EDITORIAL

PET and SPECT Imaging in the SARS-CoV-2 Pandemic

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In Europe, the annual incidence of pneumonia is variable between 1 and 1.7 per 1000 persons with an increasing mortality rate for elderly patients [1]. In the late 2019, a new coronavirus of zoonotic origin, called SARS-CoV-2 also characterized by acute respiratory consequences, was discovered in China. From December 2019 to 20th March 2020, more than 245,000 people were affected worldwide, with or without specific symptoms. In Europe, the number of infected patients is more than 100,000, until 20th March 2020.

Clinical symptoms and detection of viral RNA by nasopharyngeal tests represent the gold standard for diagnosis. However, the presence of breath shortness is further evaluated by using chest-X ray or chest computed tomography (CT) imaging. Typically, a SARS-CoV-2 pneumonia is characterized by different CT patterns, from the ground glass opacification to consolidation, with variable and less frequent pleural and thoracic lymph node involvement [2].

Nuclear medicine currently has a limited role in the diagnosis of SARS-CoV-2 pneumonia. Until to date, only 5 cases have been published by using ^{18}F-Fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT [3,4]. The authors described a typical metabolic pattern of inflammation with a more frequent mediastinal lymph node involvement, without showing a specific finding able to make a differential diagnosis with other causes. However, molecular imaging, and in particular hybrid imaging (i.e. single photon emission tomography-SPET/CT and PET/CT) can be helpful for the differential diagnosis between infectious and inflammatory pulmonary disease, for monitoring the response to therapy and for the evaluation after the end of treatment [5]. FDG PET/CT is an accurate diagnostic method able to detect infections and inflammations due to the activation of inflammatory cells associated with an increase in the expression of glucose transporters [5]. Furthermore, growth factors and cytokines released in inflammatory foci increase the affinity of glucose transporters for the deoxyglucose [6]. Several studies have confirmed that FDG uptake is proportional to the cellular metabolic rate and binds to the majority of infection and inflammation cells such as neutrophils, lymphocytes, eosinophil and macrophages [7, 8].

^{99m}Tc-HMPAO as well as FDG PET/CT have been used for the identification of pneumonia, particularly for a bacterial pneumonia, demonstrating an important role for the definition of an active vs. a chronic pattern of disease [7]. Furthermore, the presence of hybrid PET/CT or SPET/CT scanner can be helpful for monitoring early response to therapy, thanks to the concurrent anatomical and functional information, particularly in case of experimental trials. FDG PET/CT showed a high sensitivity in detection of inflammatory/infection foci, however, its specificity is not adequately sufficient, especially in case of lung infections [9], and therefore in the clinical scenario of COVID19 pandemic. CT scan, for accessibility and cost-effectiveness, represents the best tool for the identification of SARS-CoV-2 pneumonia, but, as suggested by Joob and Wiwanitkit [10], the usefulness of FDG PET/CT needs to be further analyzed, likely due to the recognition of its potential value in selected cases.

Different experiences with FDG PET/CT are now available in literature, as reported in Table **1** [3, 4, 11-13].

However, the authors underlined that the long period in PET scanner should be a possible risk for the investigation unit. Currently, the worldwide emergency needs a rapid and reproducible method to diagnose the SARS-CoV-2 complications; nevertheless, in view of new experimental therapies, information about the persistence of active inflammatory conditions or the appearance of fibrotic signs after therapy or the presence of pulmonary atelectasis or pleural effusion are strongly required. As largely demonstrated, FDG PET/CT is an optimal tool for the evaluation of an early metabolic response to chemotherapy or radiotherapy in lung cancer [14] and has shown an emerging role also for the assessment of immunotherapy that acts by simulating the immune-mediated systems [15]. Therefore, its utility in oncological filed would be translate also in other clinical scenarios.

Moreover, the recent discovery of a potential sepsis-induced coagulopathy due to SARS-CoV-2 infection [16, 17] opens the opportunity to use perfusion pulmonary scintigraphy with ^{99m}Tc-macroaggregate for the diagnosis of late embolism consequences.

In conclusion, nuclear medicine should be ready for many reasons. Firstly, the increasing diffusion of COVID19 needs particular recommendations in order to keep safe the employees and patients, as suggested by Huang *et al*. [18]. Secondly, nuclear

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Table 1. Studies employing FDG PET/CT during SARS-CoV-2 pandemia.

Author	References	Country	N of Patients	Outcome
Qin et al	[3]	China	4	FDG PET/CT can help in differential diagnosis of complex cases
Zou et al	[4]	China	1	FDG PET/CT detects SARS-CoV-2 pneumonia
Albano et al	[10]	Italy	6	Incidental findings suggestive of SARS-CoV-2 may be important in the hybrid systems, especially in asymptomatic patients
Polverari et al	[11]	Italy	1	FDG uptake in asymptomatic patients should be monitored
Kirienko et al	[12]	Italy	1	FDG reinforces CT imaging, in patients with symptomatic SARS-CoV-2

FDG: fluorodeoxyglucose; PET/CT: positron emission tomography/computed tomography.

medicine physicians need to learn the recognition of metabolic patterns of COVID19 signs and evaluate, through a multidisciplinary approach, a new diagnostic model for an accurate prediction of an early response to experimental therapies in SARS-CoV-2 complications.

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