Title

Added value of chest CT in suspected COVID-19: an analysis of 239 patients

Authors

Daniël A. Korevaar, MD PhD[1]

Ruud S. Kootte, MD PhD[2]

Loek P. Smits, MD PhD[2]

Joost G. van den Aardweg, MD PhD[1]

Peter I. Bonta, MD PhD[1]

Janke Schinkel, MD PhD[3]

René M. Vigeveno, MD[3]

Inge A.H. van den Berk, MD[4]

Maeke J. Scheerder, MD[4]

Bregtje A. Lemkes, MD PhD[5]

Abraham Goorhuis, MD PhD[5]

Ludo F.M. Beenen, MD[4]

Jouke T. Annema, MD PhD[1]

On behalf of the Amsterdam UMC location AMC COVID-19 group

[1]Department of Respiratory Medicine

[2]Department of Internal Medicine

[3]Department of Medical Microbiology and Infection Prevention

[4]Department of Radiology

[5]Department of Infectious Diseases

Amsterdam University Medical Centres, University of Amsterdam, the Netherlands

Abstract

Introduction: Clinicians have been struggling with the optimal diagnostic approach of patients with suspected COVID-19. We evaluated the added value of chest CT over RT-PCR alone.

Methods: Consecutive adult patients with suspected COVID-19 presenting to the emergency department (Academic Medical Center, Amsterdam University Medical Centers, the Netherlands) from March 16th to April 16th were retrospectively included if they required hospital admission and underwent chest CT and RT-PCR testing for SARS-CoV-2 infection. The CO-RADS classification was used to assess the radiological probability of COVID-19, where a score of 1-2 was considered as negative, 3 as indeterminate, and 4-5 as positive. CT results were stratified by initial RT-PCR results. For patients with a negative RT-PCR but a positive CT, serology or multidisciplinary discussion after clinical follow-up constituted the final diagnosis.

Results: 258 patients with suspected COVID-19 were admitted, of which 239 were included because they had both CT and RT-PCR testing upon admission. Overall, 112 patients (46.9%) had a positive initial RT-PCR, and 14 (5.9%) had a positive repeat RT-PCR. Of 127 patients with a negative or indeterminate initial RT-PCR, 38 (29.9% [95%CI 21.3-39.3%]) had a positive CT. Of these, 13 had a positive RT-PCR upon repeat testing, and 5 had positive serology. The remaining 20 patients were assessed in a multidisciplinary consensus meeting, and for 13 it was concluded that COVID-19 was 'very likely'. Of 112 patients with a positive initial RT-PCR result, CT was positive in 104 (92.9% [95%CI 89.3-97.5%]).

Conclusion: In a high-prevalence emergency department setting, chest CT showed high probability of COVID-19 (CO-RADS 4-5) in 29.9% of patients with a negative or indeterminate initial RT-PCR result. As the majority of these patients had proven or 'very likely' COVID-19 after follow-up, we believe that CT helps in the identification of patients who should be admitted in isolation.

Research letter

Introduction

Since the outbreak of the COVID-19 (coronavirus disease 2019) pandemic, clinicians have been struggling with the optimal diagnostic approach of suspected patients. RT-PCR (real-time reverse transcriptase-polymerase chain reaction) testing of respiratory samples is generally being considered as the reference standard for establishing SARS-CoV-2 infection.[1] However, RT-PCR results take hours to become available and, although highly specific, sensitivity is moderate.[2, 3] This could result in delayed and suboptimal clinical decision making.

Several reports have suggested a potential role for chest CT (computed tomography) in patients with suspected COVID-19.[4-7] Major advantages of CT are that it provides immediate results and can identify alternative diagnoses for respiratory symptoms. CT may show signs suspicious or typical of COVID-19 in patients with a negative RT-PCR, ensuring that the patient remains isolated. On the other hand, a negative CT in combination with a negative RT-PCR may exclude COVID-19 with a higher level of certainty, in which case patient de-isolation can be considered, and additional diagnostic work-up can be initiated. In this study, we evaluated the added value of chest CT over RT-PCR alone.

Methods

Consecutive patients with suspected COVID-19 who presented to the emergency department of our university hospital (Academic Medical Center, Amsterdam University Medical Centers, the Netherlands) from March 16th to April 16th were retrospectively assessed for inclusion. Patients with suspected COVID-19 were those with (1) fever, (2) cough or dyspnea, or (3) other signs suggestive of COVID-19 (e.g. gastro-intestinal symptoms). Patients were included if they were 18 years or older, required hospital admission, and underwent both chest CT and RT-PCR testing for SARS-CoV-2 infection upon admission. In our hospital, performing both these tests is standard practice for patients with suspected COVID-19 requiring admission. We excluded patients who already had a prior positive RT-PCR result. Data were extracted from patient records by one author (DAK, RSK or LPS). Formal approval from the Medical Ethics Review Committee was not required for this retrospective observational study.

A non-enhanced low-dose chest CT scan was obtained from all patients (Siemens Somatom Force, Siemens Healthineers, Forchheim, Germany). CT images were read as part of standard clinical practice by attending radiologists, with varying degrees of experience. A second read was performed daily by a dedicated acute radiologist. The radiological probability of pulmonary manifestations of COVID-19 was reported based on the 'CO-RADS classification', a standardized reporting system for patients with suspected COVID-19, ranging from 1 (very unlikely) to 5 (very likely).[8, 9] In this study, CO-RADS scores of 1-2 were considered as negative, scores of 4-5 were positive, and a score of 3 was indeterminate. CT readers were not blinded to clinical information,

but RT-PCR results were never available at the time of reading. If CT reports did not contain a CO-RADS score (n=20), images were re-read by a radiologist blinded to the RT-PCR results (LFB).

Nose and throat swabs, and, if possible, sputum samples, were obtained for RT-PCR testing of SARS-CoV-2 infection.[10] When the initial RT-PCR was negative or indeterminate, but clinical suspicion of COVID-19 remained, repeat RT-PCR testing was generally performed. In this study, patients with a positive initial or repeat RT-PCR result within 7 days after admission were considered to have COVID-19, whereas patients who only had negative RT-PCR results and a CO-RADS score of 1-3 were considered not to have COVID-19. For patients who had negative RT-PCR results but a CO-RADS score of 4-5, serological testing for SARS-CoV-2 antibodies was performed if serum was available (Biozek, COVID-19 IgG/IgM rapid test), and the final diagnosis was considered as 'COVID-19 very likely' if this was positive. If no serum was available or serology was negative, all the available clinical information (including additional microbiological tests) was assessed in a multidisciplinary meeting including two pulmonologists (PIB, JTA), an infectiologist (AG), a virologist (JCS) and a radiologist (LFB), to reach consensus about the final diagnosis, classified as 'COVID-19 very likely', 'uncertain, or 'COVID-19 very unlikely'. This meeting was held 7 days after admission of the last patient in the study.

The primary outcome was the proportion of patients with a negative initial RT-PCR result who had a positive chest CT result (i.e. CO-RADS 4-5). The full study protocol is available upon request.

Results

During the study period, 258 patients with suspected COVID-19 were admitted, of which 19 were excluded because they had a prior positive RT-PCR result (n=8), no RT-PCR was performed (n=2), or no chest CT was performed (n=9). The remaining 239 patients underwent both CT and RT-PCR testing upon admission and were included. Median age of patients was 63 years (IQR 51-71), 139 (58.2%) were male, median time since symptom onset was 7 days (IQR 3-10), and 18 (7.5%) were immediately admitted to ICU, whereas 22 (9.2%) were transferred to ICU after initial ward admission. Overall, 112 patients (46.9%) had a positive initial RT-PCR result, and 14 (5.9%) had a positive repeat RT-PCR result within 7 days after admission. Additional microbiological tests included blood culture in 206 patients (n=8 positive), sputum culture in 85 (n=12 positive), PCR for influenza virus and RSV in respiratory samples in 149 (n=2 and n=1 positive, respectively), pneumococcal urinary antigen testing in 92 (n=1 positive), Legionella urinary antigen testing in 127 (n=1), and PCR for atypical respiratory pathogens in 34 (n=0 positive). Chest CT results stratified by RT-PCR results are reported in the **Table**.

Of 127 patients with a negative or indeterminate initial RT-PCR result, 38 (29.9%) had a positive CT result (CO-RADS 4-5). Of these, 13 had a positive RT-PCR result upon repeat testing. Serological testing could be performed in 6 of the other 25 patients, and was positive for SARS-CoV-2 antibodies in 5 of them. The remaining 20 patients were assessed in a multidisciplinary consensus meeting. For 13 of them it was concluded that COVID-19 was 'very likely', for 3 that COVID-19 diagnosis was 'uncertain' (1 with negative serological

testing), and for 4 that COVID-19 was 'very unlikely'; in 3 out of these 4 patients an alternative diagnosis was found: heart failure, bacterial pneumonia, and rhinovirus pneumonia. Overall, of all 143 patients with a final diagnosis of COVID-19 after at least 7 days of follow-up, 18 (12.6%) had a negative initial or repeat RT-PCR result, but had a positive CT result (CO-RADS 4-5).

Of patients with a negative or indeterminate initial RT-PCR result, 65 (51.2%) had a negative CT result (CO-RADS 1-2), and 24 (18.9%) had an indeterminate CT result (CO-RADS 3). In 42 of these 89 patients, RT-PCR was repeated at least one time within the first 7 days after admission, and only 1 became positive. Of 112 patients with a positive initial RT-PCR result, CT was positive (CO-RADS 4-5) in 104 (92.9%), indeterminate (CO-RADS 3) in 5 (4.5%), and negative (CO-RADS 1-2) in 3 (2.7%).

Limitations

The retrospective nature of this study may be considered a limitation, but risk of selection bias is limited as only 4.4% of patients admitted with suspected COVID-19 were excluded because CT or RT-PCR testing was not performed. Although CT scans were scored by single readers with varying levels of experience, this reflects daily clinical practice. As there is currently no reliable reference standard for COVID-19, we had to rely on ruling-out other explanations and multidisciplinary consensus in patients with negative RT-PCR results, which may have led to false positive CT results.

Conclusion

In conclusion, in a high-prevalence emergency department setting, we found that chest CT showed high probability of COVID-19 (CO-RADS 4-5) in 29.9% of patients with a negative or indeterminate initial RT-PCR result. As the majority of these patients (81.6%) had a proven or 'very likely' diagnosis of COVID-19 after repeat RT-PCR testing or clinical follow-up, we believe that CT helps in the identification of patients who should be admitted in isolation.

Table

	Initial RT-PCR: Positive	Initial RT-PCR: Negative/non-interpretable	
Chest CT: CO-RADS 1-2 **(COVID-19 unlikely)**	3 2.7% (95%CI 0.0-7.3)	65* 51.2% (95%CI 42.5-60.6)	68
Chest CT: CO-RADS 3 **(COVID-19 indeterminate)**	5 4.5% (95%CI 0.9-9.1)	24** 18.9% (95%CI 10.2-28.3)	29
Chest CT: CO-RADS 4-5 **(COVID-19 likely)**	104 92.9% (95%CI 89.3-97.5)	38*** 29.9% (95%CI 21.3-39.3)	142
	112 (100%)	127 (100%)	239

*there were no 'non-interpretable' results; 22 patients had at least one repeat RT-PCR, of which 1 was positive;

**1 initial RT-PCR result was 'non-interpretable; 20 patients had at least one repeat RT-PCR, of which 0 were positive;

***7 initial RT-PCR results were 'non-interpretable'; 35 patients had at least one repeat RT-PCR, of which 13 were positive.

References

1.   Cheng MP, Papenburg J, Desjardins M, Kanjilal S, Quach C, Libman M, Dittrich S, Yansouni CP. Diagnostic Testing for Severe Acute Respiratory Syndrome-Related Coronavirus-2: A Narrative Review. *Annals of internal medicine* 2020.

2.   Long C, Xu H, Shen Q, Zhang X, Fan B, Wang C, Zeng B, Li Z, Li X, Li H. Diagnosis of the Coronavirus disease (COVID-19): rRT-PCR or CT? *European journal of radiology* 2020: 126: 108961.

3.   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.

4.   Yang S, Shi Y, Lu H, Xu J, Li F, Qian Z, Hua X, Ding X, Song F, Shen J, Lu Y, Shan F, Zhang Z. Clinical and CT features of early-stage patients with COVID-19: a retrospective analysis of imported cases in Shanghai, China. *Eur Respir J* 2020.

5.   Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, Tao Q, Sun Z, Xia L. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology* 2020: 200642.

6.   Rubin GD, Ryerson CJ, Haramati LB, Sverzellati N, Kanne JP, Raoof S, Schluger NW, Volpi A, Yim JJ, Martin IBK, Anderson DJ, Kong C, Altes T, Bush A, Desai SR, Goldin J, Goo JM, Humbert M, Inoue Y, Kauczor HU, Luo F, Mazzone PJ, Prokop M, Remy-Jardin M, Richeldi L, Schaefer-Prokop CM, Tomiyama N, Wells AU, Leung AN. The Role of Chest Imaging in Patient Management during the COVID-19 Pandemic: A Multinational Consensus Statement from the Fleischner Society. *Chest* 2020.

7.   Pan Y, Guan H, Zhou S, Wang Y, Li Q, Zhu T, Hu Q, Xia L. 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.

8.   https://radiologyassistant.nl/chest/covid-19-corads-classification.

9.   Prokop M, van Everdingen W, van Rees Vellinga T, Quarles van Ufford J, Stoger L, Beenen L, Geurts B, Gietema H, Krdzalic J, Schaefer-Prokop C, van Ginneken B, Brink M, Society C-SRWGotDR. CO-RADS - A categorical CT assessment scheme for patients with suspected COVID-19: definition and evaluation. *Radiology* 2020: 201473.

10.   Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, Bleicker T, Brunink S, Schneider J, Schmidt ML, Mulders DG, Haagmans BL, van der Veer B, van den Brink S, Wijsman L, Goderski G, Romette JL, Ellis J, Zambon M, Peiris M, Goossens H, Reusken C, Koopmans MP, Drosten C. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* 2020: 25(3).