Received: 7 May 2020 | Accepted: 25 May 2020

DOI: 10.1002/jmv.26081

REVIEW

JOURNAL OF MEDICAL VIROLOGY WILEY

The diagnosis of SARS-CoV2 pneumonia: A review of laboratory and radiological testing results

Zhong Zheng[1,2] | Zhixian Yao MD[1,2] | Ke Wu MD[1,2] | Junhua Zheng MD[1,2]

[1]Department of Evidence-based Medicine, Shanghai General Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai, China

[2]Shanghai Medical Aid Team in Wuhan, Shanghai General Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai, China

Correspondence
Ke Wu, MD, and Junhua Zheng, MD, Department of Evidence-based Medicine, Shanghai General Hospital, Shanghai Jiao Tong University, School of Medicine, Haining Road 100, 200080 Shanghai, China.
Email: doctorwuke@sjtu.edu.cn (KW) and zhengjh0471@sina.com (JZ)

Funding information
National Natural Science Foundation of China, Grant/Award Numbers: 31570775, 81772705, 81972393

Abstract

The rapid emergence of coronavirus disease 2019 (COVID-19) has necessitated the implementation of diverse pandemic control strategies throughout the world. To effectively control the spread of this disease, it is essential that it be diagnosed at an early stage so that patients can be reliably quarantined such that disease spread will be slowed. At present, the diagnosis of this infectious form of coronavirus pneumonia is largely dependent upon a combination of laboratory testing and imaging analyses of variable diagnostic efficacy. In the present report, we reviewed prior literature pertaining to the diagnosis of different forms of pneumonia caused by coronaviruses (severe acute respiratory syndrome [SARS], Middle East respiratory syndrome, and SARS-CoV-2) and assessed two different potential diagnostic approaches. We ultimately found that computed tomography was associated with a higher rate of diagnostic accuracy than was a real-time quantitative polymerase chain reaction-based approach ($P = .0041$), and chest radiography ($P = .0100$). Even so, it is important that clinicians utilize a combination of laboratory and radiological testing where possible to ensure that this virus is reliably and quickly detected such that it may be treated and patients may be isolated in a timely fashion, thereby effectively curbing the further progression of this pandemic.

KEYWORDS

chest radiography, computed tomography, coronavirus disease 2019, coronavirus pneumonia, diagnosis, polymerase chain reaction

1 | INTRODUCTION

Beginning in December 2019, a novel coronavirus (severe acute respiratory syndrome coronavirus-2 [SARS-CoV-2]) that was found to cause a form of infectious pneumonia (coronavirus disease 2019 [COVID-19]) emerged in Wuhan, China.[1-3] The first confirmed case of a patient hospitalized with COVID-19 occurred on 12 December 2019, and since that time the virus has rapidly spread throughout the world.[4] As of 17 March 2020, there were over 4 731 458 cases and 316 169 deaths confirmed to be associated with COVID-19.[5] Genetic analyses indicate that SARS-CoV-2 most likely arose from bats following passage through unknown intermediate hosts, underscoring the potential zoonotic danger of these coronaviruses.[6] While somewhat distantly related to other coronaviruses known to cause infectious pneumonia such as Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV), SARS-CoV-2 is closely related to two SARS-like coronaviruses identified in bats (bat-SL-CoVZC45 and bat-SL-CoVZXC21), and homology modeling suggests that this virus binds to human angiotensin-converting enzyme 2 (ACE2), much as does SARS-CoV.[7-9]

Zhong Zheng and Zhixian Yao contributed equally to this study.

There is clear evidence of person-to-person SARS-CoV-2 transmission in both hospital and community environments.[10] Following exposure, the median incubation period for this virus is 5.1 days, with ~99% of infected patients developing symptoms within a 14-day monitoring or isolation period.[11] Presenting symptoms most often include cough, fatigue, fever, myalgia, and dyspnea, with many other less common symptoms including allodynia, headache, diarrhea, hemoptysis, and sputum production.[12] This is consistent with the symptoms of SARS and MERS pneumonia, both of which are associated with fever in almost all infected patients upon diagnosis.[13]

Early detection is essential to slow the spread of this pandemic disease, with laboratory testing and imaging being vital to such diagnostic efforts.[14] However, the symptoms of COVID-19 can overlap with those of other serious viral illnesses.[15] Further complicating this diagnostic process is the fact that the polymerase chain reaction (PCR) tests used for COVID-19 diagnosis have a relatively significant false-negative rate.[16,17] This is a major concern, as the erroneous release of patients with false-negative test results has the potential to facilitate the rapid spread of the virus via community transmission.

In light of these facts, the present review has been designed to evaluate the diagnostic utility of early radiological and laboratory test findings in patients with coronavirus pneumonia to establish the optimal strategies for confirming infection with SARS-CoV, MERS-CoV, or SARS-CoV-2. We searched the literature in Pubmed, Web of Science, and the Cochrane Library, and summarize the findings concerning the diagnostic strategies of SARS, MERS, and COVID-19 for the consideration of clinicians in this report.

2 | STATISTICAL ANALYSIS

The Kruskal-Wallis test was used to compare continuous variables when abnormal distribution was verified by Shapiro-Wilk test, while Barlett's test was used when normal distribution was verified. The one-way analysis of variance was used to campare the difference between groups after using Levene's test for homogeneity of variance. The statistics were prepared using Excel (Microsoft Corp., Redmond, WA), and analyzed using R studio (R Foundation for Statistical Computing, Vienna, Austria). A *P* value of less than .05 was considered to be statistically significant.

2.1 | Laboratory diagnosis

Relative to macroscopic imaging approaches, serological studies, and nucleic acid testing can yield much higher specificity, allowing clinicians to correctly identify pathogenic viruses in infected patients (Table 1).[18-20] Many advances in viral diagnostic testing have been made in recent decades, including rapid antigen detection tests and high-sensitivity NAAT approaches such as PCR.[21] Rapid and simple antigen immunoassays are commonly used to detect a range of different viruses but are limited by their relatively poor sensitivity.[21]

2.1.1 | Serological testing

A number of different forms of serological testing have been employed to detect certain viruses, including neutralization assays, immunofluorescent assays (IFAs), enzyme-linked immunosorbent assays (ELISA), and immunochromatographic tests (ICT). ELISA- or chemiluminescent assay-based detection of coronavirus nucleocapsid (N) proteins has been used to detect the presence of these viral proteins in patient serum samples.[22] As a classical method for diagnosing viruses, serology test exhibited the feature of hysteresis, due to seroconversion.[23] In SARS patients, such serum tests were found to be positive in approximately 78% of infected individuals,[17,24,25] although they were only positive in 42% of MERS patients.[26] To date, emerging studies have reported on serological testing data for COVID-19 patients. Using IgG ELISA based on to the receptor-binding domain (RBD) of the spike protein to screen sera for SARS-CoV-2 antibody, followed by confirmation using 90% plaque reduction neutralization tests (PRNT90), is a valid approach for detecting COVID-19. And the average positive rate of serology tests for COVID-19 is 88%.[27-33]

2.1.2 | PCR

PCR-based diagnostic approaches including both conventional reverse-transcription PCR (RT-PCR) and real-time quantitative PCR (qPCR) are the most commonly used strategies for the detection of infectious coronaviruses in patient samples. RT-PCR and qPCR were associated with 62% and 75% average positive detection rates in SARS patients, respectively.[17,24,25,34-38] In MERS

TABLE 1 Laboratory examinations of coronavirus pneumonia

	Range (mean ± *SD*)			
Pneumonia	**RT-PCR**	**qPCR**	**Serological test**	**References**
SARS	38%-88% (62 ± 35)	50%-86% (75 ± 13)	34%-99% (78 ± 27)	17,24,25,34-38
MERS	55%-89% (72 ± 24)	58%-90% (74 ± 23)	100%[a]	26,39,40
COVID-19	/[b]	50%-97% (74 ± 14)	62%-100% (88 ± 14)	28-33,41-46

Abbreviations: COVID-19, coronavirus disease 2019; MERS, Middle East respiratory syndrome; qPCR, real-time quantitative polymerase chain reaction; RT-PCR, reverse-transcription polymerase chain reaction; SARS, severe acute respiratory syndrome.

[a]There was only one study related to the serological test of MERS.

[b]Lack of data.

patients, RT-PCR and qPCR were associated with 72% and 74% average positive detection rates, respectively.[26,39,40] In COVID-19 patients, only qPCR is generally used, with the open reading frame 1ab (ORF1ab) and nucleocapsid protein (N) gene regions of SARS-CoV-2 simultaneously tested. Primers for ORF1ab were as follows: forward primer CCCTGTGGGTTTTACACTTAA, reverse primer ACGATTGTGCATCAGCTGA, and the probe 5′-VIC-CCGTCTGCG GTATGTGGAAAGGTTATGG-BHQ1-3′. Primers for N were as follows: forward primer GGGGAACTTCTCCTGCTAGAAT, reverse primer CAGACATTTTGCTCTCAAGCTG, and the probe 5′-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3′.[41] And it has a reported 74% average positive detection rate.[41-46] No significant differences were observed between SARS and MERS with respect to the diagnostic utility of RT-PCR ($P = .4386$), nor were there any significant differences with respect to average qPCR positive detection rates for SARS, MERS, and COVID-19 ($P = .989$).

Interestingly, paired serological findings were found to be positive in 96.2% of patients among whom RT-PCR was positive in just 64% of people.[47] As seroconversion requires 2 to 3 weeks following infection in most cases,[48] such serological testing is only positive in 8.3% of patients within the first 2 weeks.[47] Based on these limitations, serological testing is unlikely to offer value as a first-line diagnostic tool in the context of rapidly evolving pandemic diseases such as COVID-19.

2.2 | Imaging diagnosis

Imaging analyses are typically considered to be auxiliary examinations, yet they are integral to the diagnosis of coronavirus pneumonia in many patients.[49,50] As such, chest radiography is recommended for all patients suspected to be infected with SARS, MERS, or COVID-19, with high-resolution computed tomography (CT) scans is considered to be the most informative. While multiple pathogens may present with similar CT findings in infected patients,[15] these rapid and straightforward imaging tests are nonetheless essential for the detection of patients suffering from coronavirus pneumonia in hotspot areas of significant known viral transmission. Patient diagnosis is typically dependent upon chest radiography and thoracic CT scans, with the former offering density specificity that enables a rapid assessment of lung lesions and the latter offering better spatial specificity as it allows clinicians to directly evaluate transverse lung sections, as well as surrounding tissues and vasculature.[51]

2.2.1 | Chest radiography

Chest radiography is generally the first test to be ordered in patients suspected to be suffering from SARS, MERS, or COVID-19 (Table 2). With the advancing technology, artificial intelligence (AI) system could be surve as a reliable support.[71] In such radiographs, 72% of SARS patients were found to exhibit abnormalities (78% consolidation, 33% ground-glass opacity [GGO]).[35,49,52-56] Similarly, 86% of MERS patients exhibit radiographic abnormalities (65% GGO, 18% consolidation, 17% bronchovascular markings, 11% air bronchogram, 4% diffuse reticulonodular patterning).[57-65] In COVID-19 patients, chest radiographic abnormalities have been observed in 62% of patients (27% GGO, 47% consolidation, and 1% pneumothorax).[12,45,46,66-70] There were no significant differences

TABLE 2 Chest radiography of coronavirus pneumonia

	Range (mean ± SD)			
Pneumonia	Abnormality	Imaging manifestation	Lesions location	References
SARS	58%-90% (72 ± 12)	GGO: 33% Consolidation: 78%	Unifocal: 55%, Multifocal: 45% Unilateral: 61% Bilateral: 39% Low lung zone: 74%	[35,49,52-56]
MERS	60%-100% (86 ± 14)	GGO: 65% Consolidation: 18% Bronchovascular markings:17% Diffuse reticulonodular pattern:4% Air bronchogram: 11%	Unifocal: 40% Multifocal: 60% Unilateral: 23% Bilateral: 77% Interstitial: 67%	[57-65]
COVID-19	15%-100% (62 ± 35)	GGO: 27% Consolidation:47% Pneumothorax:1%	Unifocal: 48% Multifocal: 52% Unilateral: 29% Bilateral: 71% Interstitial: 7% Low lung zone: 50%	[12,45,46,66-70]

Abbreviations: COVID-19, coronavirus disease 2019; GGO, ground-glass opacity; MERS, Middle East respiratory syndrome; SARS, severe acute respiratory syndrome.

in rates of radiographic abnormalities among these three coronavirus infections ($P = .1827$).

The spatial location of lesions in coronavirus pneumonia patients is also an important diagnostic and prognostic consideration. SARS patients exhibited unilateral and bilateral involvement in 61% and 39% of cases, respectively, with 55% and 45% of patients exhibiting single and multiple infiltration, respectively, and with the lower lung being more susceptible to infection (74% of patients).[35,55,56] Unilateral and bilateral involvement was observed in 40% and 60% of MERS patients, respectively, with 40% and 60% of patients similarly exhibiting single and multiple infiltration, respectively, and with interstitial infiltration having been detected in 67% of patients.[63,64,72] Unilateral and bilateral involvement has been detected in 29% and 71% of COVID-19 patients, respectively, with these patients exhibiting single, multiple, and interstitial infiltration in 48%, 52%, and 7% of cases, respectively, and with the lower lung being susceptible to infection (50% of patients).[45,67,68] These results suggest that COVID-19 and MERS are more commonly associated with bilateral lung involvement relative to SARS, whereas SARS and MERS are associated with similar infiltration rates.

Overall, extant radiographic data suggest that chest radiography can aid in the diagnosis of coronavirus pneumonia, although there is still potential for misdiagnosis. As such, further CT scans are important in affected patients.

2.2.2 | Computed tomography

CT scans are increasingly common diagnostic tools owing to recent advances in low-dose and high-resolution imaging techniques, similar to chest radiography, AI system involving (Table 3).[46,92] In CT scans, 98% of SARS patients were found to exhibit abnormalities, with 81% exhibiting GGO, 49% exhibiting consolidation, 87% exhibiting interlobular septal thickening, 74% exhibiting crazy paving pattern, and 4% exhibiting parapneumonic effusion.[55,56,73] In contrast, 100% of MERS patients were found to exhibit CT abnormalities (86% GGO, 65% consolidation, 38% pleural effusion, 35% interlobular septal thickening),[64,74] as were 89% of patients with COVID-19 (82% GGO, 45% consolidation, 48% interlobular septal thickening, 35% air bronchogram, 23% crazy paving pattern, 6% pleural effusion) (Table 3).[12,41,42,45,68,75-91] There were no significant differences in CT abnormality rates among these three groups ($P = .1481$), although rates among SARS and MERS patients were, on average, higher than among COVID-19 patients, potentially as a consequence of disease monitoring practices in China and high disease awareness such that patients are often diagnosed before the manifestation of lung disease. In addition, relatively few studies of CT findings in SARS and MERS patients have been conducted, limiting confidence in these results. Some studies found that high-resolution CT findings in SARS patients were similar to those with steroid-responsive bronchiolitis obliterans,[93,94] providing a rational basis for treating coronavirus pneumonia with such steroids.[95]

As CT scans offer excellent spatial specificity, they can be more effectively used to assess lesion variability than can radiographic scans. CT scans of SARS patients identified 61% and 39% of lesions as being unifocal and multifocal, respectively, with 74% and 26% being unilobar and multilobar, respectively, 48% being unilateral, 52% being bilateral, 71% exhibiting lower lobe involvement, and 84% exhibiting peripheral or subpleural involvement.[55,56,73] In contrast, just 14% of MERS lesions were found to be unilateral, with the remaining 86% being bilateral, and with 14% exhibiting lower lobe involvement and 71% being peripheral or subpleural.[64,74] Unifocal and multifocal lung lesions were observed in 31% and 69% of COVID-19 patients, respectively, with unilobar and multilobar lesions being detected in 25% and 75% of patients, respectively, and with 21% and 79% exhibiting unilateral and bilateral involvement, respectively, in addition to 56% exhibiting lower lobe involvement, 79% exhibiting peripheral or subpleural involvement, and 71% exhibiting central involvement.[45,77-83,89] In line with chest radiographic findings, these results suggest that MERS and COVID-19 are associated with more diffuse disease than is SARS, potentially due to underlying differences in the pathological mechanisms of these diseases. And a multicenter cohort illustrates more consolidation in upper lungs on initial CT increases the risk of adverse clinical outcome in COVID-19 patients (right: OR, 1.13; 95% CI, 1.03-1.25; $P = .01$; left: OR,1.15; 95% CI, 1.01-1.32; $P = .04$).[96]

Overall, data suggest that CT scans offer markedly higher diagnostic efficacy relative to chest radiography ($P = .0100$). However, CT scans cannot reliably identify infections associated with a specific virus, nor can they reliably differentiate between viruses.[87] Even so, owing to their excellent diagnostic utility, CT scans should be the primary mode of imaging examination in patients with suspected coronavirus pneumonia.

3 | DISCUSSION

Present guidelines indicate that formal SARS-CoV-2 diagnosis is dependent upon the results of laboratory examinations such as swab test qPCR analyses.[97] However, such laboratory testing is both time- and resource-intensive, with test kits and swabs not being available in sufficient quantities in some areas of rapid viral spread. These diagnostic approaches are also hampered by the potential for false-negative results due to laboratory errors or a lack of a sufficiently high-quality sample for analysis.[42,98]

To aid in the more precise diagnostic evaluation of patients with coronavirus pneumonia, we herein compared extant data pertaining to abnormal CT findings and qPCR results in this disease context. While no significant differences between CT and qPCR findings were observed for MERS patients owing to the relatively limited literature surrounding this emerging virus ($P = .3516$), significant differences between CT and qPCR results were observed for both SARS and COVID-19 cases ($P = .0302$, $P = .0041$) (Table 4). While qPCR analyses can achieve 100% specificity,[22,44,47] to do so they require access to a sufficient viral

TABLE 3 CT scan of coronavirus pneumonia

	Range (mean ± *SD*)			
Pneumonia	**Abnormality**	**Imaging manifestation**	**Lesions location**	**References**
SARS	93%-100% (98 ± 4)	GGO: 81% Consolidation: 49% Interlobular septal thickening: 87% Crazy paving pattern: 74% Parapneumonic effusion:4%	Unifocal: 61% Multifocal: 39% Unilobar: 74% Multilobar: 26% Unilateral: 48% Bilateral: 52% Peripheral or subpleural: 84% Lower lobe: 71%	55,56,73
MERS	100%[a]	GGO: 86% Consolidation: 52% Pleural effusion: 38% Interlobular thickening: 35%	Unilateral: 14% Bilateral: 86% Peripheral or subpleural: 71% Lower lobe: 14%	64,74
COVID-19	69%-100% (89 ± 11)	GGO: 82% Consolidation: 45% Interlobular septal thickening: 48% Air bronchogram: 35% Bronchus distortion: 18% Pleural effusion: 6% Pleural thickening: 47% Pleural retraction sign: 33% Reticular pattern: 63% Vacuolar sign: 55% Microvascular dilation sign: 45% Fibrotic streaks: 37% Subpleural line: 34% Vascular enlargement: 71% Traction bronchiectasis: 52% Crazy paving pattern: 23% Combined linear opacities: 80%	Unifocal: 31% Multifocal: 69% Unilobar: 25% Multilobar: 75% Unilateral: 21% Bilateral: 79% Peripheral or subpleural: 79% Central: 71% Lower lobe: 56%	12,41,42,45,68,75-91

Abbreviations: COVID-19, coronavirus disease 2019; CT, computed tomography; MERS, Middle East respiratory syndrome; SARS, severe acute respiratory syndrome.

[a]There were only two articles related to the abnormality rate of MERS, all of which were 100%.

specimen. While bronchoalveolar lavage fluid (BALF) samples were associated with a 100% viral positivity rate in one study, sputum samples were associated with a lower positivity rate (74.4%-88.9%), while nasal swab detection rates were lower still (53.6%-73.3%).[44] This may be a consequence of a number of different factors pertaining to sample collection methodology, timing, sample transport, and sample testing parameters. Lower respiratory samples have the potential to offer greater diagnostic sensitivity even when nasopharyngeal and oropharyngeal qPCR tests yield negative results, and serological testing should also be used as a follow-up approach in those with clinically suspected disease.[17] It is also vital that clinicians implement appropriate infection control strategies for all patients with suspected disease, including patients that exhibit negative qPCR findings but that exhibit imaging signs consistent with coronavirus pneumonia.[17] A single swab-based test is also not sufficient to reliably rule out the possibility of infection. In a study of MERS patients, while only 89% of patients were found to be positive after a single swab test, 96.5% were found to be positive following two consecutive swabs, and 97.6% were positive following three consecutive swab tests.[39] Initial negative test results have a high risk of being false-negative findings, and repeated testing is

TABLE 4 Comparison between CT scan and qPCR of coronavirus pneumonia

Pneumonia	CT Scan, range (mean ± SD)	qPCR, range (mean ± SD)	*P* value
SARS	93%-100% (98 ± 4)	50%-86% (75 ± 13)	.0302
MERS	100%	58%-90% (74 ± 23)	.3516
COVID-19	69%-100% (89 ± 11)	50%-97% (74 ± 14)	.0041

Abbreviations: COVID-19, coronavirus disease 2019; CT, computed tomography; MERS, Middle East respiratory syndrome; qPCR, real-time quantitative polymerase chain reaction; SARS, severe acute respiratory syndrome.

therefore essential to ensure appropriate patient quarantine and management.

With respect to CT scans, the relatively low rates of COVID-19 misdiagnosis (3.9%) suggest that radiologic diagnoses may be a reliable means of quickly detecting cases of coronavirus pneumonia so as to facilitate rapid and effective patient quarantine and management.[87] An AI study related to CT scan achieved a test accuracy of 96% (95% CI, 90%-98%), sensitivity 95% (95% CI, 83%-100%) and specificity of 96% (95% CI, 88%-99%) with receiver operating characteristic (ROC) AUC of 0.95 and Precision-Recall (PR) AUC of 0.90, which concluded that AI assistance improved radiologists' performance in distinguishing COVID-19 from non-COVID-19 pneumonia on chest CT.[99] These scans may also be of value in patients that initially exhibit negative PCR findings. For example, Xie et al[42] reported on five patients that were negative for SARS-CoV-2 in initial qPCR tests, but that exhibited typical COVID-19 CT findings including GGO and consolidation. These patients were isolated, and subsequent repeated qPCR testing eventually confirmed all five of these patients to be infected with SARS-CoV-2.[42] Similarly, research conducted by Ai et al[43] revealed that positive chest CT findings were detected in 75% of symptomatic patients with negative qPCR findings. Serial RT-PCR and CT scans in these patients suggested a mean interval of 5.1 ± 1.5 days between initial negative qPCR and positive qPCR findings.[43] The comprehensive strategy reached a higher sensitivity of 94% in a retrospective study (Table 4).[46]

While CT scans expose patients to higher radiation doses, the relative risks, and benefits of such exposure must be determined by radiologists and clinicians. In the context of severe pandemic disease, CT scans are a valuable tool and may be essential to accurately and quickly identify and isolate COVID-19 patients. However, a combination of both laboratory testing and imaging is essential to accurately identify COVID-19 patients with confidence, and CT scans should be ordered in patients with negative qPCR results that are nonetheless suspected to be suffering from coronavirus pneumonia. When patients test positive for SARS-CoV-2 infection, while there is a small risk of false-positive diagnosis, it is essential that they be strictly isolated from other individuals to limit the ability of this virus to spread through vulnerable communities.

4 | CONCLUSION

In summary, in the present review, we surveyed the results of prior studies of SARS, MERS, and COVID-19 patients in an effort to establish which diagnostic approaches are most efficacious in those with coronavirus pneumonia. While we found that CT scans are associated with higher detection rates than are qPCR tests, it is nonetheless important that clinicians utilize a combination of imaging and laboratory findings to inform their diagnostic process such that patients can be rapidly identified and quarantined, thus stemming the spread of these deadly pandemic viruses.

ACKNOWLEDGMENTS

We appreciate the support from Youth Science and Technology Innovation Studio of Shanghai Jiao Tong University School of Medicine. Dr. Zhong Zheng should finally like to express his gratitude to his beloved Tian Gan who has always been helping him out of difficulties and supporting without a word of complaint. The reported work was supported in part by research grants from the National Natural Science Foundation of China (no. 81972393, 81772705, 31570775).

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

JZ and KW participated in the study design; ZZ performed data collection and analysis; ZY drafted the manuscript; all authors provided a critical review of the manuscript and approved the final draft for publication.

ORCID

Zhong Zheng http://orcid.org/0000-0002-3500-9510

REFERENCES

1. Salata C, Calistri A, Parolin C, Palu G. Coronaviruses: a paradigm of new emerging zoonotic diseases. *Pathog Dis*. 2019;77(9). https://doi.org/10.1093/femspd/ftaa006
2. Tan W, Zhao X, Ma X, et al. A novel coronavirus genome identified in a cluster of pneumonia cases—Wuhan, China 2019-2020. *China CDC Weekly*. 2020;2(4):61-62.
3. Zheng Z, Yao Z, Wu K, Zheng J. Patient follow-up after discharge after COVID-19 pneumonia: considerations for infectious control [published online ahead of print May 8, 2020]. *J Med Virol*. https://doi.org/10.1002/jmv.25994
4. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet*. 2020;395(10225):689-697. https://doi.org/10.1016/s0140-6736(20)30260-9
5. WHO. Coronavirus disease 2019 (COVID-19) Situation Report—120. World Health Organization. March 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200519-covid-19-sitrep-120.pdf?sfvrsn=515cabfb_2. Accessed 20 May 2020.
6. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;579(7798):270-273. https://doi.org/10.1038/s41586-020-2012-7
7. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020;395(10224):565-574. https://doi.org/10.1016/s0140-6736(20)30251-8
8. Li R, Qiao S, Zhang G. Analysis of angiotensin-converting enzyme 2 (ACE2) from different species sheds some light on cross-species receptor usage of a novel coronavirus 2019-nCoV. *J Infect*. 2020. https://doi.org/10.1016/j.jinf.2020.02.013
9. Yao Z, Zheng Z, Wu K, Junhua Z. Immune environment modulation in pneumonia patients caused by coronavirus: SARS-CoV, MERS-CoV and SARS-CoV-2. *Aging*. 2020;12:12-7651. https://doi.org/10.18632/aging.103101
10. Chan JFW, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*. 2020;395(10223):514-523. https://doi.org/10.1016/s0140-6736(20)30154-9
11. Lauer SA, Grantz KH, Bi Q, et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases:

estimation and application. *Ann Intern Med*. 2020;172:577-582. https://doi.org/10.7326/m20-0504
12. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. https://doi.org/10.1016/s0140-6736(20)30183-5
13. Zumla A, Hui DS, Perlman S. Middle East respiratory syndrome. *Lancet*. 2015;386(9997):995-1007. https://doi.org/10.1016/s0140-6736(15)60454-8
14. Zhang N, Wang L, Deng X, et al. Recent advances in the detection of respiratory virus infection in humans. *J Med Virol*. 2020;92(4):408-417. https://doi.org/10.1002/jmv.25674
15. Koo HJ, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral pneumonia. *Radiographics*. 2018;38(3):719-739. https://doi.org/10.1148/rg.2018170048
16. Chu CM. Duration of RT-PCR positivity in severe acute respiratory syndrome. *Eur Respir J*. 2005;25(1):12-14. https://doi.org/10.1183/09031936.04.00057804
17. Tsang OTY, Chau TN, Choi KW, et al. Coronavirus-positive nasopharyngeal aspirate as predictor for severe acute respiratory syndrome mortality. *Emerg Infect Dis*. 2003;9(11):1381-1387. https://doi.org/10.3201/eid0911.030400
18. Gouel-Cheron A, Lumbard K, Hunsberger S, et al. Serial real-time RT-PCR and serology measurements substantially improve Zika and Dengue virus infection classification in a co-circulation area. *Antiviral Res*. 2019;172:104638. https://doi.org/10.1016/j.antiviral.2019.104638
19. Meyer B, Drosten C, Muller MA. Serological assays for emerging coronaviruses: challenges and pitfalls. *Virus Res*. 2014;194:175-183. https://doi.org/10.1016/j.virusres.2014.03.018
20. Bustin SA, Mueller R. Real-time reverse transcription PCR (qRT-PCR) and its potential use in clinical diagnosis. *Clinical science (London, England: 1979)*. 2005;109(4):365-379. https://doi.org/10.1042/cs20050086
21. Azar MM, Landry ML. Detection of influenza A and B viruses and respiratory syncytial virus by use of clinical laboratory improvement amendments of 1988 (CLIA)-waived point-of-care assays: a paradigm shift to molecular tests. *J Clin Microbiol*. 2018;56(7). https://doi.org/10.1128/jcm.00367-18
22. Che X, Di B, Zhao G, et al. A patient with asymptomatic severe acute respiratory syndrome (SARS) and antigenemia from the 2003-2004 community outbreak of SARS in Guangzhou, China. *Clin Infect Dis*. 2006;43(1):e1-e5.
23. Haveri A, Smura T, Kuivanen S, et al. Serological and molecular findings during SARS-CoV-2 infection: the first case study in Finland, January to February 2020. Euro surveillance: bulletin Europeen sur les maladies transmissibles. *Eur Commun Dis Bull*. 2020;25(11). https://doi.org/10.2807/1560-7917.es.2020.25.11.2000266
24. Wu HS, Chiu SC, Tseng TC, et al. Serologic and molecular biologic methods for SARS-associated coronavirus infection. *Taiwan. Emerg Infect Dis*. 2004;10(2):304-310. https://doi.org/10.3201/eid1002.030731
25. Peiris JS, Lai ST, Poon LL, et al. Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet*. 2003;361(9366):1319-1325. https://doi.org/10.1016/s0140-6736(03)13077-2
26. Arwady MA, Alraddadi B, Basler C, et al. Middle East respiratory syndrome coronavirus transmission in extended family, Saudi Arabia, 2014. *Emerging Infect Dis*. 2016;22(8):1395-1402.
27. Xu Y, Xiao M, Liu X, et al. Significance of serology testing to assist timely diagnosis of SARS-CoV-2 infections: implication from a family cluster. *Emerg Microbe Infect*. 2020;9(1):924-927. https://doi.org/10.1080/22221751.2020.1752610
28. Perera RA, Mok CK, Tsang OT, et al. Serological assays for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), March 2020. *Euro Surveillance*. 2020;25(16). https://doi.org/10.2807/1560-7917.es.2020.25.16.2000421
29. Yongchen Z, Shen H, Wang X, et al. Different longitudinal patterns of nucleic acid and serology testing results based on disease severity of COVID-19 patients. *Emerg Microbes Infect*. 2020;9(1):833-836. https://doi.org/10.1080/22221751.2020.1756699
30. Jääskeläinen AJ, Kekäläinen E, Kallio-Kokko H, et al. Evaluation of commercial and automated SARS-CoV-2 IgG and IgA ELISAs using coronavirus disease (COVID-19) patient samples. *Euro Surveillance*. 2020;25(18). https://doi.org/10.2807/1560-7917.es.2020.25.18.2000603
31. Pan Y, Li X, Yang G, et al. Serological immunochromatographic approach in diagnosis with SARS-CoV-2 infected COVID-19 patients. *J Infect*. 2020. https://doi.org/10.1016/j.jinf.2020.03.051
32. Zhao R, Li M, Song H, et al. Early detection of SARS-CoV-2 antibodies in COVID-19 patients as a serologic marker of infection. *Clin Infect Dis*. 2020. https://doi.org/10.1093/cid/ciaa523
33. Tang MS, Hock KG, Logsdon NM, et al. Clinical performance of two SARS-CoV-2 serologic assays. *Clin Chem*. 2020. https://doi.org/10.1093/clinchem/hvaa120
34. Poon LL, Wong OK, Luk W, Yuen KY, Peiris JS, Guan Y. Rapid diagnosis of a coronavirus associated with severe acute respiratory syndrome (SARS). *Clin Chem*. 2003;49(6):953-955.
35. Liu CL, Lu YT, Peng MJ, et al. Clinical and laboratory features of severe acute respiratory syndrome vis-a-vis onset of fever. *Chest*. 2004;126(2):509-517. https://doi.org/10.1378/chest.126.2.509
36. Poon LLM, Wong BWY, Chan KH, et al. A one step quantitative RT-PCR for detection of SARS coronavirus with an internal control for PCR inhibitors. *J Clin Virol*. 2004;30(3):214-217. https://doi.org/10.1016/j.jcv.2003.12.007
37. Poon LLM, Chan KH, Wong OK, et al. Early diagnosis of SARS coronavirus infection by real time RT-PCR. *J Clin Virol*. 2003;28(3):233-238. https://doi.org/10.1016/j.jcv.2003.08.004
38. Franks TJ, Chong PY, Chui P, et al. Lung pathology of severe acute respiratory syndrome (SARS): a study of 8 autopsy cases from Singapore. *Hum Pathol*. 2003;34(8):743-748. https://doi.org/10.1016/s0046-8177(03)00367-8
39. Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle East respiratory syndrome coronavirus intermittent positive cases: Implications for infection control. *Am J Infect Control*. 2019;47(3):290-293. https://doi.org/10.1016/j.ajic.2018.08.020
40. Hecht LS, Jurado-Jimenez A, Hess M, et al. Verification and diagnostic evaluation of the RealStar((R)) Middle East respiratory syndrome coronavirus (N gene) reverse transcription-PCR kit 1.0. *Future Microbiol*. 2019;14:941-948. https://doi.org/10.2217/fmb-2019-0067
41. Zhao XY, Xu XX, Yin HS, et al. Clinical characteristics of patients with 2019 coronavirus disease in a non-Wuhan area of Hubei Province, China: a retrospective study. *BMC Infect Dis*. 2020;20(1):311. https://doi.org/10.1186/s12879-020-05010-w
42. 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*. 2020:200343.
43. 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*. 2020:200642. https://doi.org/10.1148/radiol.2020200642
44. Yang Y, Yang M, Shen C, et al. Evaluating the accuracy of different respiratory specimens in the laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infections. *medRxiv*. 2020. https://doi.org/10.1101/2020.02.11.20021493
45. Yoon SH, Lee KH, Kim JY, et al. Chest Radiographic and CT Findings of the 2019 Novel Coronavirus Disease (COVID-19): Analysis of Nine Patients Treated in Korea. *Korean J Radiol*. 2020;21:494. https://doi.org/10.3348/kjr.2020.0132
46. Belfiore MP, Urraro F, Grassi R, et al. Artificial intelligence to codify lung CT in Covid-19 patients. *Radiol Med*. 2020;125(5):500-504. https://doi.org/10.1007/s11547-020-01195-x
47. Tang P, Louie M, Richardson SE, et al. Interpretation of diagnostic laboratory tests for severe acute respiratory syndrome: the Toronto experience. *CMAJ*. 2004;170(1):47-54.

48. Mahony JB, Richardson S. Molecular diagnosis of severe acute respiratory syndrome: the state of the art. *J Mol Diagnostics*. 2005;7(5):551-559. https://doi.org/10.1016/s1525-1578(10)60587-9
49. Hui DSC, Wong KT, Antonio GE, et al. Severe acute respiratory syndrome: correlation between clinical outcome and radiologic features. *Radiology*. 2004;233(2):579-585.
50. Cleri DJ, Ricketti AJ, Vernaleo JR. Severe acute respiratory syndrome (SARS). *Infect Dis Clin North Am*. 2010;24(1):175-202. https://doi.org/10.1016/j.idc.2009.10.005
51. Church TR. Chest radiography as the comparison for spiral CT in the National Lung Screening Trial. *Academic Radiol*. 2003;10(6):713-715. https://doi.org/10.1016/s1076-6332(03)80095-8
52. Tsang KW, Ho PL, Ooi GC, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. *N Engl J Med*. 2003;348(20):1977-1985.
53. Lee N, Hui D, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med*. 2003;348(20):1986-1994.
54. Booth CM. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. *JAMA*. 2003;289(21):2801-2809.
55. Peiris J, Chu C, Cheng V, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. *Lancet*. 2003;361(9371):1767-1772.
56. Zhao D, Ma D, Wang W, et al. Early X-ray and CT appearances of severe acute respiratory syndrome: an analysis of 28 cases. *Chin Med J*. 2003;116(6):823-826.
57. Al-Tawfiq JA, Hinedi K, Ghandour J, et al. Middle East respiratory syndrome coronavirus: a case-control study of hospitalized patients. *Clin Infect Dis*. 2014;59(2):160-165.
58. Arabi YM, Arifi AA, Balkhy HH, et al. Clinical course and outcomes of critically ill patients with Middle East respiratory syndrome coronavirus infection. *Ann Intern Med*. 2014;160(6):389-397.
59. Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *Lancet Infect Dis*. 2013;13(9):752-761.
60. Saad M, Omrani AS, Baig K, et al. Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: a single-center experience in Saudi Arabia. *Int J Infect Dis*. 2014;29:301-306.
61. Das KM, Lee EY, Jawder SEA, et al. Acute Middle East respiratory syndrome coronavirus: temporal lung changes observed on the chest radiographs of 55 patients. *Am J Roentgenol*. 2015;205(3):W267-S274.
62. Assiri A, McGeer A, Perl TM, et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. *N Engl J Med*. 2013;369(5):407-416.
63. Cha MJ, Chung MJ, Kim K, Lee KS, Kim TJ, Kim TS. Clinical implication of radiographic scores in acute Middle East respiratory syndrome coronavirus pneumonia: report from a single tertiary-referral center of South Korea. *Eur J Radiol*. 2018;107:196-202. https://doi.org/10.1016/j.ejrad.2018.09.008
64. Das KM, Lee EY, Enani MA, et al. CT correlation with outcomes in 15 patients with acute Middle East respiratory syndrome coronavirus. *Am J Roentgenol*. 2015;204(4):736-742. https://doi.org/10.2214/ajr.14.13671
65. Noorwali AA, Turkistani AM, Asiri SI, et al. Descriptive epidemiology and characteristics of confirmed cases of Middle East respiratory syndrome coronavirus infection in the Makkah Region of Saudi Arabia, March to June 2014. *Ann Saudi Med*. 2015;35(3):203-209. https://doi.org/10.5144/0256-4947.2015.203
66. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513. https://doi.org/10.1016/s0140-6736(20)30211-7
67. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA*. 2020.
68. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of 2019 novel coronavirus infection in China. *medRxiv*. 2020. https://doi.org/10.1101/2020.02.06.20020974
69. Wong HYF, Lam HYS, Fong AH-T, et al. Frequency and distribution of chest radiographic findings in COVID-19 positive patients. *Radiology*. 2020:201160. https://doi.org/10.1148/radiol.2020201160
70. Schiaffino S, Tritella S, Cozzi A, et al. Diagnostic performance of chest X-Ray for COVID-19 pneumonia during the SARS-CoV-2 pandemic in Lombardy, Italy. *J Thoracic Imaging*. 2020:1. https://doi.org/10.1097/rti.0000000000000533
71. Murphy K, Smits H, Knoops AJG, et al. COVID-19 on the chest radiograph: a multi-reader evaluation of an AI system. *Radiology*. 2020:201874. https://doi.org/10.1148/radiol.2020201874
72. Assiri A, McGeer A, Perl TM, et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. *N Engl J Med*. 2013;369(5):407-416. https://doi.org/10.1056/NEJMoa1306742
73. Hui JYH, Hon TYW, Yang MKW, et al. High-resolution computed tomography is useful for early diagnosis of severe acute respiratory syndrome-associated coronavirus pneumonia in patients with normal chest radiographs. *J Comput Assist Tomogr*. 2004;28(1):1-9. https://doi.org/10.1097/00004728-200401000-00001
74. Ajlan AM, Ahyad RA, Jamjoom LG, Alharthy A, Madani TA. Middle East respiratory syndrome coronavirus (MERS-CoV) infection: chest CT findings. *Am J Roentgenol*. 2014;203(4):782-787. https://doi.org/10.2214/ajr.14.13021
75. 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. https://doi.org/10.1007/s00259-020-04735-9
76. 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.
77. Pan Y, Guan H, Zhou S, et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. *Eur Radiol*. 2020;30:3306-3309. https://doi.org/10.1007/s00330-020-06731-x
78. Song F, Shi N, Shan F, et al. Emerging coronavirus 2019-nCoV pneumonia. *Radiology*. 2020:200274. https://doi.org/10.1148/radiol.2020200274
79. Wu J, Liu J, Zhao X, et al. Clinical characteristics of imported cases of COVID-19 in Jiangsu Province: a Multicenter Descriptive Study. *Clin Infect Dis*. 2020. https://doi.org/10.1093/cid/ciaa199
80. Yang W, Cao Q, Qin L, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. *J Infect*. 2020.
81. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506.
82. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513.
83. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020.
84. Xiong Y, Sun D, Liu Y, et al. Clinical and high-resolution CT features of the COVID-19 infection: comparison of the initial and follow-up changes. *Invest Radiol*. 2020;55:332-339. https://doi.org/10.1097/rli.0000000000000674
85. Zhou S, Wang Y, Zhu T, Xia L. CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. *Am J Roentgenol*. 2020:1-8. https://doi.org/10.2214/ajr.20.22975
86. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: different points from

adults. *Pediatr Pulmonol*. 2020;55:1169-1174. https://doi.org/10.1002/ppul.24718
87. Li Y, Xia L. Coronavirus disease 2019 (COVID-19): role of chest CT in diagnosis and management. *Am J Roentgenol*. 2020;214:1-7. https://doi.org/10.2214/ajr.20.22954
88. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: a multicenter study. *Am J Roentgenol*. 2020:1-6. https://doi.org/10.2214/ajr.20.22976
89. Chung M, Bernheim A, Mei X, et al. CT imaging features of 2019 novel coronavirus (2019-nCoV). *Radiology*. 2020:200230.
90. Wang K, Kang S, Tian R, Zhang X, Zhang X, Wang Y. Imaging manifestations and diagnostic value of chest CT of coronavirus disease 2019 (COVID-19) in the Xiaogan area. *Clin Radiol*. 2020;75(5):341-347. https://doi.org/10.1016/j.crad.2020.03.004
91. Miao C, Jin M, Miao L, et al. Early chest computed tomography to diagnose COVID-19 from suspected patients: A multicenter retrospective study. *Am J Emerg Med*. 2020. https://doi.org/10.1016/j.ajem.2020.04.051
92. Collins J, Stern EJ. Ground-glass opacity at CT: the ABCs. *Am J Roentgenol*. 1997;169(2):355-367.
93. Nishimura K, Itoh H. High-resolution computed tomographic features of bronchiolitis obliterans organizing pneumonia. *Chest*. 1992;102(1):26-31.
94. Epler GR, Colby TV, McLoud TC, Carrington CB, Gaensler EA. Bronchiolitis obliterans organizing pneumonia. *N Engl J Med*. 1985;312(3):152-158.
95. Wong G, Hui D. *Severe Acute Respiratory Syndrome (SARS): Epidemiology, Diagnosis and Management*. BMJ Publishing Group Ltd; 2003.
96. Yu Q, Wang Y, Huang S, et al. Multicenter cohort study demonstrates more consolidation in upper lungs on initial CT increases the risk of adverse clinical outcome in COVID-19 patients. *Theranostics*. 2020;10(12):5641-5648. https://doi.org/10.7150/thno.46465
97. Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill*. 2020;25(3).
98. Sivakorn C, Luvira V, Muangnoicharoen S, et al. Case report: walking pneumonia in novel coronavirus disease (COVID-19): mild symptoms with marked abnormalities on chest imaging. *Am J Trop Med Hyg*. 2020;102(5):940-942. https://doi.org/10.4269/ajtmh.20-0203
99. Bai HX, Wang R, Xiong Z, et al. AI augmentation of radiologist performance in distinguishing COVID-19 from pneumonia of other etiology on chest CT. *Radiology*. 2020:201491. https://doi.org/10.1148/radiol.2020201491

How to cite this article: Zheng Z, Yao Z, Wu K, Zheng J. The diagnosis of SARS-CoV2 pneumonia: A review of laboratory and radiological testing results. *J Med Virol*. 2020;92:2420–2428. https://doi.org/10.1002/jmv.26081