



# Incidental SARS-CoV-2-related findings in asymptomatic patients in [<sup>18</sup>F]-FDG-PET/CT—potential insights

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Dear Sir,

It was with great interest that we read the recent publication of Setti et al. [1], who describe a case series of asymptomatic patients with SARS-CoV-2 (COVID-19)-related incidental changes at [<sup>18</sup>F]-FDG-PET in a centre located in a known pandemic hotspot (Bergamo, Italy). The authors must be congratulated for investing valuable time to contribute their knowledge under very difficult circumstances for their country and health system. A growing number of publications, letters and brief reports show the potential benefit of [<sup>18</sup>F]-FDG-PET/CT in the diagnosis of COVID-19 [2, 3]. We note with much interest increasing numbers of reports of incidental findings of SARS-CoV-2 infection at PET/CT and in co-registered CT for SPECT/CT [4, 5], along with numerous case reports of positive chest CT findings in asymptomatic patients [6, 7]. Indeed, in a cohort of patients from the cruise liner Diamond Princess, which at the time of its publication was the second largest cohort of SARS-CoV-2 patients outside of China, of 104 positive cases identified, 76% were asymptomatic, and roughly half of asymptomatic cases (54%) nevertheless showed positive CT findings [8]. Intriguingly, a growing number of reports show superior sensitivity for chest CT compared with the existing gold standard rt-PCR (Ai et al. 97% and Fang et al. 98% for CT, compared with 71% for rt-PCR) [10, 11]. Moreover, positive CT findings can precede positive laboratory testing, making a false-negative rt-PCR finding a potential diagnostic pitfall [12].

We wholeheartedly agree with Guedj et al. who argue in this journal that nuclear medicine and molecular imaging are well placed to shed new light on this novel coronavirus [9]. We are particularly fascinated by the observation that, despite the tens of thousands of PET/CT scans performed worldwide each day, save for a small number of studies from highly affected epicentres of the pandemic [1, 3], reports of COVID-19-related findings in the asymptomatic population are sparse and limited to rare incidental findings. While [<sup>18</sup>F]-FDG-PET/CT is hardly a practicable means of screening the general population for COVID-19, we wonder whether the frequency of incidental findings might shed light on the prevalence of the disease amongst the asymptomatic but largely high-risk population of individuals undergoing PET/CT. In particular, while differences exist between the high-resolution CT performed by respiratory radiologists and the co-registered low-dose CT for PET, the CT performed is nonetheless a diagnostic CT. We posit that the frequency of findings in such imaging gives a potential new insight into disease prevalence.

Indeed, in our own patient cohort at a University Clinic in Switzerland (at the time of writing in the top 20 countries for confirmed cases), we observed no findings commensurate with COVID-19 infection in  $n = 562$  consecutive cases at PET/CT starting from the date of the first confirmed case in Switzerland. This finding suggests that the prevalence of asymptomatic patients in our catchment area is low and may give insights into local patterns of transmission. In fact, the binomial proportion confidence interval for the population prevalence can be estimated by calculating a probability of success (i.e. a positive CT finding) based on the case of  $n = 562$  negative independent Bernoulli trials by the Wilson score. Taking into account reported values of the limited test sensitivity for SARS-CoV-2 related findings (54%) and specificity (25%) for a cohort of asymptomatic individuals undergoing CT [8], we estimate the prevalence to be 0.325% (95% confidence intervals (CI) 0–0.65%). This value corresponds

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remarkably well with an estimated prevalence by rt-PCR testing in the Swiss population (0.3% at the time of writing, [<https://www.corona-data.ch/>]), as well as prevalence estimates in other populations. Indeed, one of the best current insights into the prevalence of the disease in a general population comes from the recently published Icelandic study, where 6% of the population were randomly tested by rt-PCR, giving a prevalence of 0.6% (95% CI 0.3–0.9) [10].

We argue that such insights into asymptomatic disease burden are clinically highly relevant, given the notion of the asymptomatic and pre-symptomatic patient as a potential source of infection spread [11]. Furthermore, there is an urgent need for improved epidemiological data to understand better this pandemic. While laboratory testing is the gold standard, its availability is limited and consequently few population level studies have been published to date [12], making novel or overlooked sources of data potentially valuable. From a clinical standpoint, given that COVID-19 is a notifiable disease, nuclear medicine physicians should be alert to the potential for incidental findings, and others in the nuclear medicine community are to be congratulated for their rapid formulation of guidance for such cases [13].

Finally, we urge the nuclear medicine community to continue sharing data and new insights into this novel pandemic. There is still much to be learnt about the COVID-19 virus, and molecular imaging surely has a role to play here.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article reports a statistical analysis which did not require access to patient records. It does not contain any studies with human or animals performed by any of the authors.

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