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Systematic Review and Meta-Analysis on the Value of Chest CT in the Diagnosis of Coronavirus Disease (COVID-19)

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Systematic Review and Meta-Analysis on the Value of Chest CT in the Diagnosis of Coronavirus Disease (COVID-19): *Sol Scientiae, Illustra Nos*

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OBJECTIVE. The purpose of this article is to systematically review and meta-analyze the diagnostic accuracy of chest CT in detecting coronavirus disease (COVID-19).

MATERIALS AND METHODS. MEDLINE was systematically searched for publications on the diagnostic performance of chest CT in detecting COVID-19. Methodologic quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool. Meta-analysis was performed using a bivariate random-effects model.

RESULTS. Six studies were included, comprising 1431 patients. All six studies included patients at high risk of COVID-19, and five studies explicitly reported that they included only symptomatic patients. Mean prevalence of COVID-19 was 47.9% (range, 27.6–85.4%). High or potential risk of bias was present throughout all QUADAS-2 domains in all six studies. Sensitivity ranged from 92.9% to 97.0%, and specificity ranged from 25.0% to 71.9%, with pooled estimates of 94.6% (95% CI, 91.9–96.4%) and 46.0% (95% CI, 31.9–60.7%), respectively. The included studies were statistically homogeneous in their estimates of sensitivity ($p = 0.578$) and statistically heterogeneous in their estimates of specificity ($p < 0.001$).

CONCLUSION. Diagnostic accuracy studies on chest CT in COVID-19 suffer from methodologic quality issues. Chest CT appears to have a relatively high sensitivity in symptomatic patients at high risk of COVID-19, but it cannot exclude COVID-19. Specificity is poor. These data, along with other local factors such as COVID-19 prevalence, available real-time reverse transcriptase–polymerase chain reaction tests, staff, hospital, and CT scanning capacity, can be useful to healthcare professionals and policy makers to decide on the utility of chest CT for COVID-19 detection in the hospital setting.

Coronavirus disease (COVID-19) has spread throughout the world and caused a pandemic [1–6]. Overall mortality rate based on Chinese data has been estimated to be approximately 3.6% [7]. Currently, there is no vaccine or definite treatment available [1, 5]. The social, healthcare, and economic consequences of the COVID-19 pandemic are immense [2]. Healthcare systems throughout the world are threatened to or have already become overloaded [8]. Protecting vulnerable patients (e.g., older individuals with comorbid conditions) and healthcare workers in hospitals from being infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19. COVID-19 is optimized to spread widely [9]. Infected persons are contagious even when minimally symptomatic or asymptomatic [9]. Just one hospitalized patient with occult COVID-19 can infect oth-

er patients, healthcare workers, and visitors, which in turn can infect many other people in the hospital. Hospitals need to ensure that all infected patients are placed in strict isolation to prevent an uncontrollable outbreak of COVID-19. The Centers for Disease Control and Prevention recommend rapid safe triage and isolation of patients suspected to have SARS-CoV-2 or other respiratory infection who come to the hospital [10]. At present, real-time reverse transcriptase–polymerase-chain reaction (RT-PCR) assay of nasal and pharyngeal swab specimens is considered the reference standard to detect SARS-CoV-2 [11–15]. However, given the incubation period of the infection (estimated as 2–14 days), an initial negative RT-PCR result does not rule out infection with SARS-CoV-2 [16]. Furthermore, false-negative results may be due to sampling error or laboratory error [17, 18]. Therefore, in patients with a negative RT-PCR test result but persistent clinical

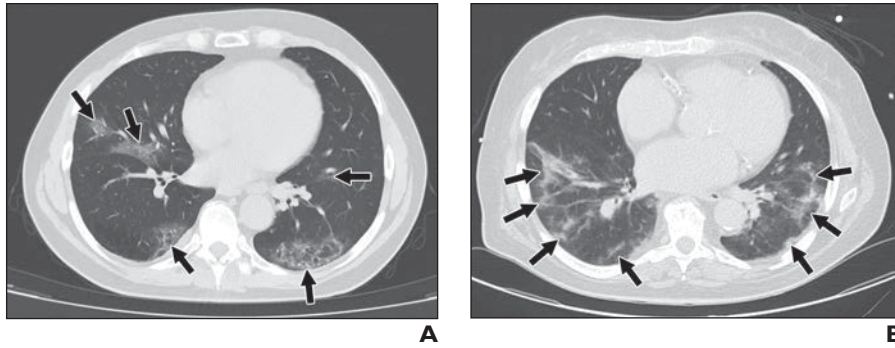


Fig. 1—CT findings of coronavirus disease (COVID-19) pneumonia with diagnosis confirmed by reverse transcriptase–polymerase chain reaction testing. **A** and **B**, Axial unenhanced CT images of 57-year-old man (**A**) and 78-year-old woman (**B**) show multifocal bilateral ground-glass opacities (arrows). Both patients had presented with fever, cough, and dyspnea.

suspicion, tests should be repeated [19, 20]. RT-PCR testing is relatively time-consuming, which puts pressure on the limited number of isolation rooms in hospitals [18, 21]. In addition, RT-PCR testing capacity remains limited with respect to the total number of eligible patients [1]. Several recent studies, which were published in rapid succession, have suggested that chest CT may be used as a tool to detect COVID-19 [17, 18, 22, 23] (Fig. 1). However, individual studies may suffer from relatively low sample sizes, concerns with respect to demographic applicability, methodologic errors, or a combination of those shortcomings. The danger lurks that clinically relevant decisions are made on the basis of incomplete or flawed data. Critical appraisal of the literature is necessary to make evidence-based decisions on the use of chest CT as a diagnostic tool in clinical practice. Therefore, the purpose of our study was to systematically review and meta-analyze the literature examining the diagnostic performance of chest CT in detecting COVID-19.

Materials and Methods

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [24].

Literature Search

MEDLINE was searched to find original studies on the diagnostic performance of chest CT in the detection of COVID-19 using the following query: (Corona OR Coronavirus OR Covid-19 OR SARS-CoV-2 OR 2019nCoV OR Wuhan-virus) AND (CT OR Computerized tomography OR CT OR CT OR CAT OR HRCT). When only an abstract was available, the study authors were contacted to request the full text version. In addition,

the journal *Radiology: Cardiothoracic Imaging* (articles published by this journal are not yet listed in MEDLINE) was manually searched for potentially relevant articles. Reference lists of included studies were also searched. The search was updated until April 12, 2020.

Selection of Studies

Original studies that investigated the diagnostic performance of chest CT in detecting COVID-19 were eligible to be included. Studies with insufficient data to construct a 2×2 contingency table (i.e., numbers of true-positive, true-negative, false-positive, and false-negative cases) to calculate sensitivity and specificity were excluded. Sensitivity and specificity are inherently related; both values are necessary to determine the overall test performance of chest CT. Therefore, by definition, studies that only enrolled patients with proven SARS-CoV-2 infection by RT-PCR testing were excluded. Reviews, conference abstracts, editorials, and studies with fewer than 10 patients were excluded. Using the selection criteria, titles and abstracts of studies that were found through the search strategy were reviewed. Full-text versions of potentially eligible articles were retrieved and reviewed. There were no language restrictions.

Extraction of Data From Included Studies

Two reviewers independently extracted principal study characteristics (date of submission, acceptance, and publication; country of origin; number, age, and sex of included patients; inclusion criteria, time between symptom onset and chest CT; CT interpreters; diagnostic CT criteria; reference standard; and COVID-19 prevalence) and true-positive, false-positive, false-negative, and true-negative values of chest CT in detecting COVID-19. Any discrepancies were solved by consensus with a third reviewer.

Assessment of Study Quality

Two reviewers independently assessed study quality with use of the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) checklist [25]. Any discrepancies were solved by consensus with a third reviewer.

Statistical Analyses

For each study, sensitivity and specificity of chest CT in detecting COVID-19 were calculated, along with 95% CIs. Heterogeneity between studies was assessed using a chi-square test (heterogeneity was defined as $p < 0.1$). Meta-analysis was performed using a bivariate random-effects model [26]. Individual studies were plotted in ROC space, as were summary estimates with a 95% confidence ellipse. The Meta-analysis of Diagnostic Accuracy Studies package in R software (R Foundation for Statistical Computing) was used for statistical analyses.

Results

Literature Search

Figure 2 sets out the study selection process. Seventy-one studies were potentially eligible for inclusion (Appendix 1). One study could not be retrieved in full text. After review of the full text of the remaining 70 studies, 57 were excluded because they investigated only patients with proven SARS-CoV-2 infection, five because they did not provide sufficient data to construct a 2×2 contingency table to calculate sensitivity and specificity, and two because they investigated fewer than 10 patients. Six studies were eventually included [23, 27–31]. Principal study characteristics are displayed in Table 1. The median number of patients per study was 110 (range, 19–1014), with a total of 1431 patients. All six studies included patients at high risk of SARS-CoV-2 infection, and five studies explicitly reported that they included only patients with symptoms of COVID-19. The mean prevalence of COVID-19 was 47.9% (range, 27.6–85.4%).

Study Quality

Figure 3 summarizes the results of QUADAS-2 quality assessments. Risk of bias regarding patient selection was deemed high in the study by Himoto et al. [29] because it excluded patients who underwent chest CT within 3 days after symptom onset. Risk of bias regarding patient selection was deemed unclear in the study by Xie et al. [31] because whether patients were enrolled consecutively or randomly assigned was unclear. Risk

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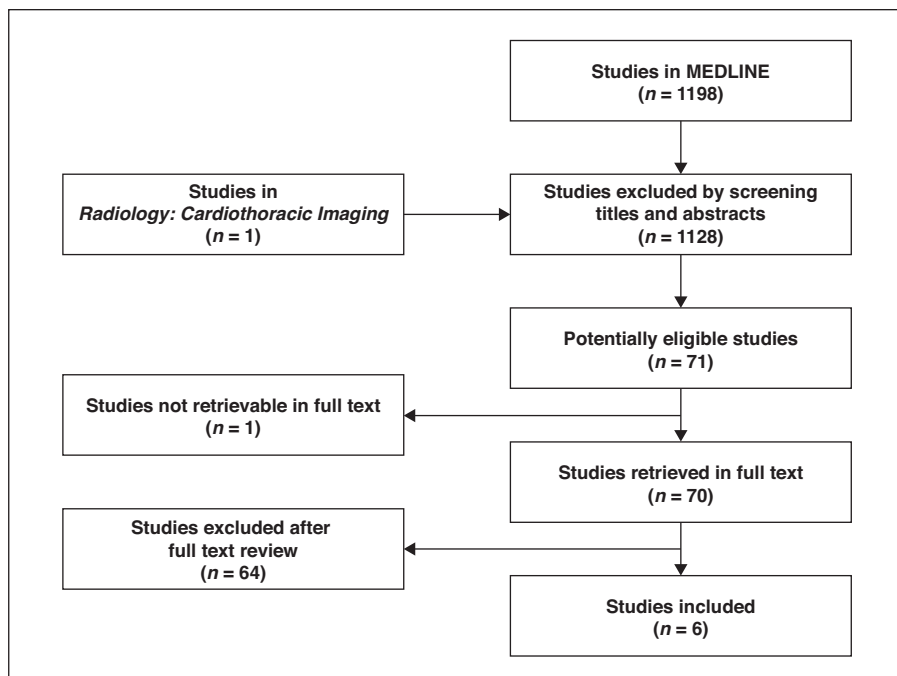


Fig. 2—Flowchart shows study selection process.

of bias regarding index test was also deemed high in the study by Himoto et al. because no prespecified diagnostic threshold was used. Risk of bias regarding index test was deemed unclear in the other five studies, because they did not report whether a prespecified threshold for positivity was used [22, 27, 30, 31] or whether chest CT was interpreted without knowledge of RT-PCR results [28, 31]. Risk of bias regarding reference standard was deemed high in Himoto et al. because careful observation for more than 2 weeks was the only reference standard (rather than RT-PCR or gene sequencing) in some patients. In addition, that study did not report the location where swab sampling was performed or whether all patients with an initial negative RT-PCR result and persistent high index of suspicion of COVID-19 underwent repeated RT-PCR testing. Risk of bias regarding reference standard was deemed unclear in two other studies; in the study by Ai et al. [22], it was not clear whether all patients with an initial negative RT-PCR result and persistent high index of suspicion of COVID-19 underwent repeated RT-PCR testing, and in the study by Zhu et al. [30], the location of the swab sampling was not reported. Risk of bias regarding flow and timing was deemed high in the study by Ai et al. because the time interval between CT and RT-PCR exceeded 72 hours (maximum, 7 days). Risk of

bias regarding flow and timing was deemed unclear in another four studies because the time interval between chest CT and RT-PCR testing was not reported [28–31]. Two studies involved applicability concerns regarding patient selection; the study by Caruso et al. [28] included patients with a previously positive RT-PCR result, and the study by Himoto et al. excluded patients who underwent chest CT within 3 days after symptom onset. There were no other applicability concerns.

Diagnostic Performance

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each included study are displayed in Table 2. Sensitivity ranged from 92.9% to 97.0% and specificity ranged from 25.0% to 71.9%, with pooled estimates of 94.6% (95% CI, 91.9–96.4%) and 46.0% (95% CI, 31.9–60.7%), respectively. The corresponding ROC plot is shown in Figure 4. The area under the summary ROC curve was 0.92. The included studies were statistically homogeneous in their estimates of sensitivity ($p = 0.578$) but statistically heterogeneous in their estimates of specificity ($p < 0.001$).

Discussion

Early and accurate diagnosis may be an essential step toward controlling the COVID-19 pandemic. Chest CT has been proposed as a rapid diagnostic tool for the detection of COVID-19. Our study systematically reviewed the literature with regard to the diagnostic performance of chest CT in detecting this disease.

Our literature search found an abundance of studies on chest CT in COVID-19. However, 57 of 70 (81.4%) potentially eligible studies had to be excluded, because they only investigated patients with SARS-CoV-2 infection proven by RT-PCR, which does not allow an assessment of the overall test performance of chest CT in terms of both sensitivity and specificity. This reason for study exclusion applied to many of the articles that have been widely circulated among the scientific community. A total of six studies remained for inclusion in

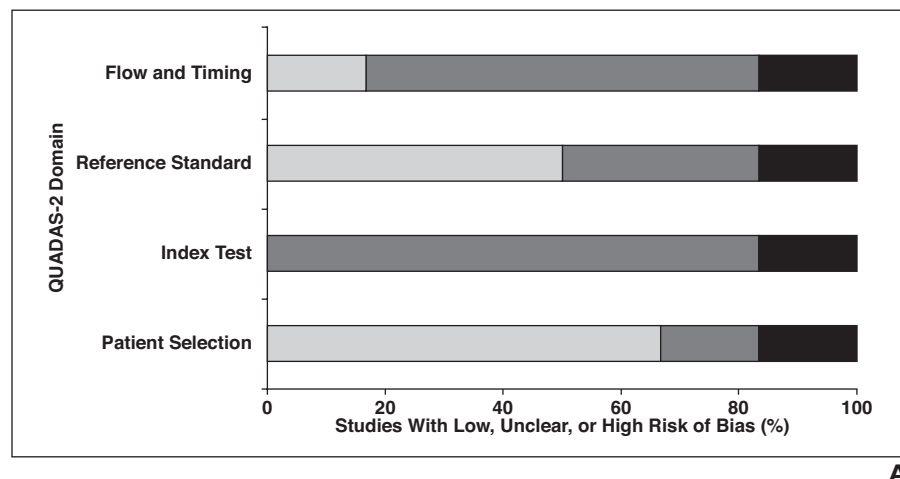


Fig. 3—Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) assessments of included studies. **A** and **B**, Graphs show performance of included studies with respect to QUADAS-2 domains addressing risk of bias (**A**) and concerns regarding applicability (**B**). Light gray = low risk, dark gray = level of risk unclear, black = high risk.

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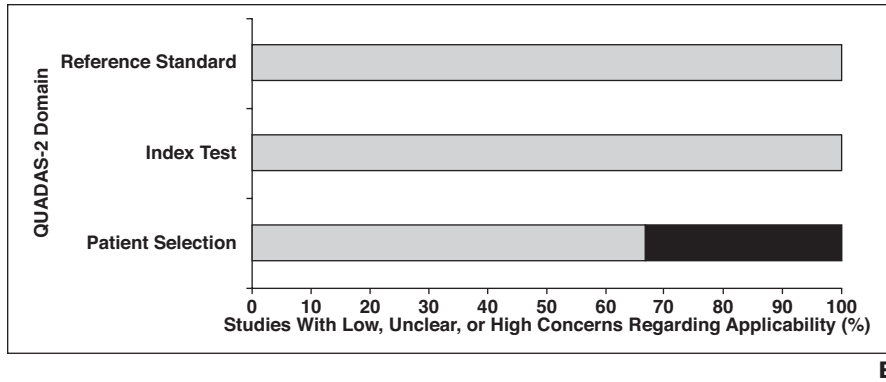


Fig. 3 (continued)—Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) assessments of included studies. **A** and **B**, Graphs show performance of included studies with respect to QUADAS-2 domains addressing risk of bias (**A**) and concerns regarding applicability (**B**). Light gray = low risk, dark gray = level of risk unclear, black = high risk.

our systematic review and meta-analysis. Importantly, all of these six studies included patients at high risk of SARS-CoV-2 infection. Not surprisingly, the prevalence of COVID-19 in patients in these studies was relatively high, with a mean of 47.9%. The majority of included studies explicitly reported that they included only patients with symptoms. The results of our systematic review and meta-analysis are therefore not applicable to a screening setting that aims to detect COVID-19 in apparently healthy people with no symptoms. Such evidence is currently lacking.

Furthermore, the six available studies that investigated the use of chest CT for COVID-19 suffered from several other methodologic flaws. There was high risk of selection bias in one study that excluded patients who underwent chest CT within 3 days after symptom onset [29]. This may have resulted in a relative overestimation of sensitivity, because patients with recent symptoms may not have lung abnormalities yet [12, 32]. All six studies had high or potential risk of bias regarding index test, because they either did not report whether a prespecified diagnostic threshold was used, because no prespecified diagnostic threshold was used, or because they did not report whether chest CT was interpreted without knowledge of RT-PCR results [22, 27–31]. A biased post hoc selection of a diagnostic threshold to optimize sensitivity, specificity, or both may lead to overestimation of diagnostic performance of chest CT [25]. Diagnostic performance is likely to be poorer in an independent sample of patients in whom the same threshold is used [25]. One study [29] had a high risk of bias regarding reference standard, because

clinical observation (rather than RT-PCR or gene sequencing) was used as the only reference standard in some patients. In addition, three studies showed potential risk of bias regarding reference standard, because it was not clear whether all patients with an initial negative RT-PCR result and persistent high index of suspicion of COVID-19 underwent repeat RT-PCR testing and because the location of the swab sampling was not reported [22, 29, 30]. These potential flaws regarding reference standard may have resulted in incorrect diagnosis of COVID-19 in some patients. One study had a high risk of disease progression bias because the time interval between CT and RT-PCR exceeded 72 hours [22]. All the aforementioned methodologic quality issues should be the topic of improvement in future studies.

Within the bounds of the aforementioned limitations, our meta-analysis found that chest CT achieves pooled sensitivity and specificity values of 94.9% (95% CI, 90.2–97.4%) and 30.9% (95% CI, 22.6–40.6%), respectively, in detecting COVID-19 in patients at high risk of being infected with SARS-CoV-2. Although overall sensitivity appears to be high, a normal chest CT does not exclude COVID-19.

There are two reasons why chest CT may suffer from false-negative results. First, patients experiencing symptoms may not have lung abnormalities in the early course of the disease [12, 32]. Second, a considerable number of patients with symptomatic upper respiratory tract infections do not develop pneumonia [11, 33]. Overall specificity of chest CT can be considered poor. False-positive chest CT findings can be encountered in patients with other viral pneumonias that

TABLE 1: Principal Characteristics of Six Included Studies

Study Characteristic	First Author [Reference]						Total no.
	Wen [27]	Caruso [28]	Himoto [29]	Zhu [30]	Xie [31]	Ai [22]	
Article date ^a							
Submitted			March 13		February 17		
Accepted			March 18		February 22		
Published	April 6	April 3	March 30	March 13	February 27	February 26	
Country	China	Italy	Japan	China	China	China	
Study design	R	P	R	R	R	R	
Patients	103	158	21	116	19	1014	

(Table 1 continues on next page)

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TABLE 1: Principal Characteristics of Six Included Studies (continued)

Study Characteristic	First Author [Reference]					
	Wen [27]	Caruso [28]	Himoto [29]	Zhu [30]	Xie [31]	Al [22]
Male	48	83	12	56	8	467
Female	55	75	9	65	11	547
Age (y)						
Mean	46	57	66	40	33	51
Median			58.5	27–53		
Range	12–98	18–89	28–87			
Inclusion criteria	WHO Interim Guidance [39]	Fever and respiratory symptoms, mild respiratory symptoms and close contact with a patient with confirmed COVID-19, or positive test result	Clinically suspected COVID-19 pneumonia	Suspected SARS-CoV-2 infection	Suspected COVID-19 infection	Suspected SARS-CoV-2 infection, chest CT, RT-PCR
Time from symptom onset to chest CT			4–26 d	5 d (median)		
CT interpreters						
No.	Three	Two ^b	Two	Two	Two ^b	Two ^b
Type	Radiologist	Radiologist	Senior radiology resident	Chest radiologist		Radiologist
Experience						
Amount (y)	8–15	15, 25	3			12, 4
Type	Chest CT	Thoracic imaging	General radiology			Chest CT
Diagnostic CT criteria	Abnormalities on CT	Diagnosis of viral pneumonia	GGOs and predominantly peripheral lesions		Bilateral patchy shadows and GGOs	
Time between CT and reference standard	< 3 days					< 7 days
Reference standard	RT-PCR ^c	RT-PCR ^d	RT-PCR, observation for > 2 wk, or both	RT-PCR ^e	RT-PCR ^f	RT-PCR ^g
Specimen type or location	Throat swab, sputum, or alveolar lavage fluid	Nasopharyngeal and oropharyngeal swabs				Throat swab
Testing interval	1–3 d	24 h				
No. (%) of patients with COVID-19	88 (85.4)	62 (39.2)	6 (28.6)	32 (27.6)	9 (47.4)	601 (59.3)

Note—R = retrospective, P = prospective, WHO = World Health Organization, COVID-19 = coronavirus disease, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, GGO = ground-glass opacity, RT-PCR = reverse transcriptase–polymerase chain reaction.

^aAll dates were in 2020.
^bReadings were performed in consensus.
^cPatients with initially negative RT-PCR results underwent repeated RT-PCR testing (up to four tests).
^dPatients were considered negative after two consecutive negative RT-PCR results.
^ePatients with a positive initial result were considered infected. Patients with a negative initial result underwent repeated RT-PCR testing. Patients with a negative second test were considered noninfected.
^fIf initial results were negative, RT-PCR of oropharyngeal swab samples were repeated for three consecutive days.
^gFor patients with multiple RT-PCR tests up to 3 days after the initial test, diagnosis of COVID-19 was confirmed when any of the test results was positive.

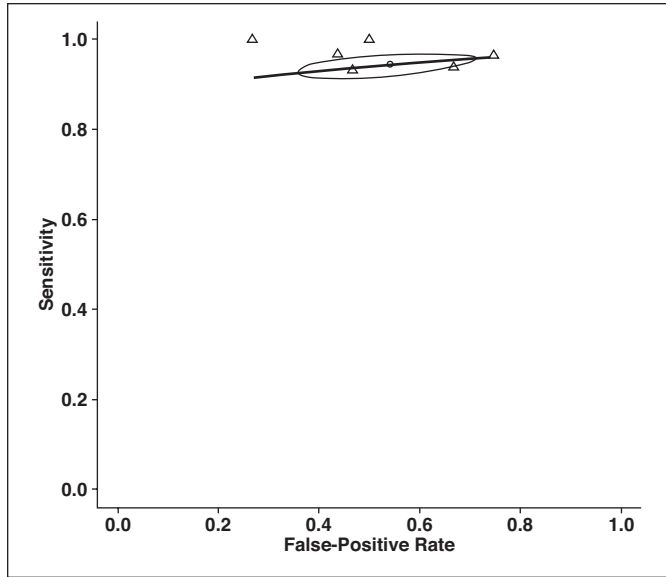


Fig. 4—ROC plot for included studies. Black line denotes summary ROC curve; gray oval shows confidence region (95% confidence ellipse of pooled sensitivity and specificity). Triangles represent data points, and circle denotes summary estimate.

TABLE 2: Diagnostic Value of Chest CT in the Diagnosis of Coronavirus Disease (COVID-19) in the Included Studies

Performance Measure	First Author [Reference]					
	Wen [27]	Caruso [28]	Himoto [29] ^{a,b}	Zhu [30]	Xie [31] ^b	Ai [22]
Sensitivity	93.2 (82/88)	96.8 (60/62)	92.2 (6/6)	93.8 (30/32)	95.0 (9/9)	96.5 (580/601)
Specificity	53.3 (8/15)	56.3 (54/96)	71.9 (11/15)	33.3 (28/84)	50.0 (5/10)	25.4 (105/413)
PPV	92.1 (82/89)	58.8 (60/102)	59.1 (6/10)	34.9 (30/86)	63.3 (9/14)	65.3 (580/888)
NPV	42.9 (6/14)	96.4 (54/56)	95.8 (54/56)	93.3 (28/30)	91.7 (5/5)	83.3 (105/126)

Note—Values are percentages with raw numbers in parentheses. PPV = positive predictive value, NPV = negative predictive value.

^aDiagnostic performance values from reader 1, using the diagnostic criterion with the highest Youden index (i.e., ground-glass opacities and peripheral-predominant lesions).

^bA standard correction of adding 0.5 to all cells of the 2 × 2 contingency table was applied because one or more of the four cells contained the number 0.

show similar imaging features [22]. This further limits the use of chest CT as a diagnostic tool for COVID-19 in regions with a higher prevalence of diseases such as various forms of flu. Interstitial lung diseases and pulmonary edema from cardiogenic and noncardiogenic causes may also have chest CT features that overlap those of COVID-19 [34]. Sensitivity values were statistically homogeneous across included studies, but specificity values were not. The latter may be due to methodologic differences between studies, including the use of different diagnostic criteria and observer variability effects, with higher specificity attained by experienced and dedicated chest radiologists than those with less experience and training.

When the use of chest CT is being considered in a hospital setting, NPV can be regarded as the most important test characteristic. A nearly perfect NPV is desired to eliminate

the risk that patients with COVID-19 remain undetected and that protective measures to prevent nosocomial spread of this disease are not undertaken. Because NPV depends on disease prevalence, the utility of chest CT for COVID-19 detection may vary by region and season. For example, assuming a simplified situation in which the pooled sensitivity and specificity values that were estimated in this study remain fixed and considering variable prevalences of COVID-19 of 10%, 20%, 40%, and 60%, the corresponding NPVs of chest CT would be 98.7%, 97.1%, 92.7%, and 85.0%, respectively. Notably, some studies were not included in this systematic review and meta-analysis because they only enrolled patients with SARS-CoV-2 infection proven by RT-PCR testing; they reported normal chest CT findings in up to 18–39% of cases [12, 35–37]. This indicates that the NPV of chest CT may be substantially low-

er. Furthermore, even when relatively high NPVs are achieved in a low disease prevalence setting, PPV may decrease to an unacceptably low level, unless future research is able to identify more specific chest CT findings of COVID-19. Other variables that need to be taken into account before embarking on any chest CT-based diagnostic algorithm in a hospital are the availability of RT-PCR tests, staff, and hospital capacity (including the number of isolation rooms). Another relevant issue is that if CT scanners are used to diagnose suspected COVID-19, thorough cleaning and disinfection of equipment and the CT examination room are necessary after each use, which may limit a high throughput of patients [10, 38].

Our study has some limitations. First, the number of included studies was relatively low. However, this underlines the fact that most of the numerous chest CT studies on COVID-19 that are currently available are of too poor quality to allow even an extraction of both sensitivity and specificity estimates. We hope that this systematic review and meta-analysis will shed scientific light on the matter and enable healthcare professionals and policy makers to make rational decisions on the value and use of chest CT for COVID-19 detection. It also emphasizes the need for more high-quality studies. Second, several factors may have affected the estimates of diagnostic performance, including chest CT criteria for COVID-19 and observer experience and skill. However, the included studies did not provide sufficient details to permit corresponding subanalyses to determine their effects on diagnostic performance. These issues are relevant for clinical practice and should be a focus of future studies.

In conclusion, diagnostic accuracy studies on chest CT in COVID-19 suffer from methodologic quality issues. Chest CT appears to have a relatively high sensitivity in patients experiencing symptoms of COVID-19 who are at high risk of infection, but it cannot exclude COVID-19. Specificity is poor. These data, along with other local factors such as COVID-19 prevalence, available RT-PCR tests, staff, hospital, and CT scanning capacity, can help healthcare professionals and policy makers to decide on the utility of chest CT for COVID-19 detection in the hospital setting.

References

1. Del Rio C, Malani PN. COVID-19: new insights on a rapidly changing epidemic. *JAMA* 2020 Feb 28 [Epub ahead of print]

Value of Chest CT for COVID-19 Detection

2. Mahase E. Covid-19: WHO declares pandemic because of “alarming levels” of spread, severity, and inaction. *BMJ* 2020; 368:m1036
3. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. *Lancet* 2020; 395:470–473
4. World Health Organization website. WHO Director-General’s opening remarks at the media briefing on COVID-19: 11 March 2020. www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. Published March 11, 2020. Accessed May 10, 2020
5. Wu YC, Chen CS, Chan YJ. The outbreak of COVID-19: an overview. *J Chin Med Assoc* 2020; 83:217–220
6. Zhu N, Zhang D, Wang W, et al. China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020; 382:727–733
7. Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. *Lancet Infect Dis* 2020 Mar 12 [Epub ahead of print]
8. Horowitz J. Italy’s health care system groans under coronavirus: a warning to the world. *The New York Times* website. www.nytimes.com/2020/03/12/world/europe/12italy-coronavirus-health-care.html. Published March 12, 2020. Accessed May 10, 2020
9. Klompas M. Coronavirus disease 2019 (COVID-19): protecting hospitals from the invisible. *Ann Intern Med* 2020 Mar 11 [Epub ahead of print]
10. Centers for Disease Control and Prevention website. Interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings. www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html. Updated April 13, 2020. Accessed May 11, 2020
11. Guan WJ, Ni ZY, Hu Y, et al.; China Medical Treatment Expert Group for COVID-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382:1708–1720
12. Bernheim A, Mei X, Huang M, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. *Radiology* 2020 Feb 20 [Epub ahead of print]
13. World Health Organization website. Coronavirus disease (COVID-19) technical guidance: laboratory testing for 2019-nCoV in humans. www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance. Accessed May 11, 2020
14. Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* 2020; 25:2000045
15. Shirato K, Nao N, Katano H, et al. Development of genetic diagnostic methods for novel coronavirus 2019 (nCoV-2019) in Japan. *Jpn J Infect Dis* 2020 Feb 18 [Epub ahead of print]
16. Sharfstein JM, Becker SJ, Mello MM. Diagnostic testing for the novel coronavirus. *JAMA* 2020 Mar 9 [Epub ahead of print]
17. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for typical 2019-nCoV pneumonia: relationship to negative RT-PCR testing. *Radiology* 2020 Mar 9 [Epub ahead of print]
18. Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis* 2020; 20:425–434
19. Song F, Shi N, Shan F, et al. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. *Radiology* 2020; 295:210–217
20. World Health Organization website. Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases: interim guidance. www.who.int/iris/bitstream/handle/10665/331329/WHO-COVID-19-laboratory-2020.4-eng.pdf. Published March 2, 2020. Accessed May 11, 2020
21. Shen M, Zhou Y, Ye J, et al. Recent advances and perspectives of nucleic acid detection for coronavirus. *J Pharm Anal* 2020; 10:97–101
22. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology* 2020 Feb 26 [Epub ahead of print]
23. Zu ZY, Jiang MD, Xu PP, et al. Coronavirus disease 2019 (COVID-19): a perspective from China. *Radiology* 2020 Feb 21 [Epub ahead of print]
24. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) website. Transparent reporting of systematic reviews and meta-analyses. www.prisma-statement.org/Default.aspx. Accessed May 11, 2020
25. Whiting PF, Rutjes AW, Westwood ME, et al.; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; 155:529–536
26. Reitsma JB, Glas AS, Rutjes AW, Scholten RJ, Bossuyt PM, Zwinderman AH. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *J Clin Epidemiol* 2005; 58:982–990
27. Wen Z, Chi Y, Zhang L, et al. Coronavirus disease 2019: initial detection on chest CT in a retrospective multicenter study of 103 chinese subjects. *Radiol Cardiothorac Imaging* [Epub 2020 Apr 6]
28. Caruso D, Zerunian M, Polici M, et al. Chest CT features of COVID-19 in Rome, Italy. *Radiology* 2020 Apr 3 [Epub ahead of print]
29. Himoto Y, Sakata A, Kirita M, et al. Diagnostic performance of chest CT to differentiate COVID-19 pneumonia in non-high-epidemic area in Japan. *Jpn J Radiol* 2020; 38:400–406
30. Zhu W, Xie K, Lu H, Xu L, Zhou S, Fang S. Initial clinical features of suspected coronavirus disease 2019 in two emergency departments outside of Hubei, China. *J Med Virol* 2020 Mar 13 [Epub ahead of print]
31. Xie C, Jiang L, Huang G, et al. Comparison of different samples for 2019 novel coronavirus detection by nucleic acid amplification tests. *Int J Infect Dis* 2020; 93:264–267
32. Pan F, Ye T, Sun P, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. *Radiology* 2020 Feb 13 [Epub ahead of print]
33. Roser M, Ritchie H, Ortiz-Ospina E. Coronavirus disease (COVID-19): statistics and research. Our World in Data website. ourworldindata.org/coronavirus. Accessed March 19, 2020
34. Nishino M, Itoh H, Hatabu H. A practical approach to high-resolution CT of diffuse lung disease. *Eur J Radiol* 2014; 83:6–19
35. Xu X, Yu C, Qu J, et al. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2. *Eur J Nucl Med Mol Imaging* 2020; 47:1275–1280
36. Xu YH, Dong JH, An WM, et al. Clinical and computed tomographic imaging features of novel coronavirus pneumonia caused by SARS-CoV-2. *J Infect* 2020; 80:394–400
37. Inui S, Fujikawa A, Jitsu M, et al. Chest CT findings in cases from the cruise ship “Diamond Princess” with coronavirus disease 2019 (COVID-19). *Radiol Cardiothorac Imaging* [Epub 2020 Mar 17]
38. Cheng LT, Chan LP, Tan BH, et al. Déjà vu or jamais vu? How the severe acute respiratory syndrome experience influenced a Singapore radiology department’s response to the coronavirus disease (COVID-19) epidemic. *AJR* 2020 Mar 4 [Epub ahead of print]
39. World Health Organization website. Clinical management of severe acute respiratory infection when COVID-19 is suspected: interim guidance. [www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](http://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected). Published March 13, 2020. Accessed May 11, 2020

(Appendix starts on next page)

APPENDIX I: Potentially Eligible Studies That Were Excluded from Systematic Review and Meta-Analysis**TABLE 3: Excluded Studies by Reason for Exclusion**

Reason for Exclusion, First Author Name	Citation
Full text not available	
Xiong Z	<i>Zhonghua Yi Xue Za Zhi</i> 2020; 100:E019
Included patients with proven coronavirus disease (COVID-19) but not patients at risk	
Bai HX	<i>Radiology</i> 2020 Mar 10 [Epub ahead of print]
Bernheim A	<i>Radiology</i> 2020 Feb 20 [Epub ahead of print]
Chen H	<i>Lancet</i> 2020; 395:809–815
Chen L	<i>Zhonghua Jie He He Hu Xi Za Zhi</i> 2020; 43:E005
Chen N	<i>Lancet</i> 2020; 395:507–513
Chung M	<i>Radiology</i> 2020; 295:202–207
Fang Y	<i>Radiology</i> 2020 Feb 19 [Epub ahead of print]
Feng K	<i>Zhonghua Er Ke Za Zhi</i> 2020; 58:E007
Guan CS	<i>Acad Radiol</i> 2020; 27:609–613
Guan WJ	<i>N Engl J Med</i> 2020; 382:1708–1720
Han R	<i>AJR</i> 2020 Mar 17 [Epub ahead of print]
Hu Z	<i>Sci China Life Sci</i> 2020; 63:706–711
Huang C	<i>Lancet</i> 2020; 395:497–506
Lei DP	<i>J Infect</i> 2020 Mar 20 [Epub ahead of print]
Li K	<i>Invest Radiol</i> 2020; 55:327–331
Li M	<i>Acad Radiol</i> 2020; 27:603–608
Li W	<i>Pediatr Radiol</i> 2020 Mar 11 [Epub ahead of print]
Li Y	<i>AJR</i> 2020 Mar 4 [Epub ahead of print]
Ling Z	<i>Eur J Radiol</i> 2020; 126:108956
Liu D	<i>AJR</i> 2020 Mar 18 [Epub ahead of print]
Liu H	<i>J Infect</i> 2020; 80:e7–e13
Liu K	<i>Chin Med J</i> 2020; 133:1025–1031
Liu KC	<i>Eur J Radiol</i> 2020; 126:108941
Liu M	<i>Zhonghua Jie He He Hu Xi Za Zhi</i> 2020; 43:E016
Pan F	<i>Radiology</i> 2020 Feb 13 [Epub ahead of print]
Pan Y	<i>Eur Radiol</i> 2020 Feb 13 [Epub ahead of print]
Peng YD	<i>Zhonghua Xin Xue Guan Bing Za Zhi</i> 2020; 48:E004
Qian GQ	<i>QJM</i> 2020 Mar 17 [Epub ahead of print]
Shi H	<i>Lancet Infect Dis</i> 2020; 20:425–434
Song F	<i>Radiology</i> 2020; 295:210–217
Wan S	<i>J Med Virol</i> 2020 Mar 21 [Epub ahead of print]
Wang D	<i>JAMA</i> 2020; 323:1061–1069
Wang D	<i>Zhonghua Er Ke Za Zhi</i> 2020; 58:E011
Wang J	<i>Zhejiang Da Xue Xue Bao Yi Xue Ban</i> [Epub 2020 Feb 24]
Wang XF	<i>Zhonghua Er Ke Za Zhi</i> 2020; 58:E008
Wang Y	<i>Radiology</i> 2020 Mar 19 [Epub ahead of print]
Wu J	<i>Zhonghua Jie He He Hu Xi Za Zhi</i> 2020; 43:E030
Wu J	<i>Clin Infect Dis</i> 2020 Feb 29 [Epub ahead of print]
Wu J	<i>Invest Radiol</i> 2020; 55:257–261

(Table 3 continues on next page)

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TABLE 3: Excluded Studies by Reason for Exclusion (continued)

Reason for Exclusion, First Author Name	Citation
Xia W	<i>Pediatr Pulmonol</i> 2020; 55:1169–1174
Xie X	<i>Radiology</i> 2020 Feb 12 [Epub ahead of print]
Xiong Y	<i>Invest Radiol</i> 2020; 55:332–339
Xu T	<i>Int J Infect Dis</i> 2020; 94:68–71
Xu X	<i>Eur J Nucl Med Mol Imaging</i> 2020; 47:1275–1280
Xu XW	<i>BMJ</i> 2020 368;m606
Xu YH	<i>J Infect</i> 2020; 80:394–400
Yang W	<i>J Infect</i> 2020 Apr 28 [Epub ahead of print]
Ye G	<i>J Infect</i> 2020; 80:e14–e17
Yuan M	<i>PLoS One</i> 2020; 15:e0230548
Zhang S	<i>Eur Respir J</i> 2020; 55:2000334
Zhang X	<i>Int J Infect Dis</i> 2020; 94:81–87
Zhao W	<i>AJR</i> 2020; 214:1072–1077
Zhao X	<i>Clin Radiol</i> 2020; 75:335–340
Zheng F	<i>Curr Med Sci</i> 2020; 40:275–280
Zhong Q	<i>Zhejiang Da Xue Xue Bao Yi Xue Ban</i> [Epub 2020 May 25]
Zhou S	<i>AJR</i> 2020 Mar 5 [Epub ahead of print]
Zhu ZA	<i>Zhonghua Xin Xue Guan Bing Za Zhi</i> 2020; 48:E007
Fewer than 10 patients included	
Chan JF	<i>Lancet</i> 2020; 395:514–523
Yoon SH	<i>Korean J Radiol</i> 2020; 21:494–500
Insufficient data for 2 × 2 contingency table	
Cheng Z	<i>AJR</i> 2020 Mar 14 [Epub ahead of print]
Li YY	<i>Zhonghua Jie He He Hu Xi Za Zhi</i> 2020; 43:E023
Long C	<i>Eur J Radiol</i> 2020; 126:108961
Zhao D	<i>Clin Infect Dis</i> 2020 Mar 12 [Epub ahead of print]
Zhao S	<i>J Cardiothorac Vasc Anesth</i> 2020; 34:1125–1131

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