Clinical PET/CT utilization during the COVID-19 pandemic: initial experience at Yale University

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Objective To determine temporal changes in PET/CT utilization during the COVID-19 pandemic and examine the impact of epidemiologic, demographic and oncologic factors on PET/CT utilization.

Methods Clinical PET-CT utilization between 1 January 2020 and 15 June 2020 at a tertiary academic center was assessed using change-point-detection (CPD) analysis. COVID-19 epidemiologic trend was obtained from Connecticut Department of Public Health records. Demographic and oncologic data were gathered from electronic medical records and PET-CT scans by four reviewers in consensus.

Results A total of 1,685 cases were reviewed. CPD analysis identified five distinct phases of PET-CT utilization during COVID-19, with a sharp decline and a gradual recovery. There was a 62.5% decline in case volumes at the nadir. These changes correlated with COVID-19 epidemiologic changes in the state of Connecticut, with a negative correlation between COVID-19 cases and PET-CT utilization ($\tau = -0.54$; $P$ value $<0.001$). Statistically significant differences in age, race, cancer type and current and prior scan positivity were observed in these five phases. A greater percentage of young patients and minorities were scanned during the pandemic relative to baseline. PET/CT scanning was less impacted for hematologic malignancies than for solid cancers, with less profound decline and better recovery.

Discussion PET-CT cancer imaging was vulnerable to the COVID-19 pandemic at our institution. Epidemiologic, demographic and oncologic factors affected PET-CT utilization. Nucl Med Commun 42: 1277–1284 Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

Keywords: cancer imaging, coronavirus disease 2019, North America, pandemics, PET/CT, severe acute respiratory syndrome coronavirus 2

Introduction Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a positive-sense RNA virus causing coronavirus disease 2019 (COVID-19), an ongoing pandemic claiming millions of lives [1–3]. Rapidly evolving SARS-CoV-2 outbreak continues with recent spikes in cases in some countries, while few have significantly curbed the numbers of new cases thanks to the recent deployment of vaccines [3]. Connecticut is a relatively small-sized northeastern state (approximate population 3.5 million) that is ranked #3 in healthcare access among the US states, according to US News data. The geographical proximity of the state of Connecticut to New York, an epicenter of the initial outbreak in the USA, resulted in the immediate spread of the virus in the Connecticut area as well. Governors of New York, New Jersey and Connecticut followed a similar course of action, and the timeline of the pandemic followed a similar path in this region. The first case in our hospital system was seen on 8 March 2020.

Decreased numbers of screening studies and elective surgeries, as well as on-in-person appointments took in place in parallel with state-wide administrative policy implementations. COVID-19 has less favorable clinical outcomes in patients with preexisting health conditions including cancer [4]. Unprecedented strain in healthcare systems and rapid development of the outbreak led to readjustment of cancer treatment, deferral of procedures and alteration of surveillance algorithms [5]. The dual danger of COVID-19 and cancer have forced practitioners to make decisions based on experience and risk/benefit analysis, particularly at the early stage of the pandemic, due mainly to the scarcity of clinical and epidemiologic data on COVID-19. Identification of factors that are potentially associated with the decline in molecular cancer imaging, will help better understand the dynamics of cancer imaging at the time of respiratory outbreaks. Providing real-world data during a pandemic may play a role in understanding potential vulnerabilities in similar future outbreaks or the future waves of COVID-19 outbreak that may ensue. This may also assist oncology practitioners to manage imaging studies of their patient population in an evidence-based approach.

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A decline in the volume of radiology studies as well as in nationwide new cancer diagnoses in 2020 as compared to prior years has been shown [6,7]. Two Italian studies recently demonstrated a potential increase in interstitial lung findings in cancer patients during the COVID-19 pandemic [8,9]. The impact of the COVID-19 pandemic on cancer imaging based on factors such as cancer types, patient demographics and imaging findings is not well-demonstrated in the literature, particularly with respect to epidemiologic dynamics. In this study, we aimed to analyze the impact of the ongoing pandemic on molecular imaging of cancer patients in a comprehensive cancer hospital by in-depth analysis of all PET/CT studies from 1 January 2020 through 15 June 2020. The aims of this study were: (1) to determine temporal changes in PET/CT utilization during the COVID-19 pandemic; (2) to correlate PET/CT utilization and state-wide number of COVID-19 cases within the same period in the light of restrictive policy implementations; (3) to examine the impact of demographic and oncological factors on PET/CT utilization and (4) to examine the number of cases discussed in multidisciplinary tumor boards during the same period.

**Materials and methods**

**Study cohort**

The study was approved by the Institutional Review Board and informed consent requirement was waived. All patients that had PET/CT scans between 1 January 2020 and 15 June 2020 at a single tertiary academic medical center/comprehensive cancer center were included in the study. All scans were done on weekdays. Patient demographics were obtained from the electronic medical records. Oncologic parameters were determined from PET/CT reports and electronic medical records.

**PET/CT review**

Three radiologists and one radiation oncologist (all have > 10 years of experience) reviewed the reports of PET/CT scans and electronic medical records. Any disputed finding was resolved with a consensus, and all reviewers jointly decided on the classification of the scans. The cancer type was classified as solid or hematologic. The solid cancers were further divided into head and neck, lung, breast, gastrointestinal, genitourinary and other solid cancers. The hematologic cancers are divided into Hodgkin lymphoma, non-Hodgkin lymphoma and other hematologic cancers. In cases with multiple malignancies, the driver cancer was determined with a consensus. The scan type was classified as initial (new diagnosis/pretreatment) or subsequent (post-treatment). The scan results were classified as positive, negative or equivocal. In patients with subsequent scans, the results of prior scan were also classified as positive, negative or equivocal. SARS-Cov-2 test statuses of patients were recorded for the last 11 weeks of the study period, and PCR positive cases were correlated with the timing and imaging findings on PET/CT.

**Table 1** Details of examined variables based on five pandemic phases detected in CPD analysis

| Pandemics phases | Baseline (7) n=670 | Early decline (5) n=389 | Late decline (2.1) n=79 | Early recovery (5.3) n=295 | Late recovery (3.1) n=252 | P value |
|------------------|--------------------|------------------------|--------------------------|---------------------------|--------------------------|---------|
| Average age      | 64.5 (15.2)        | 62.2 (17.1)            | 61.4 (16.1)              | 61.2 (17)                 | 62.2 (17)                | 0.026   |
| Sex              | Male:331           | Female:332             | Male:31                  | Male:144                  | Male:126                 | 0.408   |
|                  | Male:185           | Female:204             | Male:48                  | Female:151                | Female:126               |         |
| Race             | Caucasian:82.3%    | Caucasian:80.6%        | Caucasian:74.7%          | Caucasian:77%             | Caucasian:75.0%          | 0.033   |
|                  | African American:9.7% | African American:12.4% | African American:12.7%   | African American:11.3%    | African American:13.3%   |         |
|                  | Hispanic:4.2%      | Hispanic:6.0%          | Hispanic:6.3%            | Hispanic:5.8%             | Hispanic:4.8%            |         |
|                  | Asian:1.8%         | Asian:0.8%             | Asian:2.5%               | Asian:1.4%                | Asian:2.4%               |         |
|                  | Other:2.0%         | Other:0.3%             | Other:3.8%               | Other:4.5%                | Other:4.4%               |         |
| Cancer type      | Solid              |                        |                          |                           |                          |         |
|                  |                    |                        |                          |                           |                          |         |
|                  | Head and Neck      | 68.4%                  | 60.3%                    | 59.7%                     | 61.8%                    | 0.012   |
|                  |                    | 8.4%                   | 6.6%                     | 12.8%                     | 10.0%                    |         |
|                  | Lung               | 18.1%                  | 17.3%                    | 9.0%                      | 11.3%                    | 1.97    |
|                  |                    | 8.0%                   | 5.5%                     | 6.4%                      | 7.2%                     | 0.67    |
|                  | Gastrointestinal   | 10.7%                  | 11.0%                    | 12.8%                     | 8.2%                     | 0.88    |
|                  |                    | 9.5%                   | 10.2%                    | 11.5%                     | 14.1%                    | 0.95    |
|                  | Genitourinary      | 13.3%                  | 9.7%                     | 6.4%                      | 9.6%                     | 0.61    |
|                  |                    | 29.6%                  | 36.5%                    | 40.3%                     | 38.2%                    | 0.40    |
| Hematologic      |                    | 12.8%                  | 5.2%                     | 5.1%                      | 3.8%                     | 0.40    |
|                  |                    | 7.5%                   | 17.1%                    | 28.2%                     | 18.9%                    | 0.006   |
|                  |                    | 9.3%                   | 14.2%                    | 6.4%                      | 14.8%                    |         |
|                  |                    | 2.0%                   | 3.1%                     | 1.3%                      | 2.1%                     | <0.001  |
|                  | Non-Cancer         |                        |                          |                           |                          |         |
|                  | Scan type          | Initial: 42.1%         | Initial: 49.6%           | Initial: 46.2%            | Initial: 37.6%           |         |
|                  |                    | Subsequent: 57.9%      | Subsequent: 51.4%        | Subsequent: 53.8%         | Subsequent: 62.4%        |         |
|                  | Scan results       | Positive: 73.7%        | Positive: 74.0%          | Positive: 73.9%           | Positive: 66.8%          | 0.006   |
|                  |                    | Negative: 24.3%        | Negative: 23.9%          | Negative: 23.8%           | Negative: 31.5%          |         |
|                  |                    | Equivocal: 2.0%        | Equivocal: 2.1%          | Equivocal: 2.9%           | Equivocal: 2.7%          |         |
|                  | Prior scan results | Positive: 67.3%        | Positive: 72.8%          | Positive: 90.5%           | Positive: 75.0%          | 0.037   |
|                  |                    | Negative: 30.3%        | Negative: 24.6%          | Negative: 9.5%            | Negative: 22.8%          |         |
|                  |                    | Equivocal: 2.4%        | Equivocal: 2.6%          | Equivocal: 0%             | Equivocal: 2.2%          |         |

The number of scans and the duration (brackets) are provided for each phase. The age is expressed as mean (SD).
Multidisciplinary tumor boards review
We collected tumor board data during the study period to determine the trends in patient volumes presented at the respective boards for different malignancies.

Timeline of the pandemic and statistical analysis
R statistical Software (version 3.6.3; The R Foundation) was used for statistical analysis. To demonstrate the potential temporal relationship between the course of pandemic and its impact on PET/CT utilization, the number of new confirmed cases of COVID-19 by the Connecticut Department of Public Health was correlated with the daily number of PET/CT scans [10]. To accurately discover time points at which the number of scans changes abruptly, we adopted change-point detection (CPD) technique based on the pruned exact linear time search algorithm [11]. This algorithm divided the PET/CT utilization time series into five periods (phases). The mean values inside each segment (phase) are approximately constant over time.

Descriptive statistics was used to analyze the characteristics of patients receiving PET/CT scans during pandemics phases. Measured continuous variables are expressed

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**Fig. 1**

The five phases of PET/CT utilization during COVID-19 pandemic, identified using change-point detection analysis [pruned exact linear time (PELT) search algorithm]. The numbers of daily PET-CT utilization significantly dropped on 21 Feb and 26 Mar and started to recover on 13 April with further recovery on average numbers on 20 May, though still significantly lower than the baseline, even at the last period of the study.

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**Fig. 2**

The graph demonstrating a negative correlation between the number of confirmed daily new COVID-19 cases in the state of Connecticut vs. utilization of PET-CT. Increase in the number of COVID-19 cases preceded a decline in the number of PET-CT utilization with a 3 day lag.
as a mean ± SD. Categorical variables are expressed as percentages. A set of statistical techniques including CPD and Kendall rank correlation coefficient were applied to explore the association between the number of PET scans and the new increase in COVID-19 cases in Connecticut. For group comparisons of continuous variables, we used
a one-way analysis of variance (ANOVA) with Tukey’s multiple comparisons post hoc testing. \( \chi^2 \) tests were used to compare the groups for categorical variables. All data used in each statistical test met the distribution assumptions of the specific test. The threshold of statistical significance was \( P \leq 0.05 \).

**Results**

**Study cohort**

A total of 1685 cases were reviewed (female: \( n = 861 \)). The average age was 62.9 (SD 16.3) years. Most patients were Caucasians (79.0%), followed by African Americans (11.2%) and Hispanics (5.0%). Fifteen patients had multiple cancers. Thirty-six cases did not have a cancer diagnosis. The most common malignancy was lung cancer (15.7%) followed by non-Hodgkin lymphoma (14.9%) and gastrointestinal cancers (10.2%). There were 63.3% solid tumors vs. 36.7% hematologic cancers. Initial and subsequent PET/CT scans represented 41.5 and 59.5% of all patients, respectively. PET/CT scans were positive in 69.9% of patients.

**PET/CT utilization changes during COVID-19 pandemics (aim 1)**

The CPD analysis of the daily number of the scans identified distinctive changes in the mean of the series at days of 35 (2/21/2020), 60 (3/26/2020), 71 (4/13/2020) and 99 (5/20/2020). This yielded five distinct phases of PET/CT utilization during the pandemics, which were respectively named as baseline (pre-COVID-19), early-decline, late-decline (nadir), early-recovery and late-recovery. The duration of phases and number of scans per phase are shown in Table 1 and Fig. 1.

There were two momentous drops in the number of visits, which happened on 21 February 2020 and 27 March 2020. The number of visits nadired on 9 April, from which the average number started recovering in a slower and steadier pace. There was a 62.5% decline in case volumes between baseline and the late decline group. One-way ANOVA analysis demonstrated a statistically significant difference between five groups (\( P < 0.001 \)). To examine where the group differences lay, we ran a post hoc test (Tukey test), which demonstrated that the only nonsignificant difference was between groups 2 and 5 (\( P = 0.9 \)), the first phase of decline and the last phase of recovery, signifying an incomplete recovery as compared to baseline (prepandemic) numbers. In the last 2 weeks of the study, the average number of cancer scans was still 10% below the baseline.

**Correlation of PET/CT utilization with state-wide number of COVID-19 cases (aim 2)**

There was a significant moderate negative correlation between the number of COVID-19 cases in the state of Connecticut and the number of cancer patient visits for PET/CT scan with \( \tau = -0.54 \). (As the data was not normally distributed, therefore, Kendall rank-based correlation tests were utilized to examine the correlation between variables with \( P \) value < 0.001, see Fig. 2.). There were four distinct dates on which a major shift in cancer imaging studies had happened, and these dates were matching the pandemic timeline in the state of Connecticut. Baseline group (before 21 February 2020): in late January 2020, two students living in Connecticut were monitored for displaying COVID-19-like symptoms, who eventually turned out to be negative for SARS-CoV-2. Early decline group (21 February–26 March 2020): in late February, greater precautions were undertaken by different organizations to be prepared for the eventual spread of the virus into Connecticut. In late decline and early recovery groups (27 March–20 May 2020): CDC advised residents of the region not to travel except for essential purposes and Connecticut National Guard workers put up a Field Hospital with 646 beds at the Connecticut Convention Center on 11 April 2020. In the late recovery group (21 May–15 June 2020): Connecticut began Phase 1 of a three-phase plan to reopen Connecticut.

**Impact of demographic and oncologic factors on PET/CT utilization (aim 3)**

Descriptive statistics for demographic and oncologic variables for five phases of PET/CT utilization during COVID-19 pandemics are shown in Table 1. The factors significantly different between the phases were age, race, cancer type, scan type, scan results and prior scan results. There were no significant sex differences between the phases.

The average age of patients undergoing PET/CT was significantly lower during the decline period when compared with baseline period, this held true during the recovery period as well, although there was a slight increase in the average age in this period as compared to the decline period (Table 1). Although Caucasians were by far the most common race scanned, the relative percentage for this race declined during the pandemic (Table 1 and Fig. 3). As a result, a greater percentage of young patients and minorities were scanned during the pandemics relative to baseline. All cancer types demonstrated a significant decline during the pandemic (Table 1) and there was a significant difference between the five periods (\( P < 0.001 \)). Certain cancer types were more impacted by the pandemic. The scanning of patients with hematologic malignancies declined less than scanning of patients with solid malignancies during the pandemic (Table 1 and Fig. 4). A striking difference was observed between lymphoma types. The highest decline in the number of scanned cases was observed in Hodgkin lymphomas, and the least decline was observed in non-Hodgkin lymphomas. PET/CT scan positivity was higher at baseline and during the decline than during the recovery. In patients that had subsequent scans, prior scan positivity was higher during the pandemic phases relative to baseline.
Relationship between multidisciplinary tumor boards and PET/CT utilization (aim 4)

Soon after clusters of cases of SARS-Cov-2 were diagnosed in the west coast of the USA, there was a spike in the number of cases that were discussed in the tumor boards (Fig. 5). Subsequently, during the pandemic phases, both the number of solid and hematologic cases presented at tumor boards steadily declined. Interestingly, unlike PET/CT utilization, the number of cases at tumor boards did not show the recovery during the study period, despite the same frequency of tumor board meetings.

Discussion

This study from a single comprehensive cancer center with a large cohort demonstrates that PET/CT utilization was significantly impacted by the ongoing SARS-Cov-2 pandemic. The decline/recovery had four major steps in trends, creating five distinct phases based on the CPD analyses. After a stable prepandemic period, a sharp decline in early and late decline phases, and a relatively slow, but steady, early and late recovery phases. Two momentous drops in the number of scans happened on 21 February 2020 and 27 March 2020, and numbers reached a nadir on 9 April. The significant decline in the volume of cases recovered up to 82.3% at the late recovery period as compared to the baseline prepandemic levels. It is important to note that major shifts in the trends of patient volume matched the course of the pandemic in the state of Connecticut. In late February, greater precautions were undertaken by different organizations to be prepared for the eventual spread of the virus into Connecticut. Between late March through mid-May 2020, CDC advised against nonessential trips in the region and Connecticut National Guard workers put up a Field Hospital. With a high degree of certainty, there was a negative correlation between daily cancer scans and the daily count of COVID-19 cases in Connecticut. An increase in COVID-19 case counts strongly preceded a decline in cancer scans with up to a three-day lag. This finding may help in forecasting cancer imaging in future outbreaks, which may lead to a more planned imaging strategy and better preparedness.

Patient demographics prior to the pandemic were significantly different than those during the pandemic. We found that average age significantly dropped during the decline period, and slightly bounced back in the recovery phase, although still significantly lower than the pre-COVID phase, signifying a likely higher impact on cancer care in an elderly population. These findings suggest that
elderly patients were less likely to undergo PET/CT imaging during the pandemic, a possible explanation is the fact that the elderly population is more vulnerable to serious side effects of COVID-19, hence patients more strictly followed lockdown directions or providers selectively deferred their imaging studies. We found no significant sex difference between periods. Interestingly, there were significant racial differences between these periods. In the decline period, there was a significant decrease in the ratio of Caucasians relative to minorities, which were more likely to undergo PET/CT both during decline and recovery periods, suggesting a lower likelihood of Caucasians to visit the hospital during these periods. For example, while the percentage of Caucasian patients dropped from a prepandemic level of 82.3% down to 74.6% at late decline period, that of African Americans substantially increased during the pandemic, from 9.7% at baseline to 13.3% at the late recovery period. Previous studies have demonstrated that elderly individuals and minorities were more likely to be impacted by the COVID-19 outbreak, evidenced by overall significantly higher death counts from COVID-19 when compared with Caucasians and younger age groups [12]. Kaufman et al. [7] investigated decline in new diagnosis of six cancer types within the COVID-19 period in a large cohort from a national cancer registry and demonstrated up to 46% decline in new cancer diagnoses and they too found that patients diagnosed with cancer within the COVID-19 period were younger than those prior to COVID-19 period. In parallel to our findings, they found no significant difference in sex distribution between 2020 and prior years.

Imaging of certain cancer types was more impacted by the pandemic and the highest decline in the number of scanned cases were observed in Hodgkin lymphomas and lung cancers, respectively. The least decline was observed in non-Hodgkin lymphomas. Overall, hematologic cancers had a much lesser decline in scan numbers as compared to their solid counterparts. This outcome is due likely to the acuity of the treatment scheme in some forms of hematologic malignancies [13]. There was a fourfold increase in the relative percentage of non-Hodgkin lymphoma cases in the late decline phase when compared to its baseline phase percentages.

We found that the percentage of positive scans was higher at baseline and during decline than during the recovery. A possible explanation is more utilization of follow-up scans in the late phases of the study. In patients that had subsequent scans, prior scan positivity was higher during the pandemic phases relative to baseline, peaking at the late decline phase. These findings are likely the result of the deferral of imaging studies in patients with more stable/less urgent status of their cancers.

The uncertainty in cancer care adjustment during pandemic affected multidisciplinary tumor board discussions, where the status of the pandemic was likely an important component in decision making. We found that the number of cases that were discussed in tumor boards soared immediately after the pandemic arrived in the USA, likely due to increased complexity in decision making and anticipated reduced access during the pandemic. The number of cases at the tumor boards significantly decreased during the pandemic, likely reflecting reduced accesses to oncologic care as anticipated. Unlike PET/CT utilization, the number of cases at tumor boards did not show the recovery during the study period. One possible explanation for this finding would be that the patients were scanned during the recovery phases in the anticipation of future patient visits and presentations at tumor boards.

The main limitation of this study is the fact that this study was conducted in a single comprehensive cancer hospital. Multicentric-international studies would likely better reflect the impact of the pandemic on cancer imaging. Pandemic timeline was based on Connecticut data and may not reflect the results of the national or global course of the pandemic. Extreme sample bias may confound race analyses due to the disproportionately high percentage of the Caucasian population. Also, we used some open-source packages in the R programming languages, where external threats may be introduced.

**Conclusion**

Our institutional PET/CT utilization data in the COVID-19 pandemic demonstrated a significant vulnerability of cancer imaging to an outbreak. PET/CT utilization experienced a sharp decline and more gradual recovery during the pandemic. These changes correlated with COVID-19 epidemiologic changes in the state of Connecticut. In our population, the relative percentage of older patients and Caucasians decreased the most, while the relative percentage of scanned younger and minority patients was increased. PET/CT scanning of solid malignancies like lung cancer was disproportionately impacted as compared with hematologic malignancies, particularly non-Hodgkin lymphoma. Case volumes discussed in multidisciplinary tumor boards showed an uptick prior to pandemics followed by steady decline and unlike PET/CT scanning utilization, did not recover during the study period.

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