Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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FDG PET/CT imaging features and clinical utility in COVID-19

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ABSTRACT

Purpose: To determine the imaging findings and potential clinical utility of FDG PET/CT in patients with laboratory-confirmed COVID-19.

Methods: We performed a single institution retrospective review of patients diagnosed with COVID-19 using real time reverse transcription–polymerase chain reaction (RT-PCR) who underwent FDG PET/CT for routine cancer care between March 1, 2020 to April 30, 2020, during the height of the pandemic in New York City, New York, United States. PET/CT scans were retrospectively reviewed for imaging findings suspicious for COVID-19. For positive scans, PET and CT findings were recorded, including location, FDG avidity (SUV_{max}) and CT morphology. Patient demographics and COVID-19 specific clinical data were collected and analyzed with respect to PET/CT scan positivity, lung SUV_{max}, and time interval between PET/CT and RT-PCR.

Results: Thirty-one patients (21 males and 10 females, mean age 57 years ± 16) were evaluated. Thirteen of 31 patients had positive PET/CT scans, yielding a detection rate of 41.9%. Patients with positive scans had significantly higher rates of symptomatic COVID-19 infection (77% vs 28%, $p = 0.01$) and hospitalizations (46% vs. 0%, $p = 0.002$) compared to patients with negative scans. Eleven of 13 patients (84.6%) with positive scans had FDG-avid lung findings, with mean lung SUV_{max} of 5.36. Six of 13 patients (46.2%) had extrapulmonary findings of FDG-avid thoracic lymph nodes. The detection rate was significantly lower when the scan was performed before RT-PCR versus after RT-PCR (18.8% ($n = 3/16$) vs. 66.7% ($n = 10/15$), $p = 0.009$). Lung SUV_{max} was not associated with COVID-19 symptoms, severity, or disease course.

Conclusion: FDG PET/CT has limited sensitivity for detecting COVID-19 infection. However, a positive PET scan is associated with higher risk of symptomatic infection and hospitalizations, which may be helpful in predicting disease severity.

1. Introduction

Coronavirus disease 2019 (COVID-19), an illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has affected over 76 million people in a worldwide pandemic.[1] The virus was first reported in late December 2019 in Wuhan, China, and has since spread rapidly worldwide.[2] Of all countries, the United States has the highest number of reported cases and deaths, with over 17.8 million cases and 317,000 deaths at the time of manuscript writing.[1]

New York City (NYC) was the early major epicenter for the COVID-19 pandemic in the United States. with approximately 203,000 laboratory-confirmed cases and 18,600 deaths in the first three months.[3] The first laboratory-confirmed case of COVID-19 in NYC occurred on February 29, 2020, and cases increased rapidly in the subsequent weeks, with a peak in cases and hospitalization during the week of March 29. While NYC began surveillance testing in January 2020, testing was limited by strict criteria due to lack of availability, with routine testing of hospitalized patients starting at the end of February. As a result of shortages in testing and personal protective equipment, New York State and NYC public health officials encouraged patients with mild symptoms to remain at home rather than seek medical care.[3]

While many studies have evaluated the role of chest computed tomography (CT) and chest radiographs in COVID-19,[4,5] investigations of ^{18}F-fluorodeoxyglucose positron emission tomography/computed

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tomography (FDG PET/CT) are limited to small retrospective studies and case series, including the first report from Wuhan, China[6] and later from Europe during the COVID-19 pandemic.[7] The literature on the United States' experience is limited to case reports and small case series.[7] Therefore, we conducted a systematic analysis to determine the detection rate and clinical value of FDG PET/CT in patients with COVID-19. We hypothesize that while FDG PET/CT will be limited in detecting COVID-19, PET scan positivity and lung PET uptake intensity will correlate with disease severity and clinical course.

2. Methods

2.1. Patients

We conducted a single-institution retrospective review of cancer patients with laboratory-confirmed COVID-19 and who underwent routine oncological FDG PET/CT imaging between March 1, 2020 and April 30, 2020. All patients had positive COVID-19 nasal swab tests using real-time reverse transcription-polymerase chain reaction (RT-PCR). A search of our hospital electronic medical record was performed and yielded 64 patients with positive COVID-19 RT-PCR and FDG PET/CT imaging. Based on the known incubation period and disease course of COVID-19,[8] we included all patients who had FDG PET/CT up to 2 weeks before a positive RT-PCR test or at any time after a positive RT-PCR within the study period. Thirty-one patients met inclusion criteria and were included in our analysis. The study was approved by the Institutional Review Board (IRB), including a waiver of informed consent compliant with the Health Insurance Portability and Accountability Act (HIPAA).

2.2. Data collection

Demographic and COVID-specific clinical data were reviewed and collected, including the date of positive RT-PCR test, signs and symptoms, hospital admission, clinical course, and death. Clinical notes were reviewed for symptoms of COVID-19 at both the time of the FDG PET scan and positive RT-PCR test. The average clinical follow-up period was 4 months. The time interval between RT-PCR and PET scan (in days) was calculated as the difference between the PET scan date minus the positive RT-PCR date. Using this definition, the RT-PCR date was denoted as time "0", with negative values when the PET scan was performed before RT-PCR and positive values when the PET scan was performed after RT-PCR.

2.3. ^{18}F-FDG PET/CT imaging protocol

PET CT was performed for routine clinical care using standard scanning procedure. Before intravenous injection of ^{18}F-FDG, patients fasted for at least 6 h and blood glucose levels were confirmed to be less than 200 mg/dL. Patients were injected with approximately 444 Mbq (12 mCi) of ^{18}F-FDG and then rested for 60 min before image acquisition. PET/CT scans were obtained with GE Discovery 690 or 710 PET/CT scanners (GE Healthcare - Waukesha WI). Low-dose CT images were obtained for anatomic localization and attenuation correction. Image reconstruction was performed using standard reconstruction software with an ordered-subset expectation-maximization algorithm and a Gaussian filter.

The nuclear medicine technologists took special precautions for confirmed or suspected COVID-19 positive patients, following recommendations reported in a prior communication.[9] Technologists were required to wear personal protective equipment (PPE), including face shields and N95 masks. After scan acquisition, the PET scanner room was immediately cleaned with germicidal disposable wipes, similar to room management in patients with contact precautions.

2.4. Image interpretation

FDG PET/CT images were reviewed retrospectively by two physicians, one board-certified in both nuclear medicine and diagnostic radiology and another board-certified in diagnostic radiology. Both reviewers were aware that all patients had laboratory-confirmed COVID-19. Body PET/CT scans (skull base to mid-thigh or vertex to toe) were reviewed using PET VCAR software package on an advanced workstation (GE Advantage Workstation, GE Healthcare - Waukesha WI) with specific attention to the lungs and thoracic nodes. PET/CT images were reviewed for abnormal PET and CT findings typical for COVID-19 as described in prior studies.[4,7] For the lungs, abnormal CT findings of ground-glass opacities (GGOs), opacities, consolidation, and combinations of these findings were recorded, along with location and distribution. PET images were assessed qualitatively for the presence or absence of FDG avidity. If FDG-avid, then region-of-interests were drawn around the lung findings to measure maximum standardized uptake value (SUV_{max}). Extrapulmonary thoracic findings of pleural effusion and abnormal thoracic lymph nodes were recorded, with abnormal lymph node defined as lymphadenopathy on CT (short axis $>$ 1 cm) or focal FDG avidity in the location of a lymph node (i.e., hilar) and SUV_{max} of nodal FDG avidity was measured. In patients with multiple FDG-avid lung or nodal findings, the location and FDG uptake of all findings were recorded, however, only the SUV_{max} for the "hottest" lesion was used for analysis. PET and CT images were compared qualitatively to determine whether abnormal findings and extent of involvement were better visualized on PET, CT, or equally. For extrathoracic findings, the remaining regions of the body were reviewed for foci of increased FDG avidity suspicious for COVID-19, i.e. increased splenic FDG avidity.

2.5. Statistical analysis

Continuous and categorical data were presented as mean with standard deviation and as number and percentage, respectively. Since the primary indication for FDG PET/CT was for cancer staging and not COVID-19, the detection rate was determined and calculated as the percentage of patients who had abnormal findings on FDG PET/CT suggestive of COVID-19. Fisher's exact test was performed to test for differences in proportions of categorical data when using small samples. Unpaired two-sample Wilcoxon rank-sum (Mann-Whitney) tests and Student's *t*-test were performed to test for differences in continuous data. For single comparisons, p-values <0.05 were considered statistically significant. All statistical analyses were performed using STATA 16.1 (StataCorp, College Station, Texas).

3. Results

3.1. Patient demographics

Table 1 summarizes patient demographics, primary tumor site, PET/CT indication, and COVID-19 specific clinical data for all patients and then dichotomized into patients with positive or negative PET/CT. The mean patient age was 57 years ± 16 (38–80 years), and majority were male (68%). Thirteen patients (41.9%) had positive PET/CT scans and eighteen patients (58.1%) had negative scans. About half (48%) of the patients were symptomatic, with fever (60%), cough (40%), and dyspnea (13%) as the most common signs and symptoms. Six patients were hospitalized, and one patient died from COVID-19. There was no difference in age or gender between patients with positive and negative scans ($p > 0.05$). Compared with patients with negative PET scans, patients with positive PET scans had significantly higher rates of symptomatic COVID-19 infection (77% vs. 28%, $p = 0.01$) and hospitalizations (46% vs. 0%, $p = 0.002$). Deaths from COVID-19 did not significantly differ between the two groups ($p = 0.2$).

All 18 patients with negative PET scans had follow-up thoracic

Table 1
Patient demographics and COVID-19 characteristics.

Parameter	All patients ($N = 31$)	PET/CT positive ($N = 13$)	PET/CT negative ($N = 18$)	P-value
Age (years)				
Mean ± SD (range)	56.5 ± 16 (15–86)	55.5 ± 10 (38–80)	57.5 ± 20 (15–86)	0.7[a]
Gender				
Male	21 (68%)	8 (62%)	13 (72%)	0.7[b]
Female	10 (32%)	5 (38%)	5 (28%)	
Tumor site				
Lymphoma	8 (26%)	4 (31%)	4 (22%)	
Gastrointestinal	5 (16%)	2 (15.3%)	3 (16%)	
Breast	3 (10%)	2 (15.3%)	1 (6%)	
Head/neck	6 (19%)	2 (15.3%)	4 (22%)	
Lung	3 (10%)	2 (15.3%)	1 (6%)	
Prostate	3 (10%)	1 (8%)	2 (11%)	
Genitourinary	2 (6%)	–	2 (11%)	
Bone	1 (3%)	–	1 (6%)	
PET/CT indication				
Staging/restaging	19 (61%)	6 (46%)	13 (72%)	
Treatment response	4 (13%)	3 (23%)	1 (6%)	
Follow-up	6 (19%)	3 (23%)	3 (16%)	
Diagnosis	2 (7%)	1 (8%)	1 (6%)	
COVID-19 signs and symptoms				
No	16 (52%)	3 (23%)	13 (72%)	**0.01**[b]
Yes	15 (48%)	10 (77%)	5 (28%)	
Fever	9 (60%)	5 (50%)	4 (80%)	
Cough	6 (40%)	3 (30%)	3 (60%)	
Dyspnea	2 (13%)	2 (20%)	–	
Myalgia	1 (7%)	1 (10%)	–	
Headache	1 (7%)	1 (10%)	–	
Respiratory failure	1 (7%)	1 (10%)	–	
AKI	1 (7%)	1 (10%)	–	
Hospital admission due to COVID-19				
Yes	6 (19%)	6 (46%)	0 (0%)	**0.002**[b]
No	25 (81%)	7 (54%)	18 (100%)	
Alive/dead?				
Alive	25 (81%)	9 (69%)	16 (89%)	0.2[b]
Dead	6 (19%)	4 (31%)	2 (11%)	
COVID-19 related	1 (17%)	1 (25%)	0	
Cancer related	5 (83%)	3 (75%)	2 (100%)	

Data are presented in counts (%) unless otherwise stated.
[a] Independent sample *t*-test.
[b] Fisher's exact test.

imaging. Of these patients, only three patients had positive imaging findings: one patient had serial chest radiographs with COVID-19 findings 2 weeks later, one patient had a positive CT chest 2 weeks later, and one patient had a positive chest radiograph 1 month later. The remaining 15 patients did not have findings suggestive of COVID-19 on follow-up imaging.

3.2. COVID-19 FDG PET/CT findings

Imaging findings of COVID-19 are summarized for the 13 patients with positive FDG PET/CT scans (Table 2). Eleven of 13 patients (84.6%) had FDG-avid lung findings, with a mean lung SUV_{max} of 5.36 ± 3.36 (1.58–11.5). In comparison, two patients (15.4%) had no abnormal lung FDG avidity, including one patient with non-FDG-avid GGOs and the other patient with no lung findings on either PET or CT, but FDG-avid mediastinal lymph nodes suggestive of COVID-19. For CT lung findings, ten patients (77.0%) had either GGOs (38.5%) or a combination of opacities and GGOs (38.5%). Seven patients (53.8%) had extrapulmonary findings, including five patients (38.5%) with FDG-avid mediastinal nodes, hilar nodes, or both, one patient (7.7%) with pleural effusions, and one patient (7.7%) with both FDG-avid lymph nodes and pleural effusions. Of the six patients with FDG-avid lymph nodes, the mean nodal SUV_{max} was 6.66 ± 5.44 (2.6–18.6); in four patients

Table 2
COVID-19 FDG PET/CT findings.

	Number of patients ($n = 13$)
PET lung findings	
Lung uptake	11 (84.6%)
No lung uptake	2 (15.4%)
Lung SUV_{max}[a]	5.36 ± 3.36 (1.58–11.5)
CT lung findings	
GGO	5 (38.5%)
Opacities	1 (7.7%)
Consolidation	0 (0%)
GGO + opacities	5 (38.5%)
GGO + consolidation	1 (7.7%)
No lung findings	1 (7.7%)
No. of lobes affected	
>2 lobes bilaterally	8 (61.5%)
2 lobes bilaterally	4 (30.7%)
No lobes affected	1 (7.7%)
Extrapulmonary findings (PET and CT)	
Presence of extrapulmonary findings	7 (53.8%)
Lymph nodes	5 (38.5%)
Pleural effusion	1 (7.7%)
Pleural effusion + lymph nodes	1 (7.7%)
No extrapulmonary findings	6 (46.2%)
Nodal SUV_{max}[a]	6.66 ± 5.44 (2.6–18.6)
If FDG avid nodes, adenopathy on CT? ($n = 6$)	Yes: 2 (33.3%) No: 4 (66.7%)
PET vs. CT: qualitative comparison	
Equal	10 (76.9%)
PET > CT	2 (15.4%)
PET < CT	1 (7.7%)

Data are presented in counts (%) unless otherwise stated.
[a] Mean ± SD (range).

(66.7%), these FDG-avid nodes were only visualized on PET, with no corresponding lymphadenopathy on CT. Comparing PET vs. CT, ten patients (76.9%) had equal extent and location of PET and CT findings; in two patients (15.4%), PET showed more findings than CT (i.e., foci of lung or nodal FDG avidity greater than CT). In one patient (7.7%), the CT demonstrated more findings than PET (non-FDG avid lung opacities on CT). No patients had extra-thoracic findings related to COVID-19. Figs. 1-3 show examples of different FDG PET/CT findings of COVID-19.

3.3. Detection rate of FDG PET/CT for COVID-19

All patients had a diagnosis of COVID-19 based on RT-PCR. Of 31 patients, 13 patients had a positive PET/CT with imaging findings suggestive of COVID-19, yielding a detection rate of 41.9%. To evaluate the influence of timing on FDG PET/CT positivity, patients were stratified according to the timing of PET vis-à-vis the date of their positive COVID-19 RT-PCR test (Table 3). Detection rate was significantly lower in patients undergoing PET scan before RT-PCR (18.8%; $n = 3/16$) than those undergoing PET scan after RT-PCR (66.7%, $n = 10/15$), $p = 0.009$. Fig. 4 shows the time intervals between PET scan and RT-PCR using the PCR date as time "0". The mean time interval was 4.19 days ±15.6 (range: −13.4–36.5). Mean time interval was higher ($p = 0.012$) for patients with positive PET scans (11.2 ± 14.8, range: −11.4–36.5), than for those with negative PET scans (−0.86 days ±14.5, range: −13.41–35.7).

3.4. COVID-19 lung FDG avidity and clinical variables

Using the 11 patients with FDG-avid lung findings, mean lung SUV_{max} was compared between groups stratified by COVID-19 clinical variables. There was no significant difference in mean lung SUV_{max} between symptomatic vs. asymptomatic patients ($p = 0.346$), patients with fever vs. no fever ($p = 0.100$), and patients who were admitted to

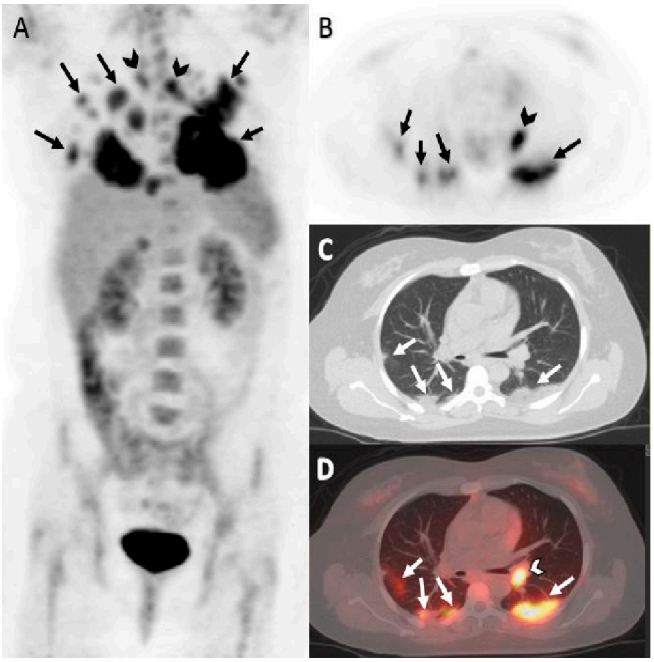

Fig. 1. 60 year old female with metastatic NSCLC with FDG PET/CT for radiation therapy planning. Patient reported muscle aches, headache and had a positive COVID-19 RT-PCR on the same day of the PET/CT. FDG PET maximum intensity projection (MIP) image (A) and axial PET, CT, and fusion PET/CT images (B-D) demonstrate newly detected FDG-avid bilateral opacities and consolidation, predominantly subpleural in location (arrows). The hottest opacity was in the left lower lobe with SUV_{max} of 11.5. FDG-avid hilar lymph nodes are also identified (arrowheads), with SUV_{max} of 6.2.

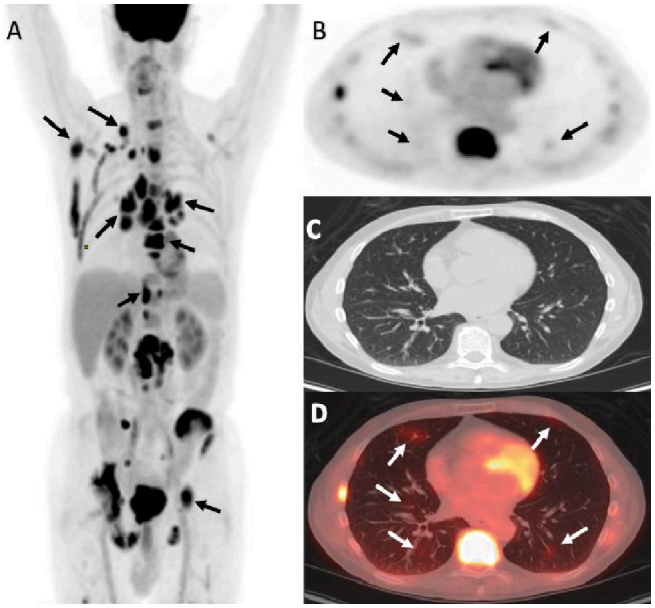

Fig. 2. 60 year old male with metastatic prostate cancer with FDG PET/CT for restaging disease following therapy. Patient reported fever and cough and had a positive COVID-19 RT-PCR 3 days after the PET/CT. FDG PET maximum intensity projection (MIP) image (A) demonstrates multiple FDG avid lymph nodes and bone lesions (black arrows) related to known history of metastatic prostate cancer. Axial PET, CT, and fusion PET/CT images (B-D) demonstrate new bilateral mildly FDG-avid scattered patchy foci with SUV_{max} of 1.56, predominantly subpleural in location (white arrows), consistent with COVID-19 pneumonia with no corresponding lesions seen on the low-dose CT (C).

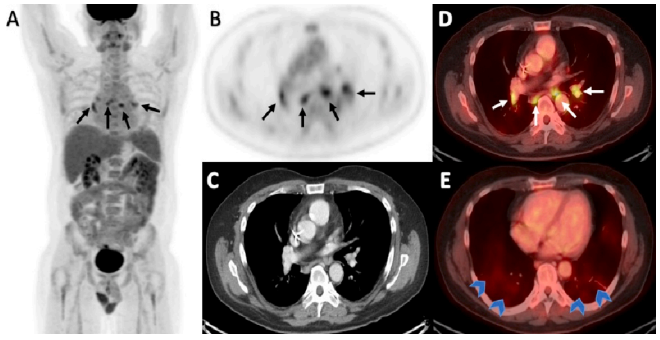

Fig. 3. 51 year old male with metastatic urothelial cancer with FDG PET/CT for restaging disease following therapy. Patient reported fever, cough and dyspnea and had a positive COVID-19 RT-PCR test 25 days before the PET/CT. FDG PET maximum intensity projection (MIP) image (A) and axial PET, CT, and fusion PET/CT images (B-D) demonstrate hypermetabolic subcarinal and hilar lymph nodes (arrows) with SUV_{max} of 4.8. No corresponding lymphadenopathy on low-dose contrast enhanced CT (C). Axial fusion PET/CT image (E) shows newly detected FDG avid opacities in the bilateral posterior lower lobes with SUV_{max} of 3.03, (blue arrowheads). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 3
Detection rate of FDG PET/CT for COVID-19 and influence of timing.

Order of tests	Number of patients (% of total)	Positive scan	Negative scan	P-value
Total patients	31 (100%)	13 (41.9%)	18 (58.1%)	
PET performed before COVID-19 RT-PCR (negative days)	16 (51.6%)	3 (18.8%)	13 (81.3%)	0.009
PET performed after COVID-19 RT-PCR (positive days)	15 (48.4%)	10 (66.7%)	5 (33.3%)	
Time interval	All patients	Positive scans	Negative scans	
Mean time from COVID-19 RT-PCR to PET scan (days)[a]	4.19 ± 15.6 (−13.4–36.5)	11.2 ± 14.8 (−11.4–36.5)	−0.86 ± 14.5 (−13.41–35.7)	0.012

[a] Mean ± SD (range).

the hospital vs. not admitted ($p = 0.247$). Results are summarized in Table 4.

4. Discussion

Cancer patients are more susceptible to infection and mortality from COVID-19.[10] This study evaluates FDG PET/CT findings and detection rate of COVID-19 in a cohort of cancer patients during the peak of the pandemic in NYC.

In our study, the detection rate of FDG PET/CT for COVID-19 was 41.9%. No prior studies have reported FDG PET/CT detection rates to allow for comparison, but the rate in our study was much lower than the pooled sensitivity of 92% for CT chest.[11] This difference may be, at least in part, because the clinical indication for CT chest in those studies was to diagnose patients with suspected COVID-19 and were therefore performed around the same time as RT-PCR (1–3 days) and the onset of symptoms.[11] In contrast, in our study, COVID-19 was incidentally detected on PET scans performed for routine cancer. Patients with positive FDG scans were more likely to have symptomatic COVID-19 infection and be hospitalized, suggesting that the presence of PET/CT findings is associated with the severity of COVID-19 infection. However, the intensity of lung FDG uptake (SUV_{max}) was unrelated to the presence

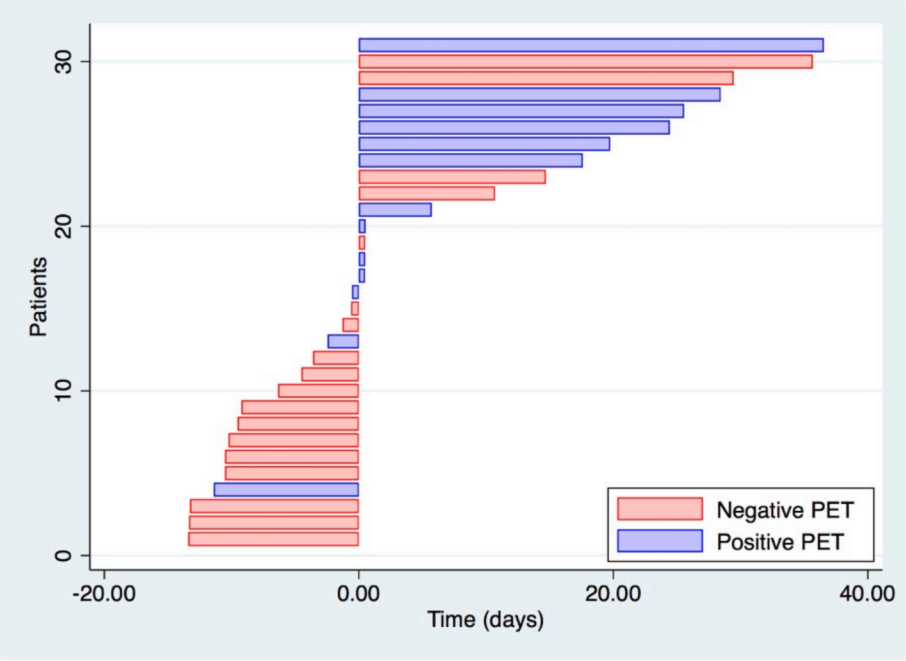

Fig. 4. Positive and Negative PET scans based on Time Interval between COVID-19 RT-PCR to PET scan. Time intervals for all patients between FDG PET/CT and COVID-19 RT-PCR using the PCR date as time "0", with negative values when the PET was performed before RT-PCR and positive values when PET was performed after RT-PCR.

Table 4
COVID-19 clinical characteristics and PET Lung SUV_{max}.

Clinical variable	Lung SUV_{max}, mean ± SD (range)	P-value
Symptoms		
Asymptomatic ($n = 2$)	6.45 ± 3.17 (4.21–8.69)	0.346
Symptomatic ($n = 9$)	5.12 ± 3.54 (1.58–11.5)	
Fever status		
No fever ($n = 5$)	6.55 ± 3.37 (3.17–11.5)	0.100
Fever (n = 6)	3.93 ± 3.07 (1.58–9.31)	
Admission status		
No admission (n = 5)	6.25 ± 3.68 (3.17–11.5)	0.247
Admission (n = 6)	4.62 ± 3.21 (1.58–9.31)	

of symptoms, fever, or hospitalization. The timing of PET scans in relation to RT-PCR influenced detection rates for COVID-19, with significantly lower rates when PET scans were performed before RT-PCR than after RT-PCR.

In contrast to prior studies, which either lacked RT-PCR confirmation or had low numbers of laboratory-confirmed cases,[12–14] COVID-19 was confirmed in all of our patients by RT-PCR. Several prior studies evaluated FDG PET/CT for findings of interstitial pneumonia suspicious for COVID-19 infection and reported the rates of such findings, ranging from 2.1% to 16.2%.[7] Three studies compared the rates of interstitial pneumonia to a date-matched control group from 2019, with two studies from Naples and Lombardy regions in Italy demonstrating significantly increased rates of interstitial pneumonia in 2020,[13,14] while one study from London, United Kingdom, did not show a difference from the 2019 control group.[12] While increased rates of interstitial pneumonia may be due to COVID-19, the presence of CT lung findings without RT-PCR confirmation lacks specificity and may be due to other infectious or inflammatory causes. Indeed, the reported specificity of CT lung features is relatively low at 25–33%, as there may be considerable overlap with other viral and bacterial pneumonias.[11]

FDG PET is known to detect inflammation due to increased anaerobic glycolysis in activated lymphocytes.[15] A few studies have investigated the potential clinical value of lung SUV_{max}. In a French study in 22 patients with suspicious CT findings, 50% had COVID-19 infection, while the other half had negative COVID-19 testing and were thought to have bacterial pneumonia. The COVID positive group had larger CT abnormalities but lower rates of consolidation and lower lung SUV_{max} compared to the COVID negative group.[16] A Spanish study in 23 patients did not find any difference in lung SUV_{max} between the COVID positive and control groups.[17] A prospective study from Monaco in 13 patients evaluated $SUV_{max} \geq 7$ vs. <7, respectively, for assessing "inflammatory" vs. "low inflammatory" findings and found no correlation of the inflammatory status with CT chest evolution or clinical outcome.[15] Similarly, in our study, lung SUV_{max} was also highly variable and not associated with COVID symptoms, severity, or disease course.

Extrapulmonary findings in our study were present in about half of patients, with mediastinal and hilar nodes as the most frequent finding, similar to the rate in another study.[17] In addition, most FDG-avid lymph nodes were only visualized on PET images without corresponding enlarged nodes on CT. This is consistent with a prior meta-analysis on CT chest, in which lymphadenopathy was a rare finding, occurring in only 3.38% of COVID-19 patients.[4]

The clinical manifestations of COVID-19 pneumonia can be non-specific and indistinguishable from other causes of viral pneumonia and other respiratory diseases.[18,19] Therefore, accurate and early detection is crucial for outbreak control and early management. Despite the high specificity of RT-PCR, it has a relatively low sensitivity of 60–70%.[20,21] The role of imaging has been evolving with possible applications for initial diagnosis and disease monitoring to assess severity, treatment response, and complications. Chest radiography and CT chest are the most commonly used imaging modalities.[22,23] Chest radiography is considered the modality of choice in hospitalized patients for baseline imaging and monitoring disease progression but has low sensitivity for detecting early or mild disease. While CT chest is more sensitive than radiography for COVID-19,[22,24] it is not recommended for screening or diagnosis in patients with mild or asymptomatic disease and instead is utilized in specific clinical settings to determine management, such as suspected disease progression, worsening respiratory status, or evaluation of additional diagnoses.[22,25–28]

FDG PET has emerged as a non-invasive technique for diagnosing and monitoring infectious diseases.[29] In the setting of acute infection,

neutrophils depend on anaerobic glycolysis to maintain cellular activity and glucose transporters are overexpressed in activated inflammatory cells, leading to increased FDG uptake. The pathophysiology of COVID-19 pneumonia involves the accumulation of alveolar macrophages and neutrophils due to immune host response and subsequent release of inflammatory cytokines.[30] FDG uptake can be detected when neutrophils are activated and sequestered within the lungs before their transendothelial migration into airways[24,31] and therefore, FDG PET has been postulated to have potential applications in detecting COVID-19 pneumonia.[30–32]

Our study has several limitations. First, the inclusion time window to include PET scans performed within two weeks before RT-PCR test was determined by the study investigators based on the COVID-19 disease time course, which may influence the time interval analysis. Second, our cohort was based on patients with positive RT-PCR tests performed at our institution. Given the circumstances of the pandemic, there may have been patients with COVID-19 and FDG PET/CT at our institution, who either did not have RT-PCR performed at our institution or did not have confirmatory testing due to limited testing,[3] and these patients were not included and limited our cohort size. Third, we used RT-PCR as the reference standard; however, the test may have limited sensitivity due to false-negatives.[4,11] Lastly, our study is limited by self-selection and referral biases, as patients may have elected to postpone cancer care and cancer imaging during that time.[9] Therefore, our cohort may have included patients with more severe illness, either due to COVID-19 or their underlying cancer. Nevertheless, our study is thus far the largest cohort of patients with confirmed COVID-19 infection who underwent FDG PET/CT imaging.

5. Conclusion

FDG PET/CT has limited sensitivity for detecting COVID-19 infection. However, a positive PET scan is associated with a higher risk of symptomatic infection and hospitalizations, which may help predict disease severity. FDG PET may also visualize reactive thoracic nodes from COVID-19 infection better than CT. These factors should be considered when interpreting FDG PET/CT in patients with suspected or known COVID-19.

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Declaration of competing interest

No potential conflicts of interest relevant to this article exist.

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