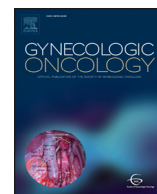




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Cancer patients affected by COVID-19: Experience from Milan, Lombardy

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HIGHLIGHTS

- There are growing concerns on the impact of COVID-19 in cancer patients.
- COVID-19 is impacting oncologic practice directly and indirectly.
- Prioritizing patients journey during COVID-19 is of paramount importance.

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ABSTRACT

Objective. SARS-CoV-2 pandemic is continuing to spread. There are growing concerns on the impact of COVID-19 in cancer patients. Several papers reporting recommendations and guidelines are published. But few data on cancer patients affected by COVID-19 are available.

Methods. This is a retrospective study including all consecutive patients affected by gynecological cancer who developed COVID-19. All patients were treated in an academic setting (in Milan, Lombardy, Italy) between February and March 2020.

Results. Overall, 355 patients had active treatment during the study period due to newly diagnosed or recurrent gynecological disease. Among those, 19 (5.3%) patients affected developed COVID-19. All patients were asymptomatic at the time of COVID-19 detection. Six patients were diagnosed before starting planned treatments; while the remaining 13 were diagnosed for COVID-19 after their started their treatments. Considering the first group of six patients, one patient died due to COVID-19 3 days after the diagnosis; while the other patients recovered from COVID-19 after a median of three weeks. The latter group of 13 patients (treatments started) included five patients who underwent surgery and eight patients who underwent chemotherapy. Focusing on five patients who were diagnosed after surgery, we observed that two patients died during postoperative course, while in other two cases prolonged hospitalization was needed. One patient had no issues. Chemotherapy was delayed for the remaining patients without sequelae.

Conclusions. Our report highlights that COVID-19 impacts the quality of treatments for cancer patients. Mortality rate is high, especially after surgery. More important, patients under active treatment for cancer are at high risk of developing severe evolution of COVID-19. Prioritizing patients journey during COVID-19 is of paramount importance.

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1. Introduction

COVID-19 spreads to Europe and US in early 2020 [1]. COVID-19 is an emerging and rapidly evolving situation. Based on currently available evidence, older adults and individuals who have serious underlying medical conditions might be at high risk for severe illness from COVID-19. Cancer is a serious underlying medical condition, and it promotes the risk of developing severe and life-threatening complications [1]. Although literature is full of expert opinions addressing the

potential impact of COVID-19 on oncologic practice [2], only few data on the impact of COVID-19 on patients affected by cancer are still available [3–6].

Recently, Liang et al., published a case series of 18 patients with history of cancer [3]. But only four (22.2%) patients received chemotherapy or surgery within the previous month; while, other patients were cancer survivors in routine follow-up after primary resection ($n = 12$) [3]. Similarly, Yu et al., reported outcomes of 12 cancer patients affected by cancer and COVID-19 [4]. Only five (41%) were under active treatments. The study included just a female patient having adjuvant radiotherapy for breast cancer [4]. Due to the paucity of data, it is not possible to weight the real impact of COVID-19 on patients (especially female patients) having active tumors or having treatment for cancer.

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Table 1
Patients' characteristics.

	n = 19
Age, yrs	65 (49, 84)
Performance status (PS)	
ECOG PS 0	14 (73.7%)
ECOG PS 1	4 (21%)
ECOG PS 2	1 (5.3%)
Diagnosis of COVID-19	
Pre treatment	6 (31.6%)
After surgery	5 (26.3%)
After starting chemotherapy	8 (42.1%)
CT scan suggestive for pneumonia	
Yes	17 (89.6%)
No	1 (5.3%)
Not done	1 (5.3%)
Impact of COVID-19 on oncologic treatments	
Delayed medical treatment	8 (42.1%)
Avoided/stopped medical treatment	3 (15.8%)
Delayed surgical treatment	2 (10.5%)
Avoided surgical treatment	2 (10.5%)
Changing in surgical plan	2 (10.5%)
Outcomes	
Recovered (at home)	14 (73.7%)
ICU-admission	2 (10.5%)
Death	3 (15.8%)

Data are reported as median (range) or number (%). Abbreviation: yrs, years; ECOG, Eastern Cooperative Oncology Group; PS, performance status; COVID-19, CORonaVirus Disease 19; CT, computed tomography; ICU, intensive care unit.

2. Methods

This is a retrospective study of women with active gynecological cancer treated between February and March 2020. All patients were treated at Fondazione IRCCS Istituto Nazionale dei Tumori di Milano (Milan, Lombardy, Italy) at the beginning of the outbreak in Italy. Data of patients developing COVID-19 were collected from Institutional database. A positive nasopharyngeal swab is necessary for the diagnosis of COVID-19. The Fondazione IRCCS Istituto Nazionale dei Tumori di Milano is a COVID-free HUB. Only patients considered to be negative for COVID-19 were admitted to our center. In order to protect the Fondazione IRCCS-Istituto Nazionale dei Tumori di Milano from the spread of COVID-19, a number of to-hospital and within-hospital filters were applied [5]. According our Institutional protocol, all patients admitted at Fondazione IRCCS Istituto Nazionale dei Tumori di Milano were clinically evaluated, and collection of anamnestic data (e.g. history

of fever, respiratory symptoms, exposure to COVID-19) is of paramount importance. Additionally, all patients scheduled for surgery had a high-resolution low-dose computed tomography (CT) scan followed by reverse transcription polymerase chain reaction (RT-PCR) detection of SARS-CoV-2 in nose-throat swabs whenever CT was suggestive of lung infection. Details of our triage protocol are reported elsewhere [5]. While, nose-throat swabs is normally used as a sole triage methods for patients scheduled for having chemotherapy or maintenance therapy.

This study was focusing just on patients admitted to the hospital to have surgery, chemotherapy and maintenance therapy. Outpatient visits were excluded since those patients were not tested for COVID-19 using specific triage methods, but only using clinical and anamnestic data. The aim of the present paper is to evaluate the impact of COVID-19 on patients affected by gynecological cancers. We aim to evaluate the prevalence of treatments' delay and to assess morbidity and mortality rates. Delay of treatments is calculated from the date in which treatment was planned to the effective date in which treatments were administered/started. Basic descriptive statistics are used to describe our study population.

3. Results

Overall, 355 single patients had active treatment during the study period due to newly diagnosed or recurrent gynecological cancers. Active treatments included surgery, chemotherapy and maintenance therapy in 86 (24.2%), 197 (55.5%), and 72 (20.3%) patients.

Among those COVID-19 was confirmed by nasopharyngeal swab in 19 patients (5.3%). Table 1 reports main characteristics of the patients, and the impact of COVID-19. All patients were asymptomatic at the time of COVID-19 detection. Nine (47%) patients developed symptoms after a median of 3 (range, 1–17) days, after COVID-19 detection; while the remaining 10 (53%) patients were asymptomatic.

Six patients were diagnosed before starting planned treatments; while the remaining 13 were diagnosed for COVID-19 after their started their treatments (including surgery and chemotherapy). Considering the first group of six patients (treatments not yet started), one patient died due to COVID-19, 3 days after the diagnosis of interstitial pneumonia at CT scan (the patient affected by suspected ovarian cancer died before receiving any treatment); while the other five patients recovered from COVID-19 after a median of three weeks. Treatments were delayed in all those patients. They started planned oncologic treatments after a median of 3 (range, 1–5) weeks (after they had two consecutive negative nasopharyngeal swabs). Table 2 shows the characteristics of those

Table 2
Characteristics of patients diagnosed for COVID-19 before starting planned treatments.

Patient	Age, years	Disease	Significant comorbidities	Treatments planned	Symptoms related to COVID-19	CT scan suggestive for pneumonia	Consequence of COVID-19 infection	Outcomes
1	84	Suspected ovarian cancer	Cardiovascular disease	Diagnostic laparoscopy	None at the time of diagnosis, but the patients developed respiratory symptoms 2 days after COVID-19 diagnosis	Yes	Treatment aborted	Died to COVID-19
2	67	High grade serous ovarian cancer	None	Interval debulking surgery	None	Yes	Surgical plan changed	Recovered
3	62	Endometrial cancer	None	Surgery	None	Yes	Delayed surgical treatment	Recovered
4	82	Isolated inguinal ovarian cancer recurrence	Chronic kidney disease	Surgery plus chemotherapy	None at the time of diagnosis, but the patients developed mild fever 1 day after COVID-19 diagnosis	Yes	Delayed surgical treatment	Recovered
5	65	Suspected ovarian cancer	None	Surgery	None	Yes	Changing in surgical plan (neoadjuvant chemotherapy followed by interval debulking surgery)	Recovered
6	62	Ovarian cancer	None	Surgery	None	Yes	Avoided surgical treatment	Recovered

Table 3
Characteristics of patients diagnosed for COVID-19 after they started planned treatments.

Patient	Age, years	Disease	Significant comorbidities	Treatments	Symptoms related to COVID-19 ^a	CT scan suggestive for pneumonia ^a	Consequence of COVID-19 infection	Outcomes
1	72	Recurrent ovarian carcinosarcoma	Cardiovascular disease	Palliative surgery	Fever, cough, and dyspnea developed 3 days after surgery	Yes (after surgery)	ICU admission	Died due to COVID-19
2	71	Ovarian cancer	Cardiovascular disease	Interval debulking surgery	Fever, dyspnea developed 7 days after surgery	Yes (after surgery)	ICU admission	Died due to COVID-19
3	60	Recurrent endometrial cancer (trocar site metastasis)	None	Surgery	Fever, developed 3 days after surgery	Yes (after surgery)	Prolonged hospitalization need; delayed medical treatment	Recovered
4	61	Ovarian cancer	Cardiovascular disease	Interval debulking surgery	Fever, developed 5 days after surgery	Yes (after surgery)	Delayed medical treatment	Recovered
5	76	Ovarian cancer	Hypothyroidism	Interval debulking surgery	None	Not done	Prolonged hospitalization need; delayed medical treatment	Recovered
6	68	Ovarian cancer	None	Chemotherapy	None	Yes (after chemotherapy)	Delayed medical treatment	Recovered
7	66	Recurrent platinum-resistant ovarian cancer	None	Chemotherapy	None	Yes (after chemotherapy)	Stopped medical treatment	Recovered
8	58	Ovarian and endometrial cancer	None	Bevacizumab maintenance	None	Yes (after chemotherapy)	Stopped medical treatment	Recovered
9	63	Ovarian cancer	None	Bevacizumab maintenance	None	Yes (after chemotherapy)	Stopped medical treatment	Recovered
10	56	Endometrial cancer	None	First line chemotherapy	Fever, developed 1 day after chemotherapy	Yes (after chemotherapy)	Delayed medical treatment	Recovered
11	59	Ovarian cancer	Hypothyroidism	Bevacizumab maintenance	Fever, developed 7 days after chemotherapy	No	Delayed medical treatment	Recovered
12	49	Recurrent cervical cancer	Plummer disease	Chemotherapy	Fever, developed 17 days after chemotherapy	Yes (after chemotherapy)	Delayed medical treatment	Recovered
13	65	Ovarian cancer	Cardiovascular disease	Chemotherapy	None	Yes (after chemotherapy)	Delayed medical treatment	Recovered

^a All patients had no symptoms nor suspected alteration at preoperative CT scan.

patients. The other group of 13 patients (treatments started) included five patients who underwent surgery and eight patients who underwent chemotherapy. Table 3 shows the characteristic of those patients. Treatments were started after the patients were considered negative for COVID-19 (they had had negative clinical evaluation, negative CT scan and negative swabs before starting the treatments). Focusing on five patients who were diagnosed after surgery, we observed that two patients died during postoperative course, while in other two cases prolonged hospitalization was needed. One patient had no issues, related to surgery. Chemotherapy was delayed ($n = 5$) or stopped ($n = 3$) for the remaining patients without *sequelae*.

4. Discussion

The present study report a case series of patients affected by both gynecological cancer and COVID-19. Although the number as small to draw conclusion on the effects of COVID-19 on cancer patients, this is one of the larger experiences investigating this issue. Only few case reports and small case series are still available. We think that those data are important since they highlight the impact of COVID-19 on patients with cancer. Mortality rate is extremely high (13.5%). Treatments should be delayed and triage methods are necessary to reduce the risk of in-hospital spread of SARS-CoV-2. Moreover, treatments plan (including delayed treatments) changed in almost all patients diagnosed with COVID-19, thus potentially impacting in our ability to treat cancers. We point out that also medical and surgical staffs need protection to reduce possible contamination [7,8].

Interestingly, a recent published paper reports evaluated the impact of COVID-19 in a series of 218 patients with cancer and COVID-19 infection who were treated in Montefiore Health system, New York from March 18th to April 8th 2020. These patients included 164 (75%)

patients with solid tumors and 54 (25%) with hematologic malignancies. A total of 61 (28%) cancer patients died from COVID-19 with a case fatality rate (CFR) of 37% (20/54) for hematologic malignancies and 25% (41/164) for solid malignancies [6]. These results corroborated our findings. The inherent biases of the retrospective study design represent the main weaknesses of the present investigation. Additionally we have to point out that there are likely undiagnosed COVID patients in population which would lower the mortality reported in our report.

Our report highlights that COVID-19 impact the quality of treatments for cancer patients. Mortality rate is high, especially after surgery. More important, patients under active treatment for cancer are at high risk of developing severe evolution of COVID-19. Prioritizing patients journey during COVID-19 is of paramount importance.

CRedit authorship contribution statement

Giorgio Bogani: Conceptualization, Methodology, Writing - original draft, Writing - review & editing. **Antonino Ditto:** Methodology, Writing - original draft, Writing - review & editing. **Sara Bosio:** Methodology, Writing - original draft, Writing - review & editing. **Claudia Brusadelli:** Methodology, Writing - original draft, Writing - review & editing. **Francesco Raspagliesi:** Conceptualization, Methodology, Project administration, Supervision, Writing - original draft, Writing - review & editing.

Declaration of competing interest

The authors declare no conflicts of interest.
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