



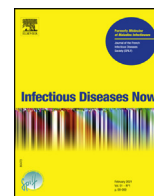
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Short communication

The additional contribution of second nasopharyngeal PCR to COVID-19 diagnosis in patients with negative initial test



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ABSTRACT

Objective: The World Health Organization (WHO) recommends performing a second test in patients with a high suspicion of novel coronavirus disease (COVID-19) whose first PCR test is negative. However, the additional contribution of the second PCR test to the diagnosis is unknown.

Patients and methods: In this study, we aimed to investigate the contribution of second SARS-CoV-2 PCR to diagnosis in patients with a suspicion of COVID-19 whose initial test was negative.

Results: A total of 1449 patients were hospitalized in infectious disease clinics with the suspicion of COVID-19 infection during the study period. We performed the second PCR test (697 nasopharyngeal sample, 5 tracheal aspirate) in 702/766 (91.6%) patients whose first tests were negative and only 6.6% (46) of them were positive.

Conclusions: The strategy of using the second nasopharyngeal PCR test to confirm or exclude the diagnosis seems to cause the loss of labor and time, and is costly, because its additional contribution to the first test is very low.

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1. Introduction

Since its appearance in mainland China at the end of 2019, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has infected more than 8 million people, and approximately 460,000 of them have died [1,2]. The diagnosis is currently based on the detection of viral RNA from respiratory samples by reverse transcriptase polymerase chain reaction (RT-PCR) [3]. However, the low sensitivity of diagnostic RT-PCR test and the undistinguishable feature of the novel coronavirus disease (COVID-19) from other respiratory infections create difficulties in diagnosis. The World Health Organization (WHO) recommends performing a second test in patients with a high suspicion of COVID-19 infection whose first PCR test is negative. Particularly, if the first test has been performed on the upper respiratory tract, it is recommended that a second test should be performed, if possible, from the lower respiratory tract. However, the contribution of a second PCR test to the diagnosis is unknown. Additionally, performing the second nasopharyngeal test causes the excessive use of tests and personal protective equipment, and the loss of labor and time, and is costly. In this study, we

aimed to investigate the contribution of second SARS-CoV-2 PCR to diagnoses in patients with a suspicion of COVID-19 infection whose initial test was negative.

This retrospective study was carried out in infectious diseases and clinical microbiology clinics in Ankara City Hospital between March 15, 2020 and June 15, 2020. Ethical approval was obtained from the Ankara City Hospital Ethical Committee 1. Patients older than 18 years old hospitalized with a high suspicion of COVID-19 infection were included in the study. The patients with fever and/or upper respiratory disease symptoms who had an epidemiological risk factor (exposure to confirmed COVID-19 patient, travel to high risk countries or regions), those who had findings of severe acute respiratory infections, and those who had cough or shortness of breath with sudden onset fever were hospitalized with the suspicion of COVID-19. The patients were categorized as mild illnesses, pneumonia, severe pneumonia according to WHO COVID-19 disease severity classification [4]. Patients diagnosed with another disease during hospitalization and those to whom PCR tests were not available were excluded from the study. The initial SARS-CoV-2 PCR test was performed on the day of hospitalization. In patients with a negative initial test, a second test was obtained 24–48 hours after the first test. We continued to follow-up the patients with a positive PCR test in the hospital until a negative control test was obtained. The patients with a negative initial test were followed-up in the hospital until their second tests were concluded. The patients with two negative consecutive tests performed at at least a

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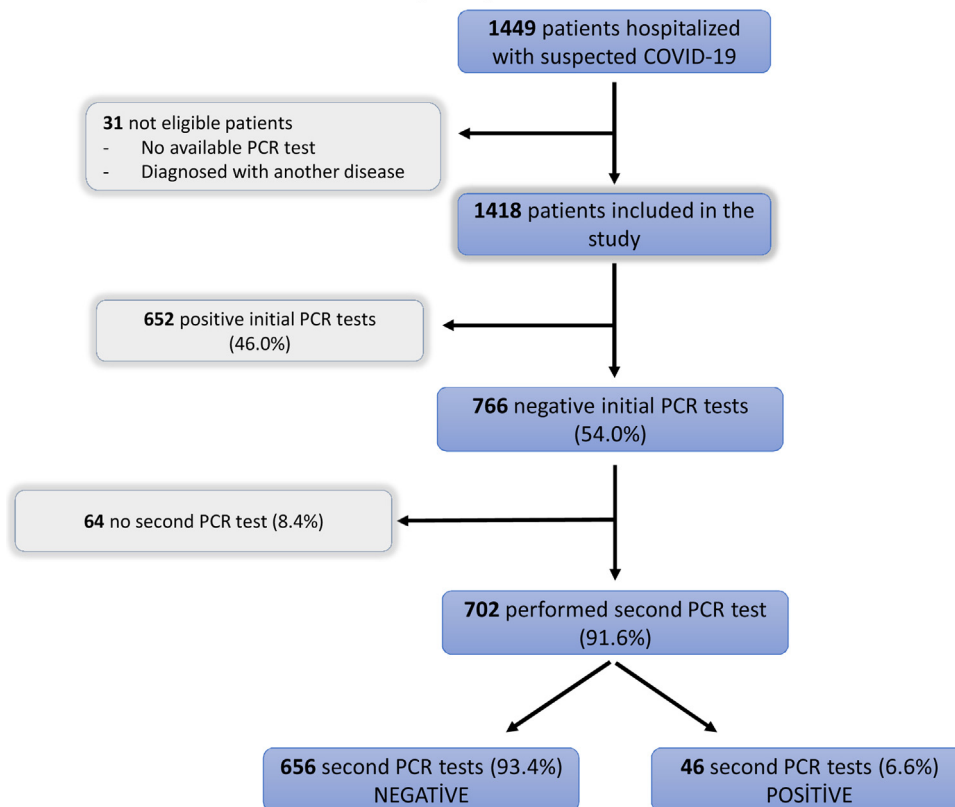


Fig. 1. The results of second PCR test in patients whose initial tests were negative for SARS-CoV-2.

24-hours interval were discharged if there was no obstacle to hospital discharge.

A total of 1449 patients were hospitalized in infectious diseases clinics with the suspicion of COVID-19 infection during the study period. Thirty-one patients who had no available PCR test results or were diagnosed with another disease were excluded from the study. The study was carried out in 1418 patients. Of these patients, 808 (57%) were male, the median age was 69 (18–92) years old. 38% of them had at least one comorbidity. The most common symptoms were fever (37.5%), coughing (52.2%) and dyspnea (26.7%). The percentage of mild illness, pneumonia and severe pneumonia patients among the tested population were 35.1%, 53.4% and 11.1%, respectively. Intensive care unit follow-up was required in 159 patients, and 69 of them died.

The initial PCR test was positive in 652 of the patients (46.0%) and negative in 766 (54.0%) (Fig. 1). The first obtained RT-PCR tests were positive in 647 of 1409 (45.9%) nasopharyngeal samples and in 5 of 9 tracheal aspirate samples (55.5%). The second PCR test was performed in 702 (91.6%) of 766 patients whose first tests were negative. Of them, 46 (6.6%) were detected positive. Fig. 2 shows the first PCR test results of 1418 patients and the second test results of 702 patients whose first test is negative by sample types. Of 697 nasopharyngeal samples with a negative initial PCR test, 44 (6.3%) were positive for SARS-CoV-2 PCR. A tracheal aspirate sample was examined in only 5 of the patients, 2 of them (40.0%) were positive (Fig. 2). When evaluated the characteristic of 46 patients whose second PCR test was positive, 25 (54.3%) were male, the median age 73 (22–81) years old. The most common symptoms were fever (43.5%), cough (41.3%) and dyspnea (32.6%). Of the patients, 11 (23.4%) had mild illness, 22 (47.8%) had pneumonia, 13 (28.2%) had severe pneumonia. Twelve patients required intensive care follow-up, 6 of them died.

All patients with suspected of COVID-19 infection should undergo PCR testing which is the referential method of diagnosis [3]. However, different sensitivity rates have been reported in literature. The sensitivity of PCR tests changes according to the type of sample, the duration of infection, the specific clinical syndrome of COVID-19, and viral load [5]. For the initial test, upper respiratory (e.g. nasopharyngeal swab test) samples are recommended. WHO and The Infectious Diseases Society of America (IDSA) recommend repeating the test in patients with intermediate/high clinical suspicion of COVID-19 infection [3,6]. IDSA recommends performing second test 24–48 hours after the initially negative tests. The lower respiratory samples are recommended for the second test in patients with signs and symptoms of lower respiratory tract infection. Following WHO and IDSA recommendations, we implemented two consecutive negative test strategies in our clinics to exclude the infection and to discharge the patients who were hospitalized for suspected COVID-19 infection. However, in almost all patients, the second test was performed from nasopharyngeal swab test due to the difficulty in taking lower respiratory tract samples, or considering upper respiratory tract infection in the foreground. The tracheal aspirate sample was taken in a limited number of patients who had been transferred to the intensive care unit because of deteriorated condition.

We have hospitalized only the cases with a high suspicion for COVID-19 and performed the second nasopharyngeal test in the patients whose initial test was negative. The patient follow up was continued in the hospital until the second test was concluded. RT-PCR was repeated in more than 90 percent of the patients whose first RT-PCR test was negative. However, the majority of patients (93.5%) remained SARS-CoV-2 PCR negative in the second nasopharyngeal test. Similarly, Long DR et al. reported that the second nasopharyngeal test had been detected positive in only 3.5% of

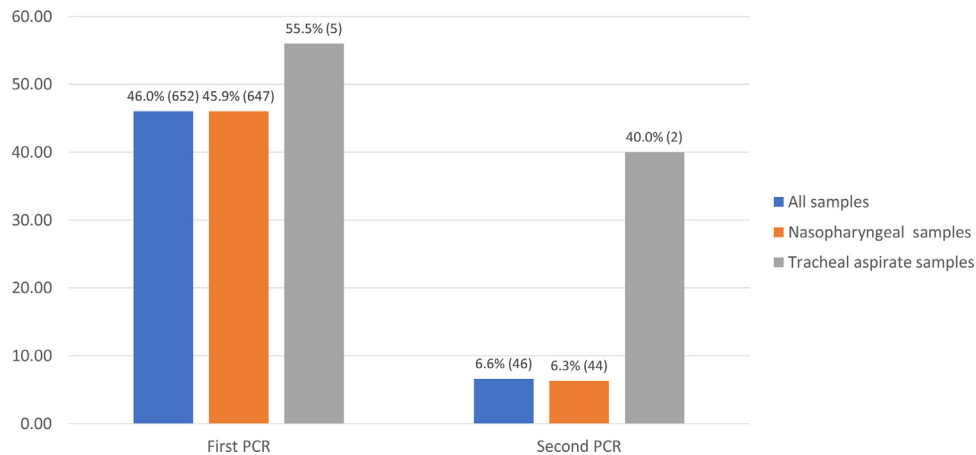


Fig. 2. The percentage of PCR test positivity according to sample order and type.

626 patients with negative initial RT-PCR test [7]. We found the sensitivity of the second tracheal aspirate test higher than second nasopharyngeal sample test, however, the result on tracheal aspirate were performed in a limited number of patients. It could be performed in only intubated patients.

In conclusion, considering that more samples have been tested due to inappropriate samples, we think that the second test strategy causes the loss of labor, time, and is costly. We recommend that the strategy of using the second nasopharyngeal PCR test to confirm or exclude the diagnosis should be reconsidered, because its additional contribution to the first test is very low. Clinical-based diagnosis by using the support of other parameters will provide a more appropriate approach in patients with an initially negative PCR test.

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Author Contributions

All authors contributed to the article, read and approved the final manuscript. Bircan Kayaaslan wrote the article.

Disclosure of Interest

The authors declare that they have no competing interest.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

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 Investigation; Methodology; Bircan Kayaaslan, Rahmet Guner
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 Resources; Software; Fatme Eser
 Supervision; Validation; Visualization; Roles/Writing – original draft; All authors

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