Received: 21 February 2021 | Accepted: 12 April 2021

DOI: 10.1111/ijcp.14231

EDITORIAL

GENERAL/SURGERY/INTERNAL

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY

Avoiding COVID-19 hospital outbreaks: RT-PCR swab and clinical assessment

Every day we face up coronavirus disease 19 (COVID-19) pandemic during our clinical practice. Despite the attention we pay in trying to detect severe acute respiratory syndrome-coronavirus-2 (Sars-Cov-2) in the hospitalised patients, often it is difficult to do, and sometimes epidemic outbreaks in hospital wards occur.

Nasopharyngeal reverse transcriptase-polymerase chain reaction (RT-PCR) swab test is a fundamental examination in COVID-19 diagnosis. However, several studies have shown a suboptimal sensitivity of this test (around 70%[1]) in detecting Sars-Cov-2; in an infected patient, the probability of a false-negative result is 67% the day before the symptom onset, 38% the day of symptom onset, 20% 3 days later and then it increases again (to 66% 2 weeks later).[2] In our experience, a critical patient (who then passed away) with strongly suggestive symptoms for COVID-19 had got four consecutive negative RT-PCR swab test results before the positive result on bronchoalveolar lavage.

This high false-negative rate may be caused by (1) the difficulty to perform the nasopharyngeal swab correctly (making this examination operator dependent), (2) a slower rise of the viral load in some patients[3] and (3) the timing of swab tests during the day. Indeed, RT-PCR test is dependent upon the viral load in detecting Sars-Cov-2, and the probability of having the highest viral load in posterior oropharyngeal saliva in early morning is 61.5%, compared to 23.1% before lunch, 7.7% at 3 PM or before dinner and 0% at bedtime[4]; therefore, assuming that this also applies to nasopharyngeal secretions, performing a swab at another time of the day could lead to a false-negative result more easily. It is reported that early morning saliva may be a better alternative specimen for detection of Sars-Cov-2.[5] Whatever diagnostic test is used, it is fundamental to identify Sars-Cov-2 infection early to avoid in-hospital contagion.

Unfortunately, the RT-PCR swab test is used mostly (and wrongly) for ruling out Sars-Cov-2 infection in hospital wards: there is often overconfidence in a negative result, without considering other important clinical features. As seen previously, some patients with clinical features suggestive for COVID-19 may have a negative result, but they may be infected anyway, thus, favouring epidemic outbreaks into hospital wards. Before the positive conversion of the RT-PCR swab test, we often observed respiratory symptoms (dyspnoea, cough, fever and sore throat), blood tests (lymphopaenia, fibrinogen, lactate dehydrogenase, C-reactive protein and ferritin above the threshold value) and chest x-ray/computed tomography (interstitial/ground-glass opacities) suggestive for Sars-Cov-2 infection. We observed also (but less frequently) elevated d-dimer and other organ damage proteins (transaminase, troponin, amylase, lipase, etc). These findings are confirmed by several studies on COVID-19 patients and the alteration degree of blood tests is often related to the severity of the disease.

Therefore, it is fundamental to always integrate the RT-PCR swab test result with the clinical assessment in the diagnostic process of COVID-19, and to suspect the disease in possibly infected patients with a negative result and manage them accordingly. The clinical situation should not be considered only before the RT-PCR test to determine pre-test probability, but also after the test to determine what degree of confidence can be attributed to a negative result.

We propose a flowchart for the management of patients who underwent nasopharyngeal RT-PCR swab test (Figure 1). If the test result is positive, immediate transfer to a COVID-19 unit should be performed (red zone); if negative without clinical features suggestive for Sars-Cov-2 infection (please see below), no further action needs to be performed (green zone). If the test result is negative but some clinical features may suggest Sars-Cov-2 infection (ie dyspnoea, cough, fever, sore throat, lymphopaenia, fibrinogen, lactate dehydrogenase, C-reactive protein and ferritin above the threshold value, interstitial/ground-glass opacities, etc), the patient should be isolated, physicians should use personal protective equipment (PPE) as in front of a COVID-19 patient and daily clinical and laboratory (body temperature, blood count, C-reactive protein, etc) monitoring and serial RT-PCR swab tests should be performed (grey zone). We must admit that similar findings can be present during other viral infections, but it is equally true that during this phase we must suspect Sars-Cov-2 primarily because of the higher danger and spread velocity compared with other viruses. Weak-positive RT-PCR swab tests should be repeated, but the possible following negative result should be integrated with the clinical assessment as seen before; we remind that RT-PCR swab test has low sensitivity but high specificity (95%)[1] and, therefore, a positive result should never be ignored.

In conclusion, COVID-19 should not be ruled out based on RT-PCR swab test alone, but also the clinical situation should be carefully assessed.[2] A cautious approach integrating RT-PCR swab tests with the clinical assessment may allow to offset the low sensitivity of swab tests and counteract in-hospital epidemic outbreaks. New diagnostic tests are necessary to reach the optimal sensitivity in detecting Sars-Cov-2. We hope that COVID-19 vaccines will help stop

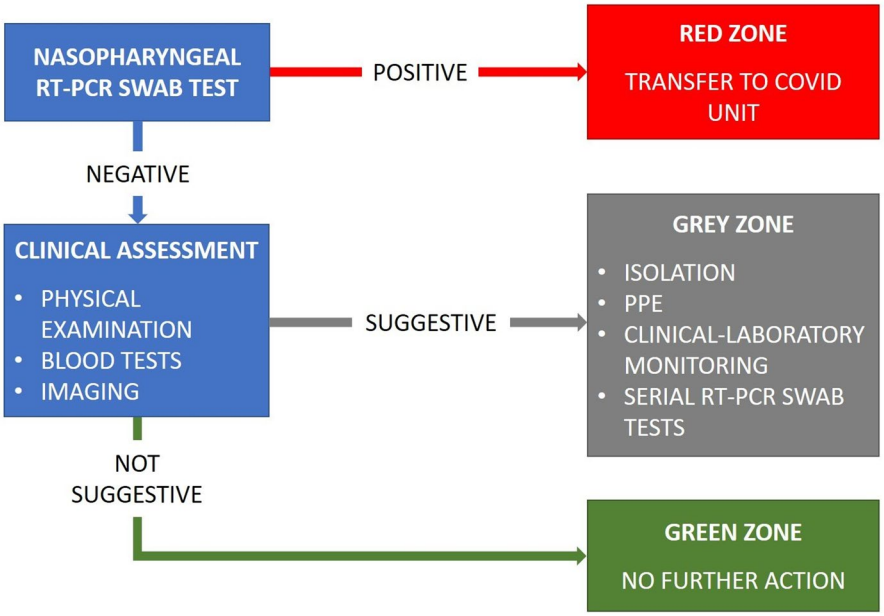

FIGURE 1 Proposed flowchart in COVID-19 diagnosis (see text for explanation)

the epidemic outbreaks into the hospital wards, which we still worry about today.

DISCLOSURE

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

Luca Allievi[1]
Amedeo Bongarzoni[2]
Guido Tassinario[2]
Stefano Carugo[1]

[1]*Department of Cardiology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy*
Email: luca.allievi@unimi.it
[2]*Department of Cardiology, ASST Santi Paolo e Carlo, Milan, Italy*

ORCID

Luca Allievi https://orcid.org/0000-0001-8960-019X

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How to cite this article: Allievi L, Bongarzoni A, Tassinario G, Carugo S. Avoiding COVID-19 hospital outbreaks: RT-PCR swab and clinical assessment. *Int J Clin Pract*. 2021;75:e14231. https://doi.org/10.1111/ijcp.14231