Use of radiographic features in COVID-19 diagnosis: Challenges and perspectives

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Abstract: The rapid surge and wide spread of the coronavirus disease-2019 (COVID-19) overshadows the entire medical industries worldwide. The stringent medical resources hinder the diagnostic capacity globally, while 84 000 of new cases confirmed within a single day of April 14, 2020. Real-time reverse-transcription polymerase chain reaction (RT-PCR) with is the current first-line diagnosis, but the false-negative rate remains concerned. Radiographic technologies and tools, including computed tomography (CT) and chest X-ray, were applied for initial screening and follow-up, from which the tools provide detail diagnosis with specific pathologic features for staging and treatment arrangement. Although the radiographic imaging is found less sensitive, numerous CT-positive patients were not screened out by RT-PCR initially and later confirmed as COVID-19 positive. Besides, the shortage of sampling kits and the longer turn-over time of PCR examinations in some areas were noticed due to logistic issues and healthcare burden. In this review, we will discuss the challenges and the future perspectives of using radiographic modalities for COVID-19 diagnosis in view of securing human lives amid the crisis.

Keywords: Chest X-ray; Computed tomography; Coronavirus disease-2019; Radiographic technologies

1. INTRODUCTION

Starting from December of 2019, the symptomatic SARS-CoV-2 virus rapidly overshadows the entire world, causing global economic and epidemic crises. By far, the confirmed number of cases has reached 1.8 million, and the death toll has passed 111 thousand lives as of April 14, 2020.[1] This pandemic has revealed various challenges across the globe particularly for the escalating spreading. Real-time reverse-transcription polymerase chain reaction (rRT-PCR) is the current first-line diagnostic measure, accompanied with computed tomography (CT) or chest radiography (CXR) for symptomatic staging and treatment arrangement.[2] Despite the recent release from American College of Radiography does not recommend the use CT or CXR for coronavirus disease-2019 (COVID-19) confirmation,[3] the debate continues as the diagnostic capacity in developing countries may not reach certain level comparing to well-developed countries, suffering from the shortage of examination kits and the long turn-over time in PCR tests.[4] Thus, this review intends to illustrate an overview of the diagnostic value of CT, CXR, and additional modalities against COVID-19.

2. THE USE OF CT IMAGING IN THE DIAGNOSIS OF COVID-19

Within a month after the COVID-19 being declared infectious, the clinical and imaging features of COVID-19 in CT have been characterized correspondingly.[5] Fever, cough, and shortness of breath in the later stage were widely observed pathologically. Diversified flu-like symptoms were documented, including sputum production, fatigue, and sore throat.[5–8] Initially, CXR was deployed for quick screening in response to the overcrowded emergency room. The common pathologic patterns of CXR are pulmonary infiltration and consolidation at the lower regions bilaterally.[9] In terms of CT imaging findings, ground-glass opacity (GGO) is an indicative feature that was initially used for diagnosis in the early stage of symptomatic patients.[5] Consolidation, referring to the signs of pathological fluids or tissues in the pulmonary parenchyma, is documented with varied occurrence rates, considerably relating to the progress of the disease.[10] Bilateral involvement and multifocal pathogenesis were found in over 50% of the patients with COVID-19.[11–13] Other imaging features were also documented while the patterns are lack of correlation with the diagnosis, for example, reticular pattern, crazy paving, and air bronchogram, etc.[14,15]

An article published by Ai et al. in late February claimed an 88% accuracy of CT diagnosis overpowered the 59% using RT-PCR in a cohort of 1014 patients.[16] In early February, a series of reports suggest the use of CT image in addition to the swab-PCR test, due to the possible false-negative rate in PCR tests. Fang et al. reported that 50 out of 51 patients were diagnosed by CT whereas only 36 out of 51 were detected with SARS-CoV-2 from the PCR.[17] Apart from this, Xie et al evaluated a total of 167 patients, of which 5 patients were tested negative by PCR

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but found positive in CT images.[18] A 2- to 7-day delay of PCR detection was found by repeating swab sampling, suggesting a very limited virus titer during the disease early-onset or latent period. Xu et al. showed three cases with initial PCR negative with pathological features in CT screening.[19] Feng et al. later reported a case with consecutive four negative PCR tests but found patchy and GGO in the initial CT imaging.[20] In addition to the false-negative rate of swab testing, the severity of COVID-19 is inconclusive in the absence of imaging results. The discrepancies in the timing of using radiography were noticed among different countries. The University of Washington, who had the most confirmed cases in the USA by mid-March, implied a policy to only screen patients infected with COVID-19 with positive PCR results. The major concerns are the stringent of personal protective equipment and the risk of cross-contamination of staff and other non-COVID-19 patients sharing the imaging facilities.[21] Meanwhile, a response from ASST Fatebenefratelli Sacco in Milan, Italy, decided to screen all symptomatic patients with imaging and discharged patients without pathological findings for quarantine to ease the burden of medical resources.[22] This could be a major challenge against the healthcare system as well as resilience in response to such surge crisis.[23] In spite of the uncertainty from PCR tests, the use of CT scan for screening is still debatable as the turnover time could be costly for repeated sanitizing, and the increased risk of aerosol spreading during the transportation, imaging, and possibly ventilation of patients. A recent retrospective study in Hong Kong evaluated the diagnostic value using CXR. In a total of 64 patients with COVID-19, Wong et al. revealed that the CXR screening only had 69% sensitivity comparing to 91% initial PCR testing; however, 6 (9%) abnormal CXR cases were initially tested negative by PCR.[24] The conundrum at the current situation is that all diagnostic tools have their blind spots and the triage, organization, logistic, and the capacity of healthcare system making the establishment of guidelines varied from regions to regions. Table 1 collected numerous studies to allow an overview among diversified results in CT diagnosis, while most of the study did not specify the false-negative rate of initial RT-PCR tests. Four out of the 20 included studies showed a 100% or better diagnostic outcomes using chest CT than RT-PCR, and the GGO is dominant among other radiographic features. Although most of the CXR were unable to be conclusive for the disease onset, plenty of the studies implied the usefulness in follow-up cases rather than the excessive radiation dose of CT scans. Only one study by Chen et al. published in early February when the diagnostic guidelines had not been issued by authorities, claiming the 100% accuracy using CXR.[25] The scenario could be the overload of the healthcare system in Hubei Province during the sudden escalating of confirmed cases. Patient admission was limited to a severe or advanced stage that certain symptoms had worsened. Other than that, the use of CXR can barely reach 50% in most presented studies. Given the fluctuating sensitivity and specificity of RT-PCR across studies, the general findings still support that RT-PCR is more consistent in COVID-19 diagnosis. CT imaging is not recommended for assessing patients with mild or no symptoms when admission in various statements, including Fleischner Society.[26,27] The radiographic imaging may be beneficial in moderate to severe case-patients; moreover, the imaging can be move to front line when the medical resources are limited.

3. PERSPECTIVES OF THE USE OF CT IMAGING IN PATIENTS WITH COVID-19

For most patients confirmed with COVID-19, the battle continues to an average period of 3–4 weeks until discharged.[28] Since the RT-PCR only answers the true-or-false question confirming the diagnosis of COVID-19, question, the progress of disease mainly relies on the imaging modalities. CT, of its advantages, provides full coverage of region-of-interests and detailed

Table 1

Summary of COVID-19 diagnosis using RT-PCR, CT, and CXR.

	Subject recruitment		RT-PCR			Chest CT					Chest X-ray	
Study	Cases	Age	Initial PCR	Positive	Negative	GGO	Consolidation	Bilateral	FP rate	FN rate	Abnormal	Bilateral
Ai et al.[16]	1014	51 ± 15	601 (59%)	601	413	409 (40.3%)[a]	447 (44.1%)	…	…	…	…	…
Bernheim et al.[11]	121	45 ± 15.6	…	121	0	91 (77.7%)	52 (43%)	73 (60%)	…	…	…	…
Caruso et al.[35]	158	57 ± 17	…	62	96	58 (96.8%)	42 (67.7%)	53 (91%)	26.58%	1.27%	…	…
Chen et al.[25]	99	55.5 ± 13.1	…	99	0	…	…	…	…	…	99 (100%)	74 (75%)
Chung et al.[36]	21	51 ± 14	…	21	0	18 (85.7%)	6 (28.6%)	16 (86%)	…	…	…	…
Fang et al.[17]	51	45 (39–55)	36 (70.6%)	51	0	50 (98%)	…	…	…	…	…	…
Guan et al.[37]	1099	47 (35–58)	…	1099	0	550/975 (56.4%)	…	505/975 (51.8%)	…	…	162/274 (59.1%)	100/274 (36.5%)
Huang et al.[5]	41	49 (41–58)	…	41	0	41 (100%)	…	40 (98%)	…	…	…	…
Kim et al.[38]	28	42.6 ± 13.4	…	28	0	16/18 (88.9%)	…	8(44.4%)	…	11.11%	15(53.6%)	6(21.4%)
Ng et al.[39]	21	56 (37–65)	…	21	0	18 (86%)	13 (62%)	…	…	9.52%	3/5 (60%)	2/5 (40%)
Pan et al.[10]	63	44.9 ± 15.2	…	63	0	54 (85.7%)	12 (19%)		…	…	…	…
Wang et al.[40]	138	56 (42–68)	…	138	0	138 (100%)[b]	…	…	…	…	…	…
Wong et al.[24]	64	56 ± 19	58 (91%)	64	0	25/28 (89.3%)	…	…	…	…	21 (33%)	32 (50%)
Wu et al.[41]	80	44 ± 11	…	80	0	73 (91.3%)	50 (62.5%)	…	…	…	…	…
Wu et al.[42]	23	29 (21–37)[c]	…	23	0	20 (87%)	…	…	…	…	…	…
Xie et al.[18]	167	Not specified	162 (97.01%)	162	5	160 (97%)	…	…	4.19%	…	…	…
Xu et al.[7]	90	50 (18–86)	…	90	0	65 (72.2%)	12 (13.3%)	53(59%)	…	…	…	…
Yuan et al.[43]	27	60 (47–69)	…	27	0	18 (66.7%)	5 (18.5%)	23 (85.2%)	…	…	…	…
Zhao et al.[44]	118	44.06 ± 13.62	…	118	0	101 (85.6%)	64 (54.2%)	94 (79.7%)	…	6.80%	…	…
Zhu et al.[45]	72	55.6 ± 12.8	…	72	0	59 (81.9%)	16 (22.2%)	…	…	13 (18%)	…	…

CT = computed tomography; CXR = chest X-ray; RT-PCR = reverse transcription polymerase chain reaction; GGO = Ground-glass opacity; FP = false positive; FN = false negative.

[a]The overall CT abnormalities were found in a total of 888 (88%) among all cases.

[b]The reference article did not specify the abnormal feature.

[c]The inclusive cohort of this study was pregnant women.

information;[29] however, the overwhelming radiation dose as well as the sanitizing procedures discourage its application. CXR becomes more reasonable when portable X-ray tubes are equipped. The machine can be exclusively used in COVID-19 ward, and the fewer patient transportation further secures the disease control. The reliability of CXR was reported by Chen et al. where they recruited hospitalized patients using CXR.[25] In addition to follow-up, the CT image may be concluded by quantitative CT score for prognostic use.[30] To the extent of artificial intelligence, elevating studies have been initiated to conduct machine learning and fast screening on a radiomics basis.[31–33] On top of it, a reputational computer science campaign, Hackathon, recently announce their highlighted projects regarding the COVID-19 research. MedCheX is honored by the competition with an automatic, high-throughput, and computational screening over CXR for COVID-19 diagnosis.[34] Yet this pandemic circumstance continues, the development of machine learning and artificial intelligence-mediated quick screening may ameliorate the contribution of radiographic imaging in the combat against COVID-19.

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