

# COVID-19 and Nuclear Medicine – Clinical Aspects

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The Coronavirus disease 2019 (COVID-19) pandemic, caused by SARS-CoV-2, has affected almost all countries worldwide. The World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020. As of February 7, 2022, a total of 676,850,919 cases and 6,776,287 deaths have been reported (1). In terms of our country, Bangladesh, we are indeed fortunate to have miraculously avoided the worst of COVID-19, as many other countries did. However, as of early 2023, it is still wreaking havoc in China, Japan, and a few other countries. We should not be relieved yet; at any time it may reappear with the ongoing mutations of the virus variants.

The COVID-19 pandemic had an impact on several medical fields, including Nuclear Medicine (NM) (2). Regarding clinical and imaging aspects, hybrid imaging techniques may provide functional and morphological information for the early diagnosis of infectious and inflammatory diseases (3), including COVID-19. Evidence-based data demonstrated that several NM procedures may incidentally detect COVID-19 lesions (e.g., interstitial pneumonia suspected for COVID-19) in patients who underwent these imaging techniques for oncological and non-oncological indications (4, 5). It has been reported that the FDG-PET/CT findings of patients with COVID-19 were increased FDG uptake in lung lesions with segmental ground-glass densities and plaques, in normal-sized or slightly enlarged lymph nodes, and in the bone marrow and spleen (6). But NM methods are currently not used in clinical practice to diagnose COVID-19, and they cannot substitute high-resolution computed tomography in this setting (7). However, incidental early diagnosis of COVID-19 through hybrid imaging techniques may be crucial for appropriate patient management (4, 5).

COVID-19 is a multisystem disease where NM techniques can play a vital role in the post-acute phases

and follow-ups. We have seen many cases of delayed complications after being released from the hospital involving the myocardium, vasculature, muscles, intestine, and the CNS. Reported cases of post-COVID myocardial ischemia or infarction are significant and one study found that, SPECT myocardial perfusion imaging (MPI) revealed a high prevalence of defects in patients with even mild or asymptomatic COVID infection who did not require hospitalization (8). Among the gastrointestinal complications, gastroparesis, i.e., prolongation of the transit time, is often seen (9). NM can provide vital information with gastric emptying studies. Some patients reported functional complaints after apparent recovery from COVID-19. This clinical presentation has been referred to as "long COVID." Patients with long COVID showed bilateral hypometabolism in the bilateral rectal/orbital gyri, including the olfactory gyrus; the right temporal lobe, including the amygdala and the hippocampus, extending to the right thalamus; the bilateral pons/medulla brainstem; and the bilateral cerebellum. These clusters of hypometabolism were significantly associated with the occurrence of certain symptoms, namely a) hyposmia and anosmia b) memory and cognitive impairment c) pain and d) insomnia (10).

Pulmonary embolism (PE) is a potentially life-threatening condition and a recognized complication of COVID-19. The ventilation portion of the V/Q scan could lead to the mechanical spread of SARS-CoV-2 to patients, technologists, and other health care workers. Therefore, the major medical imaging societies suggested that lung perfusion scans without ventilation (i.e., perfusion-only scans) should be performed to evaluate such cases. Perfusion scans interpreted as having normal or near-normal findings or those with high- or

low-probability readings can be reliably used for diagnosing acute PE (11).

Research is ongoing to find out the possibility of detecting acute inflammation in the future using NM methods. Radiopharmaceuticals that target the purinergic P2X7 receptor, for example, can be absolutely vital as inflammatory biomarkers. There are potential P2X7 inhibitors at the receptor level (12), which have shown anti-inflammatory effects in animal models (13). Future research may form the rationale for anti-inflammatory therapy principles in COVID-19. Furthermore, NM has the potential to provide evidence and clarify contradictory concepts in the use of NSAID drugs in COVID-19 by directly depicting cyclooxygenase-2 (COX2) involvement using established COX2-inhibitory radiopharmaceuticals (14). Other radiopharmaceuticals might target the cytokine signaling pathway (e.g., chemokine receptor CXCR4, interleukin IL-6), fibroblast activation protein inhibitors (FAPI), to address post-inflammatory fibrosis, or inhibitors of the type 1 angiotensin-II-receptor ATR1 (e.g., KR31173), involved in cellular internalization of SARS-CoV-2 (15). Radiolabeling of an ACE2-receptor antagonist has already been achieved for receptor autoradiography protocols (16) and could serve as a starting point for PET tracer development (17).

Several studies have reported FDG avidity in enlarged axillary lymph nodes as a specific feature of FDG-PET/CT imaging after COVID-19 vaccination. After vaccination, lymph nodes can show abnormal size and loss of fatty hilum shortly after vaccination, which could be considered to indicate malignancy. A major concern is that this discovery could lead to misdiagnosis in patients suffering from various types of cancer (18). Therefore, it is important to carefully manage the timing of the FDG-PET/CT examination with respect to the date of vaccination, and NM physicians have to be aware of FDG findings related to the immune response to vaccines.

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