

Accuracy of Emergency Department Clinical Findings for Diagnosis of Coronavirus Disease 2019

Olivier Peyrony, MD, PhD*; Carole Marbeuf-Gueye, MD; Vy Truong, MD; Marion Giroud, MD; Clémentine Rivière, MD; Khalil Khenissi, MD; Léa Legay, MD; Marie Simonetta, MD; Arben Elezi, MD; Alessandra Principe, MD; Pierre Taboulet, MD; Carl Ogereau, MD; Mathieu Tourdjman, MD, MPH; Sami Ellouze, MD, PhD; Jean-Paul Fontaine, MD

*Corresponding Author. E-mail: o.peyrony@hotmail.fr.

Study objective: We seek to describe the medical history and clinical findings of patients attending the emergency department (ED) with suspected coronavirus disease 2019 (COVID-19) and estimate the diagnostic accuracy of patients' characteristics for predicting COVID-19.

Methods: We prospectively enrolled all patients tested for severe acute respiratory syndrome coronavirus 2 by reverse-transcriptase polymerase chain reaction in our ED from March 9, 2020, to April 4, 2020. We abstracted medical history, physical examination findings, and the clinical probability of COVID-19 (low, moderate, and high) rated by emergency physicians, depending on their clinical judgment. We assessed diagnostic accuracy of these characteristics for COVID-19 by calculating positive and negative likelihood ratios.

Results: We included 391 patients, of whom 225 had positive test results for severe acute respiratory syndrome coronavirus 2. Reverse-transcriptase polymerase chain reaction result was more likely to be negative when the emergency physician thought that clinical probability was low, and more likely to be positive when he or she thought that it was high. Patient-reported anosmia and the presence of bilateral B lines on lung ultrasonography had the highest positive likelihood ratio for the diagnosis of COVID-19 (7.58, 95% confidence interval [CI] 2.36 to 24.36; and 7.09, 95% CI 2.77 to 18.12, respectively). The absence of a high clinical probability determined by the emergency physician and the absence of bilateral B lines on lung ultrasonography had the lowest negative likelihood ratio for the diagnosis of COVID-19 (0.33, 95% CI 0.25 to 0.43; and 0.26, 95% CI 0.15 to 0.45, respectively).

Conclusion: Anosmia, emergency physician estimate of high clinical probability, and bilateral B lines on lung ultrasonography increased the likelihood of identifying COVID-19 in patients presenting to the ED. [Ann Emerg Med. 2020;■:1-8.]

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INTRODUCTION

Background

The novel coronavirus disease 2019 (COVID-19) outbreak has led to major reorganizations of emergency departments (EDs) to face the significant increase of patients with suspected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ The clinical description of hospitalized patients has been reported in the literature,²⁻⁶ but to our knowledge no study has focused on clinical and diagnostic findings in the ED setting.

Importance

Among patients attending EDs, rapid triage of those with suspected COVID-19 is mandatory to appropriately

isolate them and avoid secondary transmissions. Clinical diagnosis can be challenging because the disease may present with nonspecific symptoms such as myalgia, cough, or fever.^{3,6} Medical history and clinical presentations of COVID-19 patients attending EDs need to be precisely described to facilitate early recognition by emergency physicians and promptly trigger diagnostic procedures such as real-time reverse-transcriptase polymerase chain reaction (RT-PCR).

Goals of This Investigation

The objectives of this study were to collect and describe the medical history and clinical findings of patients attending the ED who had suspected COVID-19, and to

Editor's Capsule Summary*What is already known on this topic*

The number of coronavirus disease 2019 (COVID-19) cases has been increasing significantly, but it can be challenging to diagnose this clinically.

What question this study addressed

What features are associated with a greater likelihood of COVID-19 in the emergency department?

What this study adds to our knowledge

In this prospective observational study of 391 patients for whom COVID-19 testing was performed, anosmia, emergency physician estimation of high clinical probability, and bilateral B lines on ultrasonography were associated with COVID-19 positivity.

How this is relevant to clinical practice

Emergency physicians should have a higher suspicion for COVID-19 in patients with these features.

assess utility of clinical parameters, physician gestalt (clinical judgment), and lung ultrasonography to accurately identify COVID-19 patients at ED presentation.

MATERIALS AND METHODS**Study Design and Setting**

This prospective observational study was conducted in the ED of Saint-Louis University Hospital, Paris, France. Starting March 9, 2020, we prospectively enrolled a cohort of all adult patients with suspected COVID-19 who were tested for SARS-CoV-2. This study reports the results of patients enrolled until April 4, 2020. The study was approved by the institutional review board of the French Speaking Society for Respiratory Medicine–Société de Pneumologie de Langue Française. Our study followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.⁷

Selection of Participants and Methods of Measurement

All adult patients (≥ 18 years) who were tested for SARS-CoV-2 in our ED were included after giving oral consent. Cases were identified and enrolled 24 hours per day, 7 days per week during the study period by the attending emergency physician or resident who was in charge of the patient. Testing for SARS-CoV-2 in

patients with suspected COVID-19 was left to the clinician's discretion, but most of the time, patients were tested when they were dyspneic or reported shortness of breath; when they had comorbidities that put them at risk of severe infection such as immunosuppression, chronic respiratory insufficiency, cardiovascular diseases, and obesity; if they were older than 70 years; or if they were too weak to be discharged home. Some patients without clinical suspicion of COVID-19 but needing hospitalization in non-COVID-19 areas were also tested. Patients younger than 70 years, with no comorbidities, and with no respiratory symptoms were not tested. Before the outbreak, our ED received approximately 110 to 120 patients per day, and this number decreased to approximately 50 to 60 from the beginning of the pandemic in March. During the study period, we tested approximately 10 to 20 patients per day. If patients attended the ED more than once, only the last visit was included. There were no other exclusion criteria.

When testing for SARS-CoV-2, the attending emergency physician or resident physician was asked to report in a dedicated form the patient's medical history; Eastern Cooperative Oncology Group Performance Status, which is a scale that describes patients' ability to care for themselves and perform daily activities, ranging from 0 (fully active) to 4 (completely disabled); physical examination; and chest radiograph and lung ultrasonographic findings when those were performed. Lung ultrasonography was performed with a pocket-size device (VSCAN; GE Healthcare, Chicago, IL). After medical history, physical examination, ultrasonography, and chest radiographs, attending physicians were asked to rate the clinical probability of COVID-19 based on both their clinical judgment and a predefined 3-level scale (low, moderate, and high). Because anosmia was reported in Europe at approximately the end of March, this clinical sign was added to the form on March 24, 2020.

All study data and variables with their categories were defined before the beginning of the study. Four residents who were previously trained in data abstraction completed the forms with a dedicated spreadsheet. Age, sex, vital signs at ED arrival, and any data that were missing in the forms were abstracted retrospectively from the patients' ED medical files, with the exception of clinical probability, which could be determined only prospectively. An emergency physician with expertise in research periodically monitored data abstraction. When there was disagreement between abstractors or if data were ambiguous, this

emergency physician made the final decision. No assessment of interrater reliability was performed.

The criterion standard for diagnosis was the result of SARS-CoV-2 RT-PCR via nasal swab (Cobas SARS-CoV-2 Test; Roche, Meylan, France). The patients who initially had a negative RT-PCR result in the ED but a positive test result in the next 48 hours were considered as having positive results (initial false negative).

Primary Data Analysis

Continuous variables were reported as medians with their interquartile ranges. To assess the performance of each characteristic to accurately identify COVID-19, we calculated the sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratios, and their 95% confidence intervals (CIs). We calculated posttest probabilities depending on both pretest probabilities (5%, 10%, 25%, 50%, and 75%) and the presence or absence of bilateral B lines on lung ultrasonography. Accuracy of the physician clinical probability in identifying patients with COVID-19 was assessed with a receiver operating characteristic (ROC) curve and by calculating the area under the curve with its 95% CI. Data were analyzed with R 3.5.0 software (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Characteristics of Study Subjects

During the study period, 400 patients were tested for SARS-CoV-2. After excluding 9 patients who were tested 2 times during 2 ED visits, we included 391 patients. Among those patients, 225 (57.6%) had positive test results for SARS-CoV-2 (including 5 initial false-negative results). Median age was 62 years (IQR, 48 to 71 years) and 150 (38.4%) were women. General characteristics of these patients with suspected COVID-19 are presented in Table 1. Among patients with confirmed COVID-19, 67 (29.8%) were discharged home from the ED, 134 (59.5%) were hospitalized in wards, 22 (9.8%) were admitted to the ICU, and 2 (0.9%) died in the ED.

Main Results

Patient-reported symptoms, physical examination, lung ultrasonography, and chest radiographic findings in patients with or without COVID-19 are summarized in Table 2. Among patients with confirmed COVID-19, 53 (23.6%) reported gastrointestinal symptoms such as vomiting, diarrhea, or abdominal pain, 147 (65.6%) had a temperature below 38°C (100.4°F), and 97 (43.3%) had a temperature below 37.5°C (98.6°F) on ED arrival

Table 1. General characteristics of patients with suspected COVID-19.

Variable	Total (N=391)	Missing Data, No. (%)
Age, median (IQR), y	62 (48–71)	0
Female sex	150 (38.4)	0
ECOG PS		104 (26.6)
0–2	257 (89.5)	
3–4	30 (10.5)	
Immunosuppression	195 (50.5)	5 (1.3)
Diabetes mellitus	68 (17.6)	
Solid cancer	58 (15.0)	
Hematologic malignancy	47 (12.2)	
Solid organ transplant	14 (3.6)	
HIV	23 (6.0)	
Extended corticosteroid course	22 (5.7)	
Other	16 (4.1)	
Chronic lung disease	85 (22.1)	6 (1.5)
COPD	24 (6.2)	
Asthma	22 (5.7)	
Lung cancer	8 (2.0)	
Bronchiectasis/emphysema	8 (2.0)	
Sarcoidosis/fibrosis	7 (1.8)	
Other	23 (6.0)	
Cardiovascular disease	156 (40.4)	5 (1.3)
Hypertension	122 (31.6)	
Atrial fibrillation	29 (7.4)	
Coronary disease	22 (5.7)	
Chronic heart failure	16 (4.1)	
Other	5 (1.3)	
Obesity	58 (15.2)	9 (2.3)
No comorbidity	70 (18.1)	5 (1.3)

IQR, Interquartile range; ECOG PS, Eastern Cooperative Oncology Group Performance Status; COPD chronic obstructive pulmonary disease.

Data are provided as No. (%) unless otherwise indicated.

(temperature was missing for 1 patient). When lung ultrasonography was performed on 48 patients (21.4%) with COVID-19, bilateral B lines were present in 36 (76.6%) of them.

Emergency physicians rated the clinical probability for 273 patients. Table 3 shows the proportion of patients with or without COVID-19, depending on the emergency physician's clinical probability. RT-PCR was more likely to be negative for SARS-CoV-2 when the emergency physician thought that clinical probability was low and more likely to be positive when he or she thought that it was high. The Figure shows the accuracy of physician clinical judgment in identifying COVID-19 patients (area under the curve=0.795; 95% CI 0.743 to 0.848).

Table 2. Patient-reported symptoms and clinical and chest radiographic findings in patients with or without COVID-19.

Variable	Total (N=391)	COVID-19 Positive (n=225)	COVID-19 Negative (n=166)	Missing Data, No. (%)
Patient-reported symptoms (%)				1 (0.2)
Classic symptoms				
Fever	259 (66.4)	176 (78.2)	83 (50.3)	
Cough	239 (61.3)	158 (70.2)	81 (49.1)	
Dyspnea	197 (50.5)	131 (58.2)	66 (40.0)	
Myalgia	93 (23.8)	71 (31.6)	22 (13.3)	
Rhinitis/pharyngitis	45 (11.5)	19 (8.4)	26 (15.8)	
Anosmia	34 (8.7)	31 (13.8)	3 (1.8)	
None	41 (10.5)	10 (4.4)	31 (18.8)	
Less classic symptoms				
Headache	27 (6.9)	15 (6.7)	12 (7.3)	
Gastrointestinal symptoms	94 (24.1)	53 (23.6)	41 (24.8)	
Fatigue	55 (14.1)	34 (15.1)	21 (12.7)	
Chest pain	24 (6.2)	11 (4.9)	13 (7.9)	
Dizziness/syncope	21 (5.4)	8 (3.6)	13 (7.9)	
Hemoptysis	4 (1.0)	3 (1.3)	1 (0.6)	
Symptom duration, median (IQR), days	5 (3–8)	7 (3–9)	4 (2–7)	37 (9.5)
Vital signs at ED arrival, median (IQR)				
SBP, mm Hg	130 (113–143)	129 (111–141)	131 (116–145)	6 (1.5)
DBP, mm Hg	75 (65–85)	75 (65–85)	75 (66–85)	7 (1.8)
PR, beats/min	94 (84–109)	93 (85–106)	99 (82–110)	8 (2.0)
Temperature, °C	37.3 (36.6–38.0)	37.6 (36.9–38.1)	36.9 (36.4–37.6)	6 (1.5)
RR, breaths/min	22 (19–28)	25 (20–30)	20 (17–24)	70 (17.9)
Oxygen saturation, %	100 (96–100)	99 (96–100)	100 (97–100)	1 (0.2)
Need for oxygen therapy, No. (%)	131 (34.0)	96 (43.0)	35 (21.6)	6 (1.5)
Oxygen delivery, median (IQR), L/min	3 (2–5)	3 (2–6)	2 (2–3)	5 (3.8)
Physical examination, No. (%)				
Altered mental status	28 (7.2)	15 (6.7)	13 (7.8)	1 (0.2)
Mottled skin	34 (9.1)	23 (10.7)	11 (7.0)	19 (4.9)
Lung auscultation				7 (1.8)
Normal	218 (56.8)	106 (48.4)	112 (67.9)	
Unilateral crackles	33 (8.6)	21 (9.6)	12 (7.3)	
Bilateral crackles	95 (24.7)	80 (36.5)	15 (9.1)	
Wheezing	17 (4.4)	4 (1.8)	13 (7.9)	
Lung ultrasonography				4 (1.0)
Not performed	303 (78.3)	176 (78.9)	127 (77.4)	
No bilateral B lines	44 (11.4)	11 (4.9)	33 (20.1)	
Bilateral B lines	40 (10.3)	36 (16.2)	4 (2.5)	
Chest radiograph				0
Not performed	262 (67.0)	145 (64.4)	117 (70.5)	
Normal	48 (12.3)	19 (8.4)	29 (17.5)	
1 lung involved	11 (2.8)	6 (2.7)	5 (3.0)	
Both lungs involved	43 (11.0)	35 (15.6)	8 (4.8)	
Other	27 (6.9)	20 (8.9)	7 (4.2)	

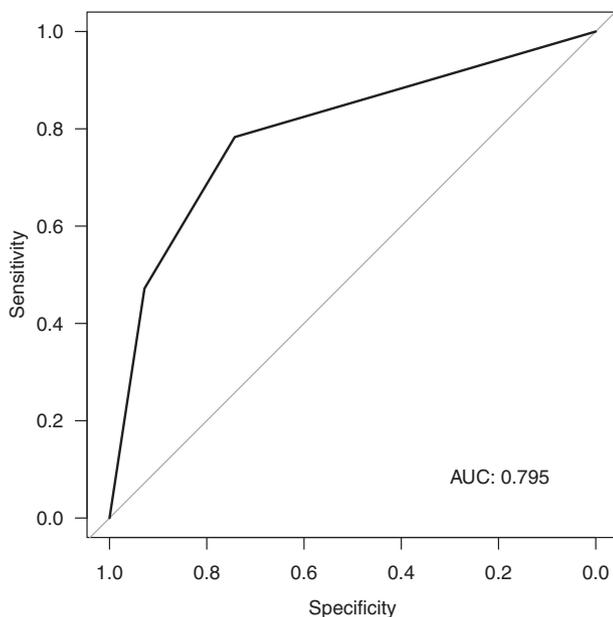
SBP, Systolic blood pressure; DBP, diastolic blood pressure; PR, pulse rate; RR, respiratory rate.

Table 3. Proportion of COVID-19 positive or negative results, depending on the emergency physician clinical probability.

Clinical Probability (N=273)	RT-PCR Result for SARS-CoV-2,	
	No. (%)	
	Positive (n=167)	Negative (n=106)
Low	12 (19.4)	50 (80.6)
Moderate	31 (48.4)	33 (51.6)
High	124 (84.4)	23 (15.6)

Table 4 shows the sensitivity, specificity, positive and negative predictive value, and positive and negative likelihood ratio for some of the patient-reported symptoms, clinical ultrasonographic findings, and chest radiographic findings. Patient-reported anosmia and the presence of bilateral B lines on lung ultrasonography had the highest positive likelihood ratio for the diagnosis of COVID-19 (7.58, 95% CI 2.36 to 24.36; and 7.09, 95% CI 2.77 to 18.12 respectively). The absence of a high clinical probability determined by the emergency physician and the absence of bilateral B lines on lung ultrasonography had the lowest negative likelihood ratio for the diagnosis of COVID-19 (0.33, 95% CI 0.25 to 0.43; and 0.26, 95% CI 0.15 to 0.45, respectively).

Table E1 (available online at <http://www.annemergmed.com>) shows the posttest probability, depending on the pretest probability (ie, prevalence) and the results of lung ultrasonography.

**Figure.** ROC curve. Accuracy of the emergency physician clinical probability in identifying patients with COVID-19. AUC, Area under the curve.

LIMITATIONS

Our study has several limitations. First, not every patient was tested for SARS-CoV-2 and testing was left to the clinician's discretion. However, despite the absence of clear predefined inclusion criteria, testing was performed in the majority of cases for patients who had severe symptoms such as dyspnea, reported shortness of breath, presented with comorbidities (eg, immunosuppression, chronic pulmonary or cardiovascular diseases), or were older than 70 years. Thus, our results may not be valid in other populations such as young people without comorbidities and those with few symptoms. Also, because our results are from a single center in France, they may not be generalizable to other centers. Second, it is possible that patients did not systematically report their symptoms, and this might have decreased the estimates of their prevalence. Third, we may have underestimated anosmia because we added this to the form only on March 24, 2020. Fourth, lung ultrasonography was not systematic and occurred for only 22.3% of the patients, which contributed to the large 95% CI observed. It is possible that emergency physicians performed lung ultrasonography in the most severe cases and that the accuracy of this examination in predicting COVID-19 is likely to be lower in patients with fewer symptoms. Fifth, our criterion standard to diagnose COVID-19 was based on the RT-PCR, which may have yielded false-negative results. To address this, we also evaluated patients who initially had negative test results for SARS-CoV-2 but were then hospitalized and secondarily had positive results, and considered them as having positive results.

DISCUSSION

To the best of our knowledge, this is the first prospective study that described patient-reported symptoms and physical examination findings in a large cohort of patients with suspected COVID-19 who attended the ED, as well as the first prospective study that estimated the accuracy of clinical findings for the diagnosis of COVID-19.

At the beginning of the epidemic in France, knowledge of the COVID-19 clinical picture was mainly extrapolated from cases in Wuhan, China. Emergency physicians prepared to face an unknown disease and attend to patients with nonspecific influenza-like symptoms with clinical signs of lung infection, or acute respiratory failure for the most severe cases.^{3,6} Since then, studies have been published about the epidemiology,¹ the risk factors for severe disease,⁴ and the description of critically ill patients⁸⁻¹¹ infected with SARS-CoV-2, but there are limited data

Table 4. Clinical and chest radiographic findings accuracy for the diagnosis of COVID-19.

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
Patient-reported symptoms						
Fever	0.78 (0.72–0.83)	0.50 (0.42–0.58)	0.68 (0.62–0.74)	0.63 (0.54–0.71)	1.56 (1.32–1.84)	0.44 (0.33–0.59)
Dyspnea	0.58 (0.51–0.65)	0.60 (0.52–0.68)	0.66 (0.59–0.73)	0.51 (0.44–0.59)	1.46 (1.17–1.81)	0.70 (0.57–0.85)
Myalgia	0.32 (0.26–0.38)	0.87 (0.81–0.91)	0.76 (0.66–0.85)	0.48 (0.42–0.54)	2.37 (1.53–3.65)	0.79 (0.71–0.88)
Anosmia	0.14 (0.10–0.19)	0.98 (0.95–1.00)	0.91 (0.76–0.98)	0.46 (0.40–0.51)	7.58 (2.36–24.36)	0.88 (0.83–0.93)
Vital signs at ED arrival						
Temperature $\geq 38^{\circ}\text{C}$	0.34 (0.28–0.41)	0.83 (0.76–0.88)	0.73 (0.64–0.81)	0.47 (0.42–0.54)	1.98 (1.35–2.90)	0.79 (0.71–0.89)
Oxygen saturation $< 95\%$	0.17 (0.12–0.22)	0.91 (0.85–0.95)	0.72 (0.58–0.83)	0.45 (0.39–0.50)	1.86 (1.06–3.26)	0.91 (0.85–0.99)
RR > 25 breaths/min	0.47 (0.39–0.54)	0.78 (0.70–0.85)	0.76 (0.68–0.84)	0.49 (0.42–0.56)	2.13 (1.49–3.06)	0.68 (0.58–0.80)
Oxygen flow ≥ 6 L/min	0.28 (0.19–0.38)	0.91 (0.75–0.98)	0.90 (0.73–0.98)	0.30 (0.21–0.40)	2.95 (0.96–9.09)	0.80 (0.68–0.94)
Physical examination						
Bilateral lung crackles	0.37 (0.30–0.43)	0.91 (0.85–0.95)	0.84 (0.75–0.91)	0.52 (0.46–0.58)	4.02 (2.41–6.71)	0.70 (0.62–0.78)
Lung ultrasonography						
Bilateral B lines	0.77 (0.62–0.88)	0.89 (0.75–0.97)	0.90 (0.76–0.97)	0.75 (0.60–0.87)	7.09 (2.77–18.12)	0.26 (0.15–0.45)
Chest radiograph						
Both lungs involved	0.16 (0.11–0.21)	0.96 (0.91–0.98)	0.83 (0.69–0.93)	0.45 (0.40–0.51)	3.67 (1.67–8.05)	0.88 (0.83–0.94)
High clinical probability	0.74 (0.67–0.81)	0.78 (0.69–0.86)	0.84 (0.77–0.90)	0.66 (0.57–0.74)	3.42 (2.36–4.97)	0.33 (0.25–0.43)

PPV, Positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR-, negative likelihood ratio.

regarding the accuracy of clinical findings in patients with suspected COVID-19. Moreover, most studies have focused on patients who were already hospitalized for the disease, which may differ from the ED population.

Prompt identification of possible cases is mandatory to avoid the spread of the virus by patients with mild or nonspecific symptoms.¹² Therefore, emergency physicians need to be cautious when they evaluate such patients and be aware of some pitfalls. Whereas fever (temperature $> 37.3^{\circ}\text{C}$) was reported in more than 90% of the patients hospitalized with COVID-19,^{4,6} we found that even if 78.2% of the patients reported fever, only 34.4% of the patients had a temperature greater than or equal to 38°C and 56.7% had one greater than or equal to 37.5°C at ED triage. It is possible that the temperature was initially decreased by antipyretics and subsequently increased during the ED stay. Nevertheless, temperature should not be used in isolation to exclude COVID-19.¹³ Consistent with other studies, we found that the most frequent reported symptoms were fever, cough, dyspnea, and myalgia.²⁻⁶ Gastrointestinal symptoms were present in 23.6% of our patients, whereas 1 small study of 18 patients found a rate of 17%¹⁴ and larger cohorts have reported these symptoms in less than 10%.²⁻⁶ Anosmia was reported by 13.8% of the patients in our cohort and was the most specific sign of COVID-19. It is likely that we underestimated this sign, which was not initially described

in the Chinese literature and was reported in Europe at approximately the end of March.¹⁵⁻¹⁷

Other findings such as bilateral crackles on lung auscultation or the rapid need for high levels of oxygen delivery at ED arrival were highly suggestive of COVID-19, especially among middle-aged or older patients with comorbidities such as diabetes or cardiovascular diseases.¹⁸ Because this disease induces endotheliitis, leading to vascular derangements,¹⁹ it is likely that new symptoms involving multiple organs such as neurologic²⁰ or skin disorders²¹ will emerge.

Besides clinical signs, lung imaging and particularly computed tomographic scans have been shown to have a high sensitivity for the diagnosis of COVID-19, particularly in severe cases, and may be valuable in patients with high clinical probability but negative RT-PCR results.²²⁻²⁴ Another option might be to perform lung ultrasonography, allowing rapid diagnosis and severity assessment at patient bedside for suspected COVID-19.^{25,26} In our study, the presence or absence of bilateral B lines with a pocket-size ultrasonographic device had the higher positive likelihood ratio and a low negative likelihood ratio, respectively.

In a study with 20 patients with COVID-19, Xing et al²⁷ found that all patients showed pleural-line abnormalities and bilateral B lines on lung ultrasonography, regardless of the severity or stage of the disease. In another

retrospective study that included 30 patients with COVID-19, interstitial pulmonary edema was present on lung ultrasonography in 90.0% of the cases.²⁸ Nonetheless, literature on this topic is scarce and more data are needed.²⁹

In the present study, we found that emergency physician clinical judgment was accurate and that only 19.4% of the patients with low clinical probability had COVID-19, whereas 15.6% of the patients with high clinical probability did not have it. The area under the curve of 0.795 seems fair for a new disease with few specific clinical signs. Emergency physician gestalt has been studied in predicting other diseases and performed equally well, with an observed area under the curve of 0.83 for appendicitis in children,³⁰ 0.75 for acute coronary syndrome,³¹ 0.86 for acute heart failure syndrome,³² and 0.81 for pulmonary embolism.³³

In summary, in this large prospective cohort study of patients attending the ED for suspected COVID-19, anosmia, emergency physician estimate of high clinical probability, and bilateral B lines on lung ultrasonography increased the likelihood of identifying COVID-19. Future studies should assess this in other EDs and the role of combining findings to develop clinical decision tools.

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Author affiliations: From the Emergency Department, Saint-Louis Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France (Peyrony, Marbeuf-Gueye, Truong, Giroud, Rivière, Khenissi, Legay, Simonetta, Elezi, Principe, Taboulet, Ogereau, Tourdjman, Ellouze, Fontaine); and Santé Publique France (Tourdjman).

Author contributions: OP, SE, and J-PF were responsible for study conception and design. OP, CM-G, VT, MG, CR, KK, LL, MS, AE, AP, PT, CO, and SE were responsible for provision of study materials for patients. OP, CM-G, VT, MG, CR, and SE were responsible for collection and assembly of data. OP was responsible for data analysis and interpretation. OP, MT, and JPF were responsible for writing the article. All authors approved the final article. OP takes responsibility for the paper as a whole.

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