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CHEST

The Potential Role for CT in the Diagnosis of Coronavirus Disease 2019

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One of the many things brought into sharp focus by the global pandemic is the value of diagnostic tests to make an accurate, rapid, and reliable diagnosis. In current times perhaps more than ever before in modern medicine, this is of paramount importance. Imaging alongside molecular testing currently is providing the majority of diagnostic information during this pandemic.

Early in the coronavirus disease 2019 (COVID-19) outbreak, typical CT findings were described that included peripheral ground glass patterns, with a relative lack of dense consolidation or pleural effusion.[1] Chest radiography findings are also well-described, and plain radiography is recognized by the World Health Organization as less sensitive, although interestingly more specific, than CT scanning[2] (this recommendation being prior to publication of this data, of course). Lung ultrasound scanning shows a typical sonographic pattern[3] and will have a role to play, although robust data looking at its effectiveness are only just starting to emerge.[4]

In this issue of *CHEST*, Lieveld et al[5] report the validation of a CT reporting tool in the diagnosis, and severity assessment, of COVID-19. Consecutive suspected cases presenting to the EDs of two academic hospitals in The Netherlands were included. As well as being among the first prospective imaging studies, it contains a large dataset of 741 patients with CT imaging and reverse transcriptase polymerase chain reaction (RT-PCR) correlation. This gives good reliability to the data.

The authors are validating a 5-point scoring system called COVID-19 Reporting and Data System, described by the Radiological Society of the Netherlands.[6] For the purposes of this study, a sixth point was added to represent 33 patients in whom the RT-PCR result was known at the time of CT reporting and who were excluded to minimize the potential for bias. The headline result is an excellent correlation between a CT diagnosis of COVID-19 (representing a COVID-19 Reporting and Data System score ≥4) with RT-PCR, with an area under the curve of 0.91 (95% CI, 0.89-0.94). This translates to a positive predictive value of 76.4% (95% CI, 71.9-80.3) and a negative predictive value of 94.6% (95% CI, 92.4-96.2), which suggests that CT imaging might be more helpful in ruling out the disease rather than ruling it in.

The second aim of the study was to validate CT imaging as a tool for the prediction of clinical outcomes in COVID-19, using a severity score ranging from 0 (no involvement of the lung parenchyma) to 25 (maximal involvement). This follows similar work in both ARDS[7] and severe acute respiratory syndrome[8] to find a CT-based outcome prediction tool, both of which have been integrated variably into routine clinical care. There was a positive association noted between per-point increasing severity scores and hospital admission, ICU admission, and 30-day mortality rate, with adjusted ORs of 1.18 (95% CI, 1.09-1.28), 1.23 (95% CI, 1.15-1.32), and 1.14 (95% CI, 1.07-1.22), respectively. Perhaps unsurprisingly, the boundaries were somewhat blurred when it came to whether an individual score would predict an individual outcome with any degree of certainty. No adjustment of the score was made for oxygen requirement; therefore, it remains unclear whether CT scanning can provide prognostic information much above that which F_{IO_2} or level of required respiratory support affords.

The primary difficulty with this study is that we have an imperfect "gold standard" reference test for the diagnosis of COVID-19. The limitations of RT-PCR

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AFFILIATIONS: From East Surrey Hospital.
FINANCIAL/NONFINANCIAL DISCLOSURES: None declared.
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DOI: https://doi.org/10.1016/j.chest.2020.12.018

testing in providing definitive positive or negative diagnoses are acknowledged within the article and should be embedded within the wider consciousness of everyone treating patients during this pandemic. Initial data suggested a 60% to 70% sensitivity of nasopharyngeal RT-PCR swabs in the detection of COVID-19,[9] meaning a significant number of patients with the disease will test negative on any given sample, purely because of technical issues around sample collection and processing. In this study, 23.8% (56/235) COVID-19 confirmed cases had a negative initial swab, serving to highlight this reality.

Therefore, using RT-PCR as the reference test (which is necessary because it is the best we have) will tend towards a falsely low specificity, positive predictive value, and likelihood ratio. The risk of this decreases where multiple swabs are sent, as is likely in patients with a high clinical suspicion who remain inpatients, but cannot be mitigated altogether. To further illustrate this, the authors suggest that of the 65 false-negative cases (CT positive scan, but RT-PCR negative result), 46 cases (70.8%) were considered to have the disease by multidisciplinary team assessment. Clinical assessment during a high-prevalence period is subject to significant biases (so this may well be an overestimate), but it does highlight the difficulties in relying on RT-PCR alone for a diagnosis. The most common alternatives in the false-positive cohort were, not surprisingly, bacterial pneumonia (25%) and decompensated heart failure (12%).

So, what do these results mean in practice? Although not strong enough evidence to support CT scanning as the first-line investigation for COVID-19, these data may well be enough to encourage the American College of Radiology and Royal College of Radiologists in the United Kingdom to review their stance that CT scanning should not be used routinely in the diagnosis of COVID-19.[10,11] These data clearly support a role for CT scanning in the diagnostic pathway of patients with suspected COVID-19, particularly where RT-PCR is not rapidly available or the result is unexpected. In low-risk cases, a negative CT scan is likely to rule out the disease and facilitate passage into "cold" or "green" zones if admission is required. Even with shifting prevalence (which, of course, will alter the diagnostic performance of any test), the high sensitivity of CT scanning should mean that this will remain an important role, because cohorting of true negative patients will continue to be of paramount importance to maintain flow and reduce nosocomial infections. Its usefulness in aiding discharge or admission decisions is less clear.

The specificity of CT scans is such that a positive scan on its own may not be enough to confirm the diagnosis; however, combined with a high clinical probability ± suggestive biochemistry (in particular lymphopenia[12]), it is likely to be confirmatory. Further research to determine a combined scoring system that includes laboratory markers and imaging would be valuable, to help overcome some of the difficulties with relying on rapidly available molecular tests or imaging alone.

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