize resource utilization is probably the single most important intervention that can help minimize delays in cancer care while optimizing resource allocation. This will help to protect COVID-19-negative patients with cancer from becoming infected and will maximize resources for patients with COVID-19.

6. In patients with confirmed COVID-19 infection who recover and need a routine bronchoscopy, we suggest the timing of the procedure is customized based on the indication for the procedure, the severity of the COVID-19 infection and time from symptom resolution (Ungraded Consensus-Based Statement).

Remarks: The exact time to perform bronchoscopy is still unknown. It would be reasonable to wait at least 30 days from resolution of symptoms with negative SARS-CoV-2 RNA tests from at least two consecutive nasopharyngeal swab specimens collected ≥24 hours apart. Further research is needed to better understand optimal timing of bronchoscopy performance relative to symptom resolution.

Patients who have confirmed COVID-19 infection continue to shed the virus from the respiratory tract for a variable period of time after resolution of symptoms.[63-67] We sought to determine the period of time after which patients who have recovered from a confirmed COVID-19 infection are no longer considered contagious and routine bronchoscopy can be performed safely without exposing HCWs to the risk of contracting the infection.

Our systematic review did not identify any study addressing time to performance of procedures in the setting of SARS-CoV-2 infection. Viral shedding in patients with COVID-19 infection varies depending on disease severity. Patients who had mild illness tend to shed the virus from the respiratory tract for a shorter period compared with those with more severe disease. Additionally, patients with mild disease tend to have an earlier viral clearance than those with severe disease. In one study, rRT-PCR test was negative in 90% of patients with mild disease by day 10 from onset of symptoms, whereas severe cases tested positive beyond day 10.[63] In another study, viral RNA was detected > 20 days from onset of symptoms.[64]

Other studies on patients with COVID-19 infections noted that rRT-PCR was positive from the respiratory tract up to 37 days from onset of symptoms and for an even longer duration in stool samples than throat swabs.[65,66] In a study comparing sputum samples with pharyngeal swabs, sputum rRT-PCR reported positive up to 39 days after pharyngeal swabs turned negative in patients with COVID-19; the duration was longer in patients who received steroids.[67]

Complicating the extended viral shedding is the performance of the rRT-PCR test because it has been shown to be false negative both in the early part of the infection and after resolution of symptoms when viral shedding may be below the threshold of detection for the test.[41]

The CDC[68] has guidance on discontinuation of transmission-based precautions using both a test-based and a non-test-based strategy. This guidance does not extend to procedure timing, but it does favor a test-based strategy in patients with severe illness, immunocompromised state, and those being transferred to long-term or assisted living facilities.

This panel reached a consensus that the timing of nonurgent bronchoscopy in patients who have recovered from COVID-19 infection will need to be individualized based on disease severity, duration of illness, and a negative SARS-CoV-2 RNA test from at least two consecutive nasopharyngeal swab specimens collected ≥ 24 h apart (total of two negative specimens). The exact time to perform bronchoscopy is still unknown, but it would be reasonable to wait at least 30 days from resolution of symptoms. Further research is needed to validate this suggested waiting period.

Discussion and Summary

The recommendation and suggestions outlined in this document were specifically created to address what were thought to be clinically common and urgent questions that frontline physicians are likely to face. We focused mainly on questions related to bronchoscopy as an AGP, but it is important to note that the primary mode of transmission for COVID-19 infection is droplets. Therefore, contact precautions (face shield, mask, gown, and gloves) are the integral components of PPE strategy to prevent the transmission of this disease, and N-95 respirators or PAPRs represent additional precautions during AGPs such as bronchoscopy.

We would like to stress that these protective strategies can be rendered completely ineffective if proper training on donning and doffing is not provided to HCWs. Proper personnel instruction and practice for wearing PPE should receive as much attention by health facilities as the chosen strategy for protection.

There are three important limitations that need to be kept in mind. The first is the overall paucity of robust and direct evidence to inform the guidance. Although this is not entirely surprising for a disease process that is brand new to humanity, it underscores the importance of multiinstitutional and multinational collaboration in

collating and rapidly disseminating clinical experiences and outcomes data under these unique circumstances. Specialty societies can play an enormously helpful role in such efforts and may be able to leverage their various networks for this, and future, novel pandemics. Second, because of the urgency of the situation, there may have been important questions that were unavoidably omitted in this particular statement. Information needs to be available at the speed of relevance and sometimes this results in a less comprehensive package. Finally, although all direct and indirect evidence was discussed with all panelists, literature search for every PICO question was performed by one panelist without an independent parallel search by a second panel member. This was unavoidable because of the limited time allotted for this effort and the desire to rapidly disseminate useful information to frontline physicians.

The strengths of this document are the multidisciplinary panel that was composed of experienced bronchoscopists and interventional pulmonologists, infectious disease specialists, intensivists, respiratory therapists, and trainees and the robust methodology to formulate specific questions, evaluate the literature with validated tools, and seek consensus while minimizing groupthink.

Physicians searching for evidence on bronchoscopy during this challenging time of the COVID-19 pandemic should use this document as general guidance and adapt it to their local situation. This statement should be envisioned as a living document that should be updated in the future as new evidence undoubtedly comes to light.

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Additional information: The e-Appendixes can be found in the Supplemental Materials section of the online article.

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