



Triage Process for the Assessment of Coronavirus Disease 2019-Positive Patients With Cancer: The ONCOVID Prospective Study

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BACKGROUND: Patients with cancer are considered at high risk for the novel respiratory illness coronavirus disease 2019 (COVID-19). General measures to keep COVID-19-free cancer divisions have been adopted worldwide. The objective of this study was to evaluate the efficacy of triage to identify COVID-19 among patients with cancer. **METHODS:** From March 20 to April 17, 2020, data were collected from patients who were treated or followed at the authors' institution in a prospective clinical trial. The primary endpoint was to estimate the cumulative incidence of COVID-19-positive patients who were identified using a triage process through the aid of medical and patient questionnaires. Based on a diagnostic algorithm, patients with suspect symptoms underwent an infectious disease specialist's evaluation and a COVID-19 swab. Serologic tests were proposed for patients who had symptoms or altered laboratory tests that did not fall into the diagnostic algorithm but were suspicious for COVID-19. **RESULTS:** Overall, 562 patients were enrolled. Six patients (1%) were diagnosed with COVID-19, of whom 4 (67%) had the disease detected through telehealth triage, and 2 patients (33%) without suspect symptoms at triage had the disease detected later. Seventy-one patients (13%) had suspect symptoms and/or altered laboratory tests that were not included in the diagnostic algorithm and, of these, 47 patients (73%) underwent testing for severe acute respiratory syndrome coronavirus 2 antibody: 6 (13%) were positive for IgG (n = 5) or for both IgM and IgG (n = 1), and antibody tests were negative in the remaining 41 patients. **CONCLUSIONS:** The triage process had a positive effect on the detection of COVID-19 in patients with cancer. Telehealth triage was helpful in detecting suspect patients and to keep a COVID-19-free cancer center. The overall incidence of COVID-19 diagnosis (1%) and antibody positivity (13%) in patients with suspect symptoms was similar to that observed in the general population. **Cancer 2020;0:1-11.** © 2020 American Cancer Society.

KEYWORDS: coronavirus disease 2019 (COVID-19), COVID-19 antibody, COVID-19 infection, triage, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

INTRODUCTION

Worldwide, health services are facing the challenge of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic.¹ The most common symptoms of the novel respiratory illness coronavirus disease 2019 (COVID-19) are fever, cough, and dyspnea; but myalgias, diarrhea, headache, cutaneous manifestations, sore throat, ageusia, and anosmia have also been reported. Although most patients present with mild symptoms, in a subset of infected individuals, patients worsen to pneumonia, multiorgan failure, and eventually die. As of June 2020, COVID-19 has spread to >200 countries worldwide, with >9.2 million affected individuals; the number of confirmed deaths is >475,000.² After China, Italy was the second country to experience the rapid spread of COVID-19. In Italy, the pandemic initially affected the Lombardy region, especially Milan, where our hospital is located; it had higher lethality here than in China and worldwide.³

Patients with immunocompromised status, like those who have cancer, are at high risk of infection. Cancer develops in an immunocompromised field, and oncologic treatments (eg, chemotherapy, radiotherapy) can increase the risk of infection.^{4,5} Medical oncologists have changed their daily clinical practice in view of the current emergency⁶ with the aid of rapidly drafted guidelines for patient management during the pandemic.⁷ However, the limited data have not led to evidence-based recommendations. Evidence suggests that COVID-19 diffusion in patients with cancer is not as

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prominent as expected; however, mortality seems to be higher than that reported for the general population and correlates with general risk factors as well as those unique to patients with cancer.⁸⁻¹² Indeed, other comorbidities (eg, cardiovascular disease, diabetes, chronic obstructive pulmonary disease) correlate with a higher risk of infection and severe events.¹³

Most treatment procedures in oncology cannot be delayed without compromising the efficacy of treatment itself. To guarantee the provision of oncology services, general measures to keep cancer centers COVID-free have been adopted, for example, the use of protective devices, patient triage with on-site temperature evaluation, and questions regarding contact and travel history in high-risk areas before accessing the hospital.¹⁴ Telehealth has replaced follow-up for nonurgent visits. Telehealth has also been used to avoid allowing patients with fever and/or recent-onset respiratory symptoms access to oncology services, with redirection to general practitioners for home care or, whenever required, to hospitalization.¹⁴

However, fever and/or respiratory symptoms can be very common findings in patients with cancer, and the interpretation of such symptoms in these patients can be challenging because they are potentially attributed to the seasonal flu, COVID-19, or may simply relate to the underlying disease and/or ongoing systemic treatment. In light of the need for appropriate resource allocation, the objective of our current study was to evaluate the frequency of COVID-19-like symptoms in patients with cancer and to identify high-risk patients to be evaluated for COVID-19 infection by using a diagnostic and decisional algorithm.

MATERIALS AND METHODS

This study was approved by our Institutional Review Board. The primary endpoint was to estimate the cumulative incidence of COVID-19-positive patients identified by triage. The exploratory endpoint was to create a diagnostic and decisional algorithm for patients with suspected COVID-19.

We prospectively collected data from all patients who were treated or followed at our institution from March 20 to April 17, 2020. Institutional guidelines, supported by the Italian Association of Medical Oncology (Associazione Italiana di Oncologia Medica), indicated rescheduling nonurgent visits. Telehealth visits replaced in-person visits. All patients accessing the hospital gave their written informed consent for the use of clinical data

for scientific purposes, whereas those undergoing telehealth visits gave their verbal agreement to participate, and informed consent was signed during their earliest in-person visit.

Patients' baseline characteristics and data regarding cancer treatment were collected. Patients were triaged using 2 paper questionnaires. Questionnaire 1 was completed by physicians in direct patient interviews and assessed the following items: performance status (according to the Eastern Cooperative Oncology Group scale), fever and/or COVID-19-like respiratory and nonrespiratory symptoms in the previous 30 days, thoracic examination, and previous or ongoing thoracic radiotherapy. A full version of the questionnaire is provided in Supporting Table 1.

Questionnaire 2 was completed by patients at the hospital and assessed the following items: smoking history; concomitant receipt of corticosteroids, acetaminophen, and antibiotics plus insulin and oxygen therapy and a possible recent increase in daily need of these treatments; respiratory illnesses (asthma, chronic obstructive pulmonary disease, emphysema); a history of pleuritis and/or pneumonitis; recent vaccinations (seasonal flu, pneumococcal); fever and/or respiratory symptoms in patients and close contacts (household, friends); and travel to high-risk areas within the previous 15 days. A full version of the patient questionnaire is provided in Supporting Table 2.

Vital signs (blood pressure, heart rate, blood oxygen saturation, and respiratory rate) were recorded by nurses before treatment administration; body temperature was measured with a digital, contactless, infrared thermometer. Pretreatment blood tests included complete blood count, lactate dehydrogenase, and C-reactive protein (CRP).

The diagnostic algorithm for patients with suspected COVID-19 came from recommendations of national guidelines and data from the literature available at the beginning of the pandemic.¹⁵⁻¹⁷ An infectious disease specialist's evaluation was promptly performed when the triage process and the medical questionnaire detected fever and new-onset respiratory symptoms; chest imaging and a SARS-CoV-2 swab were performed if clinically indicated (Fig. 1). Through the subsequent analysis of the questionnaires, patients were followed for symptom evolution. SARS-CoV-2 rapid tests (Beijing LEPU Medical Technology Company, Ltd) were offered to patients who reported suspect signs or symptoms that did not fall into the diagnostic algorithm (SARS-CoV-2 IgM and IgG: sensitivity, 88.7%;

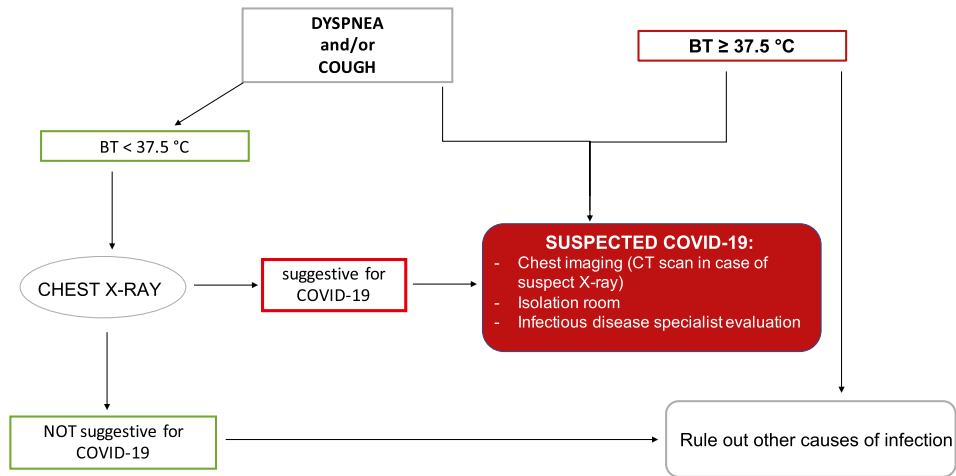


Figure 1. This is the algorithm used for the management of patients with cancer who presented with signs and symptoms suspicious for coronavirus disease 2019 (COVID-19). BT indicates body temperature; CT, computed tomography.

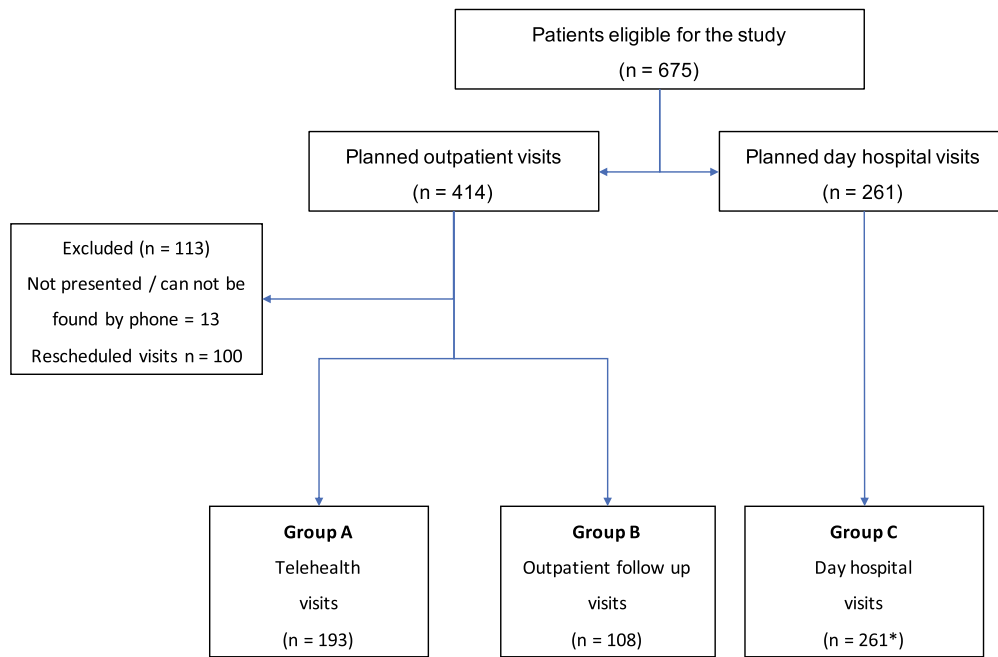


Figure 2. This is a flow diagram of the enrolled patients. *In group C, 68 outpatient on-treatment visits were included (for complete details, refer to the text).

specificity, 90.6%).¹⁸ Patients who were positive for IgM and/or IgG on rapid tests underwent chemiluminescence immunoassays (CLIAs) (LIAISON [Diasorin SpA] and MAGLUMI [Snibe Diagnostics, Shenzhen New Industries Biomedical Engineering Company, Ltd]). LIAISON is an indirect test detecting IgG against the subunits S1 and S2 of the spike viral proteins

(specificity, approximately 98%; sensitivity, 25% at <5 days, 90.4% at 5-15 days, and 97.4% at >15 days from the onset of symptoms). A negative result is defined by an IgG level <15 AU/mL, whereas a positive result is defined as an IgG level ≥15 AU/mL.¹⁹⁻²¹ MAGLUMI is a CLIA for IgM and IgG against SARS-CoV-2 S-antigen and N-protein (IgM and IgG sensitivity, 78%

TABLE 1. General Characteristics of the Study Population

Characteristic	No. (%)			
	All Patients, N = 562	Group A: Telehealth Visits, n = 193	Group B: Outpatient Visits, n = 108	Group C: Day Hospital Visits, n = 261
Age: Median [range], y	69 [26-94]	69 [36-94]	66 [31-88]	69 [26-91]
City of residence				
Milan	375 (67)	140 (73)	72 (67)	163 (62)
Milan district	106 (19)	27 (14)	19 (17)	60 (23)
Other ^a	81 (14)	26 (13)	17 (16)	38 (15)
Sex				
Men	196 (35)	58 (30)	43 (40)	95 (36)
Women	366 (65)	135 (70)	65 (60)	166 (64)
Ethnicity				
Caucasian	527 (94)	187 (97)	99 (92)	241 (92)
Asiatic	19 (3)	3 (2)	5 (4)	11 (4)
Hispanic	9 (2)	1 (<1)	4 (4)	4 (2)
African	7 (1)	2 (1)	—	5 (2)
Cancer diagnosis ^b				
Thoracic	138 (25)	25 (13)	23 (21)	90 (35)
Breast	207 (37)	96 (50)	28 (26)	83 (32)
GI tract	118 (21)	48 (24)	26 (24)	44 (17)
Head and neck	11 (2)	—	3 (3)	8 (3)
Pancreas and biliary tract	33 (6)	9 (5)	8 (7)	16 (6)
Skin: Melanoma, nonmelanoma	18 (3)	5 (3)	7 (7)	6 (2)
Genitourinary tract	23 (4)	5 (3)	8 (7)	10 (4)
Other	14 (2)	5 (2)	5 (5)	4 (1)
Active treatment				
Yes	344 (61)	58 (30)	25 (23)	261 (100)
No, follow-up	218 (39)	135 (70)	83 (77)	—
Type of treatment				
Chemo	126 (37)	3 (5)	5 (20)	118 (45)
Immunotherapy	46 (13)	1 (2)	1 (4)	44 (17)
Chemo and immunotherapy	12 (4)	—	—	12 (5)
Chemo and biologic agents ^c	38 (11)	2 (3)	1 (4)	35 (13)
Other ^d	122 (35)	52 (90)	18 (72)	52 (20)
Treatment administration				
Intravenous	185 (53)	5 (8)	4 (16)	176 (67)
Oral	112 (32)	48 (83)	20 (80)	44 (17)
Intravenous and oral	21 (6)	—	1 (4)	20 (8)
Intramuscular and oral	18 (5)	4 (7)	—	14 (5)
Intramuscular/ subcutaneous	8 (2)	1 (2)	—	7 (3)
Line of treatment				
Adjuvant/neoadjuvant	119 (35)	52 (90)	17 (68)	50 (19)
1	129 (37)	5 (8)	5 (20)	119 (46)
2	57 (17)	1 (2)	1 (4)	55 (21)
≥3	39 (11)	—	2 (8)	37 (14)

Abbreviations: Chemo, chemotherapy; GI, gastrointestinal.

^aOther indicates the remaining geographic areas outside of the Milan district.

^bSix patients (1%) had second primary cancers.

^cThese include the following monoclonal antibodies: antivasular endothelial growth factor, antiepidermal growth factor receptor, and antihuman epidermal growth factor receptor 2.

^dThese include the following treatments: cyclin-dependent kinase 4 (CDK4)/CDK6 inhibitors, hormonal treatment, oral targeted agents (eg, tyrosine kinase inhibitors, mitogen-activated pathway kinase inhibitors), and somatostatin analogues.

and 91%, respectively; IgM and IgG specificity, 97%; combined IgM and IgG sensitivity, 89.9%-95.6%; IgM and IgG specificity, 96.5%-96.0%). The IgM and IgG cutoff levels for positive tests were 1.0 and 1.1 AU/mL, respectively.²²⁻²⁴ Patients with positive CLIA serology underwent rhinopharyngeal swabs for SARS-CoV-2.

To evaluate the role of symptoms and to identify the incidence of SARS-CoV-2 positivity in asymptomatic patients,

we performed a case-control (1:1) comparison. Serologic tests were performed in patients with known COVID-19 to verify the serology in the case of documented infection.

Patients who were included in the current study were followed for COVID-19 onset. Data regarding specific characteristics of the infection were prospectively collected in a dedicated database in the case of documented SARS-CoV-2 infection.

TABLE 2. Items Assessed in Questionnaire 1 (Completed by Medical Oncologists)

Item	No. (%)			
	All Patients, N = 562	Group A: Telehealth Visits, n = 193	Group B: Outpatient Visits, n = 108	Group C: Day Hospital Visits, n = 261
ECOG PS				
0	350 (62)	150 (78)	63 (58)	137 (53)
1	168 (30)	33 (17)	35 (33)	100 (38)
≥2	44 (8)	10 (5)	10 (9)	24 (9)
History of thoracic RT				
Yes	75 (13)	27 (14)	24 (22)	24 (9)
No	487 (87)	166 (86)	84 (78)	237 (91)
Fever				
Yes	22 (4)	6 (3)	4 (4)	12 (5)
No	540 (96)	187 (97)	104 (96)	249 (95)
Symptoms				
Yes	138 (25)	12 (6)	20 (18)	106 (41)
No	424 (75)	181 (94)	88 (82)	155 (59)
COVID-19–like respiratory symptoms	30 (22)	—	4 (20)	26 (24)
Dyspnea	17 (57)	—	3 (75)	14 (54)
Stable	10 (59)	—	3 (100)	9 (64)
Worsened	7 (41)	—	—	5 (36)
Cough	9 (30)	—	—	9 (35)
Stable	3 (33)	—	—	6 (67)
Worsened	6 (67)	—	—	3 (33)
Dyspnea and cough	4 (13)	—	1 (25)	3 (11)
Stable	4 (100)	—	1 (100)	3 (100)
Worsened	—	—	—	—
COVID-19–like nonrespiratory symptoms ^a	68 (49)	6 (50)	8 (40)	54 (51)
Fatigue	47 (69)	1 (17)	4 (50)	42 (78)
Stable	42 (89)	1 (100)	4 (100)	37 (88)
Worsened	5 (11)	—	—	5 (12)
Myalgias	7 (10)	—	—	7 (13)
Stable	2 (29)	—	—	5 (71)
Worsened	5 (71)	—	—	2 (29)
Conjunctivitis	8 (12)	—	1 (12)	7 (13)
Stable	4 (50)	—	—	4 (57)
Worsened	4 (50)	—	1 (100)	3 (43)
Rhinitis/pharyngodinia	6 (9)	2 (33)	2 (25)	2 (4)
Stable	2 (33)	1 (50)	1 (50)	1 (50)
Worsened	4 (67)	1 (50)	1 (50)	1 (50)
GI symptoms ^b	7 (10)	1 (17)	1 (12)	5 (9)
Stable	5 (71)	1 (100)	—	4 (80)
Worsened	2 (29)	—	1 (100)	1 (20)
Other ^c	3 (4)	2 (33)	1 (12)	2 (4)
COVID-19–like respiratory and nonrespiratory symptoms	40 (29)	6 (50)	8 (42)	26 (24)
Dyspnea and other symptoms	18 (45)	3 (50)	4 (50)	11 (42)
Cough and other symptoms	14 (35)	3 (50)	2 (25)	9 (35)
Dyspnea, cough, and other symptoms ^c	8 (20)	—	2 (25)	6 (23)

Abbreviations: COVID-19, coronavirus disease 2019; ECOG, Eastern Cooperative Oncology Group; GI, gastrointestinal; PS, performance status; RT, radiotherapy.
^aThese included patients with ≥1 symptom(s).

^bGI symptoms included nausea (n = 5), vomiting (n = 2), diarrhea (n = 2), and decreased food intake (n = 1).

^cThese included the following symptoms: headache (n = 4), chills (n = 3), anorexia (n = 1), cutaneous rash (n = 1), noncardiac chest pain (n = 1), anxiety (n = 1), malaise (n = 1), and ageusia (n = 1).

Statistical Analysis

Basic descriptive statistics were used to describe the population. Differences in categorical variables were analyzed using the Fisher exact test. The chi-square test was used to analyze proportions when appropriate (comparing 3 groups). Odds ratios and 95% CIs were calculated for each

comparison. The *t* test and the Mann-Whitney test were used to compare continuous variables, as appropriate. *P* values <.05 were considered statistically significant. Statistical analysis was performed using GraphPad Prism version 6.0 (GraphPad Software Inc) and IBM-Microsoft SPSS version 20.0 (SPSS Statistics, IBM Inc) for Mac (Apple Inc).

TABLE 3. Items Assessed in Questionnaire 2 (Completed by Patients)

Item	No. (%)		
	All Patients: Group B and C, N = 369	Group B: Outpatient Visits, n = 108	Group C: Day Hospital Visits, n = 261
Comorbidity(ies) ^a			
None	176 (48)	52 (48)	124 (47)
1	97 (26)	25 (23)	72 (28)
2	57 (15)	17 (16)	40 (15)
≥3	39 (11)	14 (13)	25 (10)
Oxygen therapy			
Yes	16 (4)	7 (6)	9 (3)
No	353 (96)	101 (94)	252 (97)
Seasonal flu vaccination			
Yes	132 (36)	52 (48)	81 (31)
No	172 (47)	27 (25)	145 (56)
Missing data	65 (17)	29 (27)	35 (13)
Other vaccination(s)			
Yes, antipneumococcal	5 (1)	3 (2)	2 (<1)
No	297 (81)	75 (69)	223 (85)
Not assessed	67 (18)	30 (28)	36 (14)
Smoking history			
Smoker	46 (13)	12 (11)	34 (13)
Former smoker ^b	122 (33)	36 (33)	86 (33)
Never smoked	170 (46)	41 (38)	129 (49)
Unknown	31 (8)	19 (18)	12 (5)
Concomitant therapy(ies)			
Corticosteroids	75 (20)	6 (5)	69 (26)
Acetaminophen ^c	77 (21)	17 (16)	60 (23)
Antibiotics	16 (4)	4 (4)	12 (5)
High-risk contacts			
Yes	6 (1)	4 (4)	2 (1)
No	335 (91)	104 (96)	233 (89)
Unknown	28 (8)	—	26 (10)
Fever			
Yes	16 (4)	4 (4)	12 (5)
No	353 (96)	104 (96)	249 (95)
Symptoms			
Yes	120 (32)	18 (17)	102 (39)
No	249 (68)	90 (83)	159 (61)

^aRelevant comorbidities included the following: cardiovascular disease (ischemic heart disease, heart failure), hypertension, respiratory disease (asthma, pulmonary emphysema, chronic obstructive pulmonary disease), diabetes, chronic infections (hepatitis B virus, hepatitis C virus, HIV infections), autoimmune conditions (including rheumatologic diseases), hematologic disease (chronic lymphocytic leukemia, multiple myeloma), and neurologic conditions (cerebrovascular disease).

^bPatients were considered former smokers if smoking cessation happened ≥1 year ago.

^cThese included patients receiving acetaminophen as needed.

RESULTS

Baseline Patient Characteristics

Overall, 675 patients were eligible for the study, 562 patients were enrolled, and 113 patients were excluded. Figure 2 illustrates the flow of patients through the study period. Group A had 193 (34%) telehealth visits, group B had 108 (19%) outpatient ambulatory visits, and group C had 261 (47%) day hospital visits (including 68 outpatient on-treatment visits).

Table 1 lists the baseline characteristics of the study population. The median age of patients was 69 years (range, 26-94 years), with a 1:1.8 male-to-female ratio. The most common cancer diagnosis was breast cancer (37%), followed by thoracic cancer (25%), and gastrointestinal tumors (18%). In total, 344 patients (61%) were

receiving active anticancer treatment, including approximately 30% of patients in groups A and B and all patients in group C ($P < .001$). Most patients were receiving chemotherapy (37%), followed by immunotherapy (13%), chemotherapy plus monoclonal antibodies (11%), or chemotherapy plus immunotherapy (4%); and 122 patients (35%) were receiving various anticancer agents (see Table 1). Most patients in groups A and B were receiving oral therapies (83% and 80%), and a minority of patients who were receiving intravenous treatment did not access the day hospital during the study period. Conversely, 117 patients (45%) in group C were receiving intravenous chemotherapy, 44 (17%) were receiving immunotherapy, 35 (13%) were receiving chemotherapy plus biologic agents, 12 (5%) were receiving chemotherapy plus immunotherapy, and 52 (20%) were receiving oral (17%)

TABLE 4. Laboratory Analysis and Vital Signs

Variable	Group C: Day Hospital Visits, n = 261
CRP, mg/dL	
Mean ± SD	1.02 ± 1.9
Median [range]	0.28 [0.01-11.51]
No. (%)	
<ULN	171 (66)
≥ULN to ≤ULN × 3	43 (16)
>3 × ULN to ≤5 × ULN	16 (6)
>5 × ULN to ≤10 × ULN	19 (7)
>10 × ULN	12 (5)
NLR ratio	
Mean ± SD	2.8 ± 3.3
Median [range]	2.1 [0.4-41.5]
No. (%)	
<5	236 (90)
≥5	25 (10)
LDH, no. (%)	
<ULN	185 (71)
≥ULN	76 (29)
Body temperature, °C	
Mean ± SD	36 ± 0.35
Median [range]	36 [34.6-36.2]
SpO ₂ , %	
Mean ± SD	97 ± 1.8
Median [range]	98 [95-100]
Respiration rate, bpm	
Mean ± SD	16 ± 5
Median [range]	15 [10-25]

Abbreviations: bpm, breaths per minute; CRP, C-reactive protein; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio; SpO₂, blood oxygen saturation; ULN, upper limit of normal.

and intramuscular/subcutaneous therapy (3%). In group A, 90% of patients were receiving neoadjuvant/adjuvant treatment compared with 61% in group B and 19% in group C (*P* < .001). A higher proportion of patients in group C were receiving >2 lines of treatment (n = 92 [35%]; *P* < .001).

Results of the Triage Process

The items assessed in questionnaire 1 are displayed in Table 2. Overall, 138 patients (25%) reported at least 1 symptom. Of these, 30 patients (22%) reported COVID-19–like respiratory symptoms, 68 (49%) reported COVID-19–like nonrespiratory symptoms, and 40 (29%) reported both respiratory and nonrespiratory symptoms. After excluding patients with preexisting symptoms, 68 (49%) had new-onset or worsening COVID-19–like respiratory symptoms (n = 17; 25%), or nonrespiratory symptoms (n = 23; 34%), or both (n = 28; 41%). Twelve patients (2%) had increased CRP levels (ie, >10 times the upper limit of normal), either alone (n = 6) or with COVID-19–like symptoms (n = 6).

Table 3 displays the answers to questionnaire 2. The overall completion rate was 89%. In group B, 48%

of patients had no comorbidities; whereas 23%, 16%, and 13% had 1, 2, and ≥3 comorbidities, respectively. In group C, 47% of patients had no comorbidities; whereas 28%, 15%, and 10% had 1, 2, and ≥3 comorbidities, respectively. Forty-eight percent of patients in group B and 31% of those in group C received seasonal flu vaccination (*P* < .001). Most patients were former smokers (33% in both groups) or never smokers (38% in group B, 49% in group C); and 11% and 13% of patients were smokers in group B and C, respectively (*P* = .586). Compared with group B, a higher proportion of patients in group C were receiving ongoing corticosteroid therapy (26% vs 5%; *P* < .001), and a slightly (not significant) higher proportion were receiving ongoing acetaminophen therapy (23% vs 16%; *P* = .119). A minority of patients were receiving ongoing antibiotic therapy (4% vs 5%; *P* = .701). Overall, 94% of patients in group B and 88% in group C did not report high-risk contacts (*P* = .063). Fever was an uncommon finding: 96% of patients in group B and 95% in group C did not report fever within 30 days before completing the questionnaires. Similarly, the proportion of patients without suspect symptoms was 83% in group B and 61% in group C (*P* < .001).

Blood tests showed a neutrophil-to-lymphocyte ratio ≥5 in 25 patients (10%; mean ± SD, 2.8 ± 3.3); and CRP and lactate dehydrogenase levels were within the reference interval in 171 (66%) and 185 (71%) of patients, respectively. All patients had a body temperature <37 °C (mean ± SD, 36 °C ± 0.35 °C) and had adequate blood oxygen saturation (mean ± SD, 97% ± 1.8%). The mean ± SD respiratory rate was 16 ± 5 breaths per minute, and a higher rate was observed in patients who had thoracic primary or secondary tumors and was not further investigated. No medical intervention was required based on vital signs. The results of laboratory analyses and vital signs are detailed in Table 4.

Based on the medical questionnaires, 4 patients (<1%) met the algorithm criteria (3 telehealth triages and 1 ambulatory visit), and all had a COVID-19 diagnosis. Two patients (<1%) had a negative triage (1 in group B, 1 in group C) and developed fever and respiratory symptoms after 20 and 30 days from triage evaluation, respectively. These 2 patients subsequently were diagnosed with COVID-19. Based on patients’ questionnaires, no patients met the algorithm criteria to be tested for COVID-19. Patients who reported at least 1 symptom at the questionnaire and/or altered laboratory tests were followed and selected for serologic tests.

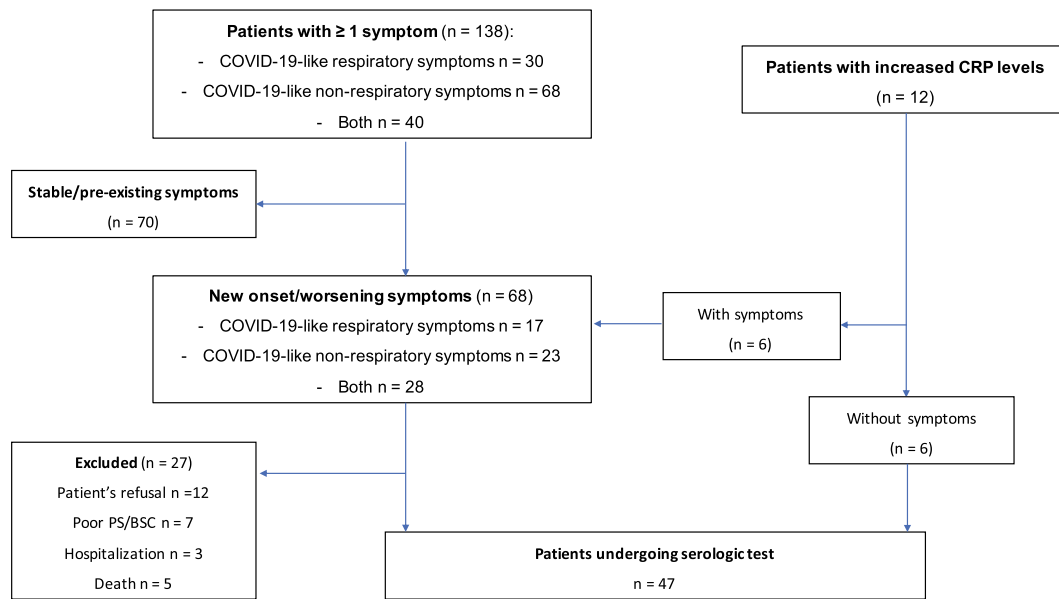


Figure 3. This is a flow diagram of symptomatic patients or patients with altered laboratory tests who were selected for coronavirus disease 2019 (COVID-19) serologic tests. CRP indicates C-reactive protein; PS, performance status; BSC, best supportive care.

Results of Serologic Tests

Figure 3 illustrates the flow of patients selected for serologic tests. Of the 74 patients who had new-onset symptoms and/or altered laboratory tests, 47 (63%) underwent rapid SARS-CoV-2 IgM/IgG tests. The remaining patients ($n = 27$; 37%) were not tested based on the patient's refusal ($n = 12$), poor performance status ($n = 7$), hospitalization ($n = 3$), or death ($n = 5$).

The control group included 47 asymptomatic patients. Table 5 displays the characteristics of patients undergoing serologic tests. Among the patients who were screened with the LEPU test, 6 (13%) were positive, including 4 who were IgG-positive, 1 who was IgM-positive, and 1 who was both IgM-positive and IgG-positive. IgG positivity was confirmed in 4 of 5 patients who were screened with the LIAISON test and in 2 of 5 patients who were screened with the MAGLUMI test (2 patients had borderline positive values); all MAGLUMI tests were negative for IgM. In the control group, 5 patients (11%) had a positive LEPU test, including 2 who were IgM-positive (weak), 1 who was IgG-positive, 1 who was IgG-positive (weak), and 1 who was both IgM-positive and IgG-positive. LIAISON and MAGLUMI tests confirmed IgG positivity in 1 IgG-positive patient and in 1 IgM-positive/IgG-positive patient; all MAGLUMI tests were negative for IgM. The prevalence of an IgM-positive/IgG-positive result using the LEPU test

was similar between patients with symptoms and the control group (13% vs 11%; $P = .748$).

All patients who had positive LEPU tests and/or CLIAs underwent rhinopharyngeal swabs at a median of 40 days (range, 35–45 days) after questionnaire completion, and all were negative except for 1 patient in the control group.

DISCUSSION

The ONCOVID study is the first prospective study collecting data from patients with cancer at the beginning of the COVID-19 outbreak using a structured triage process. From the time of study conception throughout the period of data collection, the number of COVID-19 cases increased from 22,000 to 63,000 in Lombardy and from 1550 to 6300 in the city of Milan.^{6,25,26} Therefore, the need for a triage process for oncology facilities rapidly became essential for our clinical practice. The results of our study suggest that triage can be useful for detecting COVID-19 symptoms and signs without being associated with false-positive or false-negative results. Telehealth triage seems to help with detecting suspect patients and keeping a COVID-19-free cancer center.

Data on COVID-19 and cancer are growing rapidly. Most prospective studies, however, have focused on patients who have cancer with a confirmed COVID-19

TABLE 5. Baseline Characteristics and Serologic Results of Positive Patients Among the Group of Patients With Symptoms (POLI-001–POLI-049) and in the Control Group (C01–C27)

ID No.	Sex	Age, y	ECOG PS	Diagnosis	Systemic Treatment, Line	Reason(s) for Test	Comorbidity	Colloidal Gold Immunochromatography		Liaison CLIA Test		Swab	
								IgM	IgG	IgG, AU/mL	MAGLUMI CLIA Test		
POLI-001	Man	69	1	Pleural mesothelioma	CDDP and pemetrexed, 1 line	PCR increased	CHD	Neg	Pos	<3.8	0.39	0.18	Neg
POLI-002	Man	44	0	Melanoma	Nivolumab, adjuvant	Fever, cough	None	Pos	Pos	155	0.798	0.902 ^a	Neg
POLI-026	Woman	78	0	Pleural mesothelioma	CBDCA and pemetrexed, 1 line	Fever, high risk contact	Hypertension	Neg	Pos	66.4	0.53	14.87	Neg
POLI-030	Woman	67	1	Breast cancer	Docetaxel pertuzumab and trastuzumab, 1 line	Fever, cough	Arrhythmia	Pos	Neg	<3.8	0.44	0.23	Neg
POLI-034	Woman	85	1	Breast cancer	Capecitabine and vinorelbine, 2 lines	Fever, cough, asthenia, pneumonitis	None	Neg	Pos	69.5	0.57	0.9 ^a	Neg
POLI-049	Woman	53	0	Breast cancer	Pegylated liposomal and doxorubicin, 3 lines	Fever	None	Neg	Pos	3.424	0.318	29	Neg
C01	Woman	73	0	NSCLC (ADC)	Pembrolizumab, 2 lines	—	Hypertension, obesity	Pos (weak)	Neg	<3.8	0.57	0.18	ND
C03	Man	76	1	SCLC	Topotecan, 3 lines	—	None	Pos (weak)	Neg	<3.8	0.5	0.16	ND
C12	Woman	68	0	NSCLC (ADC)	Atezolizumab, 2 lines	—	None	Neg	Pos	93.5	0.58	2.02	Pos
C20	Woman	74	1	NSCLC (ADC)	Osimertinib, 1 line	—	None	Neg	Pos (weak)	4.6	0.53	0.17	ND
C27	Man	84	1	NSCLC (ADC)	Nivolumab, 3 lines	—	Hypertension, diabetes, TIA	Pos	Pos	43.3	0.53	16.23	Neg

Abbreviations: ADC, adenocarcinoma; CBDCA, carboplatin; CHD, coronary heart disease, CLIA, chemiluminescence immunoassay; ECOG, Eastern Cooperative Oncology Group; ID, identification; ND, not done; Neg, negative; NSCLC, nonsmall cell lung cancer; PCR, polymerase chain reaction; Pos, positive; PS, performance status; SCLC, small cell lung cancer; TIA, transient ischemic attack.

^aThis value indicates borderline positive results.

diagnosis (either clinical, radiologic, or performed with serologic tests/rhinopharyngeal swabs).²⁷⁻²⁹ Overall, there does not appear to be a higher incidence of COVID-19 in patients with cancer, and the risk does not seem to be increased in those receiving anticancer treatment. Still, patients with cancer seem to be at higher risk of severe COVID-19 and reduced intensive care unit access, leading to higher mortality rates. In a recent report from the National Cancer Institute of Milan, a triage process, consisting of high-resolution, low-dose computed tomography thoracic scans followed by a rhinopharyngeal swab, was used to detect SARS-CoV-2 positivity in hospital patients.³⁰ However, the routine use of radiologic and serologic examinations may be less applicable in clinical practice. The implementation of triage could be an easy method to monitor patients in this setting of care.

The ONCOVID study provides several important findings. First, our data confirm the relatively low incidence of COVID-19 in patients with cancer. From the beginning of the pandemic over a 5-month study period—including patients who were not enrolled in the study—in total, 16 patients at our institution had a documented COVID-19 diagnosis, and 2 had a strong clinical suspicion of COVID-19. Another important finding is that the overall incidences of COVID-19 diagnosis in our study population (1%) and antibody positivity (13%) in patients with suspect symptoms were similar to those observed in patients who had cancer without suspect symptoms (11%). Therefore, data from our study suggest that most oncology activities can be safely performed during the pandemic. Simple containment measures to reduce hospital access can be pursued without compromising cancer care delivery.

Our study has some intrinsic limitations. The relatively low rate of COVID-19 diagnosis in our population might have been caused by the protective measures carried out by patients rather than a reduced risk of COVID-19. Because of the inability to perform serologic tests on all patients, the incidence of COVID-19 is not supported by secure numerators and denominators of infection for this calculation. Nevertheless, the number of positive cases seems low, suggesting that containment measures and rapid detection of symptoms with triage might help physicians to safely provide oncology care. Because of the low observed incidence of COVID-19, an excessively high number of patients should have been evaluated to confirm statistically significant results. However, the results of case-control comparisons

suggest there is a superimposable incidence of antibody positivity among the 2 groups. Finally, the low number of confirmed COVID-19 cases does not allow us to derive considerations on prognostic factors for infection and outcomes. The identification of patients who are at higher risk for COVID-19 is currently under study through the validation of a risk-assessment score in the study population (the Milano Policlinico ONCOVID score).³¹

Conclusions

In our experience, the triage process had a positive impact on the detection of COVID-19 in patients with cancer. The overall incidence of COVID-19 diagnosis and antibody positivity in patients with suspect symptoms was similar to that observed in asymptomatic patients. The identification of risk factors for COVID-19 in patients with cancer is needed to customize treatment and provide the best care in the current situation.

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AUTHOR CONTRIBUTIONS

Alice Indini: Conceptualization, data curation, formal analysis, investigation, methodology, supervision, visualization, writing—original draft, and writing—review and editing. **Monica Cattaneo:** Data curation, formal analysis, investigation, methodology, visualization, and writing—original draft. **Michele Ghidini:** Data curation, investigation, visualization, and writing—original draft. **Erika Rijavec:** Data curation, investigation, visualization, and writing—original draft. **Claudia Bareggi:** Data curation, investigation, visualization, and writing—original draft. **Barbara Galassi:** Data curation, investigation, visualization, and writing—original draft. **Donatella Gambini:** Data curation, investigation, visualization, and writing—original draft. **Rosalia Ceriani:** Data curation, investigation, visualization, and writing—original draft. **Ferruccio Ceriotti:** Methodology, project administration, supervision, and writing—review and editing. **Emilio Berti:** Funding acquisition, methodology, project administration, resources, supervision, and writing—review and editing. **Francesco Grossi:** Conceptualization, funding acquisition, methodology, project administration, resources, supervision, and writing—review and editing.

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