^{18}F-FDG PET/CT for the diagnosis of aortic inflammation in COVID-19

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A prominent component of the pathophysiology of COVID-19, which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is vascular involvement.[1] The latter includes vascular and endothelial dysfunction, as well as inflammation, i.e., vasculitis.[1] COVID-related vasculitis is challenging to diagnose clinically, necessitating the use of specific diagnostic investigations. ^{18}F-fluoro-deoxyglucose (FDG)-positron emission tomography (PET)/ computed tomography (CT) is an established technique for visualizing large-vessel inflammation.[2] The non-invasive diagnosis of vasculitis by imaging modalities, however, has not been explored very thoroughly in the context of the COVID-19 pandemic.

In the current issue of the journal, Vlachopoulos et al. performed ^{18}F-FDG PET/CT imaging in 20 severely and critically ill patients with COVID-19, who were admitted to hospital.[3] They were compared to 10 age- and sex-matched individuals with malignancies who were in remission and served as the control group.[3] PET/CT scans were performed at a median of 60 (IQR 45-74) days after the diagnosis, and no difference in aortic target-to-background ratio (TBR) was found between the patient and control groups (P = 0.422).[3] In contrast, index TBR (region with the highest TBR) differed between patients and controls, in the group where scans were performed before or at 60 days after the diagnosis (P = 0.036). A fair correlation was identified between TBR and serum C-reactive protein (CRP) levels (P = 0.004), and arterial TBR was independently associated with the time from diagnosis.[3] The results therefore suggest that ^{18}F-FDG PET/CT can be used to diagnose and monitor large-vessel involvement in COVID-19, and that it resolves over time.

Endothelial dysfunction, including vasculitis (characterized by lymphocyte infiltration) and intravascular thrombosis, has been well documented in COVID-19. Vascular dysfunction may lead to serious complications, e.g., arterial and venous thromboses, as well as coronary and aortic dissection.[1] Large-vessel inflammation can be visualized with ^{18}F-FDG PET/CT, since inflammatory cells overexpress glucose transporters which avidly take up glucose and ^{18}F-FDG.[2] While alternative techniques are available for the diagnosis of large-vessel vasculitis, e.g., biopsy, invasive angiography, ultrasound, and magnetic resonance (MR) imaging, these are impractical (e.g., biopsy), demonstrate changes only in advanced or late-stage disease (e.g., invasive angiography), and can be non-specific (e.g., ultrasound).[2] ^{18}F-FDG PET/CT, on the other hand, has a high sensitivity and specificity for the diagnosis of large-vessel vasculitis.[4] The uptake of ^{18}F-FDG into large blood vessels was correlated with acute phase reactants in a study including 26 patients with giant cell or Takayasu's arteritis—similar to the current study—suggesting that ^{18}F-FDG PET/CT is a sensitive technique for detecting early disease in conditions causing inflammation of large vessels.[2,3] The presence of inflammation in large vessels has recently been demonstrated in a study of 10 patients who had recovered from acute COVID-19, but who were suffering from persistent symptoms, i.e., ''long COVID.''[5] The current study, however, is the first to investigate the

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relation of large-vessel inflammation, diagnosed with ^{18}F-FDG PET/CT, with the time from diagnosis.[3]

Early identification of the degree of vascular inflammation in COVID-19 patients might be useful in planning management. Strategies for suppression of large-vessel vasculitis in COVID-19 still have to be defined, although the use of systemic glucocorticoids appears logical, based on the beneficial effect in large-vessel vasculitides in general, as well as serious manifestations of COVID-19.[6,7] Although the outcome implications (including the impact of the severity and duration of vascular inflammation) of large-vessel vasculitis due to COVID-19 are still unclear, the clinical use of ^{18}F-FDG PET/CT is promising, and the technique has been demonstrated to predict relapses in large-vessel vasculitides which were clinically in remission.[8] A confounder regarding the use of ^{18}F-FDG PET/CT to detect large-vessel vasculitis is the accumulation of ^{18}F-FDG in atherosclerotic plaques. This occurs in about 50% of all PET scans, although it can potentially be distinguished from vasculitis by the lower grade of uptake.[2,9] Infection control protocols are also required for the performance of PET/CT scans in patients with COVID-19, which may limit its use in daily practice. An additional consideration is the fact that PET/CT involves radiation, especially when repeat scans may be required for monitoring the degree of vascular inflammation. PET/MR and novel MR contrast agents (e.g., ultrasmall superparamagnetic iron oxide) are promising alternatives for the diagnosis and prognostication of large-vessel vasculitis without the use of radiation, but their application has not been investigated in the context of COVID-19.[10]

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