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Radiology

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Conflicts of interest are listed at the end of this article.

See also the editorial by Elicker in this issue.

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Background: Clinicians need to rapidly and reliably diagnose coronavirus disease 2019 (COVID-19) for proper risk stratification, isolation strategies, and treatment decisions.

Purpose: To assess the real-life performance of radiologist emergency department chest CT interpretation for diagnosing COVID-19 during the acute phase of the pandemic, using the COVID-19 Reporting and Data System (CO-RADS).

Materials and Methods: This retrospective multicenter study included consecutive patients who presented to emergency departments in six medical centers between March and April 2020 with moderate to severe upper respiratory symptoms suspicious for COVID-19. As part of clinical practice, chest CT scans were obtained for primary work-up and scored using the five-point CO-RADS scheme for suspicion of COVID-19. CT was compared with severe acute respiratory syndrome coronavirus 2 reverse-transcription polymerase chain reaction (RT-PCR) assay and a clinical reference standard established by a multidisciplinary group of clinicians based on RT-PCR, COVID-19 contact history, oxygen therapy, timing of RT-PCR testing, and likely alternative diagnosis. Performance of CT was estimated using area under the receiver operating characteristic curve (AUC) analysis and diagnostic odds ratios against both reference standards. Subgroup analysis was performed on the basis of symptom duration grouped presentations of less than 48 hours, 48 hours through 7 days, and more than 7 days.

Results: A total of 1070 patients (median age, 66 years; interquartile range, 54–75 years; 626 men) were included, of whom 536 (50%) had a positive RT-PCR result and 137 (13%) of whom were considered to have a possible or probable COVID-19 diagnosis based on the clinical reference standard. Chest CT yielded an AUC of 0.87 (95% CI: 0.84, 0.89) compared with RT-PCR and 0.87 (95% CI: 0.85, 0.89) compared with the clinical reference standard. A CO-RADS score of 4 or greater yielded an odds ratio of 25.9 (95% CI: 18.7, 35.9) for a COVID-19 diagnosis with RT-PCR and an odds ratio of 30.6 (95% CI: 21.1, 44.4) with the clinical reference standard. For symptom duration of less than 48 hours, the AUC fell to 0.71 (95% CI: 0.62, 0.80; $P < .001$).

Conclusion: Chest CT analysis using the coronavirus disease 2019 (COVID-19) Reporting and Data System enables rapid and reliable diagnosis of COVID-19, particularly when symptom duration is greater than 48 hours.

Online supplemental material is available for this article.

The ongoing coronavirus disease 2019 (COVID-19) pandemic, a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has brought about a need for timely and high diagnostic performance tests for detecting COVID-19. The reference standard for diagnosing COVID-19 is a SARS-CoV-2 real-time reverse-transcription polymerase chain reaction (RT-PCR) test of respiratory tract specimens. Unfortunately, RT-PCR has limited sensitivity, and clinical test performance is dependent on test sample quality, viral load kinetics, and duration of symptoms (1–5). Moreover, the time required for laboratory testing and reporting of RT-PCR results can be substantial, which is undesirable in crowded emergency departments. Hence, in hospitals there is a need for rapid and reliable diagnostics of COVID-19 for appropriate isolation in patient groups with high suspicion of disease. CT is widely available and offers

Abbreviations

AUC = area under the receiver operating characteristic curve, CO-RADS = COVID-19 Reporting and Data System, COVID-19 = coronavirus disease 2019, RT-PCR = reverse-transcription polymerase chain reaction, SARS-CoV-2 = severe acute respiratory coronavirus 2

Summary

Chest CT analysis using the coronavirus disease 2019 (COVID-19) Reporting and Data System is fast and achieves a high performance for diagnosing COVID-19, particularly when symptom duration is greater than 48 hours.

Key Results

- Radiologist interpretation of emergency department chest CT examinations from 1070 patients in six medical centers yielded an area under the receiver operating characteristics curve (AUC) of 0.87 (95% CI: 0.84, 0.89) for a diagnosis of coronavirus disease 2019 (COVID-19) with real-time reverse-transcription polymerase chain reaction as the reference standard.
- A positive chest CT interpretation showed high performance for the diagnosis of COVID-19 pneumonia, with an odds ratio of 25.9 (95% CI: 18.7, 35.9).
- For symptom duration of less than 48 hours, the AUC of chest CT for the diagnosis of COVID-19 fell to 0.71 (95% CI: 0.62, 0.80; $P < .001$).

the potential for fast triage and robust rapid diagnosis with limited burden to patients. However, the use of CT scanning to diagnose COVID-19 has been strongly debated, with mixed recommendations (6,7).

The Dutch Radiological Society has developed a standardized reporting scheme for chest CT in patients presenting with moderate to severe symptoms of COVID-19 (8). This "COVID-19 Reporting and Data System" (CO-RADS) is a likelihood classification for the presence of pulmonary involvement of COVID-19, with scores varying from 1 (very low suspicion) to 5 (very high suspicion) depending on the type and distribution of the pulmonary abnormalities (Table 1). This CT classification has moderate to substantial interobserver agreement (8). However, the performance of CO-RADS and its clinical applicability have not been validated in a real-life setting.

This multicenter study aimed to assess the performance of the CO-RADS classification for diagnosing COVID-19 in patients presenting to the emergency department with moderate to severe symptoms suspicious for COVID-19, both for the overall study group and stratified according to duration of symptoms. Chest CT was compared with two reference standards: SARS-CoV-2 RT-PCR assay and a clinical diagnostic reference standard.

Materials and Methods

Ethics

This study was approved by the institutional review boards of all participating centers. Informed consent was waived by the local institutional review boards prior to the study.

Patients

This retrospective multicenter study in four university medical centers and two large teaching hospitals evaluated consecutive adult patients presenting to the emergency department between March 20 and April 3, 2020 (April 10 for center F), with moderate to severe symptoms suspicious for COVID-19 who underwent noncontrast-enhanced CT at presentation. Suspected COVID-19 was defined as (*a*) cough and clinically relevant dyspnea requiring hospital admission with or without fever greater than 38°C, (*b*) fever without a known cause, or (*c*) fever with anosmia. As standard practice in all these hospitals, patients underwent chest CT if there was a potential indication for hospital admission.

Patients were excluded from analysis if RT-PCR was not performed or if they were transferred from other hospitals with a known, RT-PCR–proven COVID-19 diagnosis. Patients who only underwent chest CT with intravenous contrast material were also excluded. Patients without reported CO-RADS were excluded from further analysis. Demographic and clinical information, including duration of symptoms, was retrieved from electronic patient records.

Imaging and CO-RADS Reporting

Noncontrast-enhanced CT scans were obtained with various CT scanners (Canon Aquilion Vision and Canon Aquilion One Genesis [Canon Medical Systems]; Somatom Force, Somatom Definition Flash, and Somatom Definition AS+ [Siemens Healthineers]; Lightspeed 16 [GE Healthcare]; Ingenuity 128 [Philips Healthcare]) according to existing local imaging protocols, preferably a low-dose protocol (Table E1 [online]). All scans were prospectively evaluated by local radiologists with varying levels of experience as part of regular care, without knowledge of RT-PCR results. The current study exclusively used the CO-RADS classification as adjudicated in the official radiologic report.

Reference Standard

CT was compared with two reference standards. The first reference standard was SARS-CoV-2 RT-PCR assay of a clinical specimen. COVID-19 infection was considered "proven" if at least one RT-PCR for SARS-CoV-2 in a throat, nasal, sputum, bronchoalveolar lavage fluid, and/or fecal sample was positive. If initial RT-PCR was negative, subsequent RT-PCR testing was generally performed, depending on the clinical likelihood of disease.

A reference standard for COVID-19 diagnosis has yet to be established. Although RT-PCR is widely used, a large proportion of patients with negative RT-PCR results still have high clinical suspicion for COVID-19. In daily routine, this subgroup is isolated and remains in isolation until COVID-19 is ruled out clinically and/or with repeat RT-PCR to avoid nosocomial COVID-19 transmission to noninfected individuals. To address the limited sensitivity of RT-PCR and the need to avoid missing a diagnosis in patients with COVID-19 in the inpatient setting, the study established a clinical reference standard that was designed to be highly sensitive (Fig 1).

In this clinical reference standard, patients with positive RT-PCR results were designated as having proven COVID-19

Table 1: Chest CT CO-RADS Classification for the Diagnosis of COVID-19

CO-RADS Category	Level of Suspicion for Pulmonary Involvement of COVID-19	Summary
0	Noninterpretable	Scan technically insufficient
1	Very low	Normal or noninfectious
2	Low	Typical for other infection but not COVID-19
3	Equivocal	Features compatible with COVID-19 but also other diseases
4	High	Suspicious for COVID-19
5	Very high	Typical for COVID-19
6	Proven	Positive for SARS-CoV-2 at RT-PCR

Note.—Adapted, with permission, from reference 8. Typical CT features include ground-glass opacities, with or without consolidations, in lung regions close to visceral pleural surfaces, including the fissures (subpleural sparing is allowed), and multifocal bilateral distribution. In addition, one of the following confirmatory patterns is present: ground-glass regions, crazy paving, patterns compatible with organizing pneumonia, or thickened vessels within parenchymal abnormalities. Suspicious CT features are as typical findings, but they are not located in contact with the visceral pleura, are strictly unilaterally located, have a predominant peribronchovascular distribution, or are superimposed on severe diffuse preexisting pulmonary abnormalities. CO-RADS = COVID-19 Reporting and Data System, COVID-19 = coronavirus disease 2019, RT-PCR = reverse-transcription polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

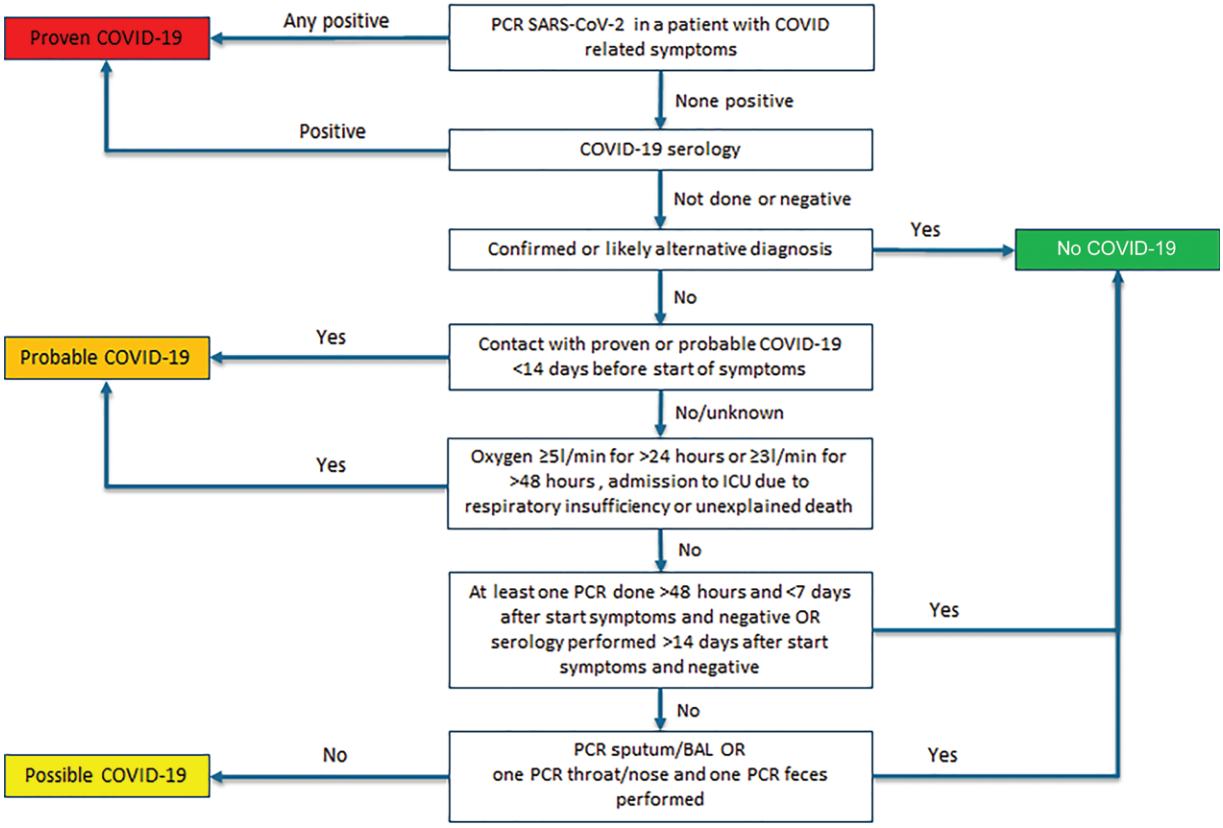

Figure 1: Flowchart of clinical reference standard. BAL = bronchoalveolar lavage, COVID-19 = coronavirus disease 2019, ICU = intensive care unit, PCR = polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

infection. Patients with negative RT-PCR results were classified as having probable, possible, or no COVID-19 infection on the basis of clinical data. These patients were classified by local teams of clinical physician assessors who were blinded to findings at CT and laboratory examination. First, assessors determined whether an alternative diagnosis explained the presenting symptoms, in which case the patient was classified as having no COVID-19. If no alternative diagnosis was established, patients were classified as having a probable diagnosis of COVID-19 if they had contact with persons with suspected or proven COVID-19, if they required high oxygen therapy (5 L O_2 for ≥24 hours or 3 L O_2 for ≥48 hours), if they required intensive care unit admission due to respiratory failure, or in the case of unexplained death during admission. The remaining patients were classified as having possible COVID-19 if their nasopharyngeal RT-PCR sample

had been collected less than 2 or more than 7 days after onset of symptoms. Classification in the proven, probable, and possible COVID-19 categories was considered positive for the clinical reference standard.

Statistical Analysis

Data from all participating centers were collected in line with General Data Protection Regulation standards. Statistical analyses were performed using software (SPSS statistics, version 25; IBM). Continuous data are presented either as means ± standard deviations or as medians and interquartile ranges. Categorical data are presented as proportions. Performance estimates are reported as proportions along with 95% CIs. Receiver operating characteristic analysis was performed to calculate the area under the receiver operating characteristic curve (AUC) for CO-RADS against both reference standards. Sensitivity, specificity, and diagnostic odds ratios at various cutoff points of the CO-RADS classification were calculated. Results are displayed per center and for all centers combined. Because pulmonary involvement may not be immediately visible, and because RT-PCR loses sensitivity at a later stage after the beginning of symptoms, subgroup analysis was performed on the basis of the duration of symptoms, grouping presentations of less than 48 hours, 48 hours through 7 days, and more than 7 days. Significance testing between subgroups of receiver operating characteristic analysis was performed with statistical software (MedCalc, version 19.3.1; MedCalc Software; *https://www.medcalc.org*). $P < .05$ represented a statistically significant difference.

Results

Patient Demographics

Of 1833 patients suspected of having COVID-19, 763 were excluded from the study group. Eighty-eight patients were excluded because they were not diagnosed in an emergency department, 403 were excluded because they had no symptoms or only mild symptoms, 129 were excluded because they did not undergo RT-PCR testing, 53 were excluded because they already had RT-PCR–proven COVID-19, 56 were excluded because they had no CO-RADS score in the original report, and 34 were excluded because they underwent contrast-enhanced CT, leaving a total of 1070 patients for inclusion in in this study (Fig 2). In the study group, 626 of the 1070 patients (59%) were men. The median patient age was 66 years (interquartile range, 54–75 years). The median duration of symptoms at admission was 7 days (interquartile range, 3–10 days). Baseline patient characteristics for each center are shown in Table 2.

Of the 1070 patients, 536 (50%) had proven COVID-19 based on a positive RT-PCR; in 497 of these 536 patients (93%), the initial RT-PCR test was positive. According to the clinical reference standard, of the 1070 patients, there were an additional 70 patients (7%) with negative RT-PCR results and probable COVID-19, 67 patients (6%) with negative RT-PCR results

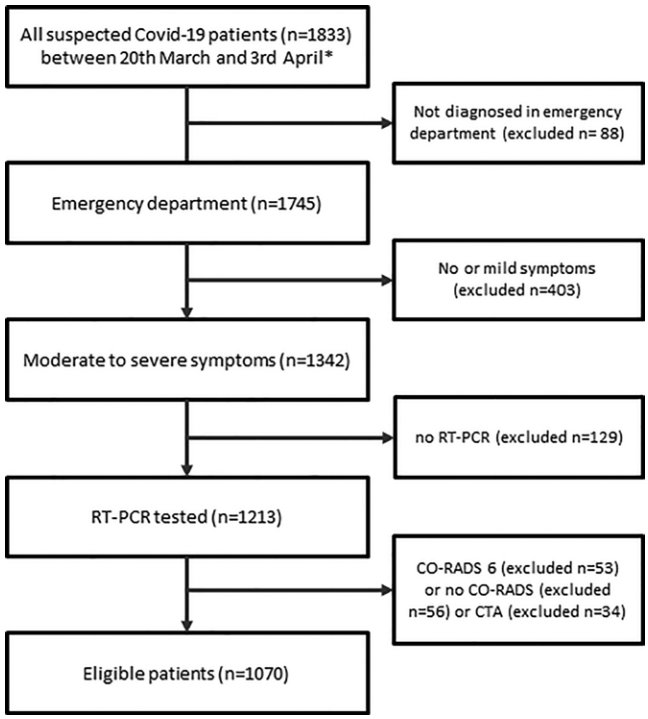

Figure 2: Inclusion flowchart. Patients were excluded when they were not diagnosed in the emergency department, when they had no symptoms or only mild symptoms, when they did not undergo reverse-transcription polymerase chain reaction (RT-PCR) testing, if coronavirus disease 2019 (COVID-19) was diagnosed with RT-PCR assay at the time of CT, or if the COVID-19 Reporting and Data System (CO-RADS) was not used in the original report. * = 10th of April for center F. CTA = CT angiography.

and possible COVID-19, and 397 (37%) with negative RT-PCR results and no COVID-19. Of the 1070 CT scans, 235 (22%) were scored as CO-RADS 1, 140 (13%) as CO-RADS 2, 134 (13%) as CO-RADS 3, 120 (11%) as CO-RADS 4, and 441 (41%) as CO-RADS 5 (Table 3).

Performance of Chest CT with CO-RADS

With use of RT-PCR as a reference standard, the AUC of CO-RADS was 0.87 (95% CI: 0.84, 0.89; range across hospitals, 0.82–0.90) (Table 4). At a CO-RADS positivity threshold of 4 or more, sensitivity was 86% (95% CI: 83, 89), specificity was 81% (95% CI: 78, 84), and the odds ratio for a COVID-19 diagnosis was 25.9 (95% CI: 18.7, 35.9).

Compared with the clinical reference standard, the AUC of CO-RADS was 0.87 (95% CI: 0.85, 0.89; range across hospitals, 0.85–0.89). At a CO-RADS positivity threshold of 4 or more, sensitivity was 77% (95% CI: 74, 81), specificity was 90% (95% CI: 87, 93), and the odds ratio for a COVID-19 diagnosis was 30.6 (95% CI: 21.1, 44.4). Results per CO-RADS category are shown in Figure 3, and results at different CO-RADS cutoffs are displayed in Table 5.

Duration of Symptoms

Pulmonary manifestations of COVID-19 at CT (CO-RADS ≥3) were seen in 67% of patients (18 of 52) with a symptom duration of less than 48 hours and in 95% of patients (449 of 471) with a symptom duration of more than 48 hours. The performance of CT in the diagnosis

Table 2: Baseline Patient Characteristics per Center

Characteristic	Center						Total
	A	B	C	D	E	F	
No. of patients	172	262	173	175	194	94	1070
M:F ratio	112:60	142:120	102:71	95:85	122:72	53:41	626:444
Median age (y)*	66 (51–74)	67 (55–76)	59 (47–70)	68 (54–76)	71 (59–79)	68 (56–76)	66 (54–75)
Duration of symptoms							
Median days of complaints*	6 (2–9)	7 (4–10)	7 (3–10)	6 (2–10)	6.5 (3–9)	7 (3–10)	7 (3–10)
<48 hours	49 (28)	32 (12)	34 (20)	42 (24)	41 (21)	22 (23)	220 (21)
>48 hours to 7 days	65 (38)	115 (44)	64 (37)	69 (39)	81 (42)	36 (38)	430 (40)
>7 days	55 (32)	104 (40)	64 (37)	55 (31)	64 (33)	34 (36)	376 (35)
Unknown	3 (2)	11 (6)	11 (6)	9 (5)	8 (4)	2 (2)	44 (4)
Reference standard							
No COVID-19	54 (31)	66 (25)	56 (32)	99 (57)	79 (41)	43 (46)	397 (37)
Possible COVID-19	16 (9)	17 (7)	21 (12)	8 (5)	1 (1)	4 (4)	67 (6)
Probable COVID-19	22 (13)	24 (9)	11 (6)	6 (3)	4 (2)	3 (3)	70 (7)
Proven COVID-19	80 (47)	155 (59)	85 (49)	62 (35)	110 (57)	44 (47)	536 (50)

Note.—Except where indicated, data are numbers of patients, with percentages in parentheses. Center A = Radboudumc, Nijmegen, the Netherlands, center B = Canisius Wilhelmina Hospital, Nijmegen, the Netherlands, center C = Amsterdam UMC, Location AMC, Amsterdam, the Netherlands, center D = Haaglanden MC, the Hague, the Netherlands, center E = Maastricht UMC, Maastricht, the Netherlands, and center F = Leiden UMC, Leiden, the Netherlands. COVID-19 = coronavirus disease 2019.

* Numbers in parentheses are the interquartile range.

Table 3: CO-RADS CT Score per Reference Standard Category

Reference Standard	CO-RADS 1	CO-RADS 2	CO-RADS 3	CO-RADS 4	CO-RADS 5	Total
No COVID-19	179	102	76	20	20	397
Possible COVID-19	21	11	14	8	13	67
Probable COVID-19	10	11	9	13	27	70
RT-PCR–proven COVID-19	25	16	35	79	381	536
Total	235	140	134	120	441	1070

Note.—CO-RADS = COVID-19 Reporting and Data System, COVID-19 = coronavirus disease 2019, RT-PCR = reverse-transcription polymerase chain reaction.

Table 4: Performance of CO-RADS

Center	RT-PCR–proven COVID-19	Clinical Reference Standard for COVID-19
A	0.86 (0.81, 0.92)	0.87 (0.82, 0.93)
B	0.82 (0.77, 0.88)	0.88 (0.83, 0.93)
C	0.89 (0.84, 0.94)	0.86 (0.81, 0.92)
D	0.87 (0.81, 0.93)	0.85 (0.78, 0.91)
E	0.87 (0.81, 0.92)	0.86 (0.80, 0.91)
F	0.90 (0.83, 0.97)	0.89 (0.82, 0.96)
All patients	0.87 (0.84, 0.89)	0.87 (0.85, 0.89)

Note.—Data are areas under the receiver operating characteristics curve of the CO-RADS for each center per reference standard, with the 95% CI in parentheses. Center A = Radboudumc, Nijmegen, the Netherlands, center B = Canisius Wilhelmina Hospital, Nijmegen, the Netherlands, center C = Amsterdam UMC, Location AMC, Amsterdam, the Netherlands, center D = Haaglanden MC, the Hague, the Netherlands, center E = Maastricht UMC, Maastricht, the Netherlands, and center F = Leiden UMC, Leiden, the Netherlands. CO-RADS = COVID-19 Reporting and Data System, COVID-19 = coronavirus disease 2019, RT-PCR = reverse-transcription polymerase chain reaction.

of COVID-19 was worse in the subgroup of patients with symptom duration of less than 48 hours (220 of 1070 patients) compared with patients with a symptom duration greater than 48 hours, with AUCs of 0.71 (95% CI: 0.62, 0.80; $P < .001$) against RT-PCR and 0.68 (95% CI: 0.60, 0.76; $P < .001$) against the clinical reference standard. In the subgroup of patients with symptom duration between 48 hours and 7 days (430 of 1070 patients), the AUC was 0.86 (95% CI: 0.83, 0.90) against RT-PCR and 0.89 (95% CI: 0.86, 0.93) against the clinical reference standard. For patients with a symptom duration of more than 7 days (376 of 1070 patients), the AUC was 0.86 (95% CI: 0.82, 0.90) against RT-PCR and 0.89 (95% CI: 0.85, 0.93) against the clinical reference standard (Fig 4).

Discussion

Large numbers of patients suspected of having coronavirus disease 2019 (COVID-19) flooded emergency departments during the first peak of COVID-19, creating the need for rapid and reliable diagnosis to guide clinicians in risk stratification, isolation strategies, and treatment decisions. During this pandemic,

we demonstrated high performance of chest CT using the COVID-19 Reporting and Data System for the diagnosis of COVID-19 in clinical practice. This high level of performance suggests that chest CT can be used to optimize and expedite emergency care for patients suspected of having COVID-19 pneumonia.

The AUC of CO-RADS for the diagnosis of COVID-19 was 0.87 (95% CI: 0.84, 0.89) when compared with RT-PCR and reached a sensitivity of 86% at a specificity of 81% at a CO-RADS positivity threshold of 4 or more. When compared with our clinical reference standard, we also found good performance of CT, reaching an AUC of 0.87 (95% CI: 0.85, 0.89) and a sensitivity of 77% at a specificity of 90% and an odds ratio greater than 30. Our subgroup analysis based on duration of symptoms showed lower performance of chest CT when performed within the first 48 hours of symptoms, with an AUC of 0.71 (95% CI: 0.62, 0.80) against RT-PCR and 0.68 (95% CI: 0.60, 0.76) against the clinical reference standard ($P < .001$).

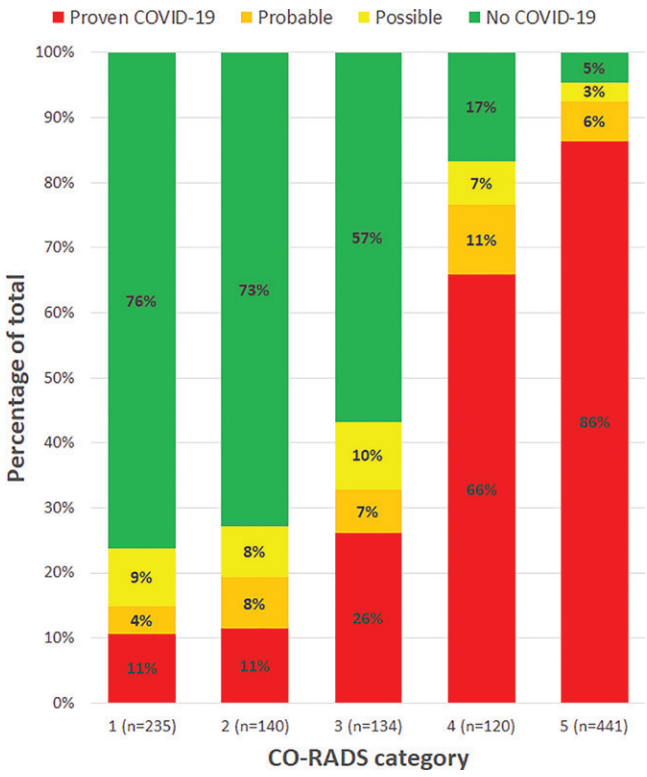

Figure 3: Performance per coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS) category. Bar chart shows percentage of patients classified with proven, probable, possible, and no COVID-19 according to CO-RADS CT score.

Previous studies have reported higher sensitivities for CT diagnosis of COVID-19 (3,9,10), but this may be exaggerated because of biased samples and cohorts (11). Reports on CT specificity are scarce and thus far disappointingly indicate values often below 50% (3,6,12–17). Previous studies did not use a well-circumscribed imaging classification system (3,10). Our study may indicate that employing CO-RADS improves CT performance in the diagnosis of COVID-19 in clinical practice. Our observation that CT demonstrated lower performance within the first 48 hours of symptoms is in line with a recent observational study (18). Because the sensitivity of RT-PCR declines after 7 days of symptoms (1,19), CT may aid in the diagnosis of COVID-19 in patients who present after a longer duration of symptoms.

Beyond diagnostic challenges, the first wave of COVID-19 also introduced patient management issues related to workflow, isolation, personal protective equipment, and treatment decisions. During initial risk estimation in the emergency department, RT-PCR results are usually not immediately available and, even when they become available, negative RT-PCR does not exclude COVID-19, especially when the pretest probability of COVID-19 is high (20). Our study showed that CT can be a useful risk stratification tool for COVID-19 and may be advantageous in counteracting emergency department crowding (21).

However, 41 of the 375 patients with a CO-RADS score of 1 or 2 (11%) had RT-PCR–proven COVID-19. Retrospective analysis of corresponding CT scans did not reveal misclassification errors in the original reporting. An explanation may be that these patients had no pulmonary manifestations of COVID-19. The proportion of patients with only extrapulmonary symptoms is not well documented but may be on the order of 3%–26% (22–24). The lack of pulmonary findings at CT for this subset of patients with positive RT-PCR results underscores the fact that CO-RADS 1 and 2 alone should not be used to rule out COVID-19 infection. Lack of pulmonary involvement on CT, however, may allow for earlier de-isolation when the initial RT-PCR result is negative.

Forty-one of the 120 patients with a CO-RADS score of 4 (34%) and 60 of the 441 with a CO-RADS score of 5 (14%) did not have a positive RT-PCR result. However, a substantial number of these patients with negative RT-PCR results—21 of 41 (51%) for CO-RADS category 4 and 40 of 60 (67%) for CO-RADS category 5—were considered as having probable or possible COVID-19 infection according to our clinical reference standard and therefore would not qualify for removal from

Table 5: Sensitivity, Specificity, and Diagnostic Odds Ratios of the CO-RADS Classification according to Different Cutoffs

	RT-PCR–proven COVID-19			Clinical Reference Standard for COVID-19		
CO-RADS Cutoff	Sensitivity (%)	Specificity (%)	Odds Ratio	Sensitivity (%)	Specificity (%)	Odds Ratio
≥3	92 (90, 94)	63 (58, 67)	20.2 (14.0, 29.0)	86 (83, 89)	71 (66, 75)	14.9 (11.0, 20.3)
≥4	86 (83, 89)	81 (78, 84)	25.9 (18.7, 35.9)	77 (74, 81)	90 (87, 93)	30.6 (21.1, 44.4)
≥5	71 (67, 75)	89 (86, 91)	19.4 (14.0, 26.9)	62 (59, 66)	95 (93, 97)	31.5 (19.6, 50.7)

Note.—Numbers in parentheses are 95% CIs. CO-RADS = COVID-19 Reporting and Data System, COVID-19 = coronavirus disease 2019, RT-PCR = reverse-transcription polymerase chain reaction.

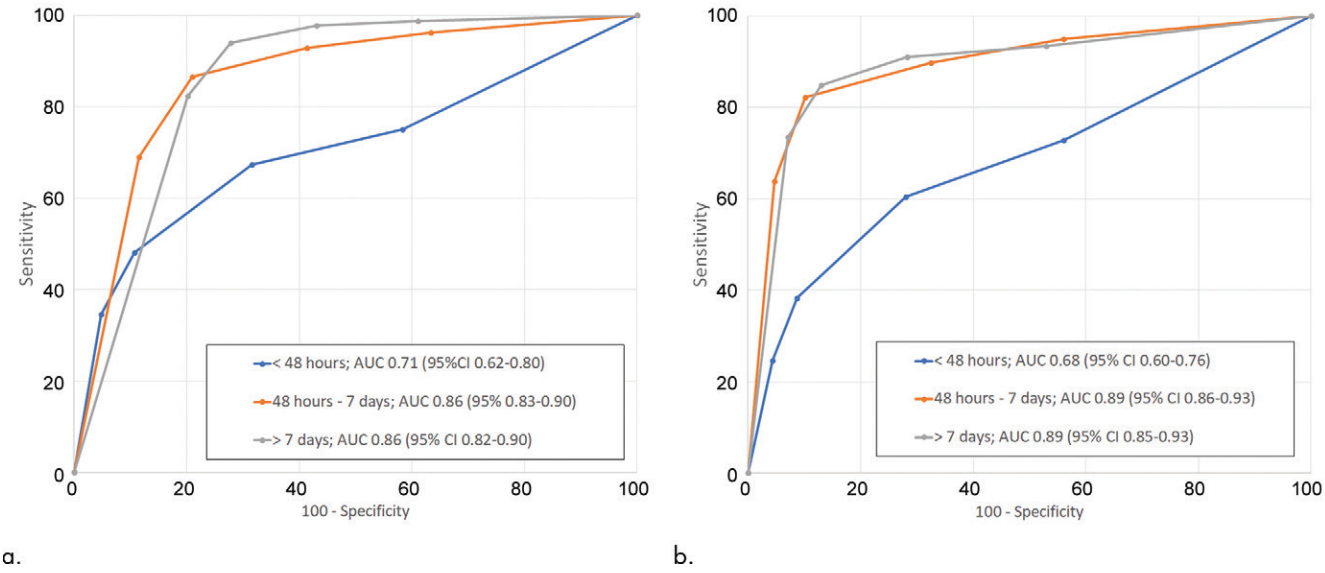

Figure 4: Results of receiver operating characteristic analysis based on durations of symptoms. **(a)** Graph shows results for comparison of the coronavirus disease 2019 Reporting and Data System (CO-RADS) against reverse-transcription polymerase chain reaction (RT-PCR) testing. **(b)** Graph shows results for comparison of CO-RADS against the clinical reference standard. Blue line indicates symptom duration of less than 48 hours (220 patients, of whom 52 had positive RT-PCR results), red line indicates symptom duration of 48 hours to 7 days (430 patients, of whom 239 had positive RT-PCR results), and gray line indicates symptom duration of more than 7 days (376 patients, of whom 232 had positive RT-PCR results). AUC = area under the receiver operating characteristic curve.

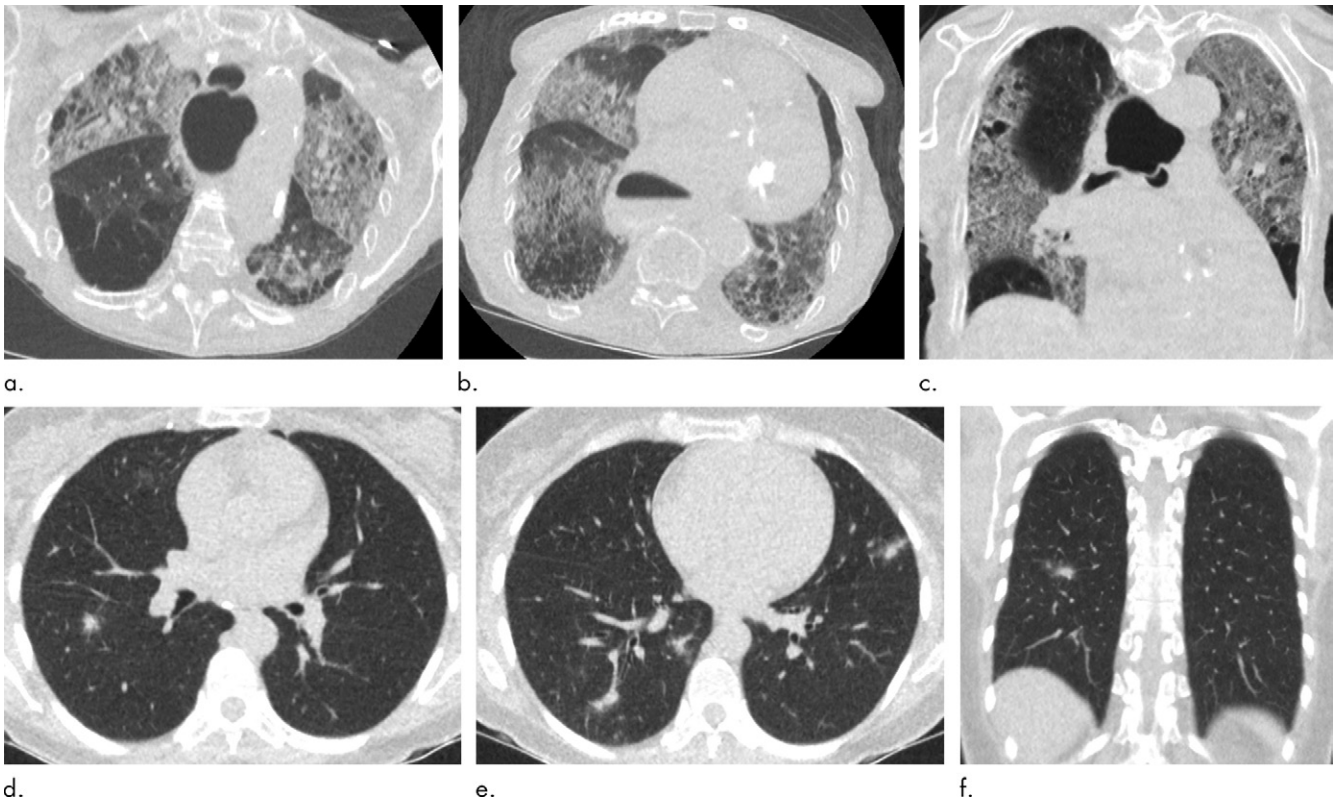

Figure 5: Example chest CT scans in patients with a true-positive and false-positive coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS) score of 4. **(a–c)** Axial (**a, b**) and coronal (**c**) CT scans in a 79-year-old woman with 9 days of symptoms. Scans show diffuse ground-glass opacities close to visceral pleural surfaces but superimposed on emphysematous changes. Also note the widened esophagus. COVID-19 was confirmed with reverse-transcription polymerase chain reaction (RT-PCR) assay. **(d–f)** Axial (**d, e**) and coronal (**f**) CT scans in a 51-year-old woman with 2 days of symptoms. Scans show bilateral multifocal areas of consolidation with halo and subtle areas of ground glass without contact to visceral pleural surfaces. RT-PCR assay for severe acute respiratory syndrome coronavirus 2 was repeatedly negative, and an alternative diagnosis of line sepsis was established with a blood culture.

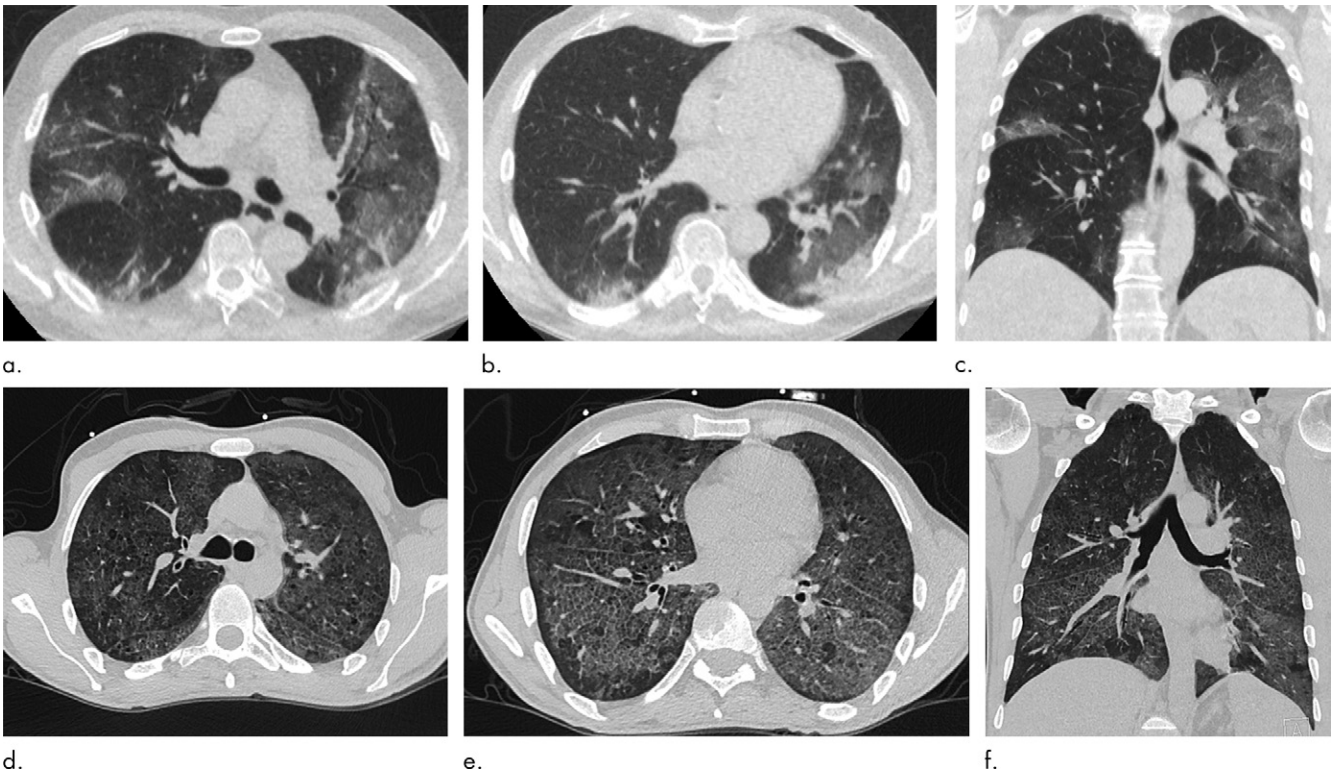

Figure 6: Example chest CT scans in patients with a true-positive and false-positive coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS) score of 5. **(a–c)** Axial (**a, b**) and coronal (**c**) CT scans in a 69-year-old man with 7 days of symptoms. Scans show bilateral multifocal areas of ground-glass opacity and consolidation in the vicinity of the visceral pleural surface. In addition, few thickened vessels in areas of ground glass are observed. COVID-2019 was confirmed with reverse-transcription polymerase chain reaction (RT-PCR) assay. **(d–f)** Axial (**d, e**) and coronal (**f**) CT scans in a 42-year-old man with more than 7 days of symptoms. Scans show diffuse ground-glass opacities in close vicinity of visceral pleural surfaces. In addition, a crazy paving pattern is observed. Results of RT-PCR assay for severe acute respiratory syndrome coronavirus 2 were negative, and *Pneumocystis jirovecii* pneumonia was diagnosed based on bronchoalveolar lavage fluid.

isolation. An alternative diagnosis, such as an alternative pulmonary infection or congestive heart failure, was established in 21 of the 40 patients (53%) with "no" COVID-19 infection who had a CO-RADS score of either 4 or 5 (Figs 5, 6; Table E2 [online]). We recommend that patients with a CO-RADS score of 4 or 5 and a negative result at RT-PCR assay remain isolated in a single bedroom until repeat RT-PCR is negative or an alternative diagnosis is found that explains the complaints.

In 134 patients with an uncertain CT diagnosis (ie, CO-RADS score of 3), 35 (26%) had a positive RT-PCR result and 76 (57%) were classified as having no COVID-19 in the clinical reference standard. The added value of CT in this group was limited. Fortunately, only 134 of all 1070 patients (13%) had a CO-RADS 3 classification. This proportion of uncertain diagnosis is still relatively high compared with other reporting and data systems, such as the Breast Imaging Reporting and Data System (1.2%–14%) (25) and the Lung Reporting and Data System (6%) (26), but is much lower than that in the Prostate Imaging Reporting and Data System (40%) (27).

Our study has limitations. The CO-RADS classification was introduced in the early phase of the first COVID-19 peak in the Netherlands. Radiologists may not have been optimally trained, which could have negatively influenced performance. In addition, we focused on patients who presented to the emergency department when the incidence of COVID-19 was high. Our findings may not be reproducible to lower-incidence settings. Our clinical reference standard was designed to be highly sensitive but was not validated in a control group and may be less specific, especially in the "possible" COVID-19 category. Furthermore, before implementation of this CT strategy, good infection control processes must be in place. Specifically, cleaning the CT scanner room and safe room turnover for the safe scanning of new patients must be considered.

The implications of our results are of potential importance. Chest CT scans interpreted using the CO-RADS system allow for a rapid test result in the emergency department for patients suspected of having COVID-19 pneumonia. This suggests a potential role for chest CT in optimizing risk stratification and isolation strategies of patients urgently presenting for hospital care during the first and second wave of this pandemic.

In conclusion, using the coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS), a chest CT reporting system for patients presenting to the emergency department, pulmonary manifestations of COVID-19 were detected in more than 95% of patients with moderate to severe upper respiratory symptoms 48 hours after symptom onset. A CO-RADS score greater than or equal to 4 provided odds ratios above 25 for the diagnosis of COVID-19.

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