

# Feasibility and Predictive Performance of a Triage System for Patients with Cancer During the COVID-19 Pandemic

GIANPIERO FASOLA,<sup>a</sup> GIACOMO PELIZZARI<sup>1</sup>,<sup>a</sup> DIEGO ZARA,<sup>a</sup> GIADA TARGATO,<sup>a</sup> GIUSEPPE PETRUZZELLIS,<sup>b</sup> ALESSANDRO MARCO MINISINI,<sup>a</sup> ALESSANDRA BIN,<sup>a</sup> RAFFAELA DONATO,<sup>a</sup> MAURO MANSUTTI,<sup>a</sup> CHIARA COMUZZI,<sup>b</sup> ANNA CANDONI,<sup>b</sup> ALESSANDRA SPEROTTO,<sup>b</sup> RENATO FANIN<sup>b,c</sup>

Departments of <sup>a</sup>Oncology and <sup>b</sup>Hematology, Santa Maria della Misericordia Hospital, Udine, Italy; <sup>c</sup>Department of Medicine, University of Udine, Udine, Italy

Disclosures of potential conflicts of interest may be found at the end of this article.

**Key Words.** COVID-19 • SARS-CoV-2 • Cancer • Containment measures • Triage

## ABSTRACT

**Background.** Triage procedures have been implemented to limit hospital access and minimize infection risk among patients with cancer during the coronavirus disease (COVID-19) outbreak. In the absence of prospective evidence, we aimed to evaluate the predictive performance of a triage system in the oncological setting.

**Materials and Methods.** This retrospective cohort study analyzes hospital admissions to the oncology and hematology department of Udine, Italy, during the COVID-19 pandemic (March 30 to April 30, 2020). A total of 3,923 triage procedures were performed, and data of 1,363 individual patients were reviewed.

**Results.** A self-report triage questionnaire identified 6% of triage-positive procedures, with a sensitivity of 66.7% (95% confidence interval [CI], 43.0%–85.4%), a specificity of 94.3% (95% CI, 93.5%–95.0%), and a positive predictive value of 5.9% (95% CI, 4.3%–8.0%) for the identification of patients who were not admitted to the hospital after

medical review. Patients with thoracic cancer (odds ratio [OR], 1.69; 95% CI, 1.13–2.53,  $p = .01$ ), younger age (OR, 1.52; 95% CI, 1.15–2.01,  $p < .01$ ), and body temperature at admission  $\geq 37^{\circ}\text{C}$  (OR, 9.52; 95% CI, 5.44–16.6,  $p < .0001$ ) had increased risk of positive triage. Direct hospital access was warranted to 93.5% of cases, a further 6% was accepted after medical evaluation, whereas 0.5% was refused at admission.

**Conclusion.** A self-report questionnaire has a low positive predictive value to triage patients with cancer and suspected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) symptoms. Differential diagnosis with tumor- or treatment-related symptoms is always required to avoid unnecessary treatment delays. Body temperature measurement improves the triage process's overall sensitivity, and widespread SARS-CoV-2 testing should be implemented to identify asymptomatic carriers. *The Oncologist* 2021;26:e694–e703

**Implications for Practice:** This is the first study to provide data on the predictive performance of a triage system in the oncological setting during the coronavirus disease outbreak. A questionnaire-based triage has a low positive predictive value to triage patients with cancer and suspected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) symptoms, and a differential diagnosis with tumor- or treatment-related symptoms is mandatory to avoid unnecessary treatment delays. Consequently, adequate recourses should be reallocated for a triage implementation in the oncological setting. Of note, body temperature measurement improves the overall sensitivity of the triage process, and widespread testing for SARS-CoV-2 infection should be implemented to identify asymptomatic carriers.

## INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-associated coronavirus disease (COVID-19) outbreak was first reported in December 2019 in China and rapidly spread worldwide [1, 2].

Italy was one of the first European countries affected by the pandemic and, for many months, had the second-highest number of confirmed COVID-19 cases globally. As of January 3, 2021, 2,119,886 cases were diagnosed, and

Correspondence: Giacomo Pelizzari, M.D., Department of Oncology, Santa Maria della Misericordia Hospital, P.le Santa Maria della Misericordia 15, 33100 Udine, Italy. Telephone: 39 0432 552751; e-mail: giacomo.pelizzari@asufc.sanita.fvg.it Received September 7, 2020; accepted for publication January 22, 2021; published Online First on February 19, 2021. <http://dx.doi.org/10.1002/onco.13706>  
No part of this article may be reproduced, stored, or transmitted in any form or for any means without the prior permission in writing from the copyright holder. For information on purchasing reprints contact [commercialreprints@wiley.com](mailto:commercialreprints@wiley.com). For permission information contact [permissions@wiley.com](mailto:permissions@wiley.com).

72,613 deaths were reported in Italy since the first diagnosed case on February 18, 2020 [3].

Patients with cancer are considered at increased risk for severe complications and death during the COVID-19 pandemic [4–7]. This might be because of the immunosuppressive action of both the tumor itself and concurrent antineoplastic treatments, the use of immunomodulatory agents, frequent hospital visits, and the older age and comorbidities usually observed among patients with cancer.

At the beginning of the COVID-19 pandemic, the Italian Ministry of Health recommended providing necessary cancer treatment during the SARS-CoV-2 outbreak [8]. Efforts were made to ensure continuing appropriate care for patients with cancer to reduce the risk of treatment delays and unfavorable outcomes [9].

Hospitals rapidly implemented containment measures to minimize SARS-CoV-2 spread and protect patients and health workers from the infection [10]. Health care authorities and scientific societies endorsed this approach with a focus on oncology and hematology departments [11–15].

Both clinicians [16, 17] and scientific societies [12, 15] strongly recommended rapidly detecting potential cases of COVID-19 among patients accessing oncology services. However, no data are currently available on the accuracy and impact of such procedures on cancer care.

Therefore, this study aimed to evaluate the feasibility and predictive performance of a triage system implemented in a cancer center during the COVID-19 pandemic.

## SUBJECTS, MATERIALS, AND METHODS

### Study Design

This retrospective cohort study was conducted on a consecutive series of 1,363 patients with solid cancer or hematological neoplasms treated at the University Hospital of Udine, Italy, during the COVID-19 outbreak.

Between March 30 and April 30, 2020, a triage questionnaire was implemented for patients seeking admission to the day unit (DU) of the oncology and hematology department as a containment measure to prevent infections among patients and health care workers. Overall, a total of 3,923 triage procedures were performed and retrospectively reviewed.

The primary objective of the present study was to assess the feasibility and predictive performance of a triage questionnaire for the identification of patients who were not admitted to the hospital after medical review. Secondly, we evaluated triage outcomes in terms of hospital admissions, oncological program variations, SARS-CoV-2 tests, and results. Finally, we identified clinicopathological predictors of positive triage questionnaire at admission.

### Triage System

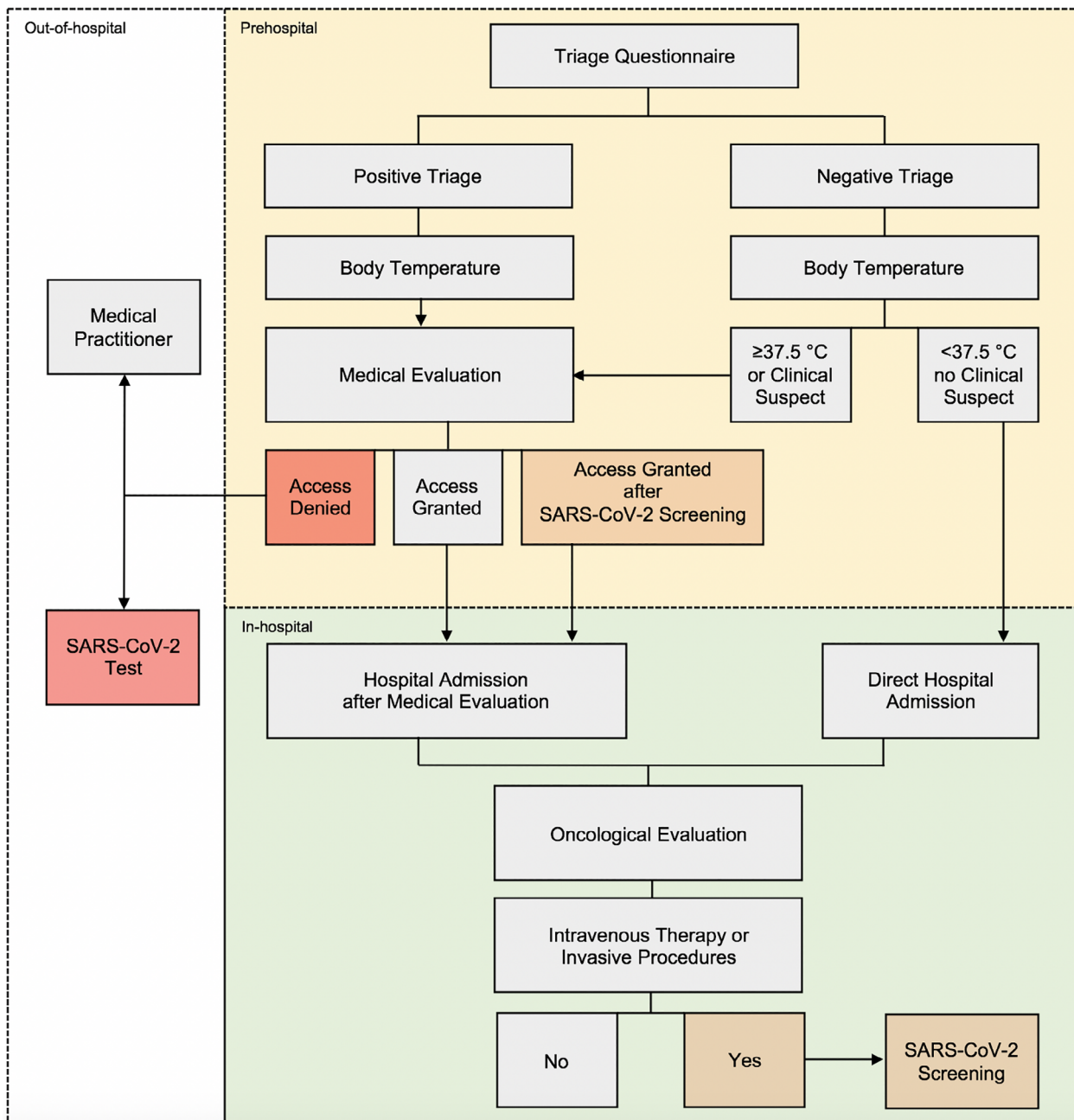
All patients seeking admission to the DU of the oncology and hematology department of the University Hospital of Udine, Italy, underwent evaluation. The triage procedure consisted of a self-report questionnaire comprising four items to assess patients' clinical status: the presence of

fever and symptoms suggestive for respiratory infection and personal exposure to the SARS-CoV-2 virus. The questionnaire included the following key questions: (a) "Have you (or one of your family members) had fever ( $\geq 37^{\circ}\text{C}$ ) in the last 14 days?" (b) "Have you (or one of your family member) had any of the following symptoms in the last 14 days: sneezing, sore throat, cough or difficulty breathing, loss of taste and smell?" (c) "Have you (or one of your family members) been in close contact with confirmed SARS-CoV-2 infected persons in the last 14 days?" (d) "Have you (or one of your family members) been asked to self-quarantine and/or have you (or one of your family members) been tested positive for the SARS-CoV-2 virus?" The triage questionnaire was considered positive if the patient reported at least one positive answer.

The questionnaire defined fever as having a body temperature (BT)  $\geq 37^{\circ}\text{C}$  (vs.  $\geq 37.5^{\circ}\text{C}$ ) [18] to limit the underestimation of possible febrile states. Indeed, the reporting of low-grade hyperpyrexia is clinically relevant for the triage of possible SARS-CoV-2 infection. Besides, patients received concurrent measurement of BT at and declared any previous SARS-CoV-2 test results.

A health care assistant carried out the triage procedures guided by a triage nurse. A dedicated medical assessment was mandatory in case of a positive triage questionnaire, actual evidence of BT  $\geq 37.5^{\circ}\text{C}$ , or symptoms requiring medical intervention. Following medical evaluation, patients were (a) not admitted to the DU (new-onset respiratory symptoms suspected for infection), (b) granted hospital access (no suspect of infection after medical evaluation), (c) or were accepted after a negative SARS-CoV-2 test (for differential diagnosis with tumor-related, preexisting respiratory symptoms). Furthermore, all patients wore a surgical mask and performed adequate hand hygiene to get access to the DU. A patient flow chart summarizing the triage system is described in Figure 1.

The DU of the oncology and hematology department consists of four patient-dedicated areas: an acute area for urgency and unplanned accesses, chemotherapy administration rooms, a nursing area for blood tests and other diagnostic procedures, and the main clinic for pretreatment evaluations. Patients may get access to the DU for pretreatment evaluations, therapy administration, blood tests, consultations, or unplanned medical evaluations. Since April 6, 2020, patients receiving intravenous treatments have been tested for SARS-CoV-2 infection before each new therapy cycle [15]. For these patients, the oncological treatment was administered only with a negative test. In the oncology department, intravenous treatments were administered the day after the oncological evaluation, with another access required. In contrast, patients receiving oral therapies, intramuscular injection, or rapid infusions (lasting less than 1 hour) were not subjected to routine tests and received the same treatment on the same day of medical evaluation. Patients were followed up for a minimum of 2 weeks after triage evaluation to identify post-triage diagnoses of SARS-CoV-2 infection. Health care professionals were also tested for SARS-CoV-2 by active surveillance with a nasopharyngeal swab every 2 weeks [19].



**Figure 1.** Triage process: patient flow chart.

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

### Triage Status Definitions

Patients were categorized as triage-positive if they reported at least a positive answer in the triage questionnaire. The triage outcomes were defined as the effect of questionnaire results on hospital admission (admission vs. refusal of admission), oncological program (evaluation, treatment, check-up performed vs. evaluation delayed), SARS-CoV-2 test (test performed vs. not performed), and detected infections (positive test vs. negative test). All triage-positive patients received a prehospital medical evaluation in a dedicated “respiratory waiting area” to get DU access. For accuracy analysis, triage-positive patients (i.e., patients with a positive triage questionnaire) were considered

false-positive if hospital admission was eventually granted after medical evaluation. Likewise, triage-negative patients were considered false-negative if hospital access was denied due to other clinical reasons.

### Data Collection

Patient-level data were collected from electronic medical records according to strict privacy standards. The study was approved by the internal review board of the department of oncology, University Hospital of Udine, and by the Regional Ethics Committee (Protocol no. CEUR-2020-Os-171). Informed consent was obtained for the use of clinical

**Table 1.** Characteristics of triage procedures and screened patients

| <b>Patients (n = 1,363)</b>   | <b>n (%)</b> |
|---|--------------|
| Number of triage procedures per patient                                 |              |
| 1   | 465 (34.1)   |
| 2   | 324 (23.8)   |
| 3   | 142 (10.4)   |
| ≥4  | 432 (31.7)   |
| Median number of triage procedures per patient (IQR)                    | 2 (1–4)      |
| Min–max   | 1–15         |
| Triage procedures: characteristics of patients <sup>a</sup> (n = 3,923) |              |
| Cancer type   |              |
| Solid malignancies  | 2,657 (67.7) |
| Hematological malignancies  | 1,266 (32.3) |
| Sex   |              |
| Male  | 1,698 (43.3) |
| Female  | 2,225 (56.7) |
| Age, years  |              |
| <65   | 1,814 (46.2) |
| ≥65   | 2,109 (53.8) |
| Median (IQR)  | 66.3 (55–73) |
| Cancer type   |              |
| Breast cancer   | 848 (21.6)   |
| Lung cancer   | 426 (10.9)   |
| Non-Hodgkin lymphoma  | 344 (8.8)    |
| Colorectal cancer   | 319 (8.1)    |
| Multiple myeloma  | 282 (7.2)    |
| Pancreatic cancer   | 214 (5.5)    |
| Acute leukemia  | 178 (4.5)    |
| Gastric cancer  | 154 (3.9)    |
| Hodgkin lymphoma  | 135 (3.5)    |
| Allogeneic bone marrow transplant                                       | 132 (3.4)    |
| Skin cancer and melanoma  | 124 (3.2)    |
| Chronic lymphocytic leukemia  | 111 (2.8)    |
| Ovarian cancer  | 111 (2.8)    |
| Head and neck cancer  | 79 (2.0)     |
| Prostatic cancer  | 76 (1.9)     |
| Urothelial cancer   | 74 (1.9)     |
| Renal cancer  | 61 (1.6)     |
| Gynecological cancer (ovarian cancer excluded)                          | 51 (1.3)     |
| Bile duct cancer  | 36 (0.9)     |
| Brain cancer  | 26 (0.7)     |
| Myeloproliferative disease  | 17 (0.4)     |
| Myelodysplastic syndrome  | 15 (0.4)     |
| Sarcoma and rare tumors   | 12 (0.3)     |
| Endocrine cancer  | 12 (0.3)     |
| Testicular cancer   | 11 (0.3)     |
| Esophageal cancer   | 8 (0.2)      |
| Other   | 67 (1.7)     |

(continued)

**Table 1.** (continued)

| <b>Patients (n = 1,363)</b>                              | <b>n (%)</b> |
|--|--------------|
| Disease stage  |              |
| Early-stage disease                                      | 946 (24.1)   |
| Advanced-stage disease                                   | 2,977 (75.9) |
| Reason for hospital admission                            |              |
| Medical evaluation for therapy or therapy administration | 3,363 (85.7) |
| Procedures/radiology                                     | 311 (7.9)    |
| Blood test   | 75 (1.9)     |
| Oncologic consultations or check-ups                     | 71 (1.8)     |
| Emergency/unplanned accesses                             | 37 (1.0)     |
| Hospitalization  | 10 (0.3)     |
| Other  | 56 (1.4)     |
| Oncologic treatment                                      |              |
| Chemotherapy   | 2,354 (60.0) |
| Immunotherapy  | 481 (12.3)   |
| Targeted therapy   | 582 (14.8)   |
| Other therapy  | 283 (7.2)    |
| No therapy   | 223 (5.7)    |

<sup>a</sup>Patients might have been screened for multiple accesses.  
Abbreviation: IQR, interquartile range.

data for purposes of clinical research from electronic records.

### Statistical Analysis

Baseline demographic and clinicopathological characteristics were summarized through descriptive analysis. Continuous variables were reported through the median and interquartile range, whereas categorical variables were described through frequency distribution. Factors associated with a positive triage were investigated through uni- and multivariate logistic regression with odds ratio (OR) calculation. A two-sided  $p < .05$  was considered statistically significant. Last, we assessed the triage questionnaire's overall accuracy for identifying patients who were not admitted to the hospital after medical review. Statistical analyses were performed in R Version 3.5.1 (R Foundation for Statistical Computing, 2016) and RStudio Version 1.1.456 (RStudio, Inc., Boston, MA).

## RESULTS

### Study Population

From March 30 to April 30, 2020, a total of 3,923 triage procedures were performed. Overall, 1,363 patients were screened with a median of two triage procedures per patient (range, 1–15). Of note, one-third of patients (31.7%) performed more than four triage procedures. The median age was 66.3 years, and 56.7% of assessed patients were female. Two-thirds of procedures (67.7%) were conducted at the oncology department and 32.3% at the hematology department. Breast cancer was the most frequent tumor in

our cohort (21.6%), followed by lung cancer (10.9%), non-Hodgkin lymphoma (8.8%), and colorectal cancer (8.1%). Almost 76% of procedures referred to patients with advanced-stage disease.

Most of the triage procedures referred to patients admitted to the DU for treatment administration (85.7%) and fewer for other reasons, including medical procedures or radiological exams (7.9%), blood tests (1.9%), oncological consultations (1.8%), medical emergencies (1.0%), or hospitalization (0.3%). Of note, 60% of triage procedures were performed on patients treated with chemotherapy-based regimens. The rest of the patients were receiving single-agent immunotherapy (12.3%), targeted therapy (14.8%), or other therapies (7.2%). Only 5.7% of patients at admission were not on active treatment. In 70% of cases, an onco-hematological treatment had been prescribed in the previous 21 days. Additional patients' characteristics and triage information are summarized in Table 1.

### Triage Procedures and Outcomes

Overall, 237 out of 3,923 triage questionnaires (6.0%) resulted positive. Specifically, 155 questionnaires (4.0%) reported fever in the previous 14 days, 94 (2.4%) reported respiratory symptoms, and 8 (0.25%) reported a previous contact with a confirmed case of SARS-CoV-2 infection. Concurrent BT was 37–37.4°C in 48 patients (1.2%) and  $\geq 37.5^\circ\text{C}$  in 16 cases (0.4%). A previous nasopharyngeal swab was performed in 41.6% of cases without any positivity (Table 2).

Direct access to the oncology and hematology department was granted in 93.5% of cases. A further 6% was accepted after medical evaluation, whereas 21 patients



**Table 2.** Triage procedures and outcomes

| Triage procedures  |  | Triage procedures<br>(n = 3,923), n (%)          |
|--|--|--|
| Triage questionnaire   |  |  |
| 1. Have you (or one of your family members) had fever ( $\geq 37^{\circ}\text{C}$ ) in the last 14 days? Yes   |  | 155 (4.0)  |
| 2. Have you (or one of your family members) had any of the following symptoms in the last 14 days: cold, sore throat, cough or breathing difficulty, loss of taste, and smell? Yes |  | 94 (2.4)   |
| 3. Have you (or one of your family members) been in close contact with confirmed SARS-CoV-2 infected persons in the last 14 days? Yes  |  | 2 (0.05)   |
| 4. Have you (or one of your family members) been asked to self-quarantine and/or have you (or one of your family members) been tested positive for the SARS-CoV-2 virus? Yes       |  | 6 (0.2)  |
| Triage questionnaire result (number of positive answers)   |  |  |
| 0  |  | 3,686 (94.0)                                     |
| 1  |  | 217 (5.5)  |
| 2  |  | 20 (0.5)   |
| 3  |  | 0 (0)  |
| 4  |  | 0 (0)  |
| Positive triage (positive triage questionnaire)  |  |  |
| Yes  |  | 237 (6.0)  |
| No   |  | 3,686 (94.0)                                     |
| Therapy administration in the last 21 days   |  |  |
| Yes  |  | 2,762 (70.4)                                     |
| No   |  | 1,161 (29.6)                                     |
| BT at admission $37\text{--}37.4^{\circ}\text{C}$  |  |  |
| Yes  |  | 48 (1.2)   |
| No   |  | 3,875 (98.8)                                     |
| BT at admission $\geq 37.5^{\circ}\text{C}$  |  |  |
| Yes  |  | 16 (0.4)   |
| No   |  | 3,907 (99.6)                                     |
| Prior SARS-CoV-2 test  |  |  |
| Yes  |  | 1,632 (41.6)                                     |
| No   |  | 2,291 (58.4)                                     |
| Prior SARS-CoV-2 test result   |  |  |
| Positive   |  | 0 (0)  |
| Negative   |  | 1,632 (100)                                      |
| <b>Triage outcomes (n = 3,923)</b>   |  |  |
| Triage outcome: hospital access  |  |  |
| Direct hospital access   |  | 3,668 (93.5)                                     |
| Hospital access after medical evaluation   |  | 234 (6.0)  |
| Access denied  |  | 19 (0.45)  |
| Access denied: patients referred to a different facility   |  | 2 (0.05)   |
| Triage outcome: therapy or evaluation postponed  |  |  |
| Yes  |  | 21 (0.5)   |
| No   |  | 3,902 (99.5)                                     |
| Triage outcome: SARS-CoV-2 test performed  |  |  |
| Yes  |  | 36 (0.9)   |
| No   |  | 3,887 (99.1)                                     |
| SARS-CoV-2 test result (n = 36)  |  |  |
| Positive   |  | 0 (0)  |
| Negative   |  | 36 (100)   |
| Triage outcome according to triage result  | Positive triage procedures<br>(n = 237), n (%) | Negative triage procedures<br>(n = 3,686), n (%) |
| Triage outcome: hospital access  |  |  |
| Direct hospital access   | 0 (0)  | 3,668 (99.5)                                     |
| Hospital access after medical evaluation   | 223 (94.1)                                     | 11 (0.3)   |
| Access denied  | 12 (5.1)                                       | 7 (0.2)  |
| Access to a different hospital facility  | 2 (0.8)  | 0 (0)  |

(continued)

**Table 2.** (continued)

| Triage outcome according to triage result       | Positive triage procedures<br>(n = 237), n (%) | Negative triage procedures<br>(n = 3,686), n (%) |
|---|--|--|
| Triage outcome: therapy or evaluation postponed |  |  |
| Yes   | 14 (5.9)                                       | 7 (0.2)  |
| No  | 223 (94.1)                                     | 3,679 (99.8)                                     |
| Triage outcome: SARS-CoV-2 test performed       |  |  |
| Yes   | 34 (16.7)                                      | 2 (0.05)   |
| No  | 203 (83.3)                                     | 3,684 (99.95)                                    |

Abbreviations: BT, body temperature; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

(0.5%) were not admitted to the DU (2 of them were referred to the infectious disease department). Thus, 21 oncological consultations or therapies were postponed (0.5%), and 36 (0.9%) nasopharyngeal swabs were performed according to clinical indication, none of them with a confirmed diagnosis of SARS-CoV-2 infection.

Hospital access was denied to 14 out of 237 triage-positive patients (5.9%), with a delay of their oncological check-ups or therapy. Among them, six patients met clinical criteria for testing for SARS-CoV-2. The rest of the triage-positive cases were admitted after medical evaluation, although 28 patients received a concurrent SARS-CoV-2 test. Regarding triage-negative patients, 11 (0.3%) still required medical evaluation: hospital access was denied to 7 patients (0.2%) because of clinical indication (6 had a BT  $\geq 37^{\circ}\text{C}$ , 1 had respiratory symptoms), and 2 of them were tested for SARS-CoV-2. Triage outcomes are summarized in the diagram flow shown in Figure 2 and Table 2.

The overall accuracy of the triage questionnaire to identify patients who were not admitted to the hospital was 94.1% (95% confidence interval [CI], 93.3%–94.8%), with a sensitivity of 66.7% (95% CI, 43.0%–85.4%), a specificity of 94.3% (95% CI, 93.5%–95.0%), a positive predictive value (PPV) of 5.9% (95% CI, 4.3%–8.0%), and a negative predictive value of 99.8% (95% CI, 99.6%–99.9%; Table 3).

As per local protocol, a post-triage nasopharyngeal swab was performed on patients requiring intravenous therapy or invasive procedures, regardless of triage outcomes. A concurrent post-triage SARS-CoV-2 test was available for 765 triage-negative patients admitted to the oncology department. Among them, one patient had a positive SARS-CoV-2 test. Moreover, during the post-triage follow-up, two out of 1,363 patients tested positive for the SARS-CoV-2 infection (days since last triage evaluation: 18 and 19). Retrospectively, all these patients were triage negative, with no suggestive symptoms and a BT  $< 37^{\circ}\text{C}$  at admission. No secondary infections were detected among health care workers and other patients who were close to these patients.

### Independent Predictors of Positive Triage

A diagnosis of thoracic cancer (OR, 1.69; 95% CI, 1.13–2.53;  $p = .01$ ), younger age (OR, 1.52; 95% CI, 1.15–2.01;  $p < .01$ ), and a BT at admission  $\geq 37^{\circ}\text{C}$  (OR, 9.52; 95% CI, 5.44–16.6;

$p < .0001$ ) were independently associated with an increased risk of positive triage (Table 4).

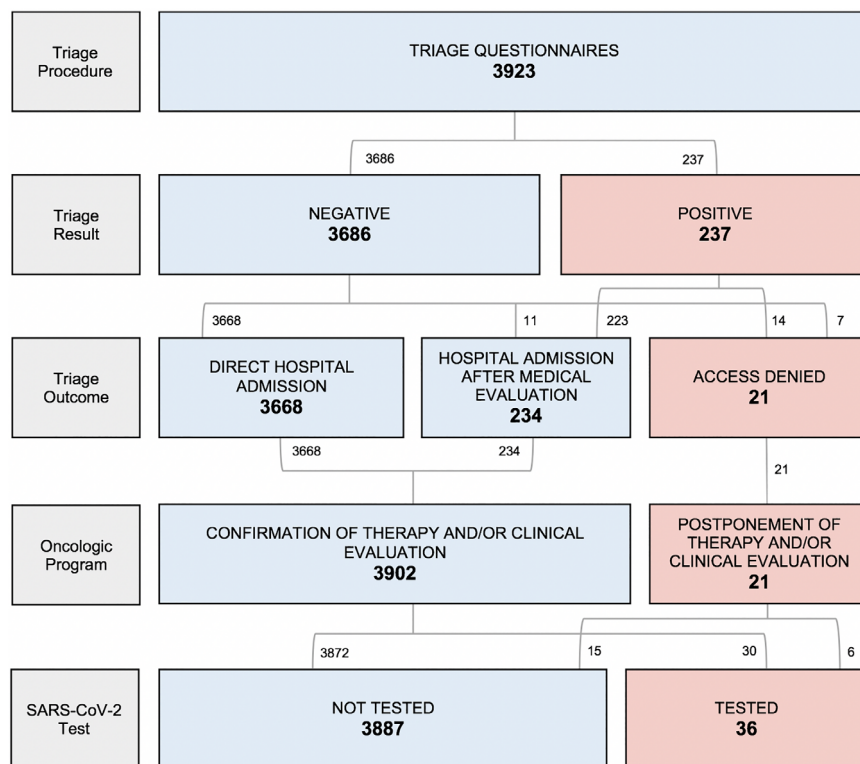
### DISCUSSION

Health care providers have deployed remarkable efforts to ensure cancer care during the COVID-19 outbreak. In early March 2020, the oncology community faced the issue of prioritizing, reorganizing, and providing cancer treatment during the pandemic, with scarce resources and limited scientific evidence [20, 21].

A first step to minimize the potential risk of infection among patients with cancer was implementing dedicated hospital pathways and triage procedures to detect, trace, and isolate infected patients [20, 22]. However, there is no evidence on the accuracy of triage procedures or standard policy upon which containment measures should be based in the oncological setting [23].

This retrospective study reviewed a large cohort of patients with cancer treated during the COVID-19 pandemic to assess the feasibility and predictive performance of a self-report questionnaire to triage patients with suspected symptoms. It was conducted in a geographic area (Friuli-Venezia Giulia Region, northeastern Italy) with an incidence of SARS-CoV-2 cases of 274.5 per 100,000 people, as of June 23, 2020 [24].

During the study period, 3,923 triage procedures were performed, and 1,363 patients were screened. Through a triage questionnaire, 6% of triage procedures were positive and required medical examination (237/3923). However, the triage questionnaire showed a low PPV at identifying patients with a real suspect of infection after medical review, and hospital access was denied only to 14 out of 237 triage-positive patients. A possible explanation could lie on how the presence of symptoms is investigated. For instance, respiratory symptoms might be mimicked by the tumor itself (e.g., paraneoplastic fever, dyspnea, and cough for patients with lung cancer or metastases) or by treatment's side effects (e.g., mucositis, dysgeusia, flu-like syndrome, interstitial pneumopathy). Also, the lower fever threshold in the self-reported questionnaire might have partially increased the number of positive screenings, but low-grade hyperpyrexia could be hard to detect for patients with cancer (they may be anergic, receive corticosteroids or painkillers with antipyretic effect, or present tumor-related fever), and many borderline or underreported cases might



**Figure 2.** Triage outcomes: patient flow chart.

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

be missed. On this point, newer triage models and diagnostic workflows should be quickly and easily implemented for the management of febrile patients with cancer: other possible threatening conditions should be evaluated (e.g., febrile neutropenia), and inappropriate treatment suspensions must be avoided (e.g., in case of paraneoplastic or treatment-related fever) [25]. Remarkably, a report from the European Institute of Oncology in Milan, Lombardy, showed that up to 45% of patients with lung cancer received a recommendation for rescheduling hospital access according to a telephone triage during the COVID-19 pandemic. As a result, 50% and 35% of intravenous and oral treatments were delayed, respectively [26]. Another cancer center in Lombardy, the Istituto Nazionale Tumori of Milan, provided similar data: up to 40%–50% of patients with head

and neck cancer postponed their oncological evaluation after telephone triage during the second and third week of March, 2020 [27]. In a warning pandemic scenario, clinicians should find an acceptable balance between containment measures and continuous cancer care. In high-prevalence areas, during the epidemic peak, and in case of scarcity of diagnostic tests, the protection of both hospitals and patients becomes crucial, and the need for strict surveillance protocols prevails. However, the low PPV of a questionnaire-based triage procedure detected in our study and the subsequent risk of unnecessary treatment delays should be considered in the oncological setting. Suggestive symptoms must be evaluated considering the oncological history, the onset (chronic vs. acute), the presence of lung or pleural disease, and concurrent treatments with potential pulmonary toxicity (e.g., immunotherapy, targeted therapy). For instance, in our cohort, patients with thoracic cancer had a higher likelihood of being triage-positive than other patients (OR, 1.69; 95% CI, 1.13–2.53;  $p = .01$ ), often presenting challenging differential diagnoses because of a compromised pulmonary function with associated dyspnea, cough, and polypnea [28]. Hence, adequate resources should be reallocated for triage implementation in the oncological setting, including trained medical professionals.

Our triage questionnaire recognized 66.7% of cases who were not admitted to DU after medical evaluation. Conversely, a negative questionnaire granted hospital access to 94.3% patients. After an internal review, six out of seven false-negative cases had a BT  $\geq 37^{\circ}\text{C}$  (two with BT  $\geq 37.5^{\circ}\text{C}$ , four with BT =  $37.4^{\circ}\text{C}$ ), which resulted in a strong and

**Table 3.** Predictive performance questionnaire-based triage system for the identification of patients refused at hospital admission

| Measure                   | Triage questionnaire, % (95% CI) |
|---------------------------|----------------------------------|
| Sensitivity               | 66.7 (43.0–85.4)                 |
| Specificity               | 94.3 (93.5–95.0)                 |
| Positive likelihood ratio | 11.7 (8.4–16.2)                  |
| Negative likelihood ratio | 0.35 (0.2–0.6)                   |
| Positive predictive value | 5.9 (4.3–8.0)                    |
| Negative predictive value | 99.8 (99.6–99.9)                 |
| Accuracy                  | 94.1 (93.3–94.8)                 |

Abbreviation: CI, confidence interval.



**Table 4.** Independent predictors of positive triage

| Factors                                    | Univariate analysis |          | Multivariate analysis |          |
|--|---------------------|----------|-----------------------|----------|
|  | OR (95% CI)         | <i>p</i> | OR (95% CI)           | <i>p</i> |
| Sex male vs. female                        | 0.71 (0.54–0.94)    | .01      | 0.78 (0.59–1.04)      | .10      |
| Age < 65 vs. ≥65 yr                        | 1.55 (1.19–2.02)    | .001     | 1.52 (1.15–2.01)      | <.01     |
| Thoracic cancer vs. other cancer types     | 1.46 (1.01–2.12)    | .5       | 1.69 (1.13–2.53)      | .01      |
| Oncology vs. hematology department         | 1.05 (0.79–1.39)    | .7       |                       |          |
| Early-stage vs. advanced-stage disease     | 1.07 (0.79–1.44)    | .6       |                       |          |
| Treatment vs. other reason for admission   | 1.00 (0.69–1.46)    | .9       |                       |          |
| Oncological treatment                      |                     |          |                       |          |
| Chemotherapy                               | Ref.                |          | Ref.                  |          |
| Immunotherapy                              | 0.82 (0.52–1.29)    | .4       | 0.79 (0.49–1.27)      | .33      |
| Other therapy                              | 1.46 (1.09–1.98)    | .01      | 1.35 (0.99–1.84)      | .051     |
| Therapy administration in the last 21 days | 1.19 (0.88–1.61)    | .2       |                       |          |
| BT ≥37°C at admission                      | 9.55 (5.63–16.2)    | <.0001   | 9.52 (5.44–16.6)      | <.0001   |

Abbreviations: BT, body temperature; CI, confidence interval; OR, odds ratio; Ref., reference.

independent predictor of positive triage (OR, 9.52; 95% CI, 5.44–16.6;  $p < .0001$ ). Hence, our data confirm that a routine BT measurement improves the triage process's overall sensitivity and should be implemented as an effective triage measure.

Overall, 36 SARS-CoV-2 nasopharyngeal swabs were performed because of our triage process (34 triage-positive and 2 triage-negative patients). None of them resulted positive, despite indicative symptoms. This result might put into discussion the effectiveness of the procedure, even if the strict application of the “stay at home when ill” policy might also explain these data. Most of the SARS-CoV-2 tests (30/36) were performed to triage-positive patients admitted to the DU after medical review. In particular, patients with a paraneoplastic fever frequently performed a SARS-CoV-2 test to avoid unnecessary treatment interruptions. Counterintuitively, most of the triage-positive patients rejected at admission were not tested (15/21). The majority of these cases, indeed, reported a fever suspected for infection in the previous 14 days, with no symptoms at evaluation, and active surveillance with fiduciary isolation was suggested instead (supplemental online Tables 1 and 2).

Because of internal regulation, a post-triage SARS-CoV-2 test was performed to 765 triage-negative asymptomatic patients who granted full hospital admission. One patient resulted positive, demonstrating how triage protocols are quite useful in detecting symptomatic patients but might be less effective for asymptomatic ones. Two additional patients resulted positive during the post-triage follow-up. Thus, a second screening barrier might detect asymptomatic carriers. Indeed, as recently reported, up to 40% of confirmed SARS-CoV-2 infections might be asymptomatic [29]. For instance, a routine SARS-CoV-2 test for new patients and before each treatment administration might offer adequate coverage. Besides, the use of masks, thorough handwashing protocols, and active staff surveillance are equally important. Thanks to an effective triage system and mandatory screening tests, we were able to identify, trace, and isolate three patients and a health care worker positive for

SARS-CoV-2 infection during the study period, with no secondary transmissions.

This study has several limitations. First, a potential limitation is the self-report questionnaire itself. Patients may exaggerate or under-report symptoms, with a considerable risk of false-positive and false-negative results. Additionally, some patients' subgroups might present different levels of social exposure and different confounders. For example, younger patients were found to have a higher risk of positive triage (OR, 1.52; 95% CI, 1.15–2.01;  $p < .01$ ). Many factors might explain this finding: possible lower compliance of older patients during the compilation of the questionnaire, greater social exposure for younger patients, or less frequent access to health care structures for elderly patients.

Further limitations of the present study are the monocentric and retrospective design, the short study period, and the local low-to-moderate prevalence of SARS-CoV-2 infection. However, we believe that our data still offer multiple suggestions for implementing an efficient triage procedure in the oncological setting. This study's strengths rely on its large numbers, the representative cohort, and the reproducibility of the triage process, which followed international recommendations.

## CONCLUSION

This is the first and largest study providing data on the feasibility and accuracy of a triage system implemented in a cancer center during the COVID-19 pandemic. A questionnaire-based triage system, even if accurate, has a low PPV to triage patients with cancer and suspected SARS-CoV-2 symptoms, and a differential diagnosis with tumor- or treatment-related symptoms is always required to avoid unnecessary treatment delays. BT measurement improves the overall sensitivity of the triage process, and widespread testing for SARS-CoV-2 infection should be implemented to identify asymptomatic carriers.

## ACKNOWLEDGMENTS

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

## AUTHOR CONTRIBUTIONS

**Conception/design:** Gianpiero Fasola, Giacomo Pelizzari, Alessandro Marco Minisini, Renato Fanin

**Provision of study material or patients:** Alessandra Bin, Raffaella Donato, Maura Mansutti, Chiara Comuzzi, Alessandra Sperotto

**Collection and/or assembly of data:** Diego Zara, Giada Targato, Giuseppe Petruzzellis

**Data analysis and interpretation:** Gianpiero Fasola, Giacomo Pelizzari, Alessandro Marco Minisini

**Manuscript writing:** Gianpiero Fasola, Giacomo Pelizzari, Diego Zara, Giada Targato, Alessandra Marco Minisini, Anna Candoni

**Final approval of manuscript:** Gianpiero Fasola, Giacomo Pelizzari, Diego Zara, Giada Targato, Giuseppe Petruzzellis, Alessandro Marco Minisini, Alessandra Bin, Raffaella Donato, Maura Mansutti, Chiara Comuzzi, Anna Candoni, Alessandra Sperotto, Renato Fanin

## DISCLOSURES

**Gianpiero Fasola:** AstraZeneca, Servier, Bristol Myers Squibb (ET), Merck, Servier, Bristol Myers Squibb (Other), Bristol Myers Squibb (IP); **Alessandro Marco Minisini:** Novartis, Merck Sharp & Dohme, Pierre Fabre (SAB); **Mauro Mansutti:** Pfizer, Novartis, Eli Lilly & Co (C/A). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

## REFERENCES

- Holshue ML, DeBolt C, Lindquist S et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med* 2020;382:929–936.
- Rothe C, Schunk M, Sothmann P et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med* 2020;382:970–971.
- Istituto Superiore di Sanità. COVID-19 integrated surveillance data in Italy. January 3, 2021. Available at <https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-dashboards>. Accessed January 4, 2021.
- Yang K, Sheng Y, Huang C et al. Clinical characteristics, outcomes, and risk factors for mortality in patients with cancer and COVID-19 in Hubei, China: A multicentre, retrospective, cohort study. *Lancet Oncol* 2020;21:904–913.
- Tian J, Yuan X, Xiao J et al. Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: A multicentre, retrospective, cohort study. *Lancet Oncol* 2020;21:893–903.
- Kuderer NM, Choueiri TK, Shah DP et al. Clinical impact of COVID-19 on patients with cancer (CCC19): A cohort study. *Lancet* 2020;395:1907–1918.
- Lee LYW, Cazier JB, Angelis T et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: A prospective cohort study. *Lancet* 2020;395:1919–1926.
- Ministero della Salute. COVID-19, raccomandazioni per i pazienti oncologici. March 12, 2020. <https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2020&codLeg=73635&parte=1%20&serie=null>. Accessed June 1, 2020.
- Curigliano G. How to guarantee the best of care to patients with cancer during the COVID-19 epidemic: The Italian experience. *The Oncologist* 2020;25:463–467.
- van de Haar J, Hoes LR, Coles CE et al. Caring for patients with cancer in the COVID-19 era. *Nat Med* 2020;26:665–671.
- Marron JM, Joffe S, Jaggi R et al. Ethics and resource scarcity: ASCO recommendations for the oncology community during the COVID-19 pandemic. *J Clin Oncol* 2020;38:2201–2205.
- ESMO. Cancer patient management during the COVID-19 pandemic. 2020. Available at <https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic>. Accessed June 1, 2020.
- Hanna TP, Evans GA, Booth CM. Cancer, COVID-19 and the precautionary principle: Prioritizing treatment during a global pandemic. *Nat Rev Clin Oncol* 2020;17:268–270.
- Rischio infettivo da Coronavirus COVID-19: Indicazioni per l'Oncologia da parte del Presidente AIOM, del Presidente eletto AIOM, del Presidente CIPOMO e del Presidente COMU. Available at [https://www.aiom.it/wp-content/uploads/2020/03/20200313\\_COVID-19\\_indicazioni\\_AIOM-CIPOMO-COMU.pdf](https://www.aiom.it/wp-content/uploads/2020/03/20200313_COVID-19_indicazioni_AIOM-CIPOMO-COMU.pdf). Accessed June 15, 2020.
- American Society of Clinical Oncology. ASCO Special Report: A Guide To Cancer Care Delivery During The Covid-19 Pandemic. American Society of Clinical Oncology; 2020. <https://www.asco.org/sites/new-www.asco.org/files/content-files/2020-ASCO-Guide-Cancer-COVID19.pdf>. Available June 15, 2020.
- Cortiua F, Pettke A, Bartoletti M et al. Managing COVID-19 in the oncology clinic and avoiding the distraction effect. *Ann Oncol* 2020;31:553–555.
- Lambertini M, Toss A, Passaro A et al. Cancer care during the spread of coronavirus disease 2019 (COVID-19) in Italy: Young oncologists' perspective. *ESMO Open* 2020;5:3000759.
- Affronti M, Mansueti P, Soresi M et al. Low-grade fever: How to distinguish organic from non-organic forms. *Int J Clin Pract* 2010;64:316–321.
- Barnes M, Sax PE. Challenges of “return to work” in an ongoing pandemic. *N Engl J Med* 2020;383:779–786.
- Ueda M, Martins R, Hendrie PC et al. Managing cancer care during the COVID-19 pandemic: Agility and collaboration toward a common goal. *J Natl Compr Canc Netw* 2020;1–4.
- Richards M, Anderson M, Carter P et al. The impact of the COVID-19 pandemic on cancer care. *Nat Cancer* 2020;1:565–567.
- Klompas M. Coronavirus disease 2019 (COVID-19): Protecting hospitals from the invisible. *Ann Intern Med* 2020;172:619–620.
- Elkin E, Viele C, Schumacher K et al. A COVID-19 screening tool for oncology telephone triage. *Support Care Cancer* 2020;1–6.
- Istituto Superiore di Sanità. Epidemia COVID-19. Aggiornamento Nazionale. June, 26, 2020. [https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19\\_23-giugno-2020.pdf](https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19_23-giugno-2020.pdf). Accessed June 1, 2020.
- Segelov E, Underhill C, Prenen H et al. Practical considerations for treating patients with cancer in the COVID-19 pandemic. *JCO Oncol Pract* 2020;16:467–482.
- de Marinis F, Attili I, Morganti S et al. Results of multilevel containment measures to better protect lung cancer patients from COVID-19: The IEO model. *Front Oncol* 2020;10:665.
- Resteghini C, Maggioni P, Di Martino V et al. Response of the Istituto Nazionale Tumori of Milan Head & Neck Cancer Unit to the COVID-19 outbreak. *Cancers Head Neck* 2020;5:7.
- Al-Shamsi HO, Alhazzani W, Alhuraiji A et al. A practical approach to the management of cancer patients during the novel coronavirus disease 2019 (COVID-19) pandemic: An International Collaborative Group. *The Oncologist* 2020;25:e936–e945.
- Lavezzo E, Franchin E, Ciavarella C et al. Suppression of COVID-19 outbreak in the municipality of Vo', Italy. *Nature* 2020;584:425–429.



See <http://www.TheOncologist.com> for supplemental material available online.