The Lancet Respiratory Medicine

Role of bronchoscopy during SARS-CoV-2 outbreak in Italy. A retrospective, multicenter study

--Manuscript Draft--

Manuscript Number:	thelancetrm-D-20-01464
Article Type:	Article (Original Research)
Keywords:	Bronchoscopy; COVID-19; BAL; SARS-CoV-2; hemoptysis
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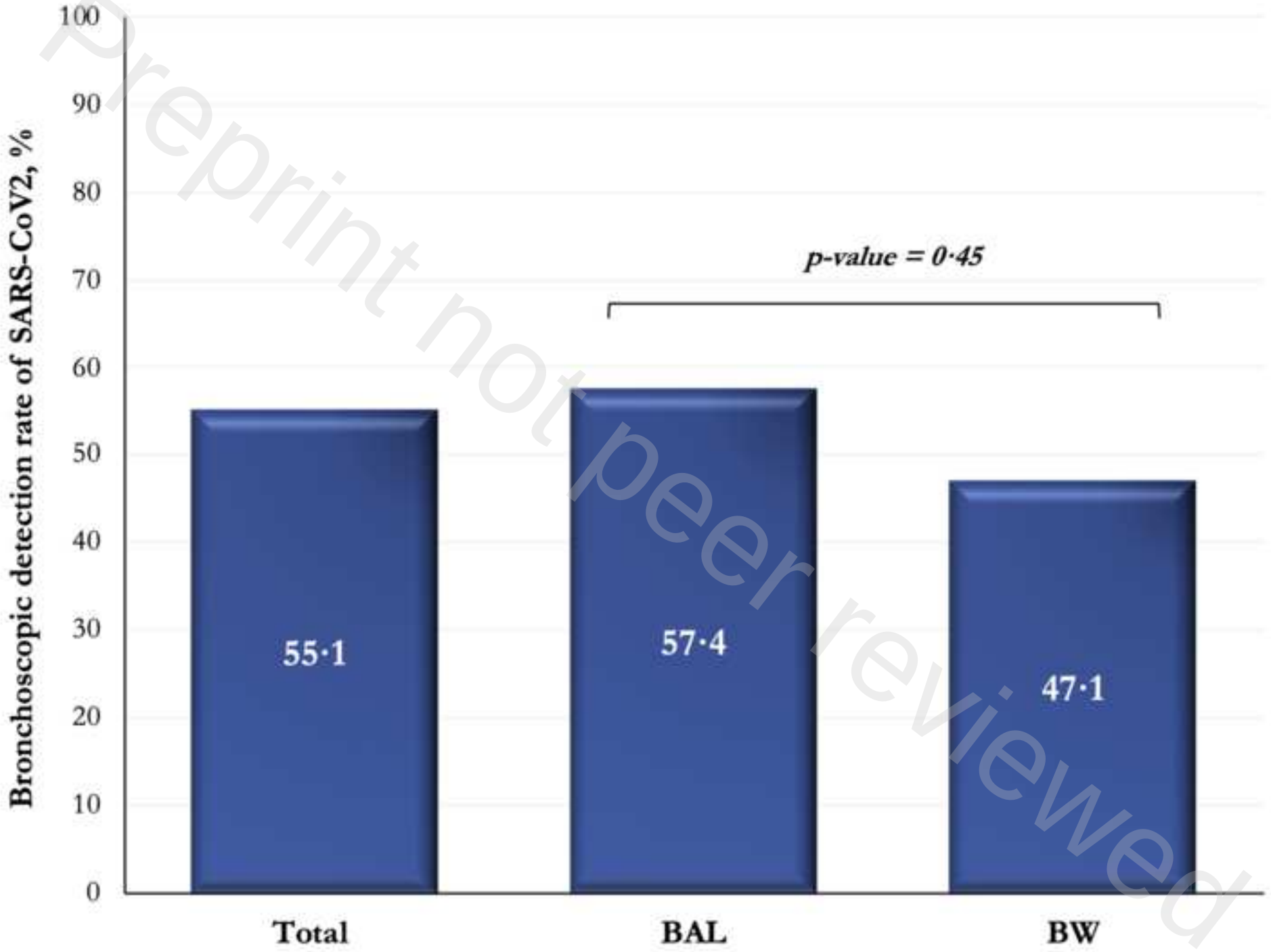
Abstract:	Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been spreading throughout Italy since February 2020. Limited data are available regarding indications, performance characteristics and safety of bronchoscopy (which is an aerosol generating procedure) in the context of SARS-CoV-

	2 outbreak. Methods: We performed a prospective, observational, multicentric study to describe the role of bronchoscopy during SARS-CoV-2 outbreak in Italy. Findings: 147 consecutive adult patients who underwent bronchoscopy between March 1st and April 15 th 2020 in five Italian hospitals were enrolled. 78/147 (53·1%) bronchoscopies were performed to detect SARS-CoV-2 in patients with negative nasopharyngeal swabs. SARS-CoV-2 was detected in 43/78 (55·1%) patients, without no difference in diagnostic yield between bronchoalveolar lavage (BAL) and bronchial washing (BW) (35/61, 57·4% and 8/17, 47·1%; p-value: 0·45). Suspected co-infections and management of obstructive atelectasis were the main indications for bronchoscopy in 31/147 (21·1%) patients with COVID-19 (respectively 11/31 (35·5%) and 7/31 (16·1%)). Suspected non-COVID-19 lower respiratory tract infections (18/38 (47·4%) and malignancy (7/38 (18·4%)) were the main indications in 38/147 (25·8%) patients without COVID-19. Overall, bronchoscopy was successfully performed for diagnostic and therapeutic purposes in 111/147 (75·5%) cases. 8/147 (5·4%) patients had mild complications related to the procedure. No procedure-related infections for patients and healthcare workers were recorded. Interpretation: bronchoscopy is a useful technique in the diagnosis of SARS-CoV-2 pneumonia in patients with negative swab. Endoscopic techniques may be safely and successfully performed for diagnostic and therapeutic purposes in the vast majority of the patients with or without SARS-CoV-2 illness. Funding: University of Milan



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Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been spreading throughout Italy since February 2020. Limited data are available regarding indications, performance characteristics and safety of bronchoscopy (which is an aerosol generating procedure) in the context of SARS-CoV-2 outbreak.

Methods: We performed a retrospective, observational, multicentric study to describe the role of bronchoscopy during SARS-CoV-2 outbreak in Italy.

Findings: 147 consecutive adult patients who underwent bronchoscopy between March 1st and April 15th 2020 in five Italian hospitals were enrolled. 78/147 (53·1%) bronchoscopies were performed to detect SARS-CoV-2 in patients with negative nasopharyngeal swabs. SARS-CoV-2 was detected in 43/78 (55·1%) patients, without no difference in diagnostic yield between bronchoalveolar lavage (BAL) and bronchial washing (BW) (35/61, 57·4% and 8/17, 47·1%; p-value: 0·45).

Suspected co-infections and management of obstructive atelectasis were the main indications for bronchoscopy in 31/147 (21·1%) patients with COVID-19 (respectively 11/31 (35·5%) and 7/31 (16·1%)). Suspected non-COVID-19 lower respiratory tract infections (18/38 (47·4%) and malignancy (7/38 (18·4%)) were the main indications in 38/147 (25·8%) patients without COVID-19. Overall, bronchoscopy was successfully performed for diagnostic and therapeutic purposes in 111/147 (75·5%) cases. 8/147 (5·4%) patients had mild complications related to the procedure.

No procedure-related infections for patients and healthcare workers were recorded.

Interpretation: bronchoscopy is a useful technique in the diagnosis of SARS-CoV-2 pneumonia in patients with negative swab. Endoscopic techniques may be safely and successfully performed for diagnostic and therapeutic purposes in the vast majority of the patients with or without SARS-CoV-2 illness.

Funding: University of Milan

Research in context

Evidence before the study: very limited data are available in the literature on the role of bronchoscopy during the SARS-CoV-2 pandemic.

Bronchoscopy might represent a useful diagnostic tool, in the presence of clinical/radiological suspicion and negative nasopharyngeal swabs. Furthermore, endoscopic techniques may be crucial to rule out other life-threatening diseases and/or in the management of serious pulmonary disorders.

According to international guidelines, bronchoscopy should have a very limited role in diagnosis and management of COVID-19 pneumonias. Indeed, bronchoscopy is an aerosol generating procedure and may be associated to increased risk of SARS-CoV-2 transmission to patients and healthcare workers.

Added value of this study: This is to our knowledge the largest study evaluating the diagnostic yield of bronchoscopy in the detection of SARS-CoV-2 in patients with negative nasopharyngeal swabs and the first to provide a comprehensive overview on the diagnostic and therapeutic role of bronchoscopy during COVID-19 outbreak. We also assess, on a large cohort of patients, the risk of procedure-related infections to patients and healthcare providers related to endoscopic procedures.

Implication of all the available evidence: Our study shows that bronchoscopy is a useful technique in the diagnostic work-up of COVID-19 pneumonia with negative nasopharyngeal swabs resulted negative.

Endoscopic techniques may be safely and successfully performed for both diagnostic and therapeutic purposes when judged urgent/life-saving and when an alternative diagnosis that would impact clinical management is suspected. We demonstrate that following WHO guidelines on airborne precautions for aerosol-generating procedures dramatically hampers the risk of infection transmission to patients and healthcare workers.

Text

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the related disease (coronavirus disease – 2019, COVID-19) has spread throughout Italy since February 2020. Increased intensive care unit (ICU) admission rates following pneumonia-related respiratory failures have been recorded countrywide.[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%).[5-7]

Bronchoscopy increases the sensitivity of the molecular diagnosis in comparison with that associated with nasopharyngeal swabs.[6] Furthermore, endoscopic techniques can rule out other life-threatening diseases (e.g., malignancies) and/or can 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]

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

Aim of the present study was to describe the diagnostic yield of bronchoscopy when nasopharyngeal swabs are negative. The safety of bronchoscopy was evaluated for both patients and healthcare workers.

Methods

Study design

An observational, retrospective, multicenter cohort study was carried out in Italy. The study protocol was approved by the ethical committees of all the participating hospitals. Written informed consent was signed by recruited patients. All the demographic, clinical, microbiological and endoscopic data were

retrieved from the Registry for COVID-19 Emergency (RECOVER) electronic database, funded by the University of Milan, Italy.

Patients and interventions

Adult patients who underwent bronchoscopy between March 1st and April 15th 2020 were consecutively recruited in five Italian hospitals.

General indication for bronchoscopy were: -diagnosis of SARS-CoV-2 pneumonia in patients with previous negative nasopharyngeal swab (clinical and radiological suspicion of pneumonia); -need for urgent/lifesaving procedures in either COVID-19 and non COVID-19 patients (e.g., massive hemoptysis, post-obstructive atelectasis, suspected severe tracheal stenosis/laceration); -suspicion of an alternative diagnosis needing an immediate clinical intervention and in which endoscopic examination could not be delayed.

Patients who refused to sign an informed consent and/or with incomplete data were excluded.

Elective bronchoscopies were postponed in all the centers.

The procedures were performed during topical anesthesia, conscious or deep sedation, or general anesthesia. Both disposable (if available) and conventional endoscopes were used.[13] All bronchoscopies were performed by pulmonologists and intensive care doctors in intensive care units, endoscopy rooms with adequate ventilation or in isolation room with negative pressure.[13]

Ten patients of the Monza cohort were described by Faverio et al. in an article under review and submitted to CHEST (manuscript ID CHEST-20-1680).

Outcome measures

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

Any procedure-related complications for both patients and healthcare workers were recorded.

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 dynamic 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.

Statistical analysis

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.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. GFSP is the recipient of a grant from the University of Milan for the RECOVER study (recovernet.org), a multicenter clinical registry of hospitalized patients affected by COVID-19 in Italy.

Results

A total of 147 adult patients (27·2% males; mean (SD) age: 61·0 (15·6) years) were enrolled.

146 (99·3%) bronchoscopies were performed with a flexible bronchoscope. 21 (14·3%) bronchoscopies were performed while patients were breathing room air, 109 (74·2%) during O2 supplementation, 6 (4·1%) during non-invasive mechanical ventilation, 9 (6·1) during tracheal

intubation and invasive mechanical ventilation, 2 (1·4%) during extracorporeal membrane oxygenation (ECMO) (1 during rigid bronchoscopy and 1 during tracheal intubation) (Table 1). In 15 (10·2%) patients bronchoscopy was performed after extubation.

BAL was performed in 104/142 (73·2%) patients, BW in 33/142 (23·2%), bronchial biopsy (BB) in 4/142 (2·8%), and transbronchial biopsy (TBB) in 1/142 (0·7%). BB and TBB were only used to diagnose a pulmonary malignancy. No endosonographies were performed (Table 1).

In 78/147 (53·1%) cases bronchoscopy was performed to diagnose SARS-CoV2 infection in patients with negative nasopharyngeal swabs (median 2 negative swabs per patient) and a clinical and radiological suspicion of COVID-19 pneumonia.

31/147 (21·1%) bronchoscopies were performed in patients with a molecular biology confirmed diagnosis of COVID-19, 38/147 (25·8%) in patients with negative nasopharyngeal swab(s) without any COVID-19 suspicion.

In all cases bronchoscopies were deemed undelayable (*i.e.*, urgent/life-saving or in the presence of a suspected alternative diagnosis impacting their clinical management) (Table 2).

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 BAL and BW (35/61, 57·4%, and 8/17, 47·1%, respectively; p-value: 0·45) (Figure 1).

SARS-CoV-2 was detected in ten patients without a clinical and radiological suspicion of COVID-19 pneumonia: non-COVID-19 lower respiratory tract infection (n= 5), severe haemoptysis (n= 2), obstructive atelectasis (n= 2). In 39/147 (26·5%) patients bronchoscopy did not help perform a definite microbiological and/or histopathological diagnosis. (Table 3)

Notably, 2/147 (1·4%) patients with previous negativity of both nasopharyngeal swabs and BAL for SARS-CoV-2 showed a positive swab (Table 4). Hence, 55/147 (37·4%) patients had a definite diagnosis of COVID-19 pneumonia. 36/147 (24·5%) patients without a microbiological and/or histopathological bronchoscopic diagnosis had the following final diagnosis: the diagnosis of SARS-

CoV-2 pneumonia was considered highly likely in 18/147 (12·2%) patients; 11/147 (7·5%) non-COVID-19 patients were diagnosed with a lower respiratory tract infection (pathogens were not detected).

Aspergillus spp. co-infection is the most frequent co-infection detected in bronchoscopic samples. One patient was co-infected by *Haemophilus influenzae* and SARS-CoV-2, one patient by *Aspergillus fumigatus* and SARS-CoV-2, and one patient by *Aspergillus spp*., *Candida albicans* and SARS-CoV-2.

Klebsiella pnemioniae, *Mycobacterium tuberculosis*, and *Haemophilus influenzae* were the most frequent pathogens detected in patients with non-COVID-19 lower respiratory tract infections (Table 5).

Complications related to the endoscopic procedure occurred in 8/147 (5·4%) patients. Fever was recorded after BAL in 3/147 (2·0%). 4/147 (2·7%) patients with a known mild respiratory failure had a worsening of their gas exchange after bronchoscopy performed during oxygen supplementation. No patients died (Table 6).

Infection related to the endoscopic procedures did not occur in patients and healthcare workers.

Discussion

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. This study provides an overview on the role of bronchoscopy during the COVID-19 outbreak. Furthermore, we assessed the risk of infection in patients and healthcare workers during endoscopic procedures.

Detection of SARS-CoV-2 in patients with negative swabs and a clinical and radiological suspicion of COVID-19 pneumonia was the main indication for bronchoscopy. 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 an optimal management.[1,2]

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

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, notably, we performed 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 several patients.[11]

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

Notably, two COVID-19 patients in whom bronchoscopy were performed in ICU for severe haemoptysis were treated with anticoagulant therapy, following the high risk for venous thromboembolism in COVID-19 patients.[14,15]

Suspected pulmonary malignancies, non-COVID-19 lower respiratory tract infections, hemoptysis and obstructive atelectasis represented the most frequent indications for endoscopic examinations in thirty-eight patients with negative swabs in whom endoscopic procedures were undelayable.

Endoscopic procedures were successfully performed for both therapeutic (e.g. obstructive atelectasis, severe hemoptysis) and diagnostic purposes. All cases of suspected pulmonary malignancies were confirmed by bronchoscopy. *Mycobacterium tuberculosis* and many other pathogens were isolated from bronchoscopic samples (mostly BAL and BW).

Very few data are available in the literature on bacterial and fungal co-infections with SARS-CoV2.[16] Lower respiratory tract co-infections were diagnosed with BAL in four patients. Prompt identification of co-infecting microorganisms is associated with an early prescription of antibiotics.[16]

Few bronchoscopy-related complications were recorded, with fever and mild respiratory failure being the most frequent. Neither severe complications nor deaths were described.

WHO recommendations on airborne precautions for aerosol-generating procedures were strictly followed in all the centers involved in the study: patients and healthcare personnel did not acquire any infection during the endoscopic procedures.[12]

Some study limitations can be found. The retrospective nature of the study does not allow to include some clinical variables, although the analysis was based on a comprehensive register, which included demographic, clinical, and epidemiological information on patients with a suspected COVID-19 diagnosis. The current molecular methods do not show a high diagnostic accuracy; then, it is difficult to ascertain a definitive diagnosis in all enrolled patients. The sample size could not have sufficient statistical power to show the statistical significance of some findings. However, this is the first multicenter study on the diagnostic yield of bronchoscopy.

In conclusion, our study shows that bronchoscopy is a useful technique in the diagnostic pathway of COVID-19 pneumonia when nasopharyngeal swabs are negative.

Endoscopic techniques may be safely and successfully performed for both diagnostic and therapeutic purposes when deemed urgent/life-saving and when an alternative diagnosis that would impact the clinical management is suspected. The risk of viral transmission to patients and healthcare workers decreased following WHO guidelines on airborne precautions for aerosol-generating procedures.

Further studies are needed to assess the accuracy of endoscopic sampling techniques in the diagnosis of SARS-CoV2 infection. Future investigations should also assess the relationship between the diagnostic yield of the technique and the severity of the disease, as well as to study the role of bronchoscopy to assess the long-term complications of severe COVID-19 (e.g., tracheal stenosis following intubation).

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Contributors:

MM and GFSP: conception and design; full access to all data in the study and responsibility for the integrity of the data and the accuracy of the data analysis.

MM and GS: writing of the manuscript

MM, GFSP, RR, SC, GS: critical revision of the report

LS and GS: statistical analysis

All Authors contributed to data acquisition, data analysis, or data interpretation, and reviewed and approved the final version.

Declaration of interests: all authors declare no competing interests

Acknowledgements: the work is funded by University of Milan in the context of the Registry for COVID19 Emergency (RECOVER) electronic database

The Authors want to acknowledge Dr. Beatrice Vigo, Mrs. Simona Gentile, Dr. Filippo Montanelli, Dr. Stefano Zucchetti, Dr. Giulia Pittalis, Dr. Laura Garzillo, Dr. Donatella Palmadessa, Dr. Luca Geroli, Dr. Giuseppe Paciocco, Dr. Vanina Rognoni, Mrs. Daniela Zanoncelli, Mrs. Isa Fenati; Mrs. Teresa Goldaniga, Mrs. Veena Arkasvipate; Mr. Saverio Bove, Dr. Giuseppe Ciaravino, for their valuable contribution to the research project.

Tables and figure legends.

Table 1. Demographic, clinical and endoscopic characteristics of the cohort

Total cohort, n (%)		147 (100)
Centers/patients enrolled, n (%)	Ancona	12 (8·2)
	Bergamo	21 (14·3)
	Lodi	23 (15·7)
	Milan	22 (14·9)
	Pavia	21 (14·3)
	Monza	48 (32·7)
Male, n (%)		40 (27·2)
Age (years), mean (SD)		61 (15·6)
Ethnicity, n (%)	Caucasian	139 (94·6)
	Hispanic	5 (3·4)
	Asian	-
	African	3 (2·0)
Bronchoscopies, n (%)	Flexible	146 (99·3)
	Rigid	1 (0·7)
Sampling technique, n (%)	BAL	104 (73·2)
	BW	33 (23·2)
	BB	4 (2·8)
	TBB	1 (0·7)
	Endosonography	-
Respiratory assistance, n (%)	Room air	21 (14·3)
	O2	109 (74·2)
	NIMV	6 (4·1)
	IMV	9 (6·1)
	ECMO	2 (1·4)

BAL: bronchoalveolar lavage; BW: bronchial washing; BB: bronchial biopsy; TBB: transbronchial biopsy; O2: oxygen; NIMV: non-invasive mechanical ventilation; IMV: invasive mechanical ventilation; ECMO: extra corporeal membrane oxygenation

Table 2: Indications for bronchoscopy

General indication	**Specific indication**	**n, (%)**
Bronchoscopies in patients with suspected COVID-19 pneumonia (negative nasopharyngeal swabs)		78/78 (100)
Bronchoscopies in known COVID-19 patients	Suspected concomitant lower respiratory tract infections	7/31 (16·1)
	Hemoptysis	4/31 (16·1)
	Suspected acute complication of tracheal intubation (tracheal laceration)	3/31 (9·7)
	Obstructive atelectasis	11/31 (35·5)
	Tracheostomy complication	3/31 (9·7)
	Suspected pulmonary TB	1/31 (3·2)
	Assess SARS-CoV2 infection resolution (in patient with tracheostomy and mucus plugging)	2/31 (6·5)
Other bronchoscopies in non-COVID-19 patients	Suspected pulmonary malignancies	7/38 (18·4)
	Suspected non-COVID-19 lower respiratory tract infection	18/38 (47·4)
	Hemoptysis	3/38 (7·9)
	Suspected acute ILD	1/38 (2·6)
	Obstructive atelectasis	6/38 (15·8)
	Suspected pulmonary TB	3/38 (7·9)

COVID-19: coronavirus disease-19; TB: tuberculosis; SARS-CoV2: severe acute respiratory syndrome coronavirus 2; ILD: interstitial lung disease.

Table 3. Bronchoscopic diagnosis/outcome in the cohort

Bronchoscopic diagnosis/outcome, n (%)	COVID-19	53 (36·5)
	Lower non-COVID-19/non-TB respiratory tract infection (pathogen identification)	21 (14·3)
	Pulmonary malignancy	7 (4·8%)
	Hemoptysis in COVID-19 (therapeutic bronchoscopy)	3 (2)
	No microbiological/cytological diagnosis	36 (2·5)
	Pulmonary tuberculosis	3 (2)
	No tracheal laceration	3 (2)
	Resolution of obstructive atelectasis in COVID-19 patients	13 (8·8)
	Resolution of obstructive atelectasis in non COVID-19 patients	4 (2·7)
	Tracheostomy complication (granulomas)	3 (2)
	Confirmed SARS-CoV2 infection resolution (in patient with tracheostomy and mucus plugging)	2 (1·4)

COVID-19: coronavirus disease-19; SARS-CoV2: severe acute respiratory syndrome coronavirus 2; TB: tuberculosis

Table 4. Final diagnosis (based on clinical, radiological and endoscopic findings) and outcomes in the cohort

Final diagnosis/outcome, n (%)	Definite COVID-19	55 (37·4)
	Highly likely COVID-19	18 (12·2)
	Concomitant lower respiratory tract infection in known COVID-19 patients	4 (2·7)
	Lower non-COVID-19/non-TB respiratory tract infection (with pathogen identification)	21 (14·3)
	Lower non-COVID-19/non-TB respiratory tract infection (without pathogen identification)	11 (7·5)
	Pulmonary malignancy	7 (4·7)
	Severe hemoptysis in patients with COVID-19 and anticoagulant therapy (therapeutic bronchoscopy)	3 (2)
	Idiopathic hemoptysis in non-COVID-19 patient	1 (0·7)
	Pneumomediastinum/pneumothorax (in the absence of tracheal laceration) due to pulmonary barotrauma related to mechanical ventilation	3 (2)
	Pulmonary tuberculosis	3 (2)
	Resolution of obstructive atelectasis in COVID-19 patients	13 (8·8)
	Resolution of obstructive atelectasis in non COVID-19 patients	4 (2·7)
	Tracheostomy complication (granulomas)	2 (1·4)
	Confirmed SARS-CoV2 infection resolution (in patient with tracheostomy and mucus plugging)	2 (1·4)

COVID-19: coronavirus disease-19; TB: tuberculosis; SARS-CoV2: severe acute respiratory syndrome coronavirus 2

Table 5. Pathogens retrieved in bronchoscopic samples.

Pathogens	Co-infection with SARS-CoV2, n (%)	Non-coinfecting pathogen, n (%)
Aspergillus spp.	1/4 (25·0)	-
Aspergillus spp. and Candida spp.	2/4 (50·0)	-
Escherichia coli	-	2/17 (11·8)
Haemophilus influenzae	1/4 (25·0)	2/17 (11·8)
Haemophilus influenzae and Mycoplasma pneumoniae	-	1/17 (5·9)
Klebsiella pneumoniae	-	3/17 (17·7)
Mycobacterium tuberculosis	-	3/17 (17·7)
Streptococcus pneumoniae	-	1/17 (5·9)
Pneumocystis jirovecii	-	1 /17(5·9)
Pneumocystis jirovecii e Citomegalovirus	-	1/17 (5·9)
Pseudomonas aeruginosa	-	2/17 (11·8)
Staphilococcus aureus	-	1/17 (5·9)

SARS-CoV2: severe acute respiratory syndrome coronavirus 2; *Spp.*: species

Table 6. Complications of bronchoscopy according to respiratory assistance in the total cohort

Type of omplication	**Respiratory assistance, n (%)**				
	Room air (21 patients)	O2 (108 patients)	NIMV (6 patients)	IMV (9 patients)	ECMO (2 patients)
No complications	19 (90·5)	102 (94·4)	6 (100.0)	9 (100)	2 (100·0)
Respiratory failure /worsening of known respiratory failure requiring O2/higher O2 flows	1 (4·8)	4 (3·7)	0 (0·0)	0 (0·0)	0 (0·0)
Worsening of respiratory failure requiring NIMV	0 (0·0)	0 (0·0)	-	-	-
Worsening of respiratory failure requiring IMV	0 (0·0)	0 (0·0)	0 (0·0)	-	-
Moderate-severe bleeding	0 (0·0)	0 (0·0)	0 (0·0)	0 (0·0)	0 (0·0)
Pneumothorax	0 (4·8)	0 (0·0)	0 (0·0)	0 (0·0)	0 (0·0)
Fever	1 (4·8)	2 (1·9)	0 (100·0)	0 (0·0)	0 (0·0)
Death	0 (0·0)	0 (0·0)	0 (0·0)	0 (0·0)	0 (0·0)

NIMV: non-invasive mechanical ventilation; IMV: invasive mechanical ventilation

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.

Tables and figure legends.

Table 1. Demographic, clinical and endoscopic characteristics of the cohort

Total cohort, n (%)		147 (100)
Centers/patients enrolled, n (%)	Ancona	12 (8·2)
	Bergamo	21 (14·3)
	Lodi	23 (15·7)
	Milan	22 (14·9)
	Pavia	21 (14·3)
	Monza	48 (32·7)
Male, n (%)		40 (27·2)
Age (years), mean (SD)		61 (15·6)
Ethnicity, n (%)	Caucasian	139 (94·6)
	Hispanic	5 (3·4)
	Asian	-
	African	3 (2·0)
Bronchoscopies, n (%)	Flexible	146 (99·3)
	Rigid	1 (0·7)
Sampling technique, n (%)	BAL	104 (73·2)
	BW	33 (23·2)
	BB	4 (2·8)
	TBB	1 (0·7)
	Endosonography	-
Respiratory assistance, n (%)	Room air	21 (14·3)
	O2	109 (74·2)
	NIMV	6 (4·1)
	IMV	9 (6·1)
	ECMO	2 (1·4)

BAL: bronchoalveolar lavage; BW: bronchial washing; BB: bronchial biopsy; TBB: transbronchial biopsy; O2: oxygen; NIMV: non-invasive mechanical ventilation; IMV: invasive mechanical ventilation; ECMO: extra corporeal membrane oxygenation

Table 2: Indications for bronchoscopy

General indication	Specific indication	n, (%)
Bronchoscopies in patients with suspected COVID-19 pneumonia (negative nasopharyngeal swabs)		78/78 (100)
Bronchoscopies in known COVID-19 patients	Suspected concomitant lower respiratory tract infections	7/31 (16·1)
	Hemoptysis	4/31 (16·1)
	Suspected acute complication of tracheal intubation (tracheal laceration)	3/31 (9·7)
	Obstructive atelectasis	11/31 (35·5)
	Tracheostomy complication	3/31 (9·7)
	Suspected pulmonary TB	1/31 (3·2)
	Assess SARS-CoV2 infection resolution (in patient with tracheostomy and mucus plugging)	2/31 (6·5)
Other bronchoscopies in non-COVID-19 patients	Suspected pulmonary malignancies	7/38 (18·4)
	Suspected non-COVID-19 lower respiratory tract infection	18/38 (47·4)
	Hemoptysis	3/38 (7·9)
	Suspected acute ILD	1/38 (2·6)
	Obstructive atelectasis	6/38 (15·8)
	Suspected pulmonary TB	3/38 (7·9)

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Table 3. Bronchoscopic diagnosis/outcome in the cohort

Bronchoscopic diagnosis/outcome, n (%)	COVID-19	53 (36·5)
	Lower non-COVID-19/non-TB respiratory tract infection (pathogen identification)	21 (14·3)
	Pulmonary malignancy	7 (4·8%)
	Hemoptysis in COVID-19 (therapeutic bronchoscopy)	3 (2)
	No microbiological/cytological diagnosis	36 (2·5)
	Pulmonary tuberculosis	3 (2)
	No tracheal laceration	3 (2)
	Resolution of obstructive atelectasis in COVID-19 patients	13 (8·8)
	Resolution of obstructive atelectasis in non COVID-19 patients	4 (2·7)
	Tracheostomy complication (granulomas)	3 (2)
	Confirmed SARS-CoV2 infection resolution (in patient with tracheostomy and mucus plugging)	2 (1·4)

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Table 4. Final diagnosis (based on clinical, radiological and endoscopic findings) and outcomes in the cohort

Final diagnosis/outcome, n (%)	Definite COVID-19	55 (37·4)
	Highly likely COVID-19	18 (12·2)
	Concomitant lower respiratory tract infection in known COVID-19 patients	4 (2·7)
	Lower non-COVID-19/non-TB respiratory tract infection (with pathogen identification)	21 (14·3)
	Lower non-COVID-19/non-TB respiratory tract infection (without pathogen identification)	11 (7·5)
	Pulmonary malignancy	7 (4·7)
	Severe hemoptysis in patients with COVID-19 and anticoagulant therapy (therapeutic bronchoscopy)	3 (2)
	Idiopathic hemoptysis in non-COVID-19 patient	1 (0·7)
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Moderate-severe bleeding	0 (0·0)	0 (0·0)	0 (0·0)	0 (0·0)	0 (0·0)
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Fever	1 (4·8)	2 (1·9)	0 (100·0)	0 (0·0)	0 (0·0)
Death	0 (0·0)	0 (0·0)	0 (0·0)	0 (0·0)	0 (0·0)

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