The Impact of COVID-19 Pandemic on Oncological Disease Extent at Staging FDG PET/CT: the ONCOVIPET Study.

Carmelo Caldarella

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Fabrizio Cocciolillo

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Silvia Taralli

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Margherita Lorusso

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Valentina Scolozzi

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Daniele Antonio Pizzuto

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Maria Lucia Calcagni

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Vittoria Rufini

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Davide Guido

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Fernando Palluzzi

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Luciano Giacò

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Alessandro Giordano

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Lucia Leccisotti (✉ lucia.leccisotti@policlinicogemelli.it)

Fondazione Policlinico Universitario Agostino Gemelli IRCCS <https://orcid.org/0000-0002-6000-2898>

Research Article

Keywords: COVID-19, FDG, oncology, pandemic, PET, staging

Posted Date: September 2nd, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-853608/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at European Journal of Nuclear Medicine and Molecular Imaging on December 8th, 2021. See the published version at <https://doi.org/10.1007/s00259-021-05629-0>.

Abstract

Purpose: To investigate whether the COVID-19 pandemic and national lockdown had an impact on the extent of cancer disease at staging using FDG PET/CT as surrogate marker.

Methods: Retrospective observational study including cancer patients submitted to FDG PET/CT for staging purposes from June 1 to October 31, 2020, and June 1 to October 31, 2021, respectively. Data regarding primary tumour, nodal (N) status and number of involved nodal stations, presence and number of distant metastases (M) were collected. Each scan was classified in limited vs advanced status. Data were aggregated across the study population and tumour type. Bi-weekly frequencies of the observed events were analysed.

Results: 611 patients were included in the study (240 in 2019 vs. 371 in 2020, respectively). A significant increase in the rate of advanced disease patients in 2020 compared to 2019 was found (rate 1.56, $p<0.001$) as well as in the rate of N+ or M+ patients (rate 1.84 and 2.09 respectively, $p<0.001$) and in the rate of patients with a greater number of involved N stations or M (rate 2.01 and 2.06 respectively, $p<0.001$). Analysis by tumour type showed a significant increase of advanced disease, N+ or M+ status and number of involved N stations or M in lung cancer and lymphoma in 2020 compared with 2019 ($p<0.003$). Advanced disease rate resulted also significantly increased in gynaecologic cancer and N rate was significantly increased in gastro-intestinal cancer ($p<0.05$).

Conclusion: The rate of cancer patients with advanced disease at staging FDG PET/CT increased by 1.5-fold in 2020, following the national lockdown due to the COVID-19 pandemic, compared to 2019 with a significant increase of patients with N involvement or M. Targeted health interventions are needed to mitigate the effects of the pandemic on patient outcome.

Introduction

The global Coronavirus disease 2019 (COVID-19) pandemic has severely affected healthcare systems, economy, work, education, and social relationships. On March 2020, the National Health Services (NHSs) of many Countries, starting with Italy, suddenly redesigned their services to increase the capacity for treating patients with COVID-19. Procedures included discharging thousands of inpatients to free up beds, postponing scheduled treatment, shifting appointments online whenever possible and redeploying healthcare staff. In addition, on March 9, 2020, the Italian Government declared a national lockdown in response to the COVID-19 pandemic, lasting until May 18, 2020. "Stay-at-home" orders were enacted to slow the spread of the SARS-CoV-2 and reduce the burden on the NHS. Consequently, the COVID-19 emergency had direct and indirect effects on the healthcare delivery process. Direct effects include the radical reorganization of health systems, on the one hand to respond to the acute needs of people infected with the SARS-CoV-2 and on the other to contain the infection to protect the most vulnerable categories and healthcare personnel. Indirect effects of the pandemic are represented by the impact on

people with acute and non-acute conditions not related to COVID-19, especially cardiovascular and oncological diseases[1–7].

In oncology, it is well known that the best outcomes are obtained in those tumours whose diagnosis is at an early stage and treatment is started straight away. Unfortunately, several diagnostic and treatment pathways used for cancer patient management have been severely affected, especially during the “first wave” of the COVID-19 pandemic [8–11]. In addition, the fear of COVID-19 transmission contributed to a lower propensity of patients with symptoms to directly refer to hospitals. Therefore, many patients are likely experiencing a delay in both diagnosis and treatment of cancer. To date, no direct population-based evidence of the impact of COVID-19 on the extent of cancer disease at staging is available.

Positron Emission Tomography/Computed Tomography with 2-deoxy-2-[18F] fluoro-D-glucose (FDG PET/CT) has become one of the cornerstones of patient management in oncology. The high diagnostic accuracy of staging FDG PET/CT for detecting lymph node and distant metastasis and the impact on patient management have been widely reported in several malignancies [12–24]. This study aims to evaluate whether delay in cancer diagnosis and initial staging, due to COVID-19 pandemic and consequent national lockdown, had an impact on disease extent in cancer patients, using staging FDG PET/CT as surrogate measure.

Material And Methods

Population, selection criteria and data extraction

We conducted a single-center retrospective observational study including all consecutive oncological patients submitted to whole body FDG PET/CT at the PET-CT Center of the “Fondazione Policlinico Universitario Agostino Gemelli IRCCS” in Rome for staging purposes, in two selected intervals: June 1 to October 31, 2020, and June 1 to October 31, 2019. These intervals were taken into consideration to evaluate the effects of any diagnostic delays on disease extent at initial staging, due to the first wave of the pandemic and the restrictions enforced during the national lockdown from 9th March to 18th May 2020.

Patients’ information was retrieved from internal medical records and PET/CT images. Only patients ≥ 18 years old with diagnosis of cancer, with FDG-avid tumours who performed a whole-body PET/CT for staging purposes were included in the study. Patients < 18 years old, with non-FDG-avid tumours or performing PET/CT for restaging purposes (e.g., suspected recurrence, therapy response evaluation) or with radiopharmaceuticals other than FDG were excluded. FDG PET/CT images of all included patients were retrieved from the Institution’s Picture Archive and Communication System (PACS) and displayed on a dedicated workstation using the software Syngo.via (Siemens®). All included patients were divided into sub-groups according to the primary tumour (lung, head & neck, gynaecologic, gastro-intestinal, breast, lymphoma, melanoma, and myeloma). PET/CT images were evaluated independently by 2 nuclear medicine physicians for each tumour sub-group, also referring to the report previously drawn up, in order

to assess disease stage according to the International Classification of Diseases for Oncology (American Joint Committee on Cancer staging manual [25]. Information regarding patients' gender, age, date of PET/CT scan, site, and histology of primary tumour (T), presence/absence of lymph node (N+/N0) involvement and number of involved nodal stations, presence/absence of distant metastases (M+/M0) and number of metastatic lesions was collected. Myeloma patients were excluded from nodal assessment because of the very rare nodal spreading of disease. In lymphoma patients all the extra-nodal sites of disease were considered metastases for statistical analysis. Based on the number of distant metastases, including extra-nodal sites of disease in lymphomas, a 4-point scale was used as follows: 0 (no distant metastases), 1 (1 to 3 lesions), 2 (4 to 7 lesions) and 3 (> 7 lesions). On the basis of such evaluation, all PET/CT scans were deemed advanced or limited stage of disease as follows: advanced stage (III and IV) or limited stage (I and II) for breast, gynaecologic, lung and head & neck cancers, lymphoma and melanoma; advanced stage (any T, any N, M1) or limited stage (M0) for gastrointestinal cancers; advanced stage (extra-skeletal disease and/or presence of lytic lesions on CT) or limited stage (no extra-skeletal disease, no lytic lesions on CT) for myeloma. For the confirmation of PET tumour staging, information on the subsequent management of the patient was also reviewed (e.g., medical records referred to tumour multidisciplinary boards, subsequent examinations performed, type of treatment).

Statistical analysis

Data were aggregated across the study population and tumour type by generating bi-weekly frequencies for the observed T, N and M events, the number of N stations and M sites, and tumours in advanced status. From June 1 to October 31, 11 bi-weekly intervals were therefore generated for each reference year. Poisson models were fitted to investigate how the year (2019 vs 2020) affected the observed frequencies. For each model, the year was used as a binary predictor and the exponential transformation of the coefficient was interpreted as rate. P values less than 0.05 indicated the significance. All the analyses were performed using R statistical environment (version 4.0.3).

Results

A total of 3551 and 3443 FDG PET/CT scans were performed in our Center from June 1 to October 31, 2019, and from June 1 to October 31, 2020, respectively (Fig. 1). According to the inclusion and exclusion criteria, 240 patients in 2019 and 371 patients in 2020 were finally included in the study. The main characteristics of study population are described in Table 1. The Table 2 shows the bi-weekly frequencies for the observed T, N + and M + events, the number of N stations and M sites, as well as tumours in advanced status over the two reference periods.

Table 1
Study population characteristics (n = 611)

	June 1-October 31, 2019	June 1-October 31, 2020
n.	240	371
Age (yrs), mean $\pm$ SD	63 $\pm$ 14	63 $\pm$ 15
Male, n (%)	106 (44)	157 (42)
Tumour type, n (%):		
Lung	75 (31.3)	112 (30.2)
Gynaecologic	53 (22.1)	76 (20.5)
Gastro-intestinal	36 (15)	47 (12.7)
Lymphoma	32 (13.3)	67 (18.1)
Breast	16 (6.7)	26 (7)
Head & neck	15 (6.2)	20 (5.4)
Myeloma	10 (4.2)	12 (3.1)
Melanoma	3 (1.2)	11 (3)
n: frequency; SD: standard deviation		

Table 2

Bi-weekly frequencies (11 intervals) for the observed T, N + and M + events, the number of N stations and M lesions, as well as tumours in advanced status in 2019 and 2020.

2019-Intervals	T	N+	M+	N stations	M sites*	Advanced disease
1	34	25	10	111	16	21
2	24	12	8	51	20	15
3	11	11	5	42	10	8
4	17	13	7	38	10	10
5	16	10	5	23	9	8
6	18	12	4	29	6	12
7	19	13	10	75	13	13
8	10	10	5	43	8	7
9	20	13	4	21	5	7
10	10	12	4	67	4	7
11	8	7	2	17	2	6
2020-Intervals	T	N+	M+	N stations	M sites*	Advanced disease
1	14	19	8	67	14	11
2	27	21	12	93	23	16
3	28	25	11	92	21	18
4	26	23	9	81	10	17
5	26	25	14	101	24	20
6	25	20	10	92	17	14
7	21	25	17	151	23	19
8	25	20	10	74	13	15
9	28	25	15	103	27	15
10	30	25	14	76	21	14
11	25	27	14	107	20	19
*Extra-nodal sites of lymphoma patients were included in the M analysis as reported in the method section.						

Advanced vs. limited disease at staging FDG PET/CT

Overall, the analysis by bi-weekly ranges (Fig. 2) showed a significant increase in the rate of tumours in advanced status in 2020 compared to 2019 (rate 1.56; 95% confidence interval [CI] 1.23–1.97; $P < 0.001$).

Nodal and metastatic disease at staging FDG PET/CT

Overall, the bi-weekly analysis demonstrated a significant increase in the rate of N + or M + patients in 2020 compared with 2019 (N+: rate 1.85, 95% CI 1.50–2.27, $P < 0.001$, Fig. 3; M+: rate 2.09, 95% CI 1.55–2.82, $P < 0.001$, Fig. 4). The rate of patients with a higher number of involved N stations or M resulted significantly increased in 2020 compared to 2019 (rate of N stations: 2.01, 95% CI 1.80–2.23, $P < 0.001$, Fig. 5; rate of M sites: 2.06, 95% CI 1.63–2.61, $P < 0.001$, Fig. 6).

Analysis by tumour type

The bi-weekly frequency analysis demonstrated a significant increase in advanced disease, N + and M+ /extranodal rate, number of involved N stations and M sites for both lung cancer and lymphoma in 2020 compared to 2019 (Table 3). Compared to 2019, advanced disease rate significantly increased in 2020 in gynaecologic cancers, as well as N rate in gastro-intestinal cancers (Table 3). Head and neck tumours, melanoma and myeloma were excluded from the analysis by tumour type for the small size sample.

Table 3
Bi-weekly analysis results for tumour type (2020 vs 2019-intervals)

	Rate	95% CI	P value
Lung cancer			
Advanced stage	1.92	1.3–2.8	< 0.001
N+	1.97	1.3–2.9	< 0.001
M+	2.25	1.3–3.8	0.0025
N (n.)	2.30	1.8–2.8	< 0.001
M (n.)	2.55	1.7–3.8	< 0.001
Lymphoma			
Advanced stage	2.68	1.5–4.8	< 0.001
N+	2.42	1.5–3.8	< 0.001
Extranodal+	2.31	1.3–3.9	0.0022
N (n.)	2.15	1.8–2.5	< 0.001
Extranodal (n.)	2.59	1.5–4.3	< 0.001
Gastro-intestinal cancer			
Advanced stage	1.63	0.7–3.4	0.1981
N+	1.99	1.1–3.5	0.0163
M+	1.62	0.6–3.9	0.2799
N (n.)	1.68	1.1–2.4	0.0053
M (n.)	1.49	0.7–2.8	0.2090
Breast cancer			
Advanced stage	1.24	0.4–3.1	0.6380
N+	1.90	0.9–3.9	0.0823
M+	3.49	0.7–16.8	0.1181
N (n.)	2.66	1.6–4.4	0.0001
M (n.)	2.99	0.9–9.3	0.0570

N+: presence of nodal involvement; M+: presence of metastatic disease, M (n.): number of metastatic sites grouped using a 4-point scale (0 [no distant metastases], 1 [1 to 3 lesions], 2 [4 to 7 lesions] and 3 [> 7 lesions]. In **bold** the significant results (P < 0.05).

	Rate	95% CI	P value
Gynaecologic cancer			
Advanced stage	0.48	0.2–0.8	0.0209
N+	1.45	0.9–2.2	0.1103
M+	2.19	0.7–6.3	0.1437
N (n.)	1.31	0.9–1.7	0.0576
M (n.)	0.99	0.4–2.3	0.9999
N+: presence of nodal involvement; M+: presence of metastatic disease, M (n.): number of metastatic sites grouped using a 4-point scale (0 [no distant metastases], 1 [1 to 3 lesions], 2 [4 to 7 lesions] and 3 [> 7 lesions]). In bold the significant results (P < 0.05).			

Discussion

The results of our study show a 1.5-fold increase in the rate of cancer patients with advanced disease at staging FDG PET/CT in 2020, following the national lockdown due to the COVID-19 pandemic, compared to 2019. In addition, we found an approximately 2-fold increase in the rate of cancer patients with nodal involvement or metastatic disease at staging, as well as in the rate of patients with a greater number of involved nodes or distant metastases. Compared to 2019, patients with lung cancer and lymphoma showed a significant (1.9 to 2.6-fold) increase in advanced disease rate at staging, nodal/extranodal involvement, metastatic status, and number of nodal stations and metastatic/extranodal sites in 2020. Additionally, gynaecological cancers showed a significant increase in advanced disease rate at staging in 2020 vs 2019 as well as gastrointestinal cancer for the rate of N + patients.

This retrospective observational study indirectly analyses the impact of the first wave of the COVID-19 pandemic and national lockdown on the extent of cancer disease at staging using whole body FDG PET/CT as a surrogate marker. Oncological FDG PET/CT is known to be the most accurate non-invasive technique for cancer staging in most histotypes because of its superiority over radiological imaging, mainly in assessing lymph node involvement and distant metastases [12]. From our data, more cancer patients showed an advanced stage of disease at staging FDG PET/CT in 2020, after the national lockdown, compared with the same reference period in 2019. An increase rate of patients with nodal involvement and metastatic disease was also demonstrated. Such increase should be mainly due to delays in accessing cancer diagnosis for many patients with the onset of the COVID-19 pandemic. The first phase of the emergency determined a reduction in inpatient and outpatient services provided to non-COVID patients i.e. the delay or suspension of important screening programs, the limitation of some diagnostic tests such as CT to the emergency context and the cancellation or delay of specialist visits and some elective procedures such as biopsies or surgeries [26–30]. Several European Countries reported that cancer diagnosis rates plummeted when the pandemic began, between 15% and 40%. In Italy, approximately 1.4 million fewer screening exams were performed in the first 5 months of 2020 compared

to the same period in 2019 [31]. Surgery was the most affected modality having been delayed or cancelled in over 10% of patients in 34% of European Centers [11]. In Italy, a significant decrease (20%-50%) in the volumes of screening tests, outpatient specialist visits and oncological interventions was reported in 2020 compared to 2019, even in the geographical areas where a lower incidence of the SARS-CoV-2 was recorded during the first wave of the pandemic [31]. In addition to the limited diagnostic capacity and hospital taking-charge patients, many subjects were reluctant to visit hospitals for fear of being infected or preferred to stay at home according to public health messages encouraging people to postpone elective care. The quarantine and financial difficulties due to lockdown had also an impact on travel and care-seeking behaviours. In fact, the incidence of cancer has not changed in recent years, and, in our context, the number of PET exams performed at our Center has not significantly changed in 2020 compared to 2019 as well as the planning of staging FDG PET/CT exams which are generally performed within 7 days of receiving the request form. We have only recorded a slight reduction in PET/CT requests for patients on treatment, due to cancellation or postponement of the examination, with a consequent greater availability of performing examinations for staging or restaging purposes.

Such delays in cancer diagnosis led to more patients being diagnosed at a more advanced stage of their disease, as demonstrated by our study. This means both that these patients could require more complex treatments than they otherwise should have and that there will be more deaths from cancer. The exact extent of the effects on survival and healthcare costs will only become evident in the next few years. After the first peak of the pandemic, forecasts on the impact of these delays on cancer diagnosis and patient survival were provided. The severity of the indirect effects of the COVID-19 pandemic was clear in November 2020 when a 4-week treatment delay was reported to be associated with a 6 to 17% increased risk of death depending on type of cancer. Delays of up to 12 weeks further increase this risk [32–35]. The real challenge now is, on the one hand, to prevent new waves of the pandemic from limiting access to cancer diagnosis and treatment and, on the other, to think of a health system that adequately responds to the needs of these advanced stage patients both during and soon post-pandemic. We hope that, with the support of all stakeholders in cancer diagnosis, treatment and health planning process, the detrimental impact of the COVID-19 pandemic on cancer patients could be mitigated.

This study has some limitations. First, its retrospective nature which indirectly allowed us to take a snapshot of real events of such an emergency period. Secondly, we focused on patients with FDG-avid tumours only and excluded other cancers such as prostate cancer or neuroendocrine tumours that are usually studied with radiopharmaceuticals other than FDG. Nevertheless, the FDG is the radiopharmaceutical most frequently used for PET and FDG-avid tumours are the most aggressive ones for which a delay in diagnosis and initiation of treatment could have the worst consequences on patients' outcome [36]. Finally, the analysis by tumour type was not feasible or the results were not significant in some tumours, mainly due to the small sample size. Further studies confirming our results are desirable, even more complex with the impact on patient outcome, survival, and healthcare costs.

Conclusion

COVID-19 pandemic has had a huge and negative impact on the diagnosis and initiation of cancer treatment. Overall, the rate of oncological patients with advanced stage of disease at staging FDG PET/CT increased by 1.5-fold in 2020 compared to 2019 with a 2-fold increase of patients with nodal involvement and distant metastases. Targeted health interventions are needed to mitigate the expected impact of the COVID-19 pandemic on the outcome of cancer patients.

Declarations

Acknowledgments:

We thank to the medical technician Marco De Summa (Medipass Advanced Medical Services spa) for his valuable collaboration in material preparation.

Data analysis was performed in the Gemelli Science and Technology Park (GSTeP) by the Bioinformatics Core Facility Research.

Funding:

No funds, grants, or other support was received for conducting this study.

Conflict of Interest:

The authors have no conflicts of interest to declare that are relevant to the content of this article.

Ethics approval:

This retrospective observational study involving human participants was in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Ethics Committee of the Fondazione Policlinico Universitario Agostino Gemelli IRCCS-Università Cattolica del Sacro Cuore approved this study (Date 15.4.2021/No. 4024).

Informed consent:

Informed consent was obtained from all individual participants included in the study.

Data availability:

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Author contributions:

All authors contributed to the study conception and design. Material preparation and data collection were performed by Carmelo Caldarella, Fabrizio Cocciolillo, Silvia Taralli, Margherita Lorusso, Valentina

Scolozzi, Daniele Antonio Pizzuto and Lucia Leccisotti. Data analysis was performed in the Gemelli Science and Technology Park (GSTeP), the Bioinformatics Core Facility Research, by Davide Guido, Fernando Palluzzi and Luciano Giacò. The first draft of the manuscript was written by Carmelo Caldarella and Lucia Leccisotti and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References

1. Patt D, Gordan L, Diaz M, Okon T, Grady L, Harmison M, et al. Impact of COVID-19 on Cancer Care: How the Pandemic Is Delaying Cancer Diagnosis and Treatment for American Seniors. *JCO Clin Cancer Inform.* 2020;4:1059-71. doi:10.1200/CCI.20.00134.
2. de Jonge L, Worthington J, van Wifferen F, Iragorri N, Peterse EFP, Lew JB, et al. Impact of the COVID-19 pandemic on faecal immunochemical test-based colorectal cancer screening programmes in Australia, Canada, and the Netherlands: a comparative modelling study. *Lancet Gastroenterol Hepatol.* 2021. doi:10.1016/S2468-1253(21)00003-0.
3. Oderda M, Callaris G, Falcone M, Fasolis G, Muto G, Oderda G, et al. How uro-oncology has been affected by COVID-19 emergency? Data from Piedmont/Valle d'Aosta Oncological Network, Italy. *Urologia.* 2021;88:3-8. doi:10.1177/0391560320946186.
4. Fabi A, Pugliese P, Falbo PT, Corsi D, Fabbri MA, Vincenzi B, et al. The Experience of Oncology Healthcare Providers in the Central Italy during the COVID-19 Lockdown. *Cancers (Basel).* 2020;12. doi:10.3390/cancers12103031.
5. Qua Quarini E, Saltalamacchia G, Presti D, Caldana G, Tibollo V, Malovini A, et al. Impact of COVID-19 Outbreak on Cancer Patient Care and Treatment: Data from an Outpatient Oncology Clinic in Lombardy (Italy). *Cancers (Basel).* 2020;12. doi:10.3390/cancers12102941.
6. Hirschfeld CB, Shaw LJ, Williams MC, Lahey R, Villines TC, Dorbala S, et al. Impact of COVID-19 on Cardiovascular Testing in the United States Versus the Rest of the World: The INCAPS-COVID Study. *JACC Cardiovasc Imaging.* 2021. doi:10.1016/j.jcmg.2021.03.007.
7. Saini KS, de Las Heras B, de Castro J, Venkitaraman R, Poelman M, Srinivasan G, et al. Effect of the COVID-19 pandemic on cancer treatment and research. *Lancet Haematol.* 2020;7:e432-e5. doi:10.1016/S2352-3026(20)30123-X.
8. Di Bidino R, Cicchetti A. Impact of SARS-CoV-2 on Provided Healthcare. Evidence From the Emergency Phase in Italy. *Front Public Health.* 2020;8:583583. doi:10.3389/fpubh.2020.583583.
9. Torzilli G, Viganò L, Galvanin J, Castoro C, Quagliuolo V, Spinelli A, et al. A Snapshot of Elective Oncological Surgery in Italy During COVID-19 Emergency: Pearls, Pitfalls, and Perspectives. *Ann Surg.* 2020;272:e112-e7. doi:10.1097/SLA.0000000000004081.
10. Albano D, Bruno A, Bruno F, Calandri M, Caruso D, Clemente A, et al. Impact of coronavirus disease 2019 (COVID-19) emergency on Italian radiologists: a national survey. *Eur Radiol.* 2020;30:6635-44. doi:10.1007/s00330-020-07046-7.

11. Onesti CE, Tagliamento M, Curigliano G, Harbeck N, Bartsch R, Wildiers H, et al. Expected Medium- and Long-Term Impact of the COVID-19 Outbreak in Oncology. *JCO Glob Oncol*. 2021;7:162-72. doi:10.1200/GO.20.00589.
12. Boellaard R, Delgado-Bolton R, Oyen WJ, Giammarile F, Tatsch K, Eschner W, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. *Eur J Nucl Med Mol Imaging*. 2015;42:328-54. doi:10.1007/s00259-014-2961-x.
13. Kostakoglu L, Agress H, Goldsmith SJ. Clinical role of FDG PET in evaluation of cancer patients. *Radiographics*. 2003;23:315-40; quiz 533. doi:10.1148/rg.232025705.
14. Kandathil A, Kay FU, Butt YM, Wachsmann JW, Subramaniam RM. Role of FDG PET/CT in the Eighth Edition of TNM Staging of Non-Small Cell Lung Cancer. *Radiographics*. 2018;38:2134-49. doi:10.1148/rg.2018180060.
15. Wartski M, Sauvanet A. 18F-FDG PET/CT in pancreatic adenocarcinoma: A role at initial imaging staging? *Diagn Interv Imaging*. 2019;100:735-41. doi:10.1016/j.diii.2019.07.006.
16. Paydary K, Seraj SM, Zadeh MZ, Emamzadehfard S, Shamchi SP, Gholami S, et al. The Evolving Role of FDG-PET/CT in the Diagnosis, Staging, and Treatment of Breast Cancer. *Mol Imaging Biol*. 2019;21:1-10. doi:10.1007/s11307-018-1181-3.
17. Ha HK, Koo PJ, Kim SJ. Diagnostic Accuracy of F-18 FDG PET/CT for Preoperative Lymph Node Staging in Newly Diagnosed Bladder Cancer Patients: A Systematic Review and Meta-Analysis. *Oncology*. 2018;95:31-8. doi:10.1159/000488200.
18. Caresia Aroztegui AP, García Vicente AM, Alvarez Ruiz S, Delgado Bolton RC, Orcajo Rincon J, Garcia Garzon JR, et al. 18F-FDG PET/CT in breast cancer: Evidence-based recommendations in initial staging. *Tumour Biol*. 2017;39:1010428317728285. doi:10.1177/1010428317728285.
19. Thanarajasingam G, Bennani-Baiti N, Thompson CA. PET-CT in Staging, Response Evaluation, and Surveillance of Lymphoma. *Curr Treat Options Oncol*. 2016;17:24. doi:10.1007/s11864-016-0399-z.
20. Perng P, Marcus C, Subramaniam RM. (18)F-FDG PET/CT and Melanoma: Staging, Immune Modulation and Mutation-Targeted Therapy Assessment, and Prognosis. *AJR Am J Roentgenol*. 2015;205:259-70. doi:10.2214/AJR.14.13575.
21. Jones M, Hruby G, Solomon M, Rutherford N, Martin J. The Role of FDG-PET in the Initial Staging and Response Assessment of Anal Cancer: A Systematic Review and Meta-analysis. *Ann Surg Oncol*. 2015;22:3574-81. doi:10.1245/s10434-015-4391-9.
22. Kaneko Y, Murray WK, Link E, Hicks RJ, Duong C. Improving patient selection for 18F-FDG PET scanning in the staging of gastric cancer. *J Nucl Med*. 2015;56:523-9. doi:10.2967/jnumed.114.150946.
23. Mak D, Corry J, Lau E, Rischin D, Hicks RJ. Role of FDG-PET/CT in staging and follow-up of head and neck squamous cell carcinoma. *Q J Nucl Med Mol Imaging*. 2011;55:487-99.
24. Yousefi-Koma A, Panah-Moghaddam M, Kalff V. The Utility of Metabolic Imaging by 18F-FDG PET/CT in Lung Cancer: Impact on Diagnosis and Staging. *Tanaffos*. 2013;12:16-25.

25. Amin MB, Edge, S., Greene, F., Byrd, D.R., Brookland, R.K., Washington, M.K., Gershenwald, J.E., Compton, C.C., Hess, K.R., Sullivan, D.C., Jessup, J.M., Brierley, J.D., Gaspar, L.E., Schilsky, R.L., Balch, C.M., Winchester, D.P., Asare, E.A., Madera, M., Gress, D.M., Meyer, L.R. (Eds.), editor. AJCC Cancer Staging Manual 2017.
26. Jereczek-Fossa BA, Pepa M, Marvaso G, Bruni A, Buglione di Monale E Bastia M, Catalano G, et al. COVID-19 outbreak and cancer radiotherapy disruption in Italy: Survey endorsed by the Italian Association of Radiotherapy and Clinical Oncology (AIRO). *Radiother Oncol.* 2020;149:89-93. doi:10.1016/j.radonc.2020.04.061.
27. Oldani C, Vanni G, Buonomo OC. COVID-19 Unintended Effects on Breast Cancer in Italy After the Great Lockdown. *Front Public Health.* 2020;8:601748. doi:10.3389/fpubh.2020.601748.
28. Fortunato L, d'Amati G, Taffurelli M, Tinterri C, Marotti L, Cataliotti L. Severe Impact of Covid-19 Pandemic on Breast Cancer Care in Italy: A Senonetwork National Survey. *Clin Breast Cancer.* 2020. doi:10.1016/j.clbc.2020.10.012.
29. Rebecchi F, Arolfo S, Ugliono E, Morino M, Asti E, Bonavina L, et al. Impact of COVID-19 outbreak on esophageal cancer surgery in Northern Italy: lessons learned from a multicentric snapshot. *Dis Esophagus.* 2020. doi:10.1093/dote/doaa124.
30. Lambertini M, Toss A, Passaro A, Criscitiello C, Cremolini C, Cardone C, et al. Cancer care during the spread of coronavirus disease 2019 (COVID-19) in Italy: young oncologists' perspective. *ESMO Open.* 2020;5. doi:10.1136/esmoopen-2020-000759.
31. <https://www.agenas.gov.it/covid19/web/index.php?r=site%2Fresilienza>. 2021.
32. Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. *BMJ.* 2020;371:m4087. doi:10.1136/bmj.m4087.
33. Gheorghe A, Maringe C, Spice J, Purushotham A, Chalkidou K, Rachet B, et al. Economic impact of avoidable cancer deaths caused by diagnostic delay during the COVID-19 pandemic: A national population-based modelling study in England, UK. *Eur J Cancer.* 2021. doi:10.1016/j.ejca.2021.04.019.
34. Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. *Lancet Oncol.* 2020;21:1023-34. doi:10.1016/S1470-2045(20)30388-0.
35. Sud A, Torr B, Jones ME, Broggio J, Scott S, Loveday C, et al. Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study. *Lancet Oncol.* 2020;21:1035-44. doi:10.1016/S1470-2045(20)30392-2.
36. Higashi K, Ueda Y, Ayabe K, Sakurai A, Seki H, Nambu Y, et al. FDG PET in the evaluation of the aggressiveness of pulmonary adenocarcinoma: correlation with histopathological features. *Nucl Med Commun.* 2000;21:707-14. doi:10.1097/00006231-200008000-00002.

Figures

Figure 1

Flow-chart of FDG PET/CT scans from June 1 to October 31, 2019 and from June 1 to October 31, 2020.

Figure 2

Bi-weekly analysis of the advanced disease rate at staging FDG PET/CT from June 1 to October 31, 2019, compared to June 1 to October 31, 2020.

Figure 3

Bi-weekly analysis of nodal involvement (N+) rate at staging FDG PET/CT from June 1 to October 31, 2019, compared to June 1 to October 31, 2020.

Figure 4

Bi-weekly analysis of metastatic disease (M+) rate at staging FDG PET/CT from June 1 to October 31, 2019, compared to June 1 to October 31, 2020.

Figure 5

Bi-weekly analysis of N-sites number at staging FDG PET/CT from June 1 to October 31, 2019, compared to June 1 to October 31, 2020.

Figure 6

Bi-weekly analysis of M-sites number at staging FDG PET/CT from June 1 to October 31, 2019, compared to June 1 to October 31, 2020.