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Scientific letter

Analysis of SARS-COV-2 in Bronchial Samples in Asymptomatic or Unsuspected Patients Who Underwent Scheduled Bronchoscopy After Negative Screening

Análisis de SARS-COV-2 en muestras bronquiales de pacientes asintomáticos o no sospechados que se sometieron a una broncoscopia programada tras un cribado negativo

Dear Editor,

Suspicion of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection may arise in the presence of associated symptoms, a history of exposure, or lung involvement confirmed by chest imaging.[1] Routine screening by reverse transcriptase-polymerase chain reaction (RT-PCR) in samples collected from the upper respiratory tract, nasopharyngeal (NP) and/or oropharyngeal (OP) swabs, are considered the gold standard for diagnosing SARS-CoV-2 infection.[2]

During the coronavirus disease 2019 (COVID-19) pandemic, bronchoscopy practices changed worldwide given contagion risks of the procedure. At the beginning, most elective bronchoscopies were suspended or rescheduled. Time devoted to safety protocols over the last two years, led to a compromise in the number of exams performed.[3,4] Some might advocate that a negative NP/OP swab in an asymptomatic or unsuspected patient could be sufficient to reinstate practices that allow the same number of procedures as in the pre-COVID-19 era.

Comparison of diagnostic yield of NP/OP swabs and bronchial secretions in suspected SARS-CoV-2 infections has been extensively addressed in literature.[5] As bronchial secretions hold higher sensitivity, they can be used to diagnose COVID-19 lower respiratory tract infection when NP/OP swabs are negative for RT-PCR SARS-CoV-2.[1,5] However, concordance rates between NP/OP swabs and samples from the lower respiratory tract among asymptomatic or unsuspected patients are unknown and can only be assessed by testing specimens concurrently.

The aim of this study was to determine the value of SARS-CoV-2 RT-PCR test in the upper respiratory tract of asymptomatic or unsuspected patients as a screening method prior bronchoscopy.

A prospective study was conducted at two Pulmonology units of the Centro Hospitalar Universitário do Algarve between March and September 2021. The study was approved by the Ethical committee of Centro Hospitalar e Universitário do Algarve (UAIF 090/2020) and individual consent was required. All consecutive patients who underwent scheduled bronchoscopy with a negative SARS-CoV-2 swab test within the 72 h prior to bronchoscopy were included. Patients with previous SARS-CoV-2 infection and pediatric patients were excluded.

For each patient demographic information, indications for bronchoscopy, radiological computed tomography (CT) characteristics, technical procedure and virological bronchoalveolar lavage (BAL) and/or bronchial washing (BW) results were collected. Patients were asked to complete a risk assessment questionnaire which evaluated SARS-CoV-2 vaccine status, previous COVID-19 contacts, use of health services and symptom evaluation in the previous month.

To diminish procedural risks BW was usually preferred to BAL. Samples were preferably collected from a lung segment or subsegment with identified disease on previous chest CT or by direct bronchoscopic visualization of airway disease. If BAL was performed during the procedure a sample would be directed for SARS-CoV-2 analysis.

During the study period, 146 patients were eligible and a total of 155 bronchoscopies were performed. One patient had a positive NP swab and was therefore excluded. Table 1 describes patients characteristics at baseline. Among these patients, 111 (76%) had one or more underlying diseases, of whom 38.3% were attributed to respiratory diseases. Eighty-three patients (53.6%) were not vaccinated for SARS-CoV-2 infection at the time of the exam.

All individuals submitted to bronchoscopy denied close contacts to patients with confirmed COVID-19 disease within the previous thirty days of the exam. A total of 141 patients (91%) had used health services during that period. The risk assessment questionnaire analysis also indicated that 117 patients (75.5%) had relevant symptoms on the day of the exam. A considerable number of patients presented with cough ($n = 78$, 66.6%), fatigue ($n = 71$, 60.7%), dyspnea ($n = 38$, 32.5%) and asthenia ($n = 32$, 27.4). Other COVID-19 commonly associated symptoms were also reported (Table 1).

The most frequent CT alterations were nodular lesions ($n = 85$, 55.9%), followed by emphysema ($n = 27$, 17.8%) and ground glass opacities ($n = 26$, 17.1%). Chest CT scans were performed at a median of 36.1 days (SD 39.9) prior to bronchoscopy.

The most frequent indications for bronchoscopy were suspected malignancy and/or cancer staging ($n = 89$, 57.4%), suspected lung infection ($n = 34$, 21.9%) and suspected interstitial lung disease ($n = 21$, 13.6). Bronchoscopies were performed at a median of 2 days (IQR 1–3) after the last NP/OP swab.

All patients recruited were living in the Algarve region, during which period the COVID-19 Rt (effective reproductive number) varied between 0.77 (95% CI, 0.75–0.80) and 1.34 (95% CI, 1.29–1.39) and incidence varied between 60 and 945.3/100 000 cases.[6]

All of BW and BAL samples collected for SARS-CoV-2 RT-PCR test results ($n = 155$) were negative, demonstrating a 100% of concordance between NP/OP swabs and bronchial secretions.

The main limitation of this study is the low number of BAL (23.2%) compared to BW technique. BAL samples are considered to

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Table 1
Baseline characteristics and clinical data of the study population ($n = 146$).

Baseline characteristics	Total
Male	93 (63.7)
Age (years)	64 (23–88)
Current or former smokers	111 (76)
Underlying diseases	
COPD	26 (17.8)
Asthma	8 (5.5)
Bronchiectasis	7 (4.8)
Post-tuberculosis lung disease	5 (3.4)
Interstitial lung disease	5 (3.4)
α-1 antitrypsin deficiency	1 (0.7)
Lung cancer	4 (2.7)
Other neoplasms	20 (13.7)
Hypertension	46 (31.5)
Diabetes	23 (15.7)
Cardiovascular disease	22 (15.1)
Other non-respiratory diseases	52 (35.6)
Number of underlying diseases per patient	
0	35 (23.9)
1	41 (28.1)
2	36 (24.7)
≥3	34 (23.3)
SARS-CoV-2 vaccine status	
Unvaccinated	83 (53.6)
1 vaccine	23 (14.8)
2 vaccines	49 (31.6)

Questionnaire	Total
Use of health services in the last 30 days (hospitals or health centers)	141 (91)
Patients with symptom manifestations 30 days prior to bronchoscopy	137 (88.4)
Patients with symptom manifestations on the day of bronchoscopy	117 (75.5)
Cough	78 (66.6)
Fatigue	71 (60.7)
Dyspnea	38 (32.5)
Asthenia	32 (27.4)
Thoracic pain	20 (1.7)
Joint pain	16 (13.7)
Nasal obstruction	15 (12.8)
Myalgia	11 (9.4)
Anosmia and/or ageusia	9 (7.7)
Headache	8 (6.8)
Abdominal pain	4 (3.4)
Conjunctivitis	4 (3.4)
Fever	3 (2.6)
Odynophagia	3 (2.6)
Diarrhea	3 (2.6)
Nausea and/or vomit	2 (1.7)
Patients submitted to NP swab	82 (52.9)
Patients submitted to NP and OP swab	73 (47.1)
Time between swab and bronchoscopy (days)	2 (1–3)

Radiologic data	Total
Time between imaging and bronchoscopy (days)	36.1 ± 39.9
CT characteristics	
Nodular lesions	85 (55.9)
Emphysema	27 (17.8)
Ground glass opacities	26 (17.1)
Cavitation	19 (12.5)
Micronodules	15 (9.9)
Bronchiectasis	15 (9.9)
Pleural effusion	14 (9.2)
Consolidation	12 (7.9)
Septal thickening	9 (5.9)
Tree in bud	4 (2.6)
Honeycombing	4 (2.6)
Crazy paving pattern	2 (1.3)
Mosaic attenuation pattern	1 (0.6)
CT characteristics per patient	
1	84 (55.3)
2	46 (30.3)
3	16 (10.5)
4	6 (0.4)

Bronchoscopy data	Total
Indications for bronchoscopy	
Suspected malignancy/cancer staging	89 (57.4)
Suspected infection	34 (21.9)
Suspected interstitial lung disease	21 (13.6)
Haemoptysis	5 (3.2)
Bronchoscopy revision of tracheal prosthesis	4 (2.6)
Foreign body removal	2 (1.3)
Bronchial washing	119 (76.8)
Bronchoalveolar lavage	36 (23.2)

Values are expressed as *n* (%), median (IQR) or median ± SD.
Definition of abbreviations: COPD: chronic obstructive pulmonary disease; CT: computed tomography; NP: nasopharyngeal; OP: oropharyngeal; SARS-CoV-2: severe acute respiratory syndrome coronavirus-2.

have higher sensitivity for lower respiratory tract infections compared to BW.

A thorough search of the relevant literature yielded only one related article that analyzed the correlation between NP swabs and BAL in asymptomatic patients.[7] The article showed similar results, with no discordances between the initial negative NP swabs and bronchoscopic BAL results, which strengthens our conclusions. Our study included additional variables and a comprehensive risk assessment questionnaire providing added information.

In conclusion, these results support the use of NP/OP swab tests as a screening method prior bronchoscopy, as the low prevalence of COVID-19 infection in patients submitted to elective bronchoscopy seems to heighten the negative predictive value of NP/OP RT-PCR. Conducting a symptom based risk assessment questionnaire before bronchoscopy does not seem to add value in identifying suspected infected patients, as most patients had COVID-19 related symptoms. This knowledge might help reduce the need for certain safety protocols and shorten the time between each bronchoscopy.

Authors' contributions

Conception and design: Tânia Sales Marques, Bruno dos Santos, Djamila Neves, Francisco Martins, Isabel Ruivo, Pedro Americano, Ulisses Brito.

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All authors have read and approved submission of the manuscript, and all fully qualify for authorship.

Ethical disclosures

The authors declare that they have followed the protocols of their work center on the publication of patient data and have obtained approval by the Ethical committee of Centro Hospitalar e Universitário do Algarve (UAIF 090/2020).

Informed consent

The authors have obtained the written informed consent of the patients mentioned in the article. The corresponding author is in possession of this documents.

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Conflicts of interest

The authors declare that they have no conflict of interest directly or indirectly related to the contents of this manuscript.

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