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## The role of CT in case ascertainment and management of COV-19 pneumonia in the United Kingdom: insights from high-incidence regions --Manuscript Draft--

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## The role of CT in case ascertainment and management of COV-19 pneumonia in the United Kingdom: insights from high-incidence regions

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COVID-19 is the seventh pathogenic human coronavirus to be identified and the third – after SARS-CoV and MERS-CoV – with a predilection for causing potentially fatal pneumonia. COVID-19 infection is highly transmissible but has a relatively low death rate (1.0 - 3.5%) except in elderly persons with co-morbidities.<sup>1,2</sup> It is estimated that 15 – 20% of those infected develop severe pneumonia and 5 – 10% require critical care.<sup>2</sup>

COVID-19 preparedness in countries with a surge in new cases have prioritized containment, rapid diagnosis and fastidious contact tracing. With sustained community transmission, real-time reverse transcriptase polymerase chain reaction (rRT-PCR) of viral nucleic acid may be supplanted by more versatile diagnostic tools because false negative results have been a concern. The recent change in diagnostic criteria in China to include computed tomography (CT) was driven by a sustained daily increase in new cases. With its short turnaround time and wide availability, CT imaging is expected to dominate in large-scale COVID-19 case ascertainment. The lower sensitivity of plain chest radiography will limit its role in diagnosing COVID-19 pneumonia.

CT abnormalities may predate rRT-PCR positivity in symptomatic patients, and in those without symptoms who subsequently test positive by rRT-PCR.<sup>3,4,5</sup> A role for CT in early diagnosis of COVID-19 infection seems likely. Against this, albeit in the minority, cases with positive rRT-PCR but normal CT (likely representing very early infection) are recognised; of 36 patients scanned within the first two days of symptoms, CT was normal in half despite the majority (>90%) being rRT-PCR positive.<sup>6</sup>

The commonest CT features reported in COVID-19 pneumonia are bilateral, sub-pleural areas of ground-glass opacification (GGO) and/or consolidation affecting the lower lobes.<sup>3,6-8</sup> Foci of abnormality may be well-demarcated, sometimes with a ‘rounded’ configuration.<sup>3,5,7,9,10</sup> In the intermediate phase of infection (4 – 14 days from symptom onset), a ‘crazy-paving’ pattern may be seen. Other CT findings (e.g. a tree-in-bud pattern, nodules, cysts, cavitation and large volume lymphadenopathy) are uncommon. Differences in the frequency of individual features between pneumonia caused by COVID-19 and other viruses have yet to be studied.

**Several aspects of the utility of CT in COVID-19 infection are worth noting:**

### CT findings in asymptomatic (pre-clinical) patients

In one study, GGO was evident in nearly all of 15 asymptomatic (but rRT-PCR positive) cases who had been in close contact with COVID-19 confirmed patients.<sup>2</sup> The extent of pulmonary involvement, defined as affected lung segments, was less than in the symptomatic group and more frequently unilateral.

### CT abnormalities in survivors of COVID-19 pneumonia

Pan and colleagues, employing serial CTs, described the radiological time course of 21 patients with confirmed mild-to-moderate infection who survived to discharge.<sup>9</sup> 'Peak' radiological abnormalities occurred at around day 10, followed by gradual regression starting two weeks after symptom onset. In a separate analysis, Ai and colleagues reported radiological improvement predating rRT-PCR becoming negative in 42% (24/57) of patients recovering from COVID-19 pneumonia.<sup>3</sup>

### Comparative sensitivity of CT against rRT-PCR

Two studies have specifically compared the performance of CT and RT-PCR: in a cohort of just over 1000 cases, the diagnostic sensitivity, positive and negative predictive value of CT was reported as 97%, 65% and 83% respectively.<sup>3</sup> CT was abnormal in 75% (308/413) of those with a negative first rRT-PCR but clinically felt to likely (48%) or probably (33%) have COVID-19 pneumonia. A comparable CT sensitivity of 98% (vs 71% for rRT-PCR;  $P < 0.001$ ) was concluded in a smaller study of 51 cases where just under a third tested negative on the initial rRT-PCR.<sup>10</sup>

### Individuals with pre-existing lung disease

There are few descriptions of COVID-19 pneumonia in individuals with pre-morbid pulmonary conditions. Shi and colleagues reported that 9/81 of confirmed cases had underlying lung disease although the specific details are not known.<sup>4</sup> The potential impact of

COVID-19 pneumonia on patients with established respiratory conditions remains unclear at this time.

CT is likely to become increasingly important for the diagnosis of COVID-19 pneumonia given the continuing rise in global cases. The observed evolution from pneumonic injury to respiratory death in this disease suggests a pathologic pathway that might be amenable to early CT detection, particularly if the patient is scanned 2 or more days after developing symptoms. Put simply, a negative CT at one week is highly likely to exclude COVID-19 pneumonia. The prognostic value of CT would be further enhanced if it was able to define early radiological abnormalities or patterns that portend a worse outcome. We propose that a practical algorithm for diagnosing COVID-19 pneumonia should combine detailed clinical history, baseline and repeat contiguous CT (the interval depending on clinical circumstances) and rRT-PCR for COVID-19 and other viruses in nasal and throat swabs.

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