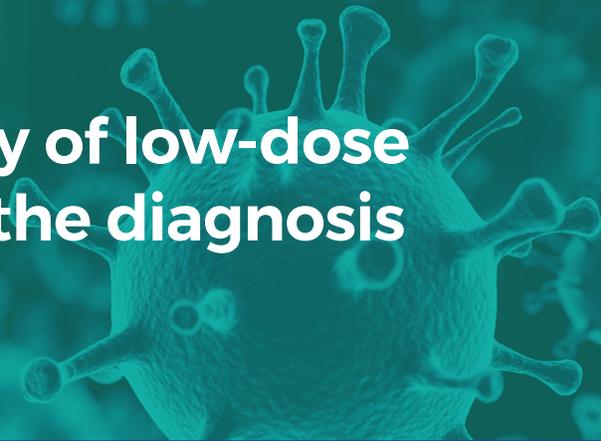


Accuracy and reproducibility of low-dose submillisievert chest CT for the diagnosis of COVID-19



Accuracy and reproducibility of low-dose submillisievert chest CT for the diagnosis of COVID-19

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Abstract

Purpose

To demonstrate the accuracy and reproducibility of low-dose submillisievert chest CT for the diagnosis of COVID-19 infection in emergency room (ER) patients.

Materials and Methods

This was a HIPAA-compliant, institutional review board-approved retrospective study. From March 14th to March 24th 2020, 192 ER patients with symptoms suggestive of COVID-19 infection were studied with low-dose chest CT and real time polymerase chain reaction (RT-PCR). Image analysis included likelihood of COVID-19 infection and semi-quantitative extent of lung involvement. CT images were analyzed by 2 radiologists blinded to RT-PCR results. Reproducibility was assessed with McNemar test and intra-class correlation coefficient (ICC). Time between CT acquisition and report was measured.

Results

When compared to RT-PCR, low-dose submillisievert chest CT demonstrated excellent sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for diagnosis of COVID-19 (86.7%, 93.6%, 91.1%, 90.3%, and 90.2%, respectively), in particular in patients with clinical symptoms for >48h (95.6%, 93.2%, 91.5%, 96.5%, and 94.4%, respectively). In patients with a positive CT, likelihood of disease increased from 43.2% (pre-test probability) to 91.1% or 91.4% (post-test probability), while in patients with a negative CT, likelihood of disease decreased to 9.6% or 3.7% for all patients or those with

clinical symptoms for >48h, respectively. The prevalence of alternative diagnoses based on chest CT in patients without COVID-19 infection was 17.6%. Mean effective radiation dose was 0.56 ± 0.25 mSv (SD). Median time between CT acquisition and report was 25 minutes (IQR: 13-49 minutes). Intra- and interreader reproducibility of CT was excellent (all ICC_{0.95}) without significant bias in Bland-Altman analysis.

Conclusion

Low-dose submillisievert chest CT allows for rapid, accurate and reproducible assessment of COVID-19 infection in ER patients, in particular in patients with symptoms lasting longer than 48 hours. Chest CT has the additional advantage of offering alternative diagnoses in a significant subset of patients.

Summary

Low-dose submillisievert chest CT allows for rapid, accurate and reproducible assessment of COVID-19 infection in ER patients. Chest CT has the additional advantage of offering alternative diagnoses in a significant subset of patients.

Key Points

- When compared to RT-PCR, low-dose submillisievert chest CT demonstrated excellent sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for the diagnosis of COVID-19 in ER patients (86.7%, 93.6%, 91.1%, 90.3%, and 90.2%, respectively), in particular in patients with clinical symptoms for >48h (95.6%, 93.2%, 91.5%, 96.5%, and 94.4%, respectively).
- In patients with a positive CT, likelihood of disease increased from 43.2% (pre-test probability) to 91.1% or 91.4% (post-test probability), while in patients with a negative CT, likelihood of disease decreased to 9.6% or 3.7% for all patients or those with clinical symptoms for >48h, respectively.

- CT results were rapidly available with median time between CT scan acquisition and report of 25 minutes (interquartile range: 13-49 minutes).

Introduction

Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) is a novel enveloped RNA betacoronavirus belonging to the same family of viruses causing severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) ⁽¹⁾. First described in December 2019 in Wuhan, the capital city of Hubei province China, the disease was named Coronavirus Disease 2019 (COVID-19) ⁽²⁾. The virus has spread rapidly across the globe and COVID-19 was declared a pandemic by the World Health Organization (WHO) on the 11th of March 2020 ⁽³⁾. Thus far there are no proven treatments for COVID-19 and current management of the pandemic mainly depends on limiting transmission of the disease by early detection and isolation of patients. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) represents the gold standard for the diagnosis of COVID-19 with very high specificity and can be easily obtained by throat swab sampling. The sensitivity of RT-PCR has been reported to be around 70% in initial reports which is rather low for screening ⁽⁴⁾. One negative RT-PCR test therefore does not exclude COVID-19 and multiple repeat tests may be required to make the final diagnosis, leading to multiple days of uncertainty for both patients and healthcare professionals.

Chest computed tomography (CT) may represent an additional tool for the initial assessment of patients with possible COVID-19 infection. COVID-19 pneumonia causes bilateral, peripheral and basal predominant areas of ground-glass opacities (GGO), typically evolving to consolidation at later stages of the disease ^(5,6). A previous study has demonstrated excellent sensitivity (97%) but poor specificity (25%) of chest CT for the diagnosis of COVID-19 ⁽⁷⁾. These results suggest a complementary approach combining the high sensitivity of chest CT with the high specificity of RT-PCR may be effective for early COVID-19 diagnosis. Given the very common and rapidly increasing clinical indication of chest CT for COVID-19 diagnosis, accurate and reproducible assessment with a low radiation dose (submillisievert) protocol may result in major radiation dose reductions on a population level ⁽⁸⁾. The purpose of this study was to investigate whether submillisievert chest CT could be used to rapidly, accurately and reproducibly stratify patients with possible COVID-19 infection.

Materials and Methods

This retrospective study was compliant with the Health Insurance Portability and Accountability Act and was approved by our institutional review board (Imelda Hospital, Bonheiden, Belgium). Informed consent was waived. From March 14th to March 24th 2020, 192 consecutive patients with possible COVID-19 infection and both RT-PCR and low-dose chest CT at presentation were included. The RT-PCR results were obtained from the patient electronic medical record. Patients who showed negative results on RT-PCR underwent repeat RT-PCR examination the following day. If this second RT-PCR was positive, the patient was considered to be COVID-19 positive. Two PCR methods were used to detect SARS-CoV-2 in nasopharyngeal swabs (eSwab, Copan Diagnostics, Brescia, Italy), both using the E-gene as target. Primers and probe sequences for the E-gene were provided by the Belgian National Reference Center (University Hospital Leuven, Leuven, Belgium). The first platform, the ARIES system (Luminex, Austin, USA), provides an open channel for lab developed tests. It is an all-in-one system with extraction, purification, amplification and detection in one cassette. Luminex SYNCT software is used to analyze and interpret PCR results. It can run up to twelve samples simultaneously with a hands-on-time of 10 min and a turn-around-time of 1h45. The second platform, the Rotorgene Q (Qiagen, Hilden, Germany), is a real-time PCR instrument. Extraction is performed on NucliSENS EasyMAG (BioMérieux, Marcy l'Étoile, France). RotorGene Q Series software is used to interpret the data. It is a higher volume, batch test, with a capacity of up to 72 samples simultaneously, but time from sample to results is at least 2h45 (due to a longer hands-on time, and separate extraction process). The sensitivity of the SARS-CoV-2 test on Aries was analyzed by testing a dilution series of an inactivated culture of SARS-CoV-2 and was similar to the assay of the Belgian National Reference Center. The sensitivity on Rotorgene Q was validated in relation to Aries analyzing samples on both platforms. No cross reactivity for other human Coronaviruses, Influenza or Respiratory Syncytial Virus (RSV) has been shown.

CT scan protocol

All patients underwent low-dose chest CT by using a Somatom Definition AS 64-slice 0.6 mm detector scanner (Siemens Healthineers, Forchheim, Germany). We used the vendor-supplied software (Care Dose 4D, Siemens Healthineers) to calculate size-specific radiation dose estimates for a low-dose chest CT protocol adapted from the protocol used for lung cancer screening ⁽⁹⁾. Reference

values in a so-called average patient were set to 100 kVp and 20 mAs with a pitch of 1.2 and 0.5 second gantry rotation time. A relatively high pitch was used to limit motion artifacts in dyspneic COVID-19 patients. Effective radiation dose was calculated by multiplying the dose-length product (DLP) by 0.014 mSv/mGy · cm as the constant k-value for thoracic imaging⁽¹⁰⁾. Images were reconstructed at 1 mm slice thickness and 0.7 mm increment with a standard lung-tissue kernel (l50f medium sharp) and at 3 mm slice thickness and 3 mm increment with a standard soft tissue kernel (l31f medium smooth) using sinogram-affirmed iterative reconstruction (SAFIRE) strength 3. All reconstructions were performed with a FOV of 450 mm and a matrix size of 512 × 512 pixels.

CT image analysis

All chest CT images were scored as suggestive for or inconsistent with COVID-19 infection based on the presence of findings as presented by Ng et al. and Shi et al.^(11,12). In summary, CT findings suggestive of COVID-19 infection were multiple GGOs, bilateral/multifocal involvement, peripheral distribution and, at a later stage, crazy paving, consolidation, and reversed halo sign. CT findings inconsistent with COVID-19 infection were tree-in-bud opacities, centrilobular/peribronchovascular distribution, cavitation, and pleural effusion. A semi-quantitative scoring system was used to estimate the extent of pulmonary involvement as reported previously^(5,13). Each lobe was scored from 0 to 5 with a total score ranging from 0 to 25; score 0, 0% involvement; score 1, <5% involvement; score 2, 5-25% involvement; score 3, 26-50% involvement; score 4, 51-75% involvement, score 5, 76-100% involvement. Two cardiothoracic radiologists (C.G. and R.S. with 8 and 7 years of cardiothoracic imaging experience, respectively) scored the CT scans by consensus and were blinded to the RT-PCR results. One reader (R.S.) reread a random sample of 50 scans after 1 week to assess intrareader reproducibility. These cases were reread by the other reader (C.G.) to assess inter-reader reproducibility.

Statistical analysis

All statistical analysis was performed by using R v.3.5.3. (Foundation for statistical computing, Vienna, Austria). Using RT-PCR as a gold standard, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, positive likelihood ratio (LR+), and negative likelihood ratio (LR-) of low-dose chest CT were calculated with 95% confidence interval (CI) by using

the reportROC and UncertainInterval packages. Fagan's nomogram (an integration of Bayes' theorem) was used to quantify the post-test probability of COVID-19 infection given the CT results and the pre-test probability⁽¹⁴⁾. Data were tested for normal distribution with the Shapiro-Wilk test. Summary statistics for all continuous variables are reported as means ± standard deviations (SD) or as medians with interquartile ranges (IQR), as appropriate. The Student t test for independent samples and the Mann-Whitney U test were used to compare continuous variables between groups. P<0.05 was considered to indicate a statistically significant difference. Intrareader and interreader agreement were assessed by using McNemar test, intraclass correlation coefficients (ICCs) and Bland-Altman analysis with 95% limits of agreement (LOAs)⁽¹⁵⁾. ICCs of >0.75 and of 0.4-0.75 indicate strong and average agreement, respectively. A difference between ICCs was considered to be statistically significant when there was no overlap between their respective 95% CI limits. No missing data was present. No patients were excluded from analysis after initial inclusion. No adverse event occurred from chest CT exams.

Results

The demographics of the patients and dose parameters of the low-dose CT scan are summarized in Table 1. There were 83 (43.2%) patients positive for COVID-19, 109 (56.8%) were negative. The mean age for all patients was 62 years ± 18 years (SD), reflecting the wide range of

Table 1: Patient characteristics and radiation dose parameters

Physical examination and demographics	All (n=192)	COVID-19 + (n=83)	COVID-19 - (n=109)	P-value
Age (y)	61.8±18.2	67.4±16.8	57.5±18.1	<0.001
male sex*	87 (45.3)	42 (50.6)	45 (41.2)	0.25
BMI (kg/m ²)	28.9±6.1	29.0±4.2	28.8±7.7	0.95
Time since symptom onset (d)†	7 (3-9)	7 (3-9)	7 (3-9)	0.99
Clinical symptoms				
Fever*	107 (55.7)	57 (68.7)	50 (45.9)	0.003
Cough*	134 (69.8)	61 (73.5)	73 (67.0)	0.41
Dyspnea*	89 (46.4)	44 (53.0)	45 (41.3)	0.14
Chest pain*	31 (16.1)	9 (10.8)	23 (21.1)	0.09
CT scan parameters				
Kilovoltage peak (kVp)				
100 kVp*	100 (52.1)	62 (56.9)	38 (45.8)	
120 kVp*	92 (47.9)	47 (43.1)	45 (54.2)	0.17
Tube current-time product (mAs)	21.5±10.7	20.9±5.6	22.0±13.3	0.45
CTDI _{vol} (mGy)	1.27±0.59	1.33±0.55	1.22±0.61	0.21
Dose-length product (DLP) (mGy.cm)	39.9±17.8	41.4±17.7	38.7±17.9	0.31
Effective dose (mSv)	0.56±0.25	0.58±0.25	0.54±0.25	0.31
Time between CT scan and result (min)†	25 (13-49)	22 (13-37)	26 (13-51)	0.40

Note: Unless otherwise specified, data are means ± SD.

* Data are numbers of patients, with percentages in parentheses.

† Data are medians, with interquartile ranges in parentheses.

Table 1. Patient characteristics and radiation dose parameters

ages susceptible to COVID-19 infection. COVID-19 positive patients were significantly older than COVID-19 negative patients (67.4±16.8 years vs 57.5±18.1 years, P<0.001) and more likely to present with a fever (68.7% vs 45.9%, P=0.003). Mean DLP for all patients was 39.9±17.8 mGy.cm, resulting in an effective radiation dose of 0.56±0.25 mSv. Median time between CT scan acquisition and report was 25 minutes (IQR: 13-49 minutes).

Accuracy and reproducibility of chest CT for COVID-19 diagnosis

When compared to RT-PCR, low-dose submillisievert chest CT demonstrated excellent sensitivity, specificity, PPV, NPV, and accuracy for the diagnosis of COVID-19 in ER patients (86.7%, 93.6%, 91.1%, 90.3%, and 90.2%, respectively) in particular in patients with clinical symptoms for more than 48 hours (95.6%, 93.2%, 91.5%, 96.5%, and 94.4%, respectively) (Table 2) (Figure 1). LR+ and LR- were 13.51 (95% CI 6.57-27.79) and 0.14 (95% CI 0.08-0.25) for all patients and 14.02 (95% CI 6.47-30.40) and 0.05 (95% CI 0.02-0.14) for patients with clinical symptoms for more than 48 hours, respectively. In patients with a positive CT, likelihood of disease increased from 43.2% (pre-test probability) to 91.1% or 91.4% (post-test probability) for all patients or those with clinical symptoms for more than 48 hours. In patients with a negative CT, likelihood of disease decreased from 43.2% (pre-test probability) to 9.6% or 3.7% (post-test probability) for all patients or those with clinical symptoms for more than 48 hours (Figure 2).

Intra- and interreader reproducibility for CT scores of lung involvement were excellent (ICC: 0.968 and 0.954; 95% CI: 0.942-0.983 and 0.918-0.974, respectively) without significant bias in Bland-Altman analysis (0.2 and -0.5, 95% LOAs: -2.0, 2.5 and -3.0, 1.9, respectively).

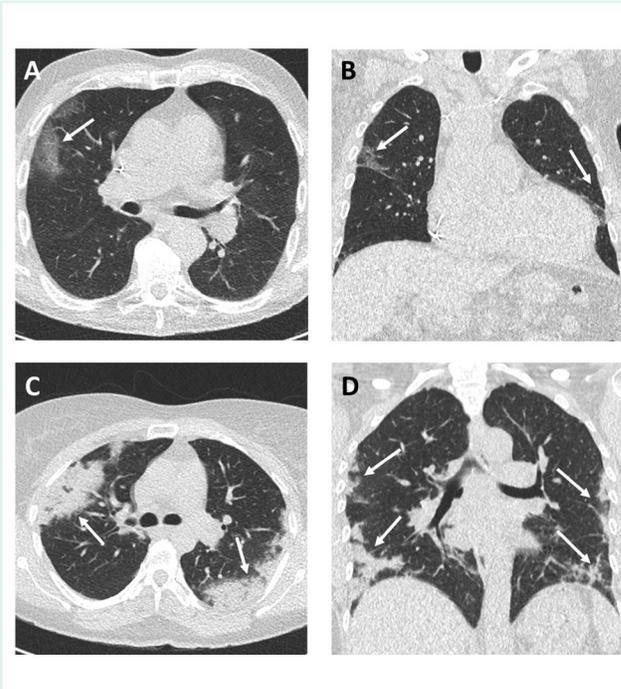


Figure 1. Example CT images in two patients with COVID-19. Axial (A) and coronal (B) CT images in an 85-year-old woman presenting with dyspnea and fever for 3 days. CT shows typical early COVID-19 findings with bilateral subpleural areas of ground-glass opacities (arrows). Total CT involvement score was 7/25. Effective radiation dose was 0.52 mSv. Axial (C) and coronal (D) CT images in a 41-year-old woman presenting with cough and fever for 14 days. CT shows typical late COVID-19 findings with multifocal bilateral subpleural areas of consolidation (arrows). Total CT involvement score was 15/25. Effective radiation dose was 0.53 mSv. Window center, -600 HU; window width 1600 HU; slice thickness, 1 mm; and increment, 0.7 mm for all images.

Table 2: Accuracy of low-dose chest CT for diagnosis of COVID-19 infection

	Results (n)				Test performance (% with 95% CI)				
	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
All patients (n=192)	72	102	7	11	86.7 (79.5-94.0)	93.6 (89.0-98.2)	91.1 (84.9-97.4)	90.3 (84.8-95.7)	90.6 (90.5-90.7)
Patients with clinical symptoms for >48h (n=156)	65	82	6	3	95.6 (90.7-99.9)	93.2 (87.9-98.4)	91.5 (85.1-98.0)	96.5 (92.5-99.9)	94.2 (94.2-94.3)

TP: true positive, TN: true negative, FP: false positive, FN: false negative, PPV: positive predictive value, NPV: negative predictive value.

Table 2. Accuracy of low-dose chest CT for diagnosis of COVID-19 infection

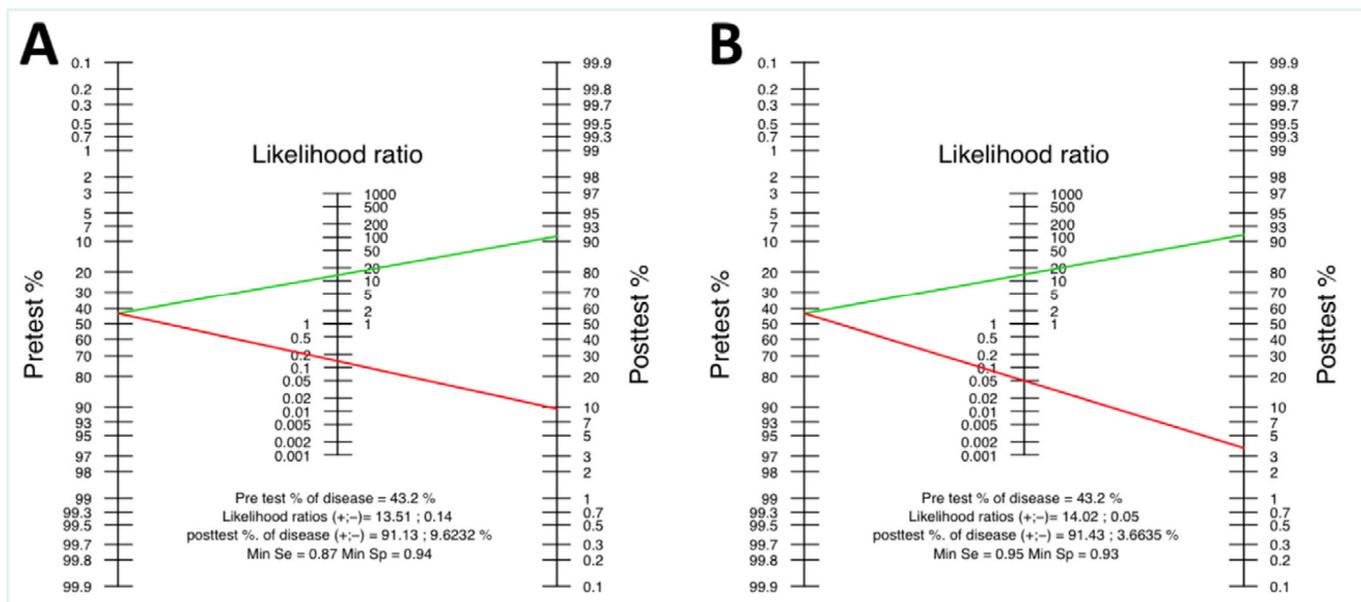


Figure 2. Fagan's nomogram for all patients (A) and patients with clinical symptoms for more than 48 hours (B) illustrating pre-test and post-test probabilities based on the LR+ and LR- of chest CT in patients with possible COVID-19 infection.

Additional information from chest CT in patients with possible COVID-19 infection

In patients with CT findings suggestive of COVID-19 infection and positive RT-PCR (true positives, n=72), CT offered additional information by suggesting the presence of associated bacterial pneumonia in 7 subjects (9.7%). In patients with findings inconsistent with COVID-19 infection and negative RT-PCR (true negatives, n=102), CT offered additional information by suggesting the presence of an alternative diagnosis in 18 subjects (17.6%) (Table 3) (Figure 3). Bacterial pneumonia (n=10) was confirmed by a combination of sputum cultures, hemocultures, and laboratory tests including RT-PCR. Lung cancer (n=3) was confirmed by biopsy to be adenocarcinoma of the lung in 2 patients. No biopsy was performed in the last patient due to comorbidities and patient refusal. Acute EBV infection (n=2) was confirmed by serologic studies. Pericarditis (n=1) was confirmed by the presence of a pericardial effusion in combination with typical ECG changes⁽¹⁶⁾. Human Metapneumovirus (n=1) was confirmed by RT-PCR. CT suggested diagnosis of sarcoidosis (n=1) was not yet confirmed at the time of submission as the patient refused biopsy. In patients with CT findings suggestive of COVID-19 infection but negative RT-PCR (false positives, n=7), another viral cause of pneumonia was identified in 2 subjects by RT-PCR (Human Metapneumovirus).

Table 3: Role of chest CT in making additional or alternative diagnoses in true positive and true negative patients, respectively

TP (n=72)	TN (n=102)
Bacterial pneumonia (n=7)	Bacterial pneumonia (n=10)
	Lung cancer (n=3)
	Epstein-Barr Virus (EBV) (n=2)
	Pericarditis (n=1)
	Human Metapneumovirus (n=1)
	Sarcoidosis (n=1)

Table 3. Role of chest CT in making additional or alternative diagnoses in true positive and true negative patients, respectively

Discussion

Low-dose chest CT may play a complementary role to RT-PCR for the early triage of patients with possible COVID-19 infection. When compared to RT-PCR, chest CT achieved high sensitivity, specificity, PPV, NPV, and accuracy (86.7%, 93.6%, 91.1%, 90.3%, and 90.2%, respectively), with further improvement when only patients with symptoms lasting longer than 48 hours were included (95.6%, 93.2%, 91.5%, 96.5%, and 94.4%, respectively). Importantly, these results were obtained by using a low-dose CT protocol with submillisievert effective radiation dose (0.56±0.25 mSv) and rapid availability of results (median: 25 min, IQR: 13-49 min).

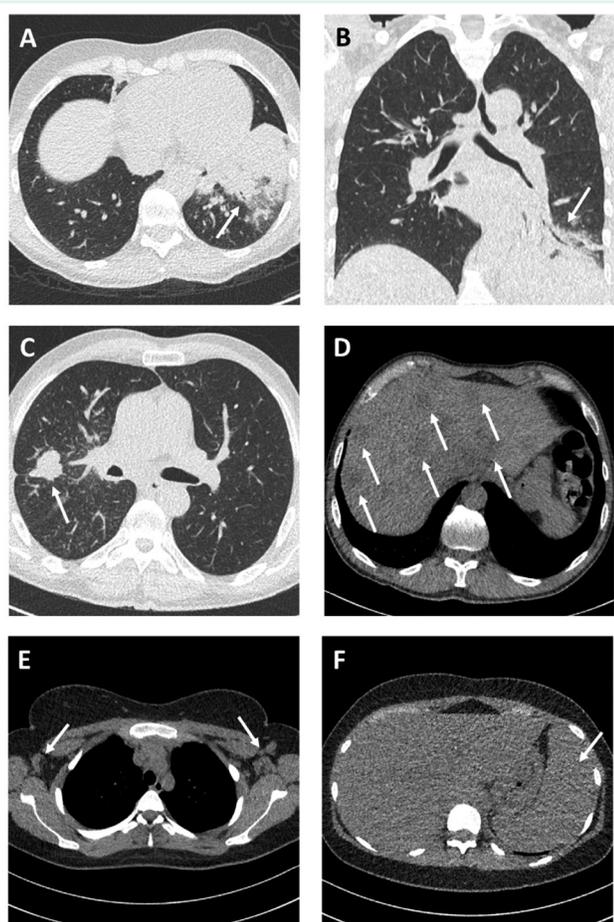


Figure 3. Example alternative diagnoses suggested by chest CT in patients with possible COVID-19 infection. Axial (A) and coronal (B) CT images in a 59-year-old woman presenting with cough and fever for 7 days. CT shows lobar consolidation of the anterior segments of the left lower lobe with surrounding ground-glass opacities compatible with bacterial lobar pneumonia (arrows). Sputum culture confirmed *Streptococcus pneumoniae* pneumonia. Axial (C) and coronal (D) CT images in a 53-year-old male presenting with cough and dyspnea for 3 weeks. CT shows an irregular mass in the right upper lobe with associated lymphangitic carcinomatosis and multiple hypodense liver lesions compatible with lung cancer with liver metastases (arrows). Biopsy confirmed adenocarcinoma of the lung with liver metastases. Axial (E,F) CT images in an 18-year-old female presenting with cough and fever for 7 days. CT shows bilateral axillary lymphadenopathy and splenomegaly compatible with Epstein-Barr virus (EBV) infection which was confirmed by EBV IgM antibody detection (arrows). Window center, -600 HU; window width 1600 HU; slice thickness, 1 mm; and increment, 0.7 mm for images A,B,C. Window center 40 HU; window width 400 HU; slice thickness, 3 mm; and increment, 3 mm for images D,E,F.

When evaluating any diagnostic test, it is important to understand how the test result affects the probability of the disease in question being present⁽⁴⁷⁾. In this regard, likelihood ratios and post-test probabilities are more informative than sensitivity and specificity analysis. At this moment of the COVID-19 pandemic, the pre-test probability of COVID-19 infection in patients presenting at the ER with appropriate clinical symptoms was very high (43.2%). However, within a short time interval (median interval between CT scan and report <30 minutes), chest CT increased this probability to >90% in those patients with CT findings suggestive of COVID-19 infection, while the post-test probability was only 4-10% for those patients with CT findings inconsistent with COVID-19 infection. This rapid and reliable differentiation with CT can play an important role in effective triage of possible COVID-19 patients, in particular during times of ER overflowing in a COVID-19 epicenter with a high pre-test probability.

When compared to the largest study to date comparing chest CT and RT-PCR by Tao et al. (7), our results indicate a significantly higher specificity of CT for the diagnosis of COVID-19. A possible explanation for this discrepancy, already mentioned by the authors in their study limitations, is their use of RT-PCR assays with a low positive rate, likely resulting in an overestimation of CT sensitivity but an underestimation of CT specificity. The use of highly sensitive RT-PCR assays in our study probably explains the higher specificity and overall accuracy in our population. However, it remains important to stress that a negative CT scan does not completely rule out COVID-19 infection and a negative CT should not trick caregivers into a false sense of security in a patient with possible COVID-19 infection. Additionally, although no exact radiation dose levels are available, reference scan settings in this study were 120 kVp and 30-70 mAs versus 100 kVp and 20 mAs in our study. When comparing these reference values, this leads to an estimated radiation dose reduction by a factor of 5. Given the widespread use of chest CT for COVID-19 detection, our results demonstrate the feasibility of using low-dose chest CT to achieve an important reduction in radiation dose on a population level during this pandemic. However, during a public health crisis it is important to note that radiation dose considerations should not be the determining factor in deciding imaging strategies.

Previous studies have suggested CT could be used to track COVID-19 lung involvement over time^(5,6). However, a key remaining issue has been to formally assess the reproducibility of CT measures of lung involvement,

essential for the validity of interpreting changes in lung involvement over time. Our results show excellent agreement rates of trained readers for determining likelihood of COVID-19 infection on low-dose chest CT (all agreement rates were 0.95). These results suggest a potential role for CT for the longitudinal follow-up of COVID-19 patients in research studies, particularly if this can be achieved with submillisievert scan protocols. However, in clinical practice CT scans should only be performed when specific clinical indications emerge and CT may help guide patient management (e.g., unexplained clinical deterioration) as recommended by the American College of Radiologists (ACR)⁽¹⁸⁾.

Of particular interest may be those patients with incongruent findings on RT-PCR and chest CT. Eleven patients had a negative chest CT but a positive RT-PCR test (false negatives). Within this subgroup, eight (72.7%) presented within 48 hours of symptom onset, highlighting the lower sensitivity of chest CT for early disease detection. Seven patients had a positive chest CT but a negative RT-PCR test (false positives). Within this subgroup, two patients (28.6%) tested positive for Human Metapneumovirus at RT-PCR, highlighting that differentiation between different types of viral pneumonia is not always possible with chest CT⁽¹⁹⁾. Finally, chest CT may offer alternative diagnoses explaining the clinical presentation suggestive of COVID-19 infection. The prevalence of alternative diagnoses based on chest CT in patients without COVID-19 infection was 17.6%: bacterial pneumonia (n=10), lung cancer (n=3), Epstein-Barr infection (n=2), pericarditis (n=1), Human Metapneumovirus (n=1), and sarcoidosis (n=1).

This study has several limitations. First, we acknowledge the inherent selection bias of this retrospective cohort study. Second, our study cohort only included patients who presented at the ER, so our cohort represents the more severe disease spectrum of COVID-19. Mild or asymptomatic cases with only upper respiratory tract involvement likely have more false negative findings on chest CT. Third, with the development of more sensitive and rapid test kits for COVID-19 with a turnaround of less than one hour, the need for COVID-19 screening with CT will reduce. Rapidly expanding knowledge on this disease and its risk factors may lead to the implementation of diagnostic algorithms allowing for a more selective implementation of chest CT in COVID-19 subjects and a lower number of true negative cases. This will ensure optimal delivery of diagnostic imaging and treatment guidance while minimizing radiation exposure and unnecessary movement of patients within the hospital.

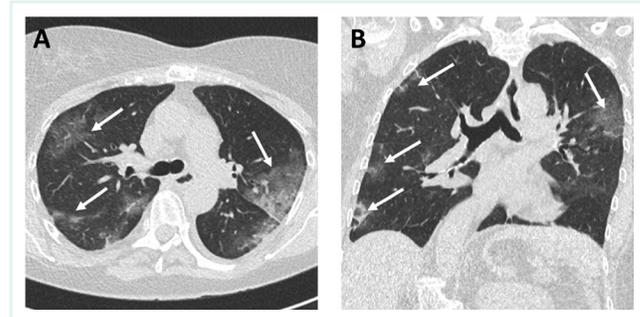


Figure 4. Example images from a 60-year-old female patient with clinical and CT findings suggestive of COVID-19 infection, but repeated negative RT-PCR analysis. Axial (A) and coronal (B) CT images show typical bilateral subpleural areas of ground-glass opacities. Patient was considered to be probably COVID-19 positive and quarantined. Note incidental finding of moderate thoracic dextroscoliosis. Window center, -600 HU; window width 1600 HU; slice thickness, 1 mm; and increment, 0.7 mm for all images.

Fourth, despite the use of new highly sensitive RT-PCR assays, this technique is not perfect. Some 'false positives' with typical CT and clinical findings but negative RT-PCR may still be COVID-19 infected (Figure 4). Further studies are warranted to examine whether these patients may have viral infection limited to the lower respiratory tract. Finally, the use of advanced deep-learning based iterative reconstruction algorithms and state-of-the-art hardware may result in better image quality at similar radiation doses.

In conclusion, low-dose submillisievert chest CT allows for rapid, accurate and reproducible assessment of COVID-19 infection in ER patients, in particular in patients with symptoms lasting longer than 48 hours. Chest CT may have the additional advantage of offering alternative diagnoses in a significant subset of patients.

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REFERENCES:

1. Corman VM, Muth D, Niemeyer D, Drosten C. Hosts and sources of endemic human coronaviruses. *Adv Virus Res.* 2018. p. 163–188. [Crossref](#), [Medline](#), [Google Scholar](#)
2. 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. [Crossref](#), [Medline](#), [Google Scholar](#)
3. World Health Organization. Coronavirus disease (COVID-19) outbreak. URL <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. 2020. [Google Scholar](#)
4. Fang Y, Zhang H, Xie J et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. *Radiology.* 2020;200432. [Link](#), [Google Scholar](#)
5. 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;200370. [Link](#), [Google Scholar](#)
6. Bernheim A, Mei X, Huang M et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. *Radiology.* 2020;200463. [Link](#), [Google Scholar](#)
7. 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. [Link](#), [Google Scholar](#)
8. Bach PB, Mirkin JN, Oliver TK et al. Benefits and harms of CT screening for lung cancer: a systematic review. *JAMA.* 2012;307(22):2418–2429. [Crossref](#), [Medline](#), [Google Scholar](#)
9. de Koning HJ, van der Aalst CM, de Jong PA et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med.* 2020;382(6):503–513. [Crossref](#), [Medline](#), [Google Scholar](#)
10. Valentin J. International Commission on Radiological Protection., 2007. The 2007 recommendations of the International Commission on Radiological Protection. *Ann ICRP.* 103. [Google Scholar](#)
11. Ng M-Y, Lee EYP, Yang J et al. Imaging profile of the COVID-19 infection: radiologic findings and literature review. *Radiol Cardiothorac Imaging.* 2020;2(1):e200034. [Link](#), [Google Scholar](#)
12. 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. [Crossref](#), [Google Scholar](#)
13. 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.* 2020;2(2):e200110. [Link](#), [Google Scholar](#)
14. Straus S, Glasziou P, Richardson WS, Haynes RB. Evidence-based medicine: How to practice and teach it, 4-th edition. Churchill Livingstone Elsevier, Edinbg. 2011. [Google Scholar](#)
15. Bland JM, Altman D. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet.* 1986;327(8476):307–310. [Crossref](#), [Google Scholar](#)
16. Lange RA, Hillis LD. Acute pericarditis. *N Engl J Med.* 2004;351(21):2195–2202. [Crossref](#), [Medline](#), [Google Scholar](#)
17. Deeks JJ, Altman DG. Diagnostic tests 4: likelihood ratios. *BMJ.* 2004;329(7458):168–169. [Crossref](#), [Medline](#), [Google Scholar](#)
18. ACR Recommendations for the use of chest radiography and computed tomography (CT) for suspected COVID-19 infection. Available at: <https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for-Suspected-COVID19-Infection>. Accessed April 7, 2020. [Google Scholar](#)
19. Shahda S, Carlos WG, Kiel PJ, Khan BA, Hage CA. The human metapneumovirus: a case series and review of the literature. *Transpl Infect Dis.* 2011;13(3):324–328. [Crossref](#), [Medline](#), [Google Scholar](#)