Utility and safety of bronchoscopy during SARS-CoV-2 outbreak in Italy: a retrospective, multicenter study

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Title: Utility and safety of bronchoscopy during SARS-CoV-2 outbreak in Italy. A retrospective, multicenter study

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Take home message: utility and safety of bronchoscopy during SARS-CoV-2 outbreak
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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the related disease (coronavirus disease – 2019, COVID-19) has been notified throughout Italy since February 2020. Intensive care unit (ICU) admission rate increased following the high incidence of pneumonia-related respiratory failure [1].

The diagnosis of pneumonia relies on viral detection in respiratory samples and on the assessment of abnormal findings on chest X-ray, ultrasounds, and computed tomography (CT) [2-5].

Viral diagnosis based on naso/oropharyngeal swabs shows suboptimal accuracy (sensitivity: 32-63%), owing to wrong handling of the specimen, sample collection during the late phase of the disease or low viral load [5-7].

Bronchoscopy increases the sensitivity of the molecular diagnosis in comparison with that associated with nasopharyngeal swabs [6]. Furthermore, endoscopic techniques may be useful to manage serious pulmonary disorders (e.g., obstructive atelectasis, severe hemoptysis) [8-12].

However, bronchoscopy generates aerosol and may increase the risk of SARS-CoV-2 transmission [8-9,12].

Limited data are available in the scientific literature on the role of bronchoscopy in cases of SARS-CoV-2 pneumonia [6-12].

The primary aim of the present study was to describe the diagnostic yield of bronchoscopy in patients with negative nasopharyngeal swab(s) and a clinical and radiological suspicion of COVID-19 pneumonia.

Indications of bronchoscopy in cases of confirmed COVID-19 patients and the assessment of the safety of bronchoscopy for healthcare workers (HCWs) were also evaluated.

An observational, retrospective, multicenter cohort study was carried out in Italy. The study protocol was approved by the ethical committees of the participating hospitals. A written informed consent was signed by recruited patients.
Adult patients who underwent bronchoscopy between 1st March 2020 and 15th April 2020 were consecutively recruited in six Italian hospitals. The indications of bronchoscopy were: -diagnosis of SARS-CoV-2 pneumonia in patients with previously negative nasopharyngeal swab (clinical and radiological suspicion of pneumonia); -need for undelayable procedures in COVID-19 patients (e.g., massive hemoptysis, post-obstructive atelectasis).

All bronchoscopies were performed according to the WHO guidelines: the number of persons in the room was decreased to achieve a size appropriate to the provision of adequate care and support (i.e., one physician and one nurse wearing FFP3 masks) [13].

The diagnosis of COVID-19 was confirmed when molecular (i.e., real time PCR) results detected SARS-CoV-2 in any respiratory sample [4,5]. The probability of COVID-19 was high in case of a negative PCR and COVID-19-related symptoms (i.e., fever, cough, fatigue, and/or shortness of breath), CT signs (i.e., ground-glass opacity, consolidation, reticulation/thickened interlobular septa, air bronchogram sign), with rapid clinical changes (progression or improvement in a short time period) [4,7].

The diagnostic yield of bronchoscopy was calculated dividing the number of patients with a molecular diagnosis of SARS-CoV-2 infection following the collection of bronchoscopic specimens by the number of patients with a suspected diagnosis of COVID-19 pneumonia.

Every HCW was carefully monitored for symptoms and clinical signs suggestive for COVID-19 for at least 15 days after the procedure.

An ad hoc electronic form was adopted to collect all study variables. Qualitative and quantitative variables were summarized with absolute (relative) frequencies and means (standard deviations, SD), respectively. The statistical software STATA version 16 (StatsCorp, Texas, USA) was used to perform all statistical computations.

A total of 109 adult patients (71% males; mean (SD) age: 60.0 (13.6) years) were enrolled.

108 (99.1%) bronchoscopies were performed with a flexible bronchoscope, 1 (0.01%) with the rigid scope. 13 (11.9%) bronchoscopies were performed while patients were breathing room air, 82 (75.3%)
during O\textsubscript{2} supplementation, 3 (2.7\%) during non-invasive mechanical ventilation, 9 (8.2\%) during invasive mechanical ventilation, 2 (1.8\%) during extracorporeal membrane oxygenation (ECMO).

In 78/109 (71.6\%) cases bronchoscopy was performed to diagnose SARS-CoV-2 infection in patients with a negative nasopharyngeal swab (median of negative swabs per patient: 2) and a clinical and radiological suspicion of COVID-19 pneumonia. Urgent/life-saving bronchoscopies were performed in 31/109 (28.4\%) patients with a confirmed diagnosis of COVID-19. The clinical indications were suspected concomitant lower respiratory tract infections or pulmonary tuberculosis, obstructive atelectasis, suspected tracheal intubation-related complication (i.e., tracheal laceration), tracheostomy complications, and severe hemoptysis.

The diagnostic yield of bronchoscopy to detect SARS-CoV-2 in patients with previous negative swabs and a clinical and radiological suspicion of COVID-19 pneumonia was 55.1\% (43/78). No differences were found between bronchoalveolar lavage (BAL) and bronchial washing (BW) (35/61, 57.4\%, and 8/17, 47.1\%, respectively; p-value: 0.45) (Figure 1).

2/109 (1.8\%) patients with previous negativity of both nasopharyngeal swabs and BAL for SARS-CoV-2 showed subsequent positive swabs. Hence, 45/78 (57.7\%) patients had a definite diagnosis of COVID-19 pneumonia.

The diagnosis of SARS-CoV-2 pneumonia was considered highly likely in 18/78 (23.1\%) patients, whereas 15/78 (19.2\%) were diagnosed with a lower respiratory tract infection.

One patient was co-infected by *Haemophilus influenzae* and SARS-CoV-2, one patient by *Aspergillus fumigatus* and SARS-CoV-2. In two patients, *Aspergillus spp.*, *Candida albicans* and SARS-CoV-2 were concomitantly found in the same BAL sample.

Complications related to bronchoscopy occurred in 5/109 (4.5\%) patients. Fever was recorded after BAL in 2/109 (1.8\%), 3/109 (2.7\%) patients with a known mild respiratory failure had a transient worsening of their gas exchange after bronchoscopy performed during oxygen supplementation. No deaths were recorded.
Infections related to the endoscopic procedure did not occur in HCWs involved in the endoscopic activities.

This is to our knowledge the largest study on the diagnostic yield of bronchoscopy in patients with negative nasopharyngeal swabs and a clinical/radiological suspicion of SARS-CoV-2 infection. An etiological diagnosis is crucial to prevent viral transmission to susceptible individuals and decrease clinical complications in infected patients [1,2]. Prompt respiratory isolation is needed to hamper the viral spread, whereas an early diagnosis of COVID-19 related complications (i.e., respiratory failure) is crucial for a good prognosis [1,2].

Our findings show that bronchoscopy might be useful in patients with suspected COVID-19 pneumonia and negative swabs, with an acceptable diagnostic performance of BAL and BW.

A recent study found a 71% detection rate of SARS-CoV-2 in 28 patients who underwent bronchoscopy in China, with 93% of positive PCR results in BAL samples [6].

Our study shows a lower diagnostic yield but we performed a bronchoscopy only in patients with two previous negative swabs [6].

Despite bronchoscopy has been relatively contraindicated during the COVID-19 pandemic, endoscopic procedures may not be postponed in some patient categories [11].

Urgent/life-saving bronchoscopies were performed in 31 patients with a confirmed COVID-19 diagnosis for obstructive atelectasis, suspected concomitant lower respiratory tract infections, severe hemoptysis, suspected tracheal lacerations in patients mechanically ventilated, tracheostomy complications, and suspected concomitant pulmonary tuberculosis. Similar findings were recently described by Torrego et al. in a Spanish cohort of COVID-19 patients who underwent bronchoscopy in ICU [12].

Few data are available on bacterial and fungal co-infections with SARS-CoV-2 [14]. Lower respiratory tract co-infections were diagnosed with BAL in 4 patients. Prompt identification of co-infecting microorganisms is associated with an early prescription of antibiotics [14].
Few bronchoscopy-related complications were recorded, with fever and mild respiratory failure being the most frequent.

The above-mentioned side effects can occur following a bronchoscopic procedure, in line with the scientific evidence published before the pandemic [15,16]. Neither severe complications nor deaths were described.

The WHO recommendations on airborne precautions for aerosol-generating procedures were strictly followed in the study centers: HCWs did not acquire any infections following the endoscopic procedures [13].

In conclusion, our study shows that bronchoscopy is a useful technique in the diagnostic pathway of COVID-19 pneumonia when nasopharyngeal swabs are negative. Urgent/life-saving procedures may be safely and successfully performed for diagnostic and therapeutic purposes in COVID-19 patients. The risk of viral transmission to HCWs is low following the WHO guidelines on airborne precautions for aerosol-generating procedures.
References


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Tables and figure legends.

Figure 1.

Bronchoscopic detection rate of SARS-CoV-2 in patients with previous negative swabs and in the presence of a clinical and radiological suspicion of COVID-19 pneumonia, in the total cohort (78 patients) and according to BAL and BW.
Bronchoscopic detection rate of SARS-CoV-2, %

- Total: 55.1%
- BAL: 57.4%
- BW: 47.1%

p-value = 0.45