Diagnostic Performance of Chest CT for SARS-CoV-2 Infection in Individuals with or without COVID-19 Symptoms

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

Background: The use of chest CT for coronavirus disease 2019 (COVID-19) diagnosis or triage in health care settings with limited severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) capacity is controversial. COVID-19 Reporting and Data System (CO-RADS) categorization of the level of COVID-19 suspicion might improve diagnostic performance.

Purpose: To investigate the value of chest CT with CO-RADS classification to screen for asymptomatic SARS-CoV-2 infections and to determine its diagnostic performance in individuals with COVID-19 symptoms during the exponential phase of viral spread.

Materials and Methods: In this secondary analysis of a prospective trial, from March 2020 to April 2020, parallel SARS-CoV-2 PCR and CT with categorization of COVID-19 suspicion was performed with CO-RADS for individuals with COVID-19 symptoms and control participants without COVID-19 symptoms admitted to the hospital for medical emergencies unrelated to COVID-19. CT with CO-RADS was categorized on a five-point scale from 1 (very low suspicion) to 5 (very high suspicion). Area under the receiver operating curve (AUC) was calculated in symptomatic versus asymptomatic individuals to predict positive SARS-CoV-2 PCR, and likelihood ratios for each CO-RADS score were used for rational selection of diagnostic thresholds.

Results: A total of 859 individuals (median age, 70 years; interquartile range, 52–81 years; 443 men) with COVID-19 symptoms and 1138 control participants (median age, 68 years; interquartile range, 52–81 years; 588 men) were evaluated. CT with CO-RADS had good diagnostic performance ($P < .001$) in both symptomatic (AUC, 0.89) and asymptomatic (AUC, 0.70) individuals. In symptomatic individuals (42% PCR positive), CO-RADS 3 or greater detected positive PCR with high sensitivity (89%, 319 of 358) and specificity of 73%. In asymptomatic individuals (5% PCR positive), a CO-RADS score of 3 or greater detected SARS-CoV-2 infection with low sensitivity (45%, 27 of 60) but high specificity (89%).

Conclusion: CT with Coronavirus Disease 2019 Reporting and Data System (CO-RADS) had good diagnostic performance in symptomatic individuals, supporting its application for triage. Sensitivity in asymptomatic individuals was insufficient to justify its use as a first-line screening approach. Incidental detection of CO-RADS 3 or greater in asymptomatic individuals should trigger testing for respiratory pathogens.

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Chest CT can help to determine the temporal disease stage and severity of coronavirus disease 2019 (COVID-19) pneumonia (1–3). In the early stage of viral replication (days 0–4), ground-glass opacities are the predominant lesion. In the progressive stage (days 5–8), crazy paving patterns mark the increased recruitment of inflammatory cells to the lung interstitium. Peak stage (days 10–13) is marked by consolidation with fibrosis and diffuse alveolar damage. These radiologic lesions are also observed in other viral pneumonia and noninfectious inflammatory lung diseases, but in a pandemic context might harbor diagnostic potential for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, especially for patient triage. The reference method for COVID-19 diagnosis, SARS-CoV-2 polymerase chain reaction (PCR), is highly specific but has variable sensitivity as low as 70% (4). In health care settings with limited PCR capacity and long turnaround times, chest CT was proposed as an alternative for COVID-19 diagnosis or triage (5). Studies supporting chest CT as a first-line diagnostic tool for COVID-19 showed several methodologic concerns (6–8). Most studies were underpowered, showed major selection biases including

Abbreviations

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

Summary

Categorization of coronavirus disease 2019 (COVID-19) suspicion by using CT with COVID-19 Reporting and Data System (CO-RADS) has good diagnostic performance in individuals with or without symptoms. Although CT screening for asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections is not recommended, incidental findings of CO-RADS 3 or greater in asymptomatic individuals have sufficient positive predictive value to trigger SARS-CoV-2 polymerase chain reaction reflex testing.

Key Results

- CT with structured coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS) scoring has good diagnostic performance for COVID-19 pneumonia in both symptomatic (area under the receiver operating characteristic curve [AUC], 0.89) and asymptomatic (AUC, 0.70) individuals ($P < .001$).
- In symptomatic individuals (42% polymerase chain reaction [PCR] positive), CO-RADS 3 or greater detected positive PCR with acceptable sensitivity (89%) and specificity (73%), resulting in a positive predictive value of 70%.
- In asymptomatic individuals (5% PCR positive), CO-RADS greater than or equal to 3 detected infection with low sensitivity (45%) but high specificity (89%) and a positive predictive value of 18%.

only individuals with COVID-19 symptoms and 40%–50% a priori risk of SARS-CoV-2 infection, and used binary scoring of CT without standardized definition of COVID-19–compatible CT. Weighed against the cost and procedural risks of CT, this sparked a controversy (8,9) leading to consensus statements by the Centers for Disease Control and Prevention, the American College of Radiology, the Society of Thoracic Radiology, the American Society of Emergency Radiology, the Fleischner Society, and the Radiological Society of North America, opposing CT as a first-line COVID-19 diagnostic tool (10–13).

In this report, we studied the diagnostic power of chest CT versus SARS-CoV-2 PCR using COVID-19 Reporting and Data System classification system (CO-RADS) (14). CO-RADS was developed by the Dutch Radiological Society to categorize the level of suspicion for COVID-19 pneumonia. It generally aligns with the structured reporting recommended by the Radiological Society of North America (13), scoring the level of COVID-19 suspicion on a scale of 1 to 5, with CO-RADS 1 corresponding to "negative" category, CO-RADS 2 to "atypical," CO-RADS 3 and 4 corresponding to "indeterminate" with "lower" or "higher" likelihood, respectively, and CO-RADS 5 equaling the Radiological Society of North America "typical" category.

The purpose of this study was to investigate the value of chest CT with CO-RADS classification to screen for asymptomatic SARS-CoV-2 infections and to determine its diagnostic performance in individuals with COVID-19 symptoms during the exponential phase of viral spread. These data should allow a more evidence-based definition of the possible role of chest CT in COVID-19 triage.
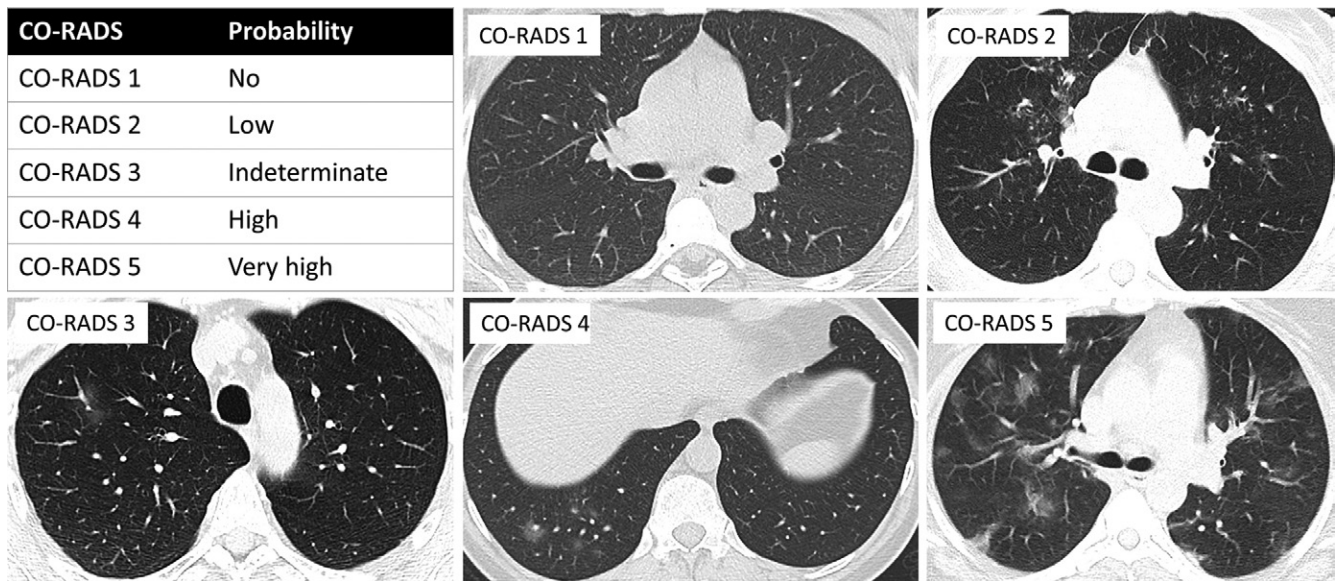
Materials and Methods

Study Participants

This is a secondary analysis of a single-center prospective trial in consecutive individuals admitted to AZ Delta General Hospital in Roeselare, Belgium, from March 19, 2020, to April 20, 2020. AZ Delta General Hospital is a central-network regional hospital that provides tertiary health care for a community of 500 000 inhabitants. Inclusion criteria were as follows: as part of the medical board–approved triage policy for COVID-19 quarantining, all individuals admitted to the hospital with clinical suspicion of COVID-19 pneumonia (hence, "symptomatic individuals") and individuals without COVID-19 symptoms but admitted for other medical emergencies, scheduled surgery, or medical procedures and psychiatric or geriatric care (hence, "asymptomatic individuals"), underwent a combined screening with chest CT and SARS-CoV-2 PCR within a 24-hour time frame. We used the COVID-19 case definition as specified by the World Health Organization interim guidance of February 27, 2020 (15), for classifying symptomatic individuals. Exclusion criteria were as follows: children younger than 14 years and pregnant individuals without COVID-19 symptoms did not undergo standard chest CT. The study was approved by the AZ Delta institutional review board with a waiver of written informed consent from study participants, considering the study is based on secondary analysis of existing data (Clinical Trial Number: IRB B1172020000008; study protocol available through the registry of the Belgian Advisory Committee on Bioethics and e-mail request to corresponding author). Authors received no specific funding for this study.

CT Protocol

Within 24 hours from admission, all individuals were imaged with multidetector CT by using either LightSpeed VCT scanner (GE Healthcare, Chicago, Ill; 1-mm section thickness), Siemens Somatom AS (Siemens Healthineers, Erlangen, Germany; 1-mm section thickness), or the GE Optmima 660 scanner (GE Healthcare; 1.25-mm section thickness). All scans were acquired without intravenous contrast agent with the patient in the supine position during end inspiration.

Image Evaluation

Two cardiothoracic radiologists with 24 years and 9 years of experience (S.G. and K.D.S., respectively) retrospectively reviewed the CT examinations on a picture archiving and communication systems workstation (Sectra Workstation IDS7; Sectra, Linköping, Sweden) with multiplanar reconstruction tools. Reviewers were blinded to symptomatic or asymptomatic status and PCR result. Final CO-RADS scoring was always reached by consensus. The Dutch CO-RADS classification system was used to categorize the level of COVID-19 suspicion, exactly as described (14): CO-RADS scores can be presented as 1 (very low level of suspicion), 2 (low level), 3 (equivocal), 4 (high level of suspicion), or 5 (very high level of suspicion) (summarized and representative images in Fig 1). See Appendix E1 (online) for detailed CT protocol.

CO-RADS	Probability
CO-RADS 1	No
CO-RADS 2	Low
CO-RADS 3	Indeterminate
CO-RADS 4	High
CO-RADS 5	Very high

Figure 1: Image shows Coronavirus Disease 2019 (COVID-19) Reporting and Data System (CO-RADS) scoring system for level of COVID-19 pneumonia suspicion. CO-RADS scores for level of COVID-19 pneumonia suspicion are summarized in upper left panel. Other panels show representative scans for CO-RADS 1 (no suspicion: normal findings), CO-RADS 2 (low level of suspicion: absence of ground-glass opacities [GGO], presence of tree-in-bud signs or endobronchial spread or bronchiolitis), CO-RADS 3 (indeterminate: unifocal GGO), CO-RADS 4 (high level of suspicion: unilateral multifocal GGO), and CO-RADS 5 (very high level of suspicion: multifocal bilateral GGO).

Comorbidities were recorded by chest CT (chronic lung disease including emphysema, fibrosis and bronchiectasis, and coronary artery disease as derived from coronary artery calcification scoring) or review of medical records (diabetes).

SARS-CoV-2 PCR was performed with multiplex reverse transcription PCR (hereafter, PCR) for E, N, and RdRP genes by using Allplex 2019-nCoV assay (Seegene, Seoul, South Korea) on nasopharyngeal swabs.

Statistical Analysis

The diagnostic performance of categorical CT assessment with CO-RADS classification was evaluated by calculating area under the receiver operating characteristics curve (AUC) compared with SARS-CoV-2 PCR positivity. Likelihood ratios (LRs; 95% CI) were calculated for each CO-RADS score in the symptomatic versus asymptomatic group and were visualized in diagrams of pretest and posttest probability. According to the Bayes theorem, posttest probability (P_{post}) can be derived from pretest probability (P_{pre}) and LR according to the formula $P_{post} = (P_{pre} \times LR)/(1 + P_{pre} \times [LR - 1])$, where P_{pre} represents the prevalence of SARS-CoV-2 PCR positivity in any population under study. Statistical differences in demographics and comorbidities were evaluated by using Mann-Whitney test (age) and χ^2 test (proportions). Statistical analyses were performed by using MedCalc (version 12.2.1; MedCalc Software, Mariakerke, Belgium) and considered to indicate statistical significance if P value was less than .05.
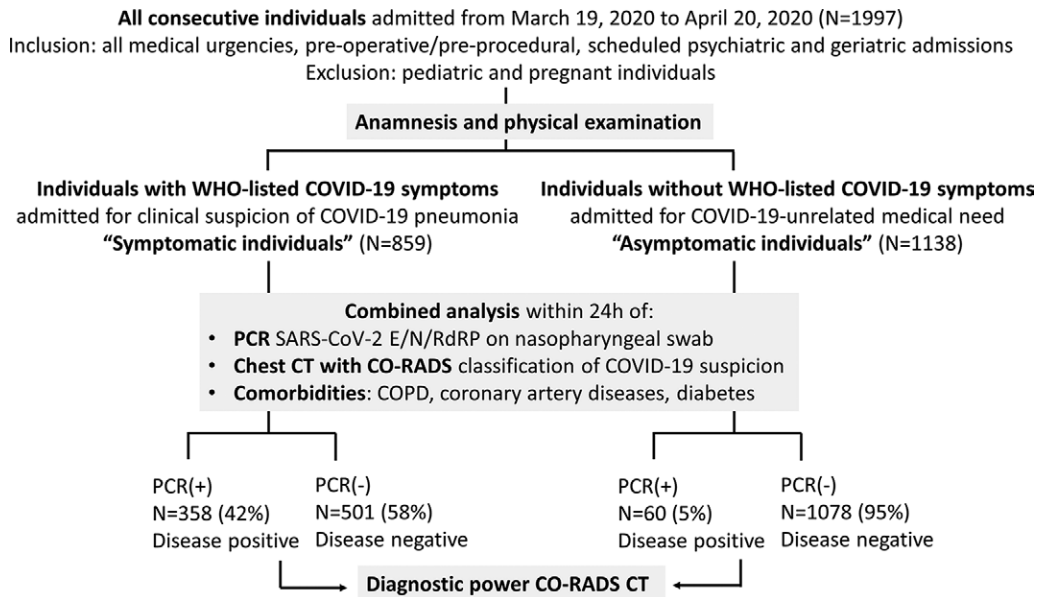
Results

Participant Characteristics

A total of 1997 consecutive individuals (Fig 2) admitted to the hospital were allocated by physical examination and anamne-

sis into two groups. First, 859 individuals were admitted with World Health Organization–listed symptoms of COVID-19 pneumonia (hence "symptomatic individuals"): 443 men (median age, 71 years; interquartile range, 54–80 years) and 416 women (median age, 68 years; interquartile range, 51–82 years) (Table 1). Second, 1138 individuals were admitted for medical needs unrelated to World Health Organization–listed COVID-19 symptoms (hence "asymptomatic individuals"): 588 men (median age, 66 years; interquartile range, 53–78 years) and 550 women (median age, 70 years; interquartile range, 50–82 years). Demographics and key clinical comorbidities are shown in Table 1; individuals with or without COVID-19 symptoms showed a similar age and sex distribution as well as a similar prevalence of diabetes and coronary artery disease. PCR-negative symptomatic individuals had higher rates of underlying chronic lung disease (28%, 140 of 501) than did PCR-positive symptomatic (22%, 77 of 358; $P < .05$) and PCR-negative asymptomatic individuals (21%, 222 of 1078; $P < .05$).

Diagnostic Performance in Symptomatic Individuals

The overall prevalence of SARS-CoV-2 infection in symptomatic individuals was 42% (358 of 859). In symptomatic individuals with CO-RADS 5, 89% (279 of 312) were PCR positive compared with only 9% (27 of 313) PCR-positive cases in symptomatic individuals with CO-RADS 1. Receiver operating characteristic analysis confirmed the diagnostic performance ($P < .001$) of CT with CO RADS with AUC of 0.89 (95% CI: 0.87, 0.91) to predict SARS-CoV-2 PCR positivity (Fig 3a). Next, we calculated LRs for each CO-RADS score in symptomatic individuals (Table 2): CO-RADS 1, 2, and the "equivocal" score CO-RADS 3 (LR, 0.34; 95% CI: 0.20, 0.59) significantly lowered the odds of PCR positivity (CI of LR excluding LR, 1). CO-RADS 4 did not further increase post-

All consecutive individuals admitted from March 19, 2020 to April 20, 2020 (N=1997)
Inclusion: all medical urgencies, pre-operative/pre-procedural, scheduled psychiatric and geriatric admissions
Exclusion: pediatric and pregnant individuals

Anamnesis and physical examination

Individuals with WHO-listed COVID-19 symptoms admitted for clinical suspicion of COVID-19 pneumonia **"Symptomatic individuals" (N=859)**

Individuals without WHO-listed COVID-19 symptoms admitted for COVID-19-unrelated medical need **"Asymptomatic individuals" (N=1138)**

Combined analysis within 24h of:
- **PCR** SARS-CoV-2 E/N/RdRP on nasopharyngeal swab
- **Chest CT with CO-RADS** classification of COVID-19 suspicion
- **Comorbidities**: COPD, coronary artery diseases, diabetes

PCR(+)
N=358 (42%)
Disease positive

PCR(-)
N=501 (58%)
Disease negative

PCR(+)
N=60 (5%)
Disease positive

PCR(-)
N=1078 (95%)
Disease negative

Diagnostic power CO-RADS CT

Figure 2: Flow diagram of study. CO-RADS = COVID-19 Reporting and Data System, COPD = chronic obstructive pulmonary disease, COVID-19 = coronavirus disease 2019, PCR = polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, WHO = World Health Organization.

Table 1: Demographics and Key Clinical Data of Study Participants

| Characteristic	Positive PCR Result	Negative PCR Result	*P* Value
Symptomatic individuals (*n* = 859)			
No. of participants	358	501	…
Sex			
Women	165 (46)	251 (50)	.28
Men	193 (54)	250 (50)	
Age (y)*	68 (53–80)	71 (52–81)	.84
Chronic lung disease	77 (212)	140 (28)*	.04
Coronary artery disease	194 (54)	281 (56)	.63
Diabetes	48 (13)	60 (12)	.61
Asymptomatic individuals (*n* = 1178)			
No. of participants	60	1078	…
Sex			
Women	28 (47)	522 (48)	.90
Men	32 (53)	556 (52)	
Age (y)*	73 (51–82)	68 (52–80)	.65
Chronic lung disease	11 (18)	222 (21)†	.79
Coronary artery disease	34 (57)	564 (52)	.60
Diabetes	5 (8)	136 (13)	.43

Note.—Unless otherwise specified, data are numbers, with percentages in parentheses. Symptomatic individuals are participants with coronavirus disease 2019 (COVID-19) symptoms and asymptomatic individuals are participants admitted for non–COVID-19 indications. For each group, key comorbidities were listed as recorded by chest CT (chronic lung disease, coronary artery disease) or review of medical records (diabetes). *P* < .05 was considered to indicate statistical significance. PCR = polymerase chain reaction.

* Data are medians, with interquartile ranges in parentheses.

† Additional symptomatic to asymptomatic subgroup comparisons for prevalence of comorbidities for which *P* < .05 was considered to indicate statistical significance.

(95% CI: 90.9, 95.4) and high overall accuracy of 87.0% (95% CI: 84.5, 89.1). Dichotomization of suspected CT at CO-RADS 4 or greater and 3 or greater increased sensitivity to 84.3% (95% CI: 80.8, 88.5) and 89.1% (95% CI: 85.4, 92.1) at a specificity of 84.8% (95% CI: 68.3, 76.3) and 72.5% (95% CI: 68.3, 76.3), respectively (Table 2). Table 2 and Figure 3b show the associated shift from pretest probability (overall prevalence of positive PCR) to post-test probability (positive predictive value) of SARS-CoV-2 as function of individual CO-RADS scores or dichotomizations.

Screening potential of chest CT in asymptomatic individuals in a SARS-CoV-2 pandemic setting.—The prevalence of SARS-CoV-2 PCR positivity (pretest probability) in asymptomatic individuals was 5.3% (60 of 1138). Only 7% (79 of 1138) of asymptomatic individuals showed a CO-RADS score of 4 (high suspicion) or 5 (very high suspicion); 87% (990 of 1138) showed a CO-RADS 2 or less with low to very low suspicion of COVID-19 (Table 2). Receiver operating characteristic analysis indicated that CT with CO-RADS in asymptomatic individuals had diagnostic performance (*P* < .001) to predict SARS-CoV-2 PCR positivity with AUC of 0.70 (95% CI: 0.67, 0.73) (Fig 3a), albeit less than in symptomatic individuals. The percentage of PCR-positive cases was 3%, 8%, 12%, 18%, and 32% in CO-RADS 1, 2, 3, 4, and 5, respectively. Analysis of LR (Table 2, Fig 3c) indicated that only a CO-

test probability. CO-RADS 5, however, strongly increased the odds of a positive PCR (LR, 11.8; 95% CI: 8.5, 16.5) (Fig 3b). A CO-RADS 5 score in symptomatic individuals identified SARS-CoV-2 PCR positivity with a sensitivity of 77.9% (95% CI: 73.3, 82.1) at high specificity of 93.4%

a.

b.

c.
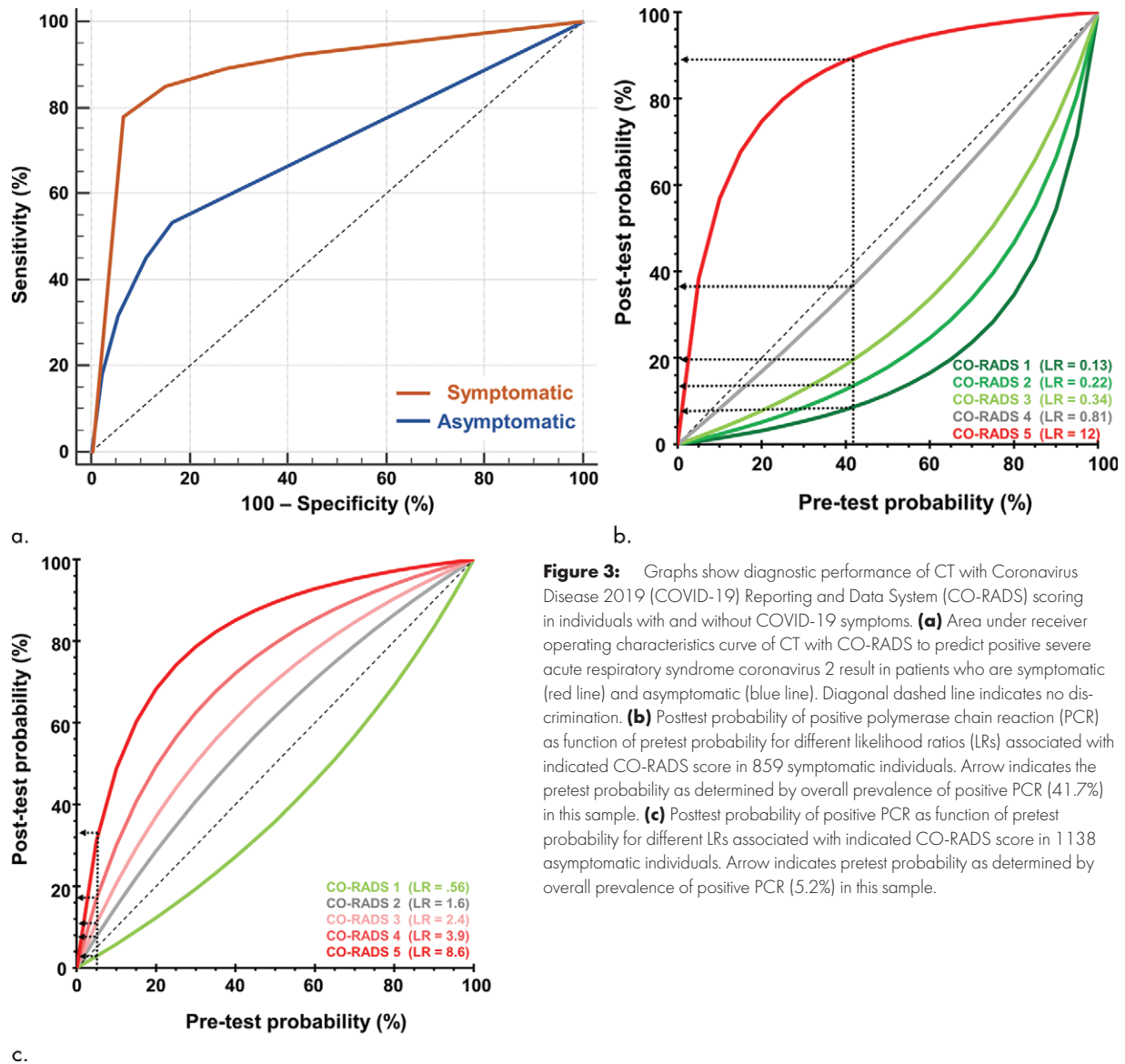
Figure 3: Graphs show diagnostic performance of CT with Coronavirus Disease 2019 (COVID-19) Reporting and Data System (CO-RADS) scoring in individuals with and without COVID-19 symptoms. **(a)** Area under receiver operating characteristics curve of CT with CO-RADS to predict positive severe acute respiratory syndrome coronavirus 2 result in patients who are symptomatic (red line) and asymptomatic (blue line). Diagonal dashed line indicates no discrimination. **(b)** Posttest probability of positive polymerase chain reaction (PCR) as function of pretest probability for different likelihood ratios (LRs) associated with indicated CO-RADS score in 859 symptomatic individuals. Arrow indicates the pretest probability as determined by overall prevalence of positive PCR (41.7%) in this sample. **(c)** Posttest probability of positive PCR as function of pretest probability for different LRs associated with indicated CO-RADS score in 1138 asymptomatic individuals. Arrow indicates pretest probability as determined by overall prevalence of positive PCR (5.2%) in this sample.

RADS 1 result significantly lowered the odds of a positive PCR (LR, 0.56; 95% CI: 0.43, 0.73). A CO-RADS 2 result had no diagnostic meaning since the 95% CI around the LR included the value 1. At CO-RADS score of 3 or higher, however, chest CT increased the odds of a positive PCR, resulting in a positive shift from pretest to posttest probability (Fig 3c). In particular, CO-RADS 5 had good diagnostic performance in asymptomatic individuals, with LR of 8.6 (95% CI: 4.4, 17), predicting SARS-CoV-2 infection at high specificity of 97.9% (95% CI: 96.8, 98.6) but low sensitivity of 18.3% (95% CI: 9.5, 30). Dichotomization of suspected CT at CO-RADS 4 or greater preserved a high specificity of 94.4% (95% CI: 93, 96), resulting in a posttest probability (positive predictive value) of 24.1% (95% CI: 20, 28) (Table 2, Fig 3c). Its sensitivity was low at 31.7% (95% CI: 20, 45), resulting in a negligible shift in pretest to posttest probability in the case of a negative test result (3.9%; 95% CI: 3.2, 4.2), arguing against the use of chest CT as a screening test for asymptomatic infections.

Representative clinical images.—A summary of the CO-RADS scoring system and representative CT images for CO-RADS 1 to 5 are shown in Figure 1. Figures 4–6 highlight individual cases with a brief clinical summary of a false-positive CO-RADS 5 in a PCR-negative symptomatic individual (Fig 4), false-negative CO-RADS 1 in a PCR-positive symptomatic individual (Fig 5), and true-positive CO-RADS 5 in a PCR-positive asymptomatic individual.

Discussion

We aimed to investigate the performance of CT with Coronavirus Disease 2019 (COVID-19) Reporting and Data System (CO-RADS) to diagnose SARS-CoV-2 polymerase chain reaction (PCR) positivity in individuals with COVID-19 symptoms and to screen for asymptomatic SARS-CoV-2 infection in control individuals in a setting with high prevalence of SARS-CoV-2 infections. In symptomatic patients, the pretest probability of SARS-CoV-2 infection, as marked by the preva-

Table 2: Diagnostic Performance of CO-RADS for Symptomatic and Asymptomatic Setting at Different CO-RADS Cutoffs and Multiple Result Intervals

| CO-RADS Cutoff	PCR (Positive)	PCR (Negative)	Likelihood Ratio	Sensitivity (%)	Specificity (%)	Posttest Probability (%)
Symptomatic individuals (n = 859)	358	501	…	…	…	…
CO-RADS ≥3						
CO-RADS 1–2	39	363	0.15 (0.11, 0.20)	89 (85, 92)	73 (68, 76)	9.7 (7.3, 13)
CO-RADS 3–5	319	138	3.2 (2.8, 3.8)	…	…	70 (67, 73)
CO-RADS ≥4						
CO-RADS 1–3	54	425	0.18 (0.14, 0.23)	85 (81, 89)	85 (68, 76)	11 (9.1, 14)
CO-RADS 4–5	304	76	5.6 (4.5, 6.9)	…	…	80 (76, 83)
CO-RADS ≥5						
CO-RADS 1–4	79	468	0.24 (0.19, 0.29)	78 (73, 82)	93 (91, 95)	15 (12, 17)
CO-RADS 5	279	33	12 (8.5, 17)	…	…	89 (86, 92)
Multiple results intervals						
CO-RADS 1	27	286	0.13 (0.09, 0.19)	…	…	8.5 (6.0, 12)
CO-RADS 2	12	77	0.22 (0.12, 0.40)	…	…	14 (7.9, 22)
CO-RADS 3	15	62	0.34 (0.20, 0.59)	…	…	20 (13, 30)
CO-RADS 4	25	43	0.81 (0.51, 1.3)	…	…	37 (27, 48)
CO-RADS 5	279	33	12 (8.5, 16)	…	…	89 (86, 92)
Asymptomatic individuals (n = 1138)	60	1078	…	…	…	…
CO-RADS ≥3						
CO-RADS 1–2	33	957	0.62 (0.49, 0.78)	45 (32, 58)	89 (87, 91)	3.3 (2.7, 4.2)
CO-RADS 3–5	27	121	4.0 (2.9, 5.6)	…	…	18 (14, 24)
CO-RADS ≥4						
CO-RADS 1–3	41	1018	0.72 (0.61, 0.86)	32 (20, 45)	95 (93, 96)	3.9 (3.2, 4.2)
CO-RADS 4–5	19	60	5.6 (4.5, 6.9)	…	…	24 (20, 28)
CO-RADS ≥5						
CO-RADS 1–4	49	1055	0.83 (0.74, 0.94)	18 (9.5, 30)	98 (97, 99)	4.4 (4.0, 5.0)
CO-RADS 5	11	23	8.6 (4.4, 17)	…	…	32 (20, 48)
Multiple results intervals						
CO-RADS 1	28	901	0.56 (0.43, 0.73)	…	…	3.0 (2.3, 3.9)
CO-RADS 2	5	56	1.6 (0.67, 3.9)	…	…	8.2 (3.6, 18)
CO-RADS 3	8	61	2.4 (1.2, 4.7)	…	…	11 (6.2, 21)
CO-RADS 4	8	37	3.9 (1.9, 8.0)	…	…	18 (9.5, 31)
CO-RADS 5	11	23	8.6 (4.4, 17)	…	…	32 (20, 48)

Note.—Unless otherwise specified, data in parentheses are 95% CIs. Pretest probability for symptomatic individuals (ie, those with coronavirus disease 2019 [COVID-19] symptoms) was 41.7%, and for asymptomatic individuals was 5.3%. This table shows the distribution of asymptomatic and symptomatic individuals over multiple result intervals (COVID-19 Reporting and Data System [CO-RADS] score 1 to 5) and various possible dichotomization approaches, with their associated number of positive or negative polymerase chain reaction (PCR) tests and the associated likelihood ratios (LRs; 95% CI) to predict positive PCR. The sensitivity and specificity with 95% CIs are calculated for various test dichotomizations. The right column indicates the posttest probability of SARS-CoV-2 PCR positivity as an indicator of positive and negative predictive value, calculated according to the formula in the Methods section, taking the measured prevalence of PCR positivity in either group as pretest probability.

lence of PCR positivity, was high at 41.7%. A CO-RADS score of 3 or greater strongly increased posttest probability to 69.8%, and CO-RADS 5 to 89.4%. For infection control policies, CO-RADS 5 could thus be used as a triage tool to quarantine symptomatic individuals in settings with bottlenecks in PCR testing. Yet, scores less than CO-RADS 3 were still associated with a posttest probability of 9.7% (corresponding to a 90.3% negative predictive value), indicating that chest CT cannot replace PCR as a diagnostic test. In our asymptomatic control participants, prevalence of SARS-CoV-2 PCR positivity was 5.3%, which is in line with the secondary attack rate at population level of 6.6% during the exponential phase of viral spread (16). This control group was thus suit-

able for investigation of whether chest CT can be used to screen for asymptomatic SARS-CoV-2 infection. Also, in asymptomatic individuals, CT with CO-RADS showed good diagnostic performance. However, various dichotomization scenarios failed to reach the high sensitivity required for a screening test. CO-RADS 4 or greater attained sensitivity of only 31.7%. A negative test (CO-RADS <4) shifted pretest to posttest probability only from 5.3% to 3.9%, which was insufficient to justify the procedural risk of CT. The specificity of CO-RADS greater than or equal to 4 in asymptomatic individuals, however, was high (94.4%) and resulted in meaningful increase in posttest probability to 24.1%. In a pandemic setting, we propose that such incidental findings
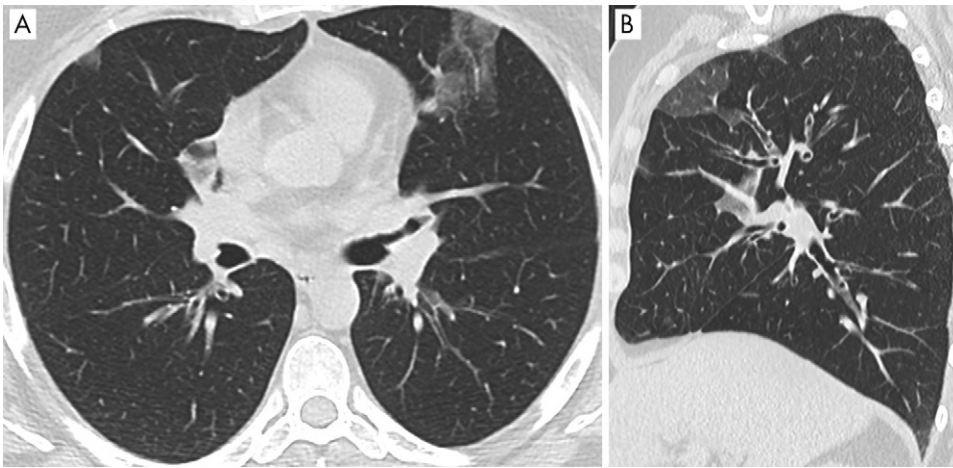
Figure 4: Images show false-positive Coronavirus Disease 2019 (COVID-19) Reporting and Data System (CO-RADS) 5 in symptomatic individual with negative severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR). *A,* Axial and, *B,* sagittal CT scan in symptomatic individual with CO-RADS 5 but negative SARS-CoV-2 PCR test. Clinical summary: 49-year-old woman with medical history of hemochromatosis and psoriatic arthritis was admitted with wheezing, dry cough, and increasing dyspnea since 2 weeks. She was subfebrile and hypoxic (89% SpO2). Blood test showed increased C-reactive protein level (32.8 mg/L) and leukocytosis with eosinophilia ($1.1 \times 10^3/\mu L$). CT showed no pleural effusion, but multifocal bilateral ground-glass opacities were present and scored as CO-RADS 5. SARS-CoV-2 PCR was repeatedly negative on nasopharyngeal swab. Extended syndromic PCR testing for 33 respiratory pathogens including 14 respiratory viruses was negative. Bronchoalveolar lavage was also repeatedly negative for SARS-CoV-2 PCR but showed high load of eosinophils (52% of 65×10^4 nucleated cells per millileter), supporting diagnosis of acute eosinophilic pneumonia. Woman was successfully treated with corticosteroids.
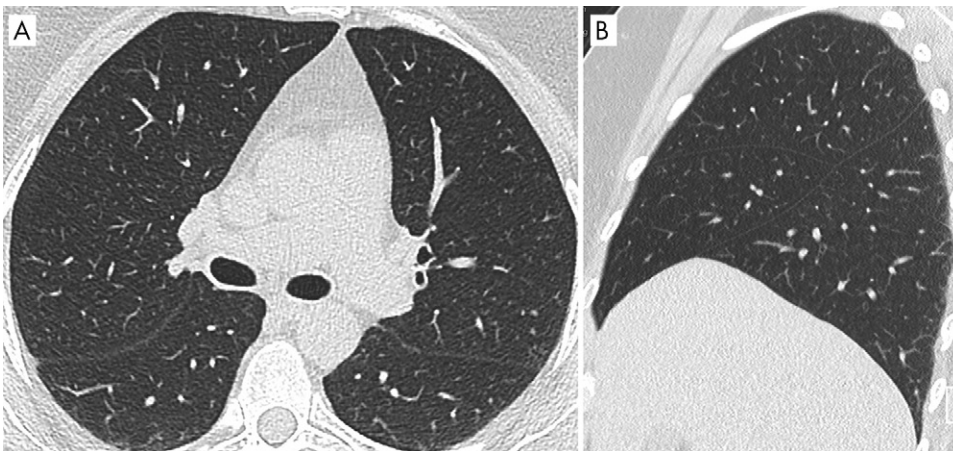
Figure 5: Images show false-negative Coronavirus Disease 2019 (COVID-19) Reporting and Data System (CO-RADS) 1 in patient who was symptomatic with positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR). *A,* Axial and, *B,* sagittal CT scan of symptomatic individual with CO-RADS 1 and positive SARS-CoV-2 PCR test. Clinical summary: 57-year-old woman presented with headache, flulike symptoms, and dry cough for more than 10 days since returning from Hanoi, Vietnam. She was subfebrile, and blood test showed slightly increased C-reactive protein level (5.3 mg/L), normal leukocyte count, no lymphocytopenia, and normal *D*-dimer and lactate dehydrogenase level. Chest CT showed no abnormalities. PCR for influenza A/B and respiratory syncytial virus was negative, but SARS-CoV-2 PCR was positive.

should be reported as "compatible with COVID-19 pneumonia" rather than as "viral pneumonia," as suggested by the Radiological Society of North America (13), and should trigger SARS-CoV-2 PCR or syndromic panel–based PCR testing for other respiratory pathogens before exclusion of noninfectious inflammatory lung diseases.

The developers of CO-RADS reported a good diagnostic performance in a pilot study (14) in 105 individuals with COVID-19 symptoms and 50.5% PCR positivity with AUC of 0.91 (95%

CI: 0.85, 0.97). Our study confirms this finding with similar AUC on a much larger sample. Compared with previous studies supporting chest CT for CO-VID-19 diagnosis or screening (3,17–19), our study answered the urgent call for well-powered data sets (18), and its prospective design on consecutive unselected individuals with similar demographics, comorbidities, and upfront clinical grouping according to absence or presence of COVID-19 symptoms minimizes selection biases. Another strength is the use of structured reporting of chest CT data and the attribution of LRs to each level of suspicion. Most studies thus far used dichotomization of CT results as positive or negative, often without a clear definition of a positive CT. One large study in China (3) reported a sensitivity of 97% of chest CT for COVID-19 diagnosis but with a poor specificity of 25%, possibly explained by a low subjective interpretation threshold to maximize sensitivity (19).

Like sensitivity and specificity, LR are test properties that, in defined patient populations, are independent of disease prevalence, unlike the positive and negative predictive values that both strongly depend on disease prevalence (19). Using LR, the posttest probability as an indicator of positive predictive value can simply be calculated (see formula in Methods section) by taking the observed prevalence of PCR positivity as pretest probability. Similarly, negative predictive value is 1 minus the posttest probability. Positive predictive value is mathematically most influenced by specificity (19). Meta-analysis showed a low pooled specificity of dichotomic chest CT of 37% for COVID-19 diagnosis (20) with low associated positive predictive value from 1.5% to 8.3% in low prevalence (<10%) settings. Our data illustrate that CO-RADS categorization improves specificity and thus discloses higher positive predictive value as LR increase. Negative predictive value is mostly influenced by sensitivity (19). In our data set, sensitivity of chest CT was insufficient to exclude SARS-CoV-2 infection both in

symptomatic and asymptomatic patients. This supports the consensus statements that chest CT should not be used as a diagnostic test.

Our study had limitations. It was conducted in a time frame with high rates of SARS-CoV-2 infections and low prevalence of other viral pneumonia. Higher incidence of seasonal respiratory viral infections will likely decrease specificity of CT with CO-RADS. Regarding selection bias, the study included mostly individuals older than 50 years admitted to the hospital and excluded pediatric and pregnant individuals. Paucisymptomatic infections in home-quarantined older individuals and asymptomatic infections in younger individuals are underrepresented in our data set.

In conclusion, our data show that CT with structured Coronavirus Disease 2019 (COVID-19) Reporting and Data System (CO-RADS) scoring had good diagnostic performance for COVID-19 pneumonia but cannot replace severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction as a diagnostic test. It can be used as an alternative triage tool in individuals with COVID-19 symptoms but not for the screening of asymptomatic SARS-CoV-2 infections.

Figure 6: Images show true-positive Coronavirus Disease 2019 (COVID-19) Reporting and Data System (CO-RADS) 5 in asymptomatic individual with positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR). A, Axial and, B, sagittal CT scan of asymptomatic individual with CO-RADS 5 and positive SARS-CoV-2 PCR. Clinical summary: 31-year-old woman was admitted with diarrhea and left iliac fossa pain. She presented no respiratory symptoms, myalgia, loss of taste or smell, or abnormal fatigue. Fever (temperature of 39.4°C) was attributed to suspected diverticulitis but CT of abdomen was negative. Standard chest CT scan as part of COVID-19 infection control policy showed multifocal bilateral ground-glass opacities and crazy paving pattern, scored as CO-RADS 5. Blood testing showed increased C-reactive protein level (48.4 mg/L), normal leukocyte count ($6.8 \times 10^3/\mu$L), and no lymphocytopenia but increased D-dimer (1428 ng/mL) and increased lactate dehydrogenase (669 U/L) levels.

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