



# The role of $^{18}\text{F}$ -FDG PET for COVID-19 infection: myth versus reality

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To date, the whole population is at risk of infection with the coronavirus COVID-19 (SARS-CoV-2); in particular, older people, often frail and subject to multimorbidity, are at highest risk for severe and fatal disease.

COVID-19 infection can be confirmed based on the patient's history, clinical manifestations, imaging characteristics, and laboratory tests [1]. Nucleic acid testing (RT-PCR) is the gold standard for the diagnosis of COVID-19 infection, but with a non-negligible false-negative rate.

About imaging methods, based on available data, chest CT is the routine-preferred method for screening, diagnosis and monitoring of COVID-19 pneumonia. Multiple and bilateral patchy ground glass opacities with peripheral distribution involving several pulmonary lobes are typical chest CT imaging features of the COVID-19 pneumonia [1].

Fluorine-18 fluorodeoxyglucose positron emission tomography/CT ( $^{18}\text{F}$ -FDG PET/CT) has been proposed as a non-invasive imaging method for detecting infectious or inflammatory diseases. The ability of  $^{18}\text{F}$ -FDG PET/CT to identify sites of inflammation and infection is mainly related to the glycolytic activity of the cells involved in the inflammatory response. In this regard, it has been demonstrated

that cells involved in infection and inflammation, especially neutrophils and the monocyte/macrophage family, are able to express high levels of glucose transporters and hexokinase activity. Notably,  $^{18}\text{F}$ -FDG PET/CT may early detect pathophysiological changes in affected tissues in patients with infectious or inflammatory diseases and these functional changes may occur before anatomical changes detected by conventional imaging techniques. Enough evidence-based data in the literature already exist about the usefulness of  $^{18}\text{F}$ -FDG PET/CT in the diagnosis and management of several infectious and inflammatory diseases [2].

Recently, some case reports and small case series have shown  $^{18}\text{F}$ -FDG PET/CT findings in patients with acute respiratory disease caused by COVID-19 infection. In particular, in the most large series described by Qin et al. [3],  $^{18}\text{F}$ -FDG PET/CT results from four patients with suspicious COVID-19 infection were described. The patients were admitted to the hospital with respiratory symptoms and fever when the COVID-19 outbreak was still unrecognized and the virus infectivity was unknown. All patients had typical chest CT imaging features of the COVID-19 pneumonia as described above. At  $^{18}\text{F}$ -FDG PET/CT, lung lesions were characterized by increased  $^{18}\text{F}$ -FDG uptake and there was evidence of lymph node involvement. Conversely, disseminated disease was absent suggesting that COVID-19 has pulmonary tropism. In their conclusion, the authors suggested a potential clinical usefulness of  $^{18}\text{F}$ -FDG PET/CT in patients with suspicious COVID-19 infection, especially at early stages when clinical symptoms are not specific and differential diagnosis is challenging [3].

Unfortunately, based on objective data, the “myth” of the potential usefulness of  $^{18}\text{F}$ -FDG PET/CT in patients with known or suspicious COVID-19 infection (as suggested by Qin et al.) collides with the “reality”.

The findings of increased metabolic activity in pulmonary or lymph nodal lesions in patients with COVID-19 infection is not surprising as acute inflammatory and infectious

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pulmonary lesions are usually characterized by increased  $^{18}\text{F}$ -FDG uptake. Furthermore, these  $^{18}\text{F}$ -FDG PET/CT findings are not specific for COVID-19 infection, and they cannot be used for the differential diagnosis of pulmonary infections or inflammatory diseases.

$^{18}\text{F}$ -FDG PET/CT should not be recommended for the evaluation of patients with known or suspicious COVID-19 infection. Chest CT remains the suggested imaging method to evaluate COVID-19 pneumonia and it is yet demonstrated that radiological pattern is more accurate than RT-PCR. There are currently no data suggesting an added value of  $^{18}\text{F}$ -FDG PET/CT compared to chest CT in the management or outcome of patients with COVID-19 infection. Conversely,  $^{18}\text{F}$ -FDG PET/CT is more complex than chest CT leading a possible increased risk of disease spreading due to the longer time of  $^{18}\text{F}$ -FDG PET/CT procedure compared to chest CT. Most importantly, specific safety and prevention protocols should be followed in the Nuclear Medicine departments during the outbreak of COVID-19 to allow for safe nuclear medicine diagnosis and treatment procedures [4, 5].

Therefore, the hypothesis that  $^{18}\text{F}$ -FDG PET/CT is useful in the evaluation of COVID-19 pneumonia due to the peculiar metabolic behavior of this infection is excessive and not clearly demonstrated until now. On the other hand, nuclear medicine physicians should pay attention to incidental CT findings of interstitial pneumonia (with ground-glass opacities) suspected for COVID-19 infection detected at  $^{18}\text{F}$ -FDG PET/CT, as demonstrated by some recent reports [6, 7]. In clinical practice, the risk to have asymptomatic patients with COVID-19 infection who undergo nuclear medicine procedures including  $^{18}\text{F}$ -FDG PET/CT is not negligible [6, 7] and this is the “reality” about  $^{18}\text{F}$ -FDG PET/CT and COVID-19 infection.

## Compliance with ethical standards

**Conflict of interest** The author declares that he has no financial or non-financial competing interests.

**Ethical approval** This article does not contain any studies with human participants or animals.

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