Diagnosis of SARS-CoV-2 Infection based on CT scan vs. RT-PCR: Reflecting on Experience from MERS-CoV

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As of 29th February 2010 the World Health Organization had reported a total of 83 652 COVID-19 cases in 51 countries in addition of China [1]. The diagnosis of respiratory viruses such as Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and SARS-CoV relies on detection of the virus by real-time RT PCR (rRT-PCR) for in vitro qualitative detection. The current recommendations are likewise to use rRT-PCR for the detection of SARS-CoV-2 in respiratory samples. There are many knowledge gaps facing the global health community in dealing with the new emerging SARS-CoV-2. Among the most pertinent is early identification of cases to facilitate application of isolation policies. The currently available RT-PCR kits are variable, offering sensitivities ranging between 45 and 60%; thus, especially early in the course of an infection, repeat testing may be required to make a diagnosis. This is not easy to apply with the global shortage of testing kits. This mirrors experience with MERS-CoV. In a study of 336 MERS patients, 89% had a positive result after 1 swab, 96.5% had a positive result after 2 consecutive swabs, and 97.6% had a positive result after 3 swabs (Figure 1) [2]. China has changed the case definition over the last 2 months to improve the ability to detect new cases. Data have emerged on the value of CTscan of chest in early diagnosis of cases. Multiple reports published to date have revealed higher sensitivity of CT chest in early detection of SARS-CoV-2 cases [3]. In a study of 51 patients, the positivity rate for a single respiratory swab was 70%, an additional 24% (94% cumulative) after a second test, and an additional 3.9% (98% cumulative) after a third test (Figure 1) [4]. However, an abnormal CT scan findings compatible with viral pneumonia was seen in 98% of patients [4]. This difference had resulted in the recommendations of authors to state that CT scan is more sensitive than PCR. Reasons for low sensitivity of PCR may include insensitive nucleic acid detection methods and variations in the accuracies of different tests, low initial viral load or improper clinical sampling [4]. An additional reason may be that lower respiratory samples may be better than upper respiratory samples, as is the cases with MERS-CoV [5] [6].

In another study of 167 patients, concordant CT scan and PCR test results were observed in 93% of patients, and a discordant results were observed in 4% (positive PCR but negative CT scan) and in 3% (negative initial PCR and positive CT scan) [7]. In a larger study of 1014 SARS-CoV-2 patients, 59% had positive RT-PCR and 88% had positive CT scan; using RT-PCR as a reference, the sensitivity of chest CT imaging was 97% [8].

Growing evidence of the limitations of rRT-PCR prompts further consideration of the limitations of this diagnostic test. First, there are already over 7 different SARS-CoV-2 nucleic acid PCR tests [9]. When considering the viral load in samples, it has shown that upper respiratory tract samples have their peak viral loads 3 days after onset of symptoms, and that nasal, rather than throat samples have the highest viral loads [10]. As the current SARS-CoV-2 epidemic evolves globally we need better diagnostic tests that are rapid, reliable, validated and widely available. For hospitalized patients diagnostic algorithms based on a combination of RT-PCR and CT scan of the chest may prove to be necessary in order to ensure accurate detection of cases and to facilitate infection prevention measures. It is also very important to learn from the previous MERS-CoV epidemic and reflect on that experience, especially that a single negative upper respiratory sample is not enough to rule out infection. It may be prudent to keep those patients in isolation while we obtain additional swabs or be able to safely get lower respiratory samples for definite diagnosis.

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Figure 1: Cumulative Positive Rate of Swabs for the diagnosis of SARS-CoV-2 and MERS-CoV based on RT-PCR