Potential Role of Molecular Imaging with \(^{18}\)F-FDG in Diagnostic Triage and Follow-Up of Suspects with COVID-19 Infection

Dear Editor,

Within 2 months after the WHO declared COVID-19 an epidemic, the number of confirmed cases has crossed three million worldwide, with an overall death toll of more than 0.2 million. Currently, RT-PCR is the standard of testing for COVID-19 suspects; however, recent published data show that RT-PCR can be true negative or false negative in the initial period despite positive computed tomographic (CT) findings, and on the other hand, it is reported to be positive even after 5–13 days or more after the discharge of patients after recovery. Similarly, the reported data showed that the new rapid immunology kits detecting serum IgM and IgG levels may also be negative in initial 5–7 days due to the absence or delay in immune response from the body. The disadvantage of the CT chest itself emerged as the fact that 50% of the patients lack CT findings in the initial incubation period and showed positive findings even after the clinical resolution of disease.\(^1\) Guan et al. reported 1099 cases stating that no CT changes were found in the 17.9% of the nonsevere and even 2.9% of the severe cases. Therefore, in the light of above scenarios, where initial RT-PCR/CT are true negative, false negative, or there is suspicion of disseminated disease or multiorgan involvement, especially cardiac involvement, we suggest that the potential role of \(^{18}\)F-FDG PET/CT needs further evaluation in COVID-19 pandemic.\(^2\)

\(^{18}\)F-FDG: A Radiopharmaceutical in Detecting Early Pneumonitis

Inflammatory cytokines and cells are an integral part of the immune system and are known to take up \(^{18}\)F-FDG at the place of inflammation, allowing this agent to play an important role in the early diagnosis of inflammatory diseases. In acute lung injury, the rate of \(^{18}\)F-FDG uptake reflects the state of inflammatory process activation, i.e., C-reactive protein, CD4, CD8, and interleukin-6, pointing to an acute inflammatory response. COVID-19 infection is believed to comprise initial infiltration of inflammatory cytokines into the lung, followed by delayed morphological changes that are apparent on high-resolution CT (HRCT) approximately 4–5 days’ postinfection with a peak reported between 6 and 11 days, which gives \(^{18}\)F-FDG the opportunity to detect/image early inflammation many days before anatomical changes of CT chest and help early triage/isolation of such patients.\(^3\)

Quantification of Inflammation and Prediction of Recovery Time

\(^{18}\)F-FDG PET/CT offers functional quantification of inflammation in terms of standardized uptake values (SUVs) and lesion glycolysis amid inflammation (LGAI), reflecting disease severity. This in turn can guide physicians in titration of medical therapy on case-to-case basis by categorizing them as mild, moderate, and severe. The recent data by Qin et al.\(^3\) showed that \(^{18}\)F-FDG PET scan can be used to monitor response to respiratory therapy and help determine a patient’s recovery time by correlating with SUV. They showed that high \(^{18}\)F-FDG uptake in COVID-19 pneumonia was related with longer recuperative times [Figure 1].

Response Evaluation and Detection of Recurrent/Residual Disease

\(^{18}\)F-FDG PET/CT not only can differentiate inflammation from noninflammatory lesions on CT but can also detect inflammatory changes in the lung, earlier than the CT. As the cellular level metabolic changes occur first in pneumonitis followed by morphological CT changes, therefore the resolution of active inflammatory disease is seen earlier on 18F-FDG, than CT alone, which in turn can

Figure 1: (a) MIP PET whole-body image demonstrating mutiorgan imaging in a single setting. (b-d) Coronal, sagittal, and axial (top to bottom) computed tomography, PET, and fused PET/computed tomographic images showing localization of \(^{18}\)F-FDG in ground glass opacities (GGOs) of COVID-19 pneumonia. (e-g) Axial images of multiple FDG-positive nodes in the mediastinum (Courtesy of Lan et al.)\(^3\)
help in differentiate and follow residual lung inflammation, if any, post-discharge of COVID19 patient. Demirev et al. showed that HRCT performed immediately following 18F-FDG PET in the suspected case of pneumonia did not show any abnormalities in the lungs [Figure 2] until 3 days of onset of inflammation.[4]

In addition to early detection of COVID-19 pneumonia as discussed above, 18F-FDG PET/CT whole-body scan can concomitantly image multiorgan (involvement if any) in a single setting, which is not possible using a CT alone setting.

**Myocarditis Post-COVID-19 Infection**

COVID-19 can effect cardiovascular system, effecting myocardium, pericardium, and vessels, and even preexisting ischemic conditions are worsened secondary to viral hypoxemia. Microvascular damage, myocyte damage, and changes in the fatty acid metabolism in viral myocarditis can be readily imaged with 18F-FDG PET/CT at an early stage and if detected at early stage can save valuable lives.[5]

Regarding cost issues, 18F-FDG PET/CT is free in the entire gulf for their nationals, and for other regions, high cost of the imaging can be covered through research funding projects and grants wherever applicable.

In a nutshell, in the current COVID-19 pandemic, 18F-FDG PET/CT though high cost, if properly adjusted in protocol [Figure 2], can provide high sensitivity for early detection of pneumonitis, concomitant assessment of multiorgan involvement through whole-body imaging, quantification of inflammation using SUV/LGAI, follow-up of response to treatment, detecting residual disease, and recurrence, whereas CT scan is initially unremarkable and fails to detect subtle residual inflammation, and moreover, CT findings remains unchanged for a longer time period after recovery.

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**Conflicts of interest**

There are no conflicts of interest.

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