Original Article

Incidentally Detected COVID-19 Lung Changes during Oncologic Fluorodeoxyglucose Positron Emission Tomography-Computerized Tomography Studies: Experience from Tertiary Care Cancer Hospital

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Abstract

Objective: The objective is to evaluate incidental detection of COVID-19 lung involvement in asymptomatic individuals who undergo fluorodeoxyglucose (FDG) positron emission tomography-computerized tomography (PET/CT) scans for oncologic indications. **Patients and Methods:** The study was conducted in a tertiary care oncology hospital and included patients who were asymptomatic for COVID-19 infection and underwent FDG PET/CT scans for standard oncologic indications between April 15, 2020, and September 30, 2020. Patients who showed CO-RADS category 4/5 changes (high level of suspicion) on the CT chest component of the PET/CT study were considered for analysis. CT severity score, presence of FDG uptake, and maximum standardized uptake value of FDG avid lung involvement were noted and correlated with reverse transcriptase-polymerase chain reaction (RT-PCR) test. **Results:** 1982 PET/CT scans were performed, 78 (3.9%) patients showed lung changes with high degree of suspicion of COVID-19 pneumonia (CO-RADS 4/5). Hematolymphoid and head-neck cancer were the most common tumor types (23%), and restaging/response evaluation was the most common PET/CT indication. Of the patients who underwent RT-PCR testing, 70% showed a positive result. The mean CT severity score was 6 (standard deviation 5.9) with no significant difference seen between the RT-PCR positive and negative groups. FDG avidity in lung lesions was noted in 41 out 57 (72%) patients. A significant correlation was seen between the RT-PCR positivity and FDG uptake in lung lesions. **Conclusion:** A small but significant proportion of patients undergoing routine oncologic PET/CT scans showed incidental COVID-19 lung involvement. Lung involvement in these asymptomatic patients showed a low CT severity score in all patients and FDG avidity in majority. Timely detection of such incidental cases can initiate further confirmatory RT-PCR testing and isolation measures that not only influence patient's cancer treatment protocols but also have a larger community impact of limiting the spread of infection.

Keywords: *COVID-19, fluorodeoxyglucose positron emission tomography, lung*

Introduction

SARS-COV-2 a novel coronavirus of zoonotic origin initially detected in Wuhan, China, in December 2019, caused an aggressive type of respiratory syndrome called COVID-19.[1] Rapidly, it became a global pandemic spreading across many countries. Commonly described symptoms of mild COVID-19 infection are fever, cough, dyspnea, and fatigue though a vast majority of infected people remain asymptomatic.[1,2] Reverse transcriptase-polymerase chain reaction (RT-PCR) testing from nasal and nasopharyngeal mucosal swabs is the accepted standard for diagnosis of COVID-19; however, false-negative results are seen in approximately 30% cases.[3-6] Asymptomatic individuals and those with a falsely negative RT-PCR test can potentially infect their family members and spread infection in the community. Several reports have described imaging features of COVID-19 pneumonia on computerized tomography (CT) scans such as subpleural ground-glass opacities (GGOs) and consolidations.[3-6] PET is not recommended in the evaluation of COVID-19 pneumonia; however, a few recent reports have described the pattern of COVID-19 lung involvement incidentally seen on fluorodeoxyglucose (FDG) positron emission tomography-CT (PET/CT)

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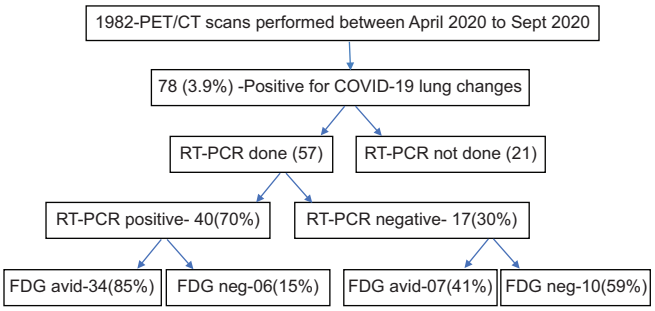
when they were performed for oncologic indications.[7-15] Asymptomatic but infected individuals with incidentally detected COVID-19 lung changes can be further subjected to RT-PCR testing for confirmation. This has implications on patient management by modifying or delaying the planned treatment. It can further promote and re-emphasize adherence to strict containment measures by the Nuclear Medicine department personnel to limit the spread of infection in such situations. After the 1st case was detected in India on January 30, 2020, infections started showing a rising trend from March 2020 onward.[16] Although there was a nationwide lockdown to curb the spread of pandemic, hospitals such as ours continued to provide comprehensive cancer care with certain modified protocols and strategies.[17,18] Being an essential part of cancer diagnostics, PET/CT facility was functional and provided regular service to cancer patients during the pandemic. The purpose of this study was to evaluate the role of routine oncologic PET/CT studies in incidental detection of COVID-19 infection in asymptomatic individuals.

Patients and Methods

The study was conducted in a tertiary care oncology center and included asymptomatic patients whose FDG PET/CT scans were performed for standard oncologic indications between April 15, 2020, and September 30, 2020. According to the institute COVID-19 protocol, all patients were triaged on the basis of temperature screening and careful history-taking prior to initial access to the hospital and then again before entering the PET/CT unit and were deemed to be asymptomatic for COVID-19 infection. Demographic, clinical, and pathological data were obtained from electronic medical records, and imaging data were acquired from hospital picture archival and communications systems. Protocol was approved by the institutional ethics committee, and individual patient consent was waived due to the retrospective nature of the study. Telephonic consents were obtained for patients imaged after July 30, 2020, due to amendment in the study protocol.

Fluorodeoxyglucose positron emission tomography-computerized tomography technique

After confirming the blood glucose levels to be <150 mg/dl, PET/CT studies were performed 60–90 min following intravenous injection of 5 MBq/kg of ^{18}F-FDG. All patients were fasting for at least 6 h prior to the intravenous administration of ^{18}F-FDG. Scans were performed using Philips Gemini time of flight (TOF) TF 16/64 slice PET/CT scanners (PET crystal-LYSO), Philips Healthcare (Cleveland, OH, USA). Whole-body CT scanning was performed in craniocaudal direction (120 kV, automated mA) without any breath-hold instructions. Eighty milliliters of low osmolar nonionic IV contrast was administered in all eligible patients at a rate of 1.8 ml/second, and scan delay was 50 s. Contrast-enhanced CT was used for diagnostic purpose and for attenuation correction of the PET data.



Flow Chart 1: STARD type diagram demonstrating selection and flow of patients in the study with test results. FDG: Fluorodeoxyglucose, RT-PCR: Reverse transcriptase polymerase chain reaction, PET/CT: Positron emission tomography-computerized tomography, COVID-19

A separate sequence with breath holding was acquired prior to the whole body contrast CT for the evaluation of the lungs (120 kV, 250 mAs). PET scanning was performed immediately after the CT acquisition, without changing the patient position with an acquisition time of 90 s for each bed position. PET scans were acquired in three-dimensional mode and images were reconstructed iteratively using row action maximum likelihood algorithm. CT attenuation correction, decay correction, and dead time correction were applied. The maximum standardized uptake values (SUVs) were automatically generated according to the following equation: $SUV_{max\ (bw)} = C_{tis}/D_{inj}/bw$, where $SUV_{max\ (bw)}$ is the maximum SUV normalized for the bodyweight, C_{tis} is tissue concentration expressed as megabecquerels per milliliter, D_{inj} is injected dose expressed as megabecquerels, and bw is bodyweight expressed as kilograms.

Image and data analysis

CT chest component of the whole-body PET/CT scan acquired as a separate breath-holding sequence was evaluated for COVID-19 lung changes. Data of only those patients who showed category 4/5 changes (high level of suspicion) on the COVID-19 reporting and data system (CO-RADS) was used for analysis.[19] CO-RADS developed by the Dutch Radiological Society provides a framework for structured and fast reporting of COVID-19 pulmonary involvement increasing interobserver agreement and reducing ambiguity. CT severity score was calculated based on percentage involvement of each lobe, with 0 as no involvement, 1 being the lowest, and 25 being the highest score.[20,21] The presence or absence of FDG uptake in the areas of lung involvement was also noted. CT severity score, presence of FDG uptake, and SUV_{max} of FDG avid lung involvement was correlated with RT-PCR test. PET/CT studies and CT chest were reviewed and interpreted by experienced nuclear physician and radiologists. Categorical variables were represented as numbers and percentages, whereas descriptive statistics were used for quantitative data.

Results

Between April 15, 2020, and September 30, 2021, 1982 patients underwent FDG PET/CT scans for standard

oncologic indications. 78 (3.9%) patients (M:F, 51:27) with a median age of 51 years (range 38–62) showed lung changes with high degree of suspicion of COVID-19 pneumonia (CO-RADS 4/5) and were considered for analysis. Table 1 shows the patient characteristics, primary tumor type and PET/CT indication and month-wise distribution of cases. All patients were asymptomatic for COVID-19, and the lung changes were detected incidentally. The highest number of patients with positive findings were seen in the month of June (24/78, 31%) followed by September (18/78, 23%). Indication for PET/CT for the 78 patients with COVID-19 pneumonia was as follows: Diagnosis and initial staging 21 (27%), restaging and response evaluation 54 (69%), surveillance and follow-up 3 (4%). Primary tumor site distribution was as follows: Hematolymphoid-18 (23%), head-neck-18 (23%), thoracic-17 (22%), breast-8 (10%), Genito-urinary-7 (9%), gastro-intestinal-6 (8%), bone soft tissue-4 (5%). Fifty-seven patients underwent RT PCR testing within a week of the PET/CT study. 40 out of the 57 (70%) patients who underwent testing showed a positive RT-PCR result. Repeat RT-PCR testing was not done in patients with initial negative test result. The mean CT severity score was 6 (standard deviation 5.9). No significant difference was seen in the CT severity scores between the RT-PCR positive (median 6, range, 3–13) and negative (median 6, range 3–8) groups (P = 0.366). FDG avidity was noted in 41 out 57 (72%) patients. Out of the 40 patients who showed a positive RT-PCR test, 34 showed FDG avidity thus showing a strong correlation between the two (34/40, p-0.004). No significant correlation was seen between SUV_{max} and RT-PCR positivity (median SUV_{max} 4.11 vs. 4.08, P = 0.967). Study results are summarized in the form of a STARD type diagram [Flow chart 1].

Table 1: Patient characteristics, primary tumor type and positron emission tomography/computerized tomography indication and month wise distribution of cases

Variable	*n*=78
Gender	
Male	51
Female	27
Indication	
Initial staging	21
Restaging	54
Follow up	3
Primary site	
Hematolymphoid	18
Head-neck	18
Thoracic	17
Breast	8
Genitourinary	7
Gastrointestinal	6
Bone-soft tissue	4
Month	
April	4
May	13
June	24
July	8
August	11
September	18

Discussion

Since the outbreak of the global pandemic there has been a plethora of scientific reports and investigations evaluating the utility of chest CT in diagnosis and severity assessment of COVID-19 pneumonia. Objective scores like the CO-RADS and disease severity indices like the CT severity score are routinely used in clinical practice. Diagnostic accuracy and prognostic utility of these CT chest parameters have been primarily tested in symptomatic patients. However, there is paucity of information regarding the utility of CT chest and other imaging techniques in diagnosing COVID-19 infection in individuals who are asymptomatic. This is expected because imaging is not routinely recommended for screening of asymptomatic individuals or close contacts of RT-PCR-positive patients. Since the most modern PET/CT protocols include a CT chest component, it would be a worthwhile exercise to evaluate its utility in diagnosing asymptomatic COVID-19 lung involvement in cancer patients. It would also help us understand the metabolic characteristics of pulmonary lesions, intensity of FDG uptake, and its relation with RT-PCR and CT severity scores. Nearly 4% of the total PET/CT scans performed during the study period showed lung findings suggestive of COVID-19 pneumonia on the CT chest component of the examination. These findings were unilateral or bilateral GGOs with or without consolidation classically described in literature as CO-RADS category 4/5.[18] Data from Nantes-France and Lombardy-Italy of asymptomatic patients undergoing oncologic PET/CT scans during the pandemic period showed a percentage of cases with lung involvement similar to ours (4.2% and 3.8%).[12,13] Studies from other regions in northern and southern Italy reported a higher percentage (9%), with the highest incidence reported from Egypt (11.3%).[10,14,15] These differences could be attributed to variations in the prevalence of COVID-19 in the community across various regions. Majority of patients (69%) who showed incidental COVID-19 lung changes were undergoing active cancer treatment or had recently completed it (response evaluation and restaging). Effects of cancer itself and anti-cancer therapy adversely impact the immune status rendering these patients more susceptible to infection and its resultant complications. Utilizing PET/CT in detecting asymptomatic COVID-19 infections in such patients provides an added benefit beyond its oncologic usefulness.

A significant proportion of patients (57/78, 73%) who had lung changes on PET/CT underwent a confirmatory RT-PCR

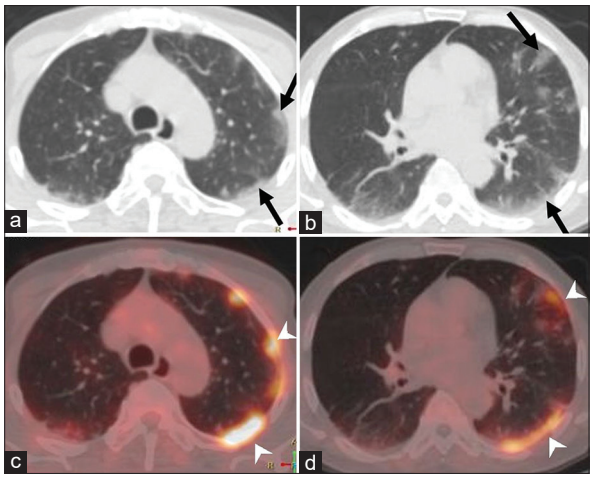


Figure 1: COVID-19 lung changes showing fluorodeoxyglucose uptake. Restaging fluorodeoxyglucose positron emission tomography- computerized tomography in a 61 year old man with non-Hodgkins lymphoma. Axial computerized tomography images of the lungs (a and b) at different levels show bilateral subpleural ground glass opacities (arrows). Fused positron emission tomography- computerized tomography images (c and d) show fluorodeoxyglucose avidity in the ground glass lung opacities (arrowheads)

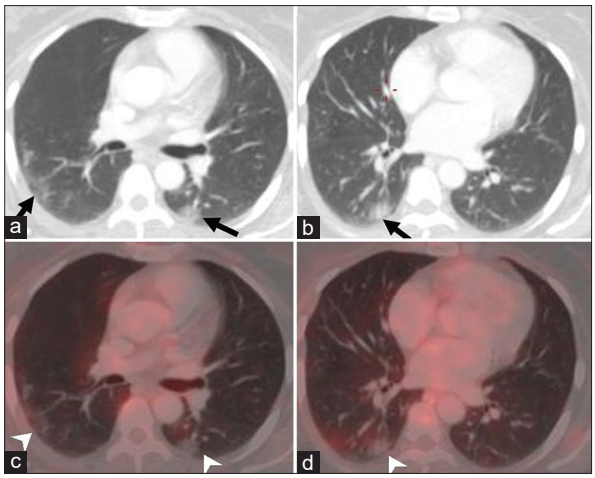


Figure 2: COVID-19 lung changes with no fluorodeoxyglucose uptake. Staging fluorodeoxyglucose positron emission tomography- computerized tomography in a 49 year old lady with lymphoma of the central nervous system. Axial computerized tomography images of the lungs (a and b) at different levels show bilateral subpleural ground glass opacities (arrows). Fused positron emission tomography- computerized tomography images (c and d) shows absence of fluorodeoxyglucose uptake in the ground glass lung opacities (arrowheads)

test within a week of the scan, with 70% (40/57) showing a positive test result confirming COVID-19 infection. These patients were asked to quarantine with initiation of contact tracing measures. Planned cancer treatment was also modified in these patients as per hospital norms instituted during the pandemic. The availability of RT-PCR correlation in majority of cases is one of the strengths of our study. Except for the Egyptian study by Ali *et al*.[14] most of the other larger studies involving PET/CT do not have RT-PCR confirmation of imaging findings. This could be because of the prevailing health policies at that time of not subjecting asymptomatic patients to RT-PCR testing. As the pandemic evolved and with a better understanding of the utility of CT chest as a diagnostic tool, there was increased RT-PCR testing of asymptomatic patients with positive lung findings on PET/CT scans. In our study, 70% of patients (40/57) with CO-RADS category 4/5 changes tested positive on RT-PCR. Egyptian study by Ali *et al*.[14] showed that 60% of patients with features of COVID-19 pneumonia on FDG PET/CT tested positive on RT-PCR, which is similar to the findings in our study. However, when patients were subjected to repeat RT-PCR testing, the sensitivity increased from 60% to 96%. RT-PCR retesting for asymptomatic patients with an initial negative result was not performed in our hospital at the time of the study. Studies comparing detection rates of CT chest and RT-PCR have shown that in case of discordant findings, a significantly high number of patients showed a positive CT and negative RT-PCR result.[5] This could be due to known false negativity of RT-PCR test probably because of inadequate viral load or technical issues during nucleic acid extraction.[4,6] Since our cohort consisted of individuals who were asymptomatic for COVID-19, a moderate detection rate of 70% for PET/CT was not unexpected. Likewise, the low CT severity index (mean, 6) reflects limited lung involvement probably due to a low viral load and resultant lack of clinical symptoms. Similar observations were also reported in a few published studies wherein low CT severity score was seen in patients with mild symptoms or no symptoms.[20,21]

FDG uptake in the lung changes was observed in 72% of patients in our study [Figures 1 and 2]. Varying degree of FDG avidity in the COVID-19 lung changes on PET/CT has been reported.[7-14] This is not entirely surprising as FDG is known to concentrate in infectious/inflammatory pulmonary lesions as was observed during the H1N1 influenza pandemic.[22] We could also find a statistically significant correlation between the RT-PCR positivity and FDG uptake. 85% (34/40, $P = 0.004$) of RT-PCR positive patients showed FDG uptake in the pulmonary lesions. Although a correlation was observed between the two parameters, it is difficult to ascertain the reasons behind it and conclusions that could be drawn from it. Unfortunately, we could not compare these findings with published studies as they have not focused on establishing a correlation between FDG uptake and RT-PCR results.

Conclusion

Although FDG PET/CT is not recommended for the evaluation of patients with suspected or known COVID-19 infection, this hybrid imaging technology which fuses anatomical CT scan to PET can be put to effective use during a pandemic. Physicians should pay careful attention and familiarize themselves with typical lung findings to detect COVID-19 pneumonia on PET/CT scans performed for oncologic indications. Although such incidentally

detected COVID-19 cases are a small fraction of the total number of patients undergoing PET/CT scans; they assume significance when one considers their potential to spread the infection to health care workers, family members, and the community in general. An astute nuclear medicine physician by ensuring timely detection of such cases can initiate further confirmatory testing and isolation measures. This will not only influence patient's cancer treatment protocols but also have a larger community impact of limiting the spread of infection.

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Conflicts of interest

There are no conflicts of interest.

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