Radiology

What is the Performance and Role of CT in Suspected COVID-19 Infection?

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See also the article by Schalekamp et al.

The coronavirus (COVID-19) pandemic represents one of the greatest acute threats to human health since the 1918 influenza outbreak, which over a three-year period resulted in a worldwide death toll estimated to be greater than 50 million. By comparison, COVID-19 has resulted in a worldwide death toll of over 1 million as of October 2020 (1). This has put a significant burden on health care resources with localized outbreaks in specific regions resulting in a higher mortality as resources have become strained. Early diagnosis is most important in allowing patients to isolate themselves, thus limiting the potential for spread of the virus to others.

The diagnosis of COVID-19 primarily relies upon a real-time reverse-transcriptase polymerase chain reaction test (RT-PCR) which detects viral specific deoxyribonucleic acid. Imaging, both chest radiographs and CT, has been proposed as an adjunct to RT-PCR. While there are some fairly clear roles for imaging, other roles have yet to be defined. Imaging is, undoubtedly, useful in the evaluation of patients with suspected or known COVID-19 in whom other diagnoses, such as pulmonary embolism, are possible alternative causes of symptoms. However, the role of CT in the diagnosis of COVID-19 infection itself is still evolving with certain societies having established guidelines that recommend against its use for this express purpose (2,3). That being said, RT-PCR has several limitations of its own including reduced sensitivity in early disease, variable performance characteristics, long processing times in certain settings, and reduced accessibility in certain regions. Using imaging in these contexts might provide a complementary method of diagnosis, however, this would necessitate understanding its performance characteristics.

Several CT classification schemes have been developed as a guide to radiologists in better understanding the spectrum of typical and atypical manifestations of COVID-19. These schemes also serve a useful role in the research realm by providing a standardized way of reporting CT findings and their likelihood of representing COVID-19 infection. Many of the earlier studies investigating the use of CT in this arena simply used a binary determination of CT findings that were compatible with viral infection or not. While overlap invariably exists between COVID-19 and other processes, including other viral infections, there are CT findings that may be somewhat more specific and have a higher positive predictive value for COVID-19, particularly in a population with a relatively high prevalence of disease (4). These include peripheral areas of bilateral ground glass opacity and consolidation associated with the reversed halo sign and perilobular opacities. These findings suggest that organizing pneumonia is a significant component of the lung reaction to COVID-19 infection.

In this article in *Radiology*, Schalekamp et al (5) investigate the performance of a classification scheme developed by the Dutch Radiological Society (6) which categorizes CT findings into five main categories according to the likelihood of COVID-19 including:

1. CO-RADS 1: normal or findings compatible with a non-infectious etiology
2. CO-RADS 2: typical for other infection but not COVID-19
3. CO-RADS 3: features compatible with COVID-19 but also other diseases
4. CO-RADS 4: suspicious for COVID-19
5. CO-RADS 5: typical for COVID-19

The authors evaluate the performance characteristics by comparing the CT findings to both RT-PCR results and a clinical reference standard in a cohort of 1070 patients presenting with respiratory symptoms suggestive of COVID-19 to the emergency departments of six different medical centers. The clinical reference standard aims to compensate for the less than ideal performance characteristics of RT-PCR, and more specifically the lower sensitivity of RT-PCR in early disease. This clinical reference standard incorporates several factors including: RT-PCR results and when RT-PCR is obtained in relation to the onset of symptoms, the presence of an alternative cause of symptoms, contact with a COVID-19 positive person, the need for high oxygen therapy or ICU admission, and unexplained death during admission.

The performance of CT in this article is notable for a sensitivity and specificity of 86% and 81% respectively compared to RT-PCR when using a threshold of CO-RADS 4 or higher. As expected, when a threshold of CO-RADS 5 is used, the sensitivity decreases (71%), and the specificity increases (89%). When compared to the clinical reference standard as opposed to RT-PCR, CT has a lower sensitivity (77% using CO-RADS 4 or higher and 62% using CO-RADS 5 as a threshold) and higher specificity (90% using CO-RADS 4 or higher and 95% using CO-RADS 5 as a threshold). These numbers are similar to the article by Ciccarese et al (7) in which the RSNA classification scheme was applied to the chest CTs of 569 patients in Italy. The RSNA scheme divides the CT findings into the following main categories: typical, indeterminate, atypical, and negative for COVID-19. The "typical" category had a 71.6% sensitivity, 91.6% specificity for COVID-19 infection.

What does the data tell us about the clinical utility of CT in practice? CT has several theoretical uses which have the potential to impact management decisions. First, CT could be used to identify alternative or superimposed causes of pulmonary symptoms such as pulmonary embolism or bacterial infection. This may occur at presentation or in a patient with known COVID-19 who subsequently demonstrates a worsening clinical status. This is generally accepted as an appropriate and important role of CT. To this end, the Fleischner Society recommends (8) obtaining baseline imaging in COVID-19 positive patients presenting with moderate to severe symptoms which then may then be used as a comparison to follow-up imaging if the patient worsens, however it doesn't specify if chest radiographs or CTs are most appropriate and leaves this determination up to the specific scenario.

Second, CT could be used in conjunction with RT-PCR in the decision to isolate a patient. The need for isolation involves incorporating multiple factors including the presence and nature of pulmonary symptoms, exposures to others with known or suspected COVID-19, and the potential of an individual to spread COVID-19 to others. While a positive RT-PCR test is confirmatory and generally necessitates isolation, a negative test does not necessarily exclude active infection with the sensitivity of RT-PCR estimated to range between 58-96% in one article (9). In patients with a high clinical suspicion of disease and a negative RT-PCR result, CT could theoretically serve as a complementary examination to detect patients with false negative RT-PCR results.

The ideal test characteristics for a test to fill such a role would be a high sensitivity and high negative predictive value (NPV). Unfortunately, in this study CT demonstrated a sensitivity that only ranged from 62-86% and NPV of 60-85% depending upon the CO-RADs threshold and reference standard used. Even using a lower CO-RADs threshold of 3, CT demonstrated a sensitivity of 86-92% and NPV of 75-89%. In contrast, in another study Ai et al (10) demonstrated a very high sensitivity (97%) of chest CT compared to RT-PCR. In this other article, CT showed abnormalities in many patients deemed later to have an initial false negative PCR. The conclusion of the Ai et al article is that CT may, in fact, be more sensitive in the diagnosis of COVID-19 compared to RT-PCR. In the study by Ai et al, however, a classification scheme, such as CO-RADS, was not utilized. CTs were classified in a binary fashion as having findings compatible with COVID-19 or not. It is important to note that a classification system, such as CO-RADS, places its primary emphasis on specificity, whereas a binary system places its primary emphasis on sensitivity. Using a binary threshold in the decision to isolate a patient might allow CT to be used as a screening test given its high negative predictive value, however the cost and radiation exposure that CT imparts are significant detractors. That being said, CT could possibly be used in tandem with RT-PCR, focusing on patients who have a high likelihood of having a false negative RT-PCR result. Another potential role of CT in the diagnosis of COVID-19 infection is its use in resource limited settings in which RT-PCR is unavailable, slow to process, or inaccurate. The Fleischner Society recommends the use of imaging, in this context, in patients with moderate to severe disease presenting in resource limited environments (8).

The last area in which CT could theoretically be helpful is in treatment decisions. The current National Institutes of Health treatment recommendations for COVID-19 include the use of Remdesivir with or without dexamethasone, however this is only applicable to patients who are hospitalized and require supplemental oxygen. While treatment of mild cases of COVID-19 is not indicated at this time, it is possible that new therapies could be developed that are effective at preventing the progression to more severe disease. In such case, the early detection of COVID-19 infection might allow for early treatment and thus a combination of RT-PCR and CT might be most efficient at identifying the greatest number of eligible patients. Another theoretical role of CT is the identification of morphologic features that might be more responsive to specific treatments. In reviewing the multiple studies that have described the typical features of COVID-19 infection it appears that organizing pneumonia is a pattern that is more commonly present than in other infections, even other viral infections. As organizing pneumonia is a corticosteroid responsive disease, CT might be able to identify patients with a predominance of morphologic features consistent with this pattern. Both of these areas require significant additional research to elucidate if CT has any role in these contexts.

In summary, the article by Schalekamp et al (5) demonstrates an excellent, albeit far from perfect, performance of CT in the evaluation of patients with suspected COVID-19 infection in comparison to RT-PCR and a clinical reference standard. Given that RT-PCR is considered the reference standard for COVID-19 infection, the role of CT in its diagnosis is still evolving. While CT is helpful in the detection and characterization of alternative causes of pulmonary symptoms, such as pulmonary embolism, it's role directly related to COVID-19 infection itself still has yet to be determined. The results of this study, however, can form a foundation for other investigations whose goal is to further elucidate the potential roles of CT in the detection and characterization of this deadly disease.

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References

1. COVID-19 Coronavirus Pandemic. 2020.https://www.worldometers.info/coronavirus/. Accessed October 12, 2020.

2. STR/ASER COVID-19 Position Statement. 2020.https://thoracicrad.org/. Accessed October 12, 2020.

3. ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection. 2020;https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for-Suspected-COVID19-Infection.

4. Bai HX, Hsieh B, Xiong Z, et al. Performance of Radiologists in Differentiating COVID-19 from Non-COVID-19 Viral Pneumonia at Chest CT. Radiology. Radiological Society of North America. 2020;296:E46–E54.

5. Schalekamp S, Bleeker-Rovers CP, Beenen LFM et al. Chest CT in the Emergency Department for Diagnosis of COVID-19 Pneumonia: Dutch Experience. Radiology 2020 (in press).

6. Prokop M, van Everdingen W, van Rees Vellinga T, et al. CO-RADS: A Categorical CT Assessment Scheme for Patients Suspected of Having COVID-19-Definition and Evaluation. Radiology. Radiological Society of North America. 2020;296:E97–E104.

7. Ciccarese F, Coppola F, Spinelli D, et al. Diagnostic Accuracy of North America Expert Conesnsus Statement on Reporting CT Findings in Patients with Suspected COVID-19 Infection: An Italnian Single Center Experience. Radiology. 2020.

8. Rubin GD, Ryerson CJ, Haramati LB, et al. The Role of Chest Imaging in Patient Management During the COVID-19 Pandemic: A Multinational Consensus Statement From the Fleischner Society. Chest. 2020. pp. 106–116.

9. Green DA, Zucker J, Westblade LF, et al. Clinical Performance of SARS-CoV-2 Molecular Tests. McAdam AJ, editor. J Clin Microbiol. American Society for Microbiology Journals. 2020;58:265.

10. Ai T, Yang Z, Hou H, et al. Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology. Radiological Society of North America. 2020;296:E32–E40.