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Universal testing for COVID-19 in patients undergoing cancer treatment during the second outbreak in Brescia

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Abstract

Background: The impact of coronavirus disease 2019 (COVID-19) has been overwhelming on patients with cancer, who may be at higher risk of developing severe disease. During the second COVID-19 outbreak in Italy, we planned universal microbiologic screening for patients scheduled for antineoplastic treatment.

Methods: All patients with planned active treatment at Brescia University Radiation Oncology Department were screened for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA with repeated nasopharyngeal swabs (NPS) from October 31, 2020. Treatment continuation, suspension, or delay was modulated for patients testing positive according to clinical presentation.

Results: From October 31, 2020, to February 6, 2021, 636 patients were enrolled and 1243 NPS were performed, of which 28 (2.25%) were positive. The infection rate was 2.52%; 81.3% of the patients with a positive NPS were asymptomatic, 2 had mild disease, and 1 severe disease that led to death. All patients already on treatment with mild or asymptomatic COVID-19 carried on the therapy with no or minimal delay. Median delay for patients with infection detected before treatment start was 16.5 days.

Conclusions: Detected incidence of COVID-19 was lower during the second outbreak in our patients (2.52% vs 3.23%), despite the extensive testing schedule, and substantiates the high rate of asymptomatic infections and the low mortality among patients with COVID-19 (6.3% vs 38.5% during the first outbreak). Universal SARS-CoV-2 screening for all patients with planned treatment might allow early identification of patients with COVID-19, resulting in timely management that could improve clinical outcomes and prevent spread of the infection.

Keywords

COVID-19, radiotherapy, SARS-CoV-2, screening, cancer, chemotherapy

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Introduction

The impact of coronavirus disease 2019 (COVID-19) on healthcare has been overwhelming, especially for patients with cancer, who may be at higher risk of developing severe disease and endure consequences of treatment delay.[1–3] Presentation of COVID-19 is often asymptomatic and differential diagnosis from neoplastic and treatment manifestations could be difficult.[4] Multiple guidelines and sometimes conflicting guidelines[5–10] have been published regarding the modulation of radiation therapy prescription and administration during this pandemic, focusing on the need to provide life-saving and urgent treatments and at the same time minimizing the risk of infection. Italy was the first western country affected by COVID-19 and, as during the first wave clinical data were scarce, uncertainty

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and fear of contagion led to a significant disruption of the activity of many radiation oncology centers.[11,12] Conversely, through complete reorganization of the workflow and the adoption of dedicated measures, the activity of our Department faced only a slight reduction.[13] Mortality among patients with COVID-19 on active anticancer treatment at our institution was relatively high, as reported in a previous article.[14] The large majority of infections and deaths was reported during the first week, when the entity of COVID-19 was largely underestimated and thus preventive measures were suboptimal, especially outside of the hospital.[13] The systematic deployment of personal protective equipment (PPE) and the institution of targeted triage and clinical monitoring was effective in reducing COVID-19 incidence. Nevertheless, the shortage of supplies did not allow universal screening for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), thus hindering the detection of a large number of asymptomatic infections, the main source of the outbreak spread.[15] With the aim to halt the diffusion of the virus and to identify early infections, we planned a universal microbiologic screening for all patients scheduled for antineoplastic treatment during the second COVID-19 outbreak in Italy.

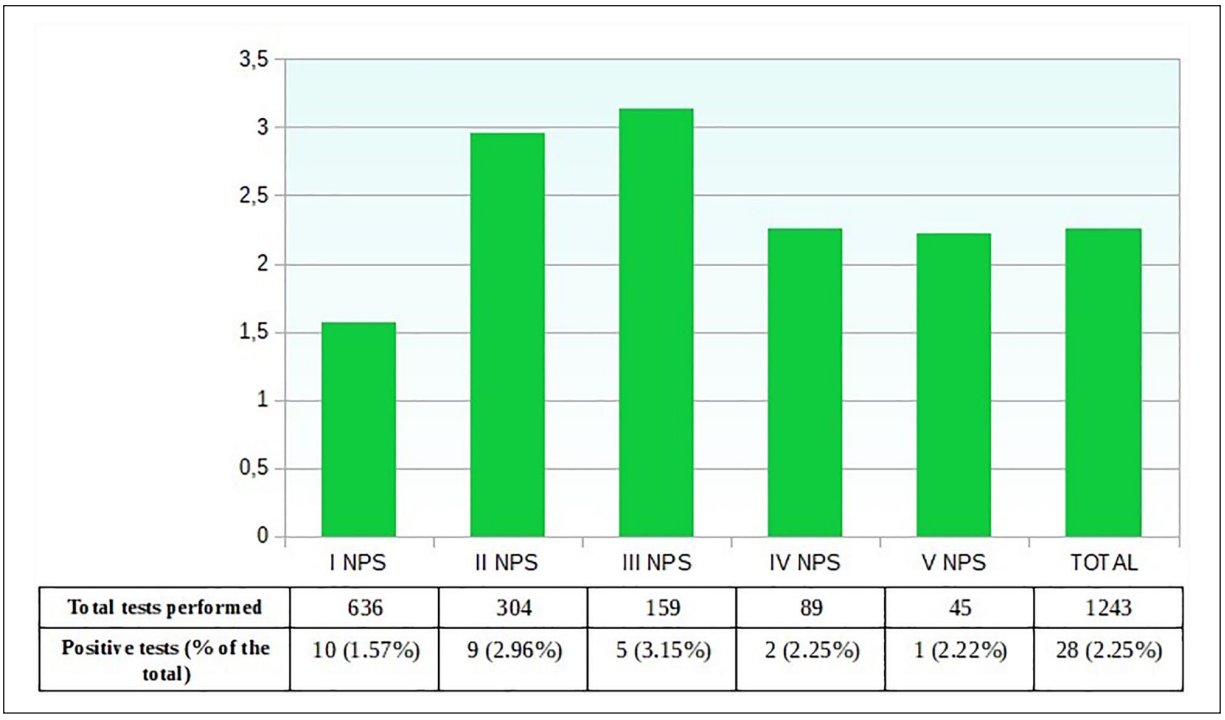
Methods

All patients with planned anticancer treatment at the Brescia University Radiation Oncology Department, Spedali Civili Hospital, Brescia, Italy, were screened from October 31, 2020. The analyzed population included only the patients who started treatment after that date and thus were screened for SARS-CoV-2 before beginning the therapy. A dedicated triage process was developed. Every patient filled in a questionnaire regarding specific symptoms and contacts at risk. All the patients were submitted to a nasopharyngeal swab (NPS) to test the presence of SARS-CoV-2 through real-time polymerase chain reaction (RT-PCR), with this timing: 2 days before systemic or local treatment start and then weekly for patients undergoing radiation therapy or radiochemotherapy; 2 days before each cycle for patients undergoing systemic therapy. Additional tests were performed at the physician's discretion in case of suspect symptoms or positive RT-PCR; in case of positive RT-PCR, treatment start was held until symptoms resolution and two consecutive negative tests (unless urgent and in asymptomatic/mildly symptomatic patients). For patients with RT-PCR becoming positive during treatment, suspension was mandatory in case of severe clinical presentation, while for asymptomatic or mildly symptomatic patients, treatment continuation was evaluated on a case-by-case basis taking into account the risk/benefit balance. Hypofractionated validated schemes were adopted in these cases when feasible. The Radiation Oncology inpatient ward was accessed only after a negative RT-PCR; inpatients were tested weekly with NPS and, if they had a positive test, were transferred to a COVID-19 dedicated ward. All the healthcare staff underwent RT-PCR on a three-weekly basis. Our experience during the first 2 months of the first COVID-19 outbreak has been recently published[13]: on that occasion, NPS were performed only in presence of suspect symptoms or high-risk contacts. We report here the results of the intensive testing applied during the second wave of the outbreak and the differences observed versus the previous strategy.

Results

From October 31, 2020, to February 6, 2021, 636 patients were enrolled and 1243 NPS were performed, of which 28 (2.25%) were positive; the infection rate was 2.52% (16/636 patients). Results of sequential NPS are summarized in the Figure: the rate of positive tests was overall stable (respectively 1.57%, 2.96%, 3.15%, 2.25%, 2.22% from the first to the fifth test performed) among the sequential examinations. Although the majority of SARS-CoV-2 infections were detected at the first test (10/16 [62.5%]), almost half of the positive cases were identified at sequential procedures (3 patients [18.8%] at second NPS and 1 [6.3%] each at third, fifth, and up to the seventh test performed in a previously negative patient). Characteristics of COVID-19–positive patients enrolled in this analysis and (for comparison) in our previous experience during the first COVID-19 outbreak[13] are summarized in the Table. Of the 16 patients with a positive NPS, 13 (81.3%) were asymptomatic, 2 (12.5%) had mild disease (fever and diarrhea), and 1 (6.3%) severe disease that led to death 63 days after diagnosis.

Eleven of the patients testing positive (68.8%) had NPS conversion to negative after a median time of 16.5 days. Five patients already on treatment tested positive: one undergoing adjuvant chemotherapy for an oligodendroglioma (no treatment suspension), one receiving chemotherapy for stage IIIB lung cancer (the deceased patient; the only case of definitive treatment suspension), two undergoing radical radiotherapy for advanced head and neck cancers (respectively no suspension and 2 days suspension, with therapy performed while positive at the end of the shift on a dedicated accelerator, as recommended elsewhere[6]), and one on treatment with adjuvant durvalumab after radical radiochemotherapy for stage IIIB lung cancer (13 days delay of durvalumab cycle). Four asymptomatic patients started radiotherapy while positive for SARS-CoV-2 to avoid treatment delay: one radiochemotherapy for stage 3 oropharyngeal carcinoma, two high-dose palliative treatments for stage 4 gynecologic and head and neck cancer, and one palliative treatment for metastatic nasopharyngeal cancer; no unexpected toxicities were detected. Six other patients tested positive before the start of the treatment (which was withheld until two negative NPS were obtained with a median delay of 16.5 days



	I NPS	II NPS	III NPS	IV NPS	V NPS	TOTAL
Total tests performed	636	304	159	89	45	1243
Positive tests (% of the total)	10 (1.57%)	9 (2.96%)	5 (3.15%)	2 (2.25%)	1 (2.22%)	28 (2.25%)

Figure. Incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positivity on sequential nasopharyngeal swabs (NPS) performed during the analyzed period (October 31, 2020– February 6, 2021).

for the four patients who started treatment at time of writing; two are awaiting treatment start as they are still positive) and one had no indication for active treatment at first evaluation.

Discussion

Among the challenges posed by the COVID-19 pandemic was reconciling public health ethics, required to limit the diffusion of the infection, and the patient-centered paradigm that usually characterizes oncology practice.[16] Since the first outbreak, we advocated for the continuation of antineoplastic treatments in selected patients, for whom a discontinuation or delay could be detrimental, through adequate preventive measures. During the first wave, the emergency state and the lack of information and adequate countermeasures likely contributed to infection diffusion and worse outcomes.

Detected incidence of COVID-19 was lower during the second outbreak in our patients with cancer (2.52% vs 3.23%), despite the extensive testing schedule that also substantiates the high rate of asymptomatic infections and the low mortality (6.3% compared to 38.5% during the first outbreak). This result could be partly explained by the stricter rules regarding the use of PPE, lockdown, and isolation procedures implemented since the beginning of the second outbreak in Italy. The intensive universal testing regimen itself is among the factors that might have contributed to halting the viral spread. Transmission from presymptomatic or asymptomatic carriers is an important, if not the main, source of SARS-CoV-2 infection.[15] In this scenario, the only chance to limit the diffusion of the virus is early detection with a molecular test on NPS.

Of note, although 62.5% of positive patients were identified at the first NPS round, almost half of the cases were detected at subsequent testing and the percentage of positive results was overall stable from first to fifth test, highlighting the importance of periodic repetition.

The results from our experience during the first wave,[13] consistently with reports from other centers,[17,18] confirmed the feasibility of continuing radiation oncology activity through adequate selection of patients and targeted preventive measures. The endorsement of systematic NPS screening for SARS-CoV-2 likely contributed to a further reduction in COVID-19 incidence and to a remarkable reduction of severe presentations and mortality. Our experience suggests that universal screening for all patients with planned treatment allows early identification of COVID-19, resulting in timely management that could improve clinical outcomes and prevent the spread of infection.

The rearrangement of the new routine should envisage an antifragile perspective,[19] allowing not only resilience to the unprecedented pandemic situation, but also a reorganization and optimization of the procedures compared with the prepandemic era[20] with a further improvement of clinical practice.

Table. Characteristics of samples analyzed and coronavirus disease 2019 (COVID-19)–positive patients during the first and second outbreaks at our institution.

	First outbreak (24 February–24 April 2020)	Second outbreak (31 October 2020–06 February 2021
Analyzed population	402 patients (on active treatment)	636 patients (on active treatment, tested before and during therapy)
Total NPS performed	52	1243
Total patients who had NPS	23	636
Positive NPS	15 (28.8)	28 (2.25)
COVID-19+	13 (56.5)	16 (2.52)
COVID-19 incidence in the analyzed population	13/402 (3.23)	16/636 (2.52)
COVID-19–positive population		
Total positive patients	13	16
Male/female	11/2 (84.6/15.4)	10/6 (62.5/37.5)
Mean/median age, y	69.8/69.7	61.2/57.2
Most frequent tumors, %	NSCLC, 61.5; HNSCC, 15.4	HNSCC, 43.8; NSCLC, 18.8
Disease stage, I/II/III/IV/undefined, %	7.7/0/53.8/30.8/7.7	6.3/6.3/25/50/12.5
Treatment indication, %	Radical, 53.8; SBRT/high-dose RT for oligometastatic disease, 15.4; palliative, 15.4; adjuvant, 7.7; neoadjuvant, 7.7	Radical, 37.5; adjuvant, 37.5; SBRT/high-dose RT for oligometastatic disease, 12.5; palliative, 6.3%; no indication (clinical evaluation only), 6.3
Mean/median comorbidities, n (% ⩾3)	2.1/2 (38.5)	1.5/1 (31.3)
Symptomatic COVID+ (% of total COVID+)	13 (100)	3 (18.8)
Asymptomatic COVID+ (% of total COVID+)	0	13(81.3)
Patients requiring supplemental oxygen	10 (76.9)	1 (6.3)
Severe COVID+ (% of total COVID+)	6 (46.2)	1 (6.3)
Death of COVID-19 (% of total COVID+)	5 (38.5)	1(6.3)
Patients who experienced treatment delay	1 (7.7)	6 (37.5)
Median duration of treatment delay, d	45	16.5
Patients who continued/started treatment while positive	6 (46.2)	9 (56.3)
Patients who experienced temporary treatment discontinuation	0	2 (12.5)
Patients who experienced definitive treatment discontinuation	6 (46.2)	1 (6.3)

HNSCC: head and neck squamous cell carcinoma; NPS: nasopharyngeal swab; NSCLC: non-small cell lung cancer; RT: radiotherapy; SBRT: stereotactic body radiation therapy.
Values are n (%) unless otherwise indicated.

Declaration of conflicting interests

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