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

To the Editor:

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 radiography, ultrasound scanning 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 haemoptysis) [8–12]. However, bronchoscopy generates aerosols 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 for bronchoscopy in cases of confirmed COVID-19 patients and the assessment of the safety of bronchoscopy for healthcare workers were evaluated.

An observational, retrospective, multicentre cohort study was performed in Italy. The study protocol was approved by the ethical committees of the participating hospitals. Written informed consent was signed by recruited patients.

Adult patients who underwent bronchoscopy between March 1, and April 15, 2020 were consecutively recruited in six Italian hospitals. The indications for bronchoscopy were diagnosis of SARS-CoV-2 pneumonia in patients with previously negative nasopharyngeal swab (clinical and radiological suspicion of pneumonia) and need for undelayable procedures in COVID-19 patients (*e.g.* massive haemoptysis, post-obstructive atelectasis).

All bronchoscopies were performed according to the World Health Organization (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 filtering facepiece class 3 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), with rapid clinical changes (progression or improvement in a short time period) [4, 7].

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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 healthcare worker was carefully monitored for symptoms and clinical signs suggestive for COVID-19 for ⩾15 days after the procedure.

An *ad hoc* electronic form was adopted to collect all study variables. Qualitative and quantitative variables were summarised with absolute (relative) frequencies and mean±SD, respectively. The statistical software STATA (version 16; StataCorp, College Station, TX, USA) was used to perform all statistical computations.

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 and one (0.01%) with the rigid scope. 13 (11.9%) bronchoscopies were performed while patients were breathing room air; 82 (75.3%) during oxygen supplementation; three (2.7%) during noninvasive mechanical ventilation; nine (8.2%) during invasive mechanical ventilation; and two (1.8%) during extracorporeal membrane oxygenation.

In 78 (71.6%) out of 109 cases, bronchoscopy was performed to diagnose SARS-CoV-2 infection in patients with a negative nasopharyngeal swab (median of two negative swabs per patient) and a clinical and radiological suspicion of COVID-19 pneumonia. Urgent/life-saving bronchoscopies were performed in 31 (28.4%) out of 109 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 haemoptysis.

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 out of 78). No differences were found between bronchoalveolar lavage (BAL) and bronchial washing (35 (57.4%) out of 61 and eight (47.1%) out of 17, respectively; p=0.45) (figure 1).

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

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

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

Complications related to bronchoscopy occurred in five (4.5%) out of 109 patients. Fever was recorded after BAL in two (1.8%) out of 109. Three (2.7%) out of 109 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.

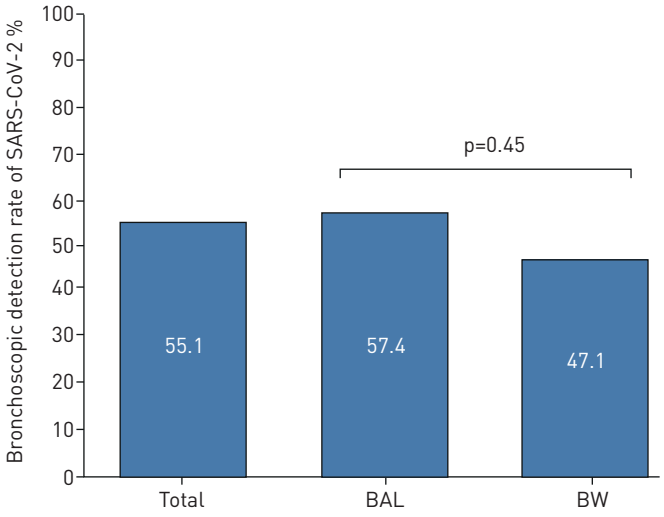

FIGURE 1 Bronchoscopic detection rate of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in patients with previous negative swabs and in the presence of a clinical and radiological suspicion of coronavirus disease 2019 pneumonia, in the total cohort (78 patients) and according to bronchoalveolar lavage (BAL) and bronchial washing (BW).

Infections related to the endoscopic procedure did not occur in healthcare workers involved in the endoscopic activities.

To our knowledge, this is 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 aetiological 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 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 bronchial washing.

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].

Although 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 haemoptysis, suspected tracheal lacerations in mechanically ventilated patients, tracheostomy complications and suspected concomitant pulmonary tuberculosis. Similar findings were described recently by Torrego *et al.* [12] in a Spanish cohort of COVID-19 patients who underwent bronchoscopy in the ICU.

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 four patients. Prompt identification of co-infecting micro-organisms 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 aforementioned side-effects can occur following a bronchoscopic procedure, in the 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 centres; healthcare workers 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 healthcare workers is low when following the WHO guidelines on airborne precautions for aerosol-generating procedures.

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