Comment

COVID-19 pneumonia: what has CT taught us?

In late December, 2019, a cluster of cases of viral pneumonia was linked to a seafood market in Wuhan (Hubei, China), and was later determined to be caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously known as 2019-nCoV).[1] The genome sequence of SARS-CoV-2 is similar to, but distinct from, those of two other coronaviruses responsible for large-scale outbreaks in the past: severe acute respiratory syndrome coronavirus (SARS-CoV; about 79% sequence identity) and Middle East respiratory syndrome coronavirus (MERS-CoV; about 50%).[2]

CT has been an important imaging modality in assisting in the diagnosis and management of patients with coronavirus disease 2019 (COVID-19) pneumonia, and reports on the radiological appearances of COVID-19 pneumonia are emerging. In *The Lancet Infectious Diseases*, Heshui Shi and colleagues[3] discuss the CT findings and temporal changes of COVID-19 pneumonia with reference to the time of onset of symptoms, in the largest cohort thus far reported. The predominant CT findings included ground-glass opacification, consolidation, bilateral involvement, and peripheral and diffuse distribution. These findings concur with other reports in smaller cohorts and with our own experience.[4–6] Notably, in Shi and colleagues' study, the asymptomatic (subclinical) group of patients showed early CT changes, supporting what was first observed in a familial cluster with COVID-19 pneumonia.[7] Conversely, other studies have shown positive RT-PCR results for SARS-CoV-2 in the absence of CT changes, or abnormal CT findings with initial false-negative RT-PCR results.[8] As the epidemic evolves, we are starting to observe the varied presentations of COVID-19 pneumonia, with symptomatic patients showing concordant CT and RT-PCR findings.[8] Nevertheless, this small number of individuals with COVID-19 pneumonia poses a diagnostic dilemma given the varied manifestations.

The evolution of the disease on CT is not well understood. Shi and colleagues reported the presence of unilateral ground-glass opacities in a subgroup of 15 asymptomatic patients with COVID-19 pneumonia, substantiating previous anecdotal reports that asymptomatic patients could have CT changes before symptom onset. This finding suggests that CT is a sensitive modality with which to detect COVID-19 pneumonia, even in asymptomatic individuals, and could be considered as a screening tool—together with RT-PCR—when a patient has significant travel history or has had close contact with an infected individual. Furthermore, CT might be a particularly important screening tool in the small proportion of patients who have false-negative RT-PCR results. Shi and colleagues also showed that the lesions that were present in asymptomatic individuals progressed to bilateral diffuse disease with consolidation at around the first to second week after symptom onset.[9]

In Hubei, there was a surge of diagnoses of COVID-19 on Feb 12 because of the introduction of new diagnostic criteria that included CT changes. These criteria were employed to ensure timely treatment and isolation measures, because of the delays associated with laboratory testing and a large number of patients presenting with respiratory symptoms in the province.

As the predominant pattern seen in COVID-19 pneumonia is ground-glass opacification, detecting COVID-19 with use of chest radiography—on which this type of abnormality is often imperceivable, particularly in patients with few symptoms or low severity—is likely to be challenging. By contrast, chest radiographs were used frequently in the diagnosis of SARS as both ground-glass opacification and consolidation were present early.[10,11]

The current literature is partly skewed by the geographical distribution of COVID-19 pneumonia and the preferential use of CT over chest radiograph in China. This preference might be due to the ease of access to CT in China and the lack of requirement for intravenous contrast agent for the examination. Therefore, it is unclear whether the threshold for performing CT evaluation of potential lung changes should be lower when chest radiographs are normal. Further research is needed to better select patients for CT examination, to define the utility of CT in COVID-19 pneumonia, and to explore the application of artificial intelligence in screening chest radiographs in suspected cases.

Overall, we congratulate Shi and colleagues in adding valuable information to the current literature. The authors carefully evaluated the CT findings in a

large cohort of patients with COVID-19 pneumonia, providing indirect evidence of the evolution of the CT changes with reference to the onset of symptoms. There is more to be learnt about this novel contagious viral pneumonia; more research is needed into the correlation of CT findings with clinical severity and progression, the predictive value of baseline CT or temporal changes for disease outcome, and the sequelae of acute lung injury induced by COVID-19.

We declare no competing interests.

*Elaine Y P Lee, Ming-Yen Ng, Pek-Lan Khong
eyplee77@hku.hk

Department of Diagnostic Radiology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, China

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Oral influenza vaccination—a possible solution for the next pandemic?

Influenza is a vaccine-preventable disease caused by a constantly mutating virus, which means that the vaccine composition must be updated almost every year. The burden of seasonal influenza is high,[1] but the emergence of a pandemic virus can cause substantially more damage to both populations and health-care systems.[2] When a pandemic starts, demand for the specific vaccine soars, leading to a global shortage.

One possible approach to solving this problem is offered by a new technology based on a non-replicating adenovirus type-5 viral vector. This approach has been assessed in a phase 2 study by David Liebowitz and colleagues[3] published in *The Lancet Infectious Diseases*. The orally delivered, adenovirus-vectored VXA-A1.1 vaccine is produced using egg-independent technology. It does not require specific equipment, such as syringes, needles, and spray devices, and thus produces less potentially biohazardous waste than do injectable or nasal vaccines. Additionally, it is highly stable at ambient temperatures, which allows it to be distributed and administered quickly.[4]

In 2015, the same authors reported the results of a phase 1 study of VXA-A1.1 in healthy adults. The vaccine showed an exceptional safety and immunogenicity profile, inducing high influenza virus-specific haemagglutination inhibition (HAI) and microneutralisation antibody titres after a single dose.[4] In the present study, Liebowitz and colleagues[3] not only established the efficacy of the vaccine, but also attempted to identify immune correlates of this protection, by doing a human challenge study in which they compared VXA-A1.1 with a licensed, quadrivalent, split-virion, inactivated influenza vaccine (IIV). The challenge virus was administered 90 days after immunisation, reflecting the real interval between seasonal vaccination campaigns and annual influenza epidemics. Although VXA-A1.1 induced substantially lower anti-haemagglutinin serum antibody titres than did the IIV, both vaccines showed an overall similar protective efficacy against the challenge virus (HAI geometric mean titre on day 30 after vaccination was 31·4 in the VXA-A1.1 group *vs* 186·7 in the IIV group). These data suggest the vaccines have distinct immune correlates