

SARS-CoV-2 and cancer: a single-institutional approach on the clinical impact of COVID-19 on cancer patients

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Abstract. Objective: In this study we aimed to identify the impact of COVID-19 on systemic oncologic treatments (chemotherapy, hormone therapies, etc) delays and outcomes of the patients in our institution. Material and method: 107 cancer patients were diagnosed with SARS-CoV-2 infection at Medisprof Cancer Center in Cluj-Napoca, Romania, between March 2020 and February 2021. 88 of these patients met the pre-specified inclusion criteria: medical history, concomitant medication, smoking status, body mass index, cancer type, severity of infection (hospitalisation needed or not), delay of cancer treatment and impact on the overall cancer evolution. Data was analyzed using descriptive statistics, one-way ANOVA and Pearson correlation methods. Results: Average age of the patients was 59 years, with an Eastern Cooperative Oncology Group performance status (ECOG PS) of 1 in 77.3 % of the cases. 54.6% were active or former smokers. The prevalent cancer types were gastrointestinal tumors (38.6%), followed by breast cancer (20.5%). 31 patients (35.2%) were under no treatment (follow-up or not yet treated), while 57 patients (64.7%) were on active anticancer treatment. Data showed significant differences between the number of days of delayed treatment and the types of treatment prescribed ($F(4,75)= 18.46, p<0.005$); targeted therapies had the longest delays with an average of 27 days ($M=26.66, SD=4.92$). 10 patients had progressive disease after COVID-19, there was a significant correlation between persistence of symptoms after SARS-CoV-2 infection and cancer progression ($p=0.013$). 5 patients died after COVID-19, mortality rate was higher among patients admitted for hospital care ($p=0.003$) and those presenting dyspnea ($p<0.005$). Conclusion: In our study, type of cancer therapy influenced the delays of oncologic treatment. Mortality rate due to SARS-CoV-2 infection was correlated with dyspnea and the need for hospital admission.

Key Words: cancer, COVID-19, outcome, oncologic treatment.

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Introduction

Since coronavirus disease became pandemic, the concern for risks and impact on patients with cancer has grown. Therefore, accumulating evidence suggested that cancer patients, especially those undergoing active anticancer treatments, are more vulnerable, being at higher risk of COVID-19 infection and having higher morbidity and mortality rates than the general population (Al-Shamsi et al 2020; Lee et al 2021; Miyashita et al 2020). Even though the prevalence of COVID-19 infection varies among studies focused on cancer patients, in a large research performed in U.S. the prevalence was 7.8%, higher among patients with hematologic malignancies compared to those with solid tumors (10.9% vs. 7.8%). In these patients mortality attributed to COVID-19 was 10.9% (Fillmore et al 2021). There is specific data, mainly from retrospective studies, referring to medical and cancer history, antitumor treatment, laboratory testing, medical course of SARS-CoV-2 infection in cancer patients (Al-Shamsi et al 2020; Fillmore et al 2021; Yarza et al 2020). In this study we aimed to describe the characteristics, clinical manifestations and outcomes of patients tested positive for SARS-CoV-2 infection in our cancer center.

Material and methods

In the context of COVID-19 pandemic, between March 2020 and February 2021, we routinely screened at Medisprof Cancer Center in Cluj-Napoca, 12501 cancer patients, using SARS-CoV-2 antigen tests, as well as RT-PCR testing. Each sampling was performed by dedicated nurses and RT-PCR test results were provided by an accredited laboratory. Of these patients, 107 were diagnosed with SARS-CoV-2 infection and 88 patients were considered eligible according to clinical characteristics including age, medical history, concomitant medication, smoking status, body mass index, oncologic diagnosis and therapy, delay of cancer treatment and impact on the overall cancer evolution. Clinical data was collected by reviewing the patient electronic file and information regarding SARS-CoV-2 infection such as severity of infection, specific and non-specific applied therapy, was obtained following a telephonic discussion led by a physician from the study team as well as from medical documents provided by hospitalized patients. Our study was in accord with the current ethical guidelines and all patients in the present research provided informed consent for participation. In the present research, the statistical analysis was performed with the IBM SPSS v.20. Descriptive statistics were used to

summarize the clinical characteristics. The quantitative variables were summarized as means and standard deviations, while qualitative variables were expressed as absolute and relative frequencies (%). In order to test the bivariate association between various quantitative and qualitative nominal variables one-way ANOVA test was used. A significance level of 0.05 was used for all two-sided statistical tests, and a test result was considered significant when p was lower than 0.05.

Results

In the cohort of patients tested positive for SARS-CoV-2 infection in our center in the specified period, the mean age was 59 years (range, 28–83 years), 42 were women (47.7%) and 46 were men (52.3%), with an ECOG performance status of 1 in most of the cases (77.3%), only 7.9% of patients were ECOG PS 2 and 3. More than half of the patients (54.6%) were active or former smokers. Medical history of the patients, with associated comorbidities is summarized in Table 1. The most prevalent cancer types were gastrointestinal tumors (38.6%), breast cancer (20.5%), followed by urogenital (13.6%), gynecological (11.4%), lung (10.2%). Less frequent cancer types were melanoma (2.3%), thyroid (1.1%), peritoneum (1.1%), brain (1.1%).

Table 1. Medical history in the studied group

Comorbidities	Frequency	%	
High blood pressure	no	41	46.6
	yes	47	53.4
Cardio-vascular pathology	no	64	72.7
	yes	24	27.3
Obesity	no	60	68.2
	yes	28	31.8
Diabetes	no	74	84.1
	yes	14	15.9
Pulmonary pathology	no	82	93.2
	yes	6	6.8
Autoimmune pathology	no	84	95.5
	yes	4	4.5
ACEI treatment	no	62	70.5
	yes	26	29.5

Thirty-one patients (35.2%) were under no treatment (follow-up or not yet treated), while 57 patients (64.7%) were on treatment, most of them on chemotherapy (34.1%) or hormone therapy (15.9%), as shown in Table 2.

Of all patients, 63 (71.6%) have developed a symptomatic COVID-19 infection and 13 (14.8%) needed hospitalization. The symptoms described by the patients are presented in Table 3. 12.5% of the patients underwent specific therapy for COVID-19 and 4.5% needed oxygen therapy; a summary of other therapies used by the patients are shown in Table 4. 18 patients (20.5%) remained with post-infection sequelae and 5 patients (5.7%) died after COVID-19.

Oncologic treatments were postponed in the majority of cases during COVID-19 infection. Our analysis shows significant differences in the number of days of delayed oncologic treatment

Table 2. Oncologic treatments in the studied group

Oncologic Treatment	Frequency	%
Chemotherapy	30	34.1
Radiotherapy	4	4.5
Immunotherapy	1	1.1
Hormone therapy	14	15.9
Targeted agents	7	8.0
Neuroendocrine therapy	1	1.1
No treatment	31	35.2
Total	88	100.0

Table 3. COVID-19 symptoms in the studied group

COVID-19 Symptoms	Frequency	%	
Rhinorrea	no	83	94.3
	yes	5	5.7
Nasal congestion	no	77	87.5
	yes	11	12.5
Fatigue	no	41	46.6
	yes	47	53.4
Cough	no	59	67.0
	yes	29	33.0
Fever	no	58	65.9
	yes	30	34.1
Dyspnea	no	75	85.2
	yes	13	14.8
Hyposmia/ Ageusia	no	68	77.3
	yes	20	22.7
Myalgia	no	61	69.3
	yes	27	30.7
Headache	no	78	88.6
	yes	10	11.4
Vertigo	no	84	95.5
	yes	4	4.5
Diarrhea	no	83	94.3
	yes	5	5.7

between the types of treatment prescribed ($F(4,75)=18.46$, $p<0.05$) (Fig.1). Patients in the hormone therapy group did not have any treatment delays ($M=0.00$, $SD=0.00$), in the radiotherapy group there was an average of 15 days treatment delay ($M= 15.25$, $SD= 2.50$), in the chemotherapy group an average of 20 days delay ($M= 20.17$, $SD= 12.43$) and in the molecular targeted therapy group an average of 27 days of treatment delay ($M= 26.66$, $SD= 4.92$).

The first oncological evaluation after COVID-19 infection showed that 77 patients (87.5%) had stable disease, 1 patient had remission of the disease and 10 patients (11.4%) had progressive disease. There was a significant correlation between persistence of symptoms after SARS-CoV-2 infection and cancer progression ($p=0.013$). Mortality rate was significantly higher

Table 4. Treatments applied to COVID-19 positive patients

Treatment	Frequency	%	
Paracetamol	no	31	35.2
	yes	57	64.8
Cortisone	no	78	88.6
	yes	10	11.4
Oxygen therapy	no	84	95.5
	yes	4	4.5
Antibiotics	no	57	64.8
	yes	31	35.2
Anticoagulants	no	59	67.0
	yes	29	33.0
VIT C	no	17	19.3
	yes	71	80.7
VIT D + Zinc	no	25	28.4
	yes	63	71.6
COVID-19 specific therapy	no	77	87.5
	yes	11	12.5

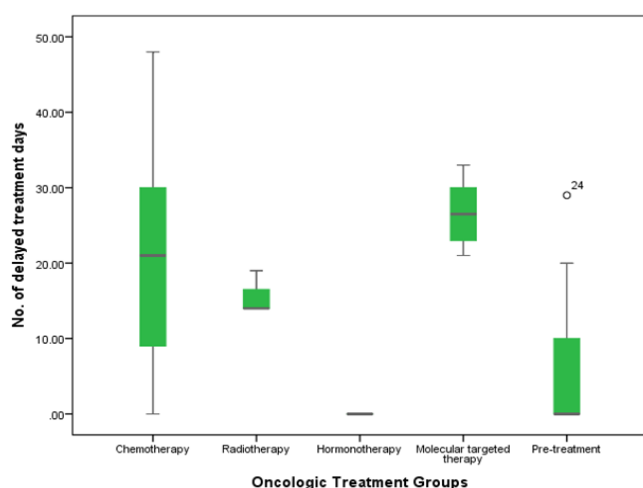


Fig. 1 Treatment delay due to COVID-19 in each treatment group

among patients admitted for hospital care ($p=0.003$) and those presenting dyspnea ($p<0.05$).

Discussion

We investigated a cohort of cancer patients diagnosed with COVID-19 infection after routine testing in our centre. According to our internal procedure patients were tested at each visit or more than 48 hours after the last RT-PCR test. The aim of the study was to identify risk factors for COVID-19 susceptibility, outcomes related to infection and the impact on the oncologic treatment of cancer patients. There are studies performed in United States that showed that the prevalence of COVID-19 among cancer patients appeared to be lower than in the general population (Miyashita et al 2020). Even in the US, a real prevalence could not be assumed since a significant number of cancer patients have not been tested, especially in cases of asymptomatic disease (Miyashita et al 2020).

Our results showed that both men and women were similarly affected by COVID-19 infection, symptomatic or not. The mean age was of 59 years old and only 7.9% presented an ECOG PS ≥ 2 . Data from another study suggest that elderly (80 years or older) patients with cancer were more commonly affected by COVID-19 (Miyashita et al 2020). In our study we did not find a correlation between older age and more frequent symptoms, sequelae or risk of death related to infection. A large study that analyzed data from the the COVID-19 and Cancer Consortium (CCC19) registry database, showed that in addition to increased age, smoking status and number of comorbidities were independent factors associated with increased 30-day mortality. On the other hand, obesity, type of cancer and type of oncologic therapy were not associated with mortality related to COVID-19 (Kuderer et al 2020). In our cohort, more than half of the patients were smokers or former smokers and almost one third were obese. These numbers were lower in similar studies from more western countries (about a third current or past smokers and a quarter with obesity) (Lee et al 2021). However, neither smoking nor obesity or comorbidities were associated with the severity of COVID-19 infection (data not shown). The most frequent associated pathology was high blood pressure, followed by other cardio-vascular pathology, diabetes or pulmonary pathology. Other studies reported similar figures (Lee et al 2021; Fillmore et al 2021), except for lung pathology that might be underdiagnosed in our country.

Symptoms most commonly associated with COVID-19 infection were fatigue, fever, cough, myalgia, hyposmia/ageusia and dyspnoea. A study performed in Spain reported quite similar values for associated comorbidities, whereas the frequency of COVID-19 related symptoms was generally higher (Yarza et al 2020). In their study, higher rates of respiratory symptoms might be explained by the highest incidence of COVID-19 infections in lung cancer subjects, followed by colorectal cancer (Fillmore et al 2021). Patients with lung cancer might be more vulnerable due to associated symptoms such as dyspnea, cough and also decreased pulmonary function, being at higher risk of severe forms of COVID-19 infection (Liang et al 2020). In our study, COVID-19 infection was more often encountered in patients with gastrointestinal tumors, followed by breast cancer. A large study from U.S. noted an unexpected reduced frequency of COVID-19 infection among patients with malignancies related to smoking such as lung, head and neck, and urothelial cancers (Miyashita et al 2020).

Most of the subjects developed symptomatic COVID-19 infection, of which almost 15% required hospitalisation, 12.5% received specific COVID-19 therapy, such as Remdesivir or Plaquenil and 5 patients died in the context of infection or complications. Among the potential risk factors studied, such as smoking, comorbidities, type of cancer, type of treatment, no statistically significant associations with more severe forms of COVID-19 infection were observed (data not shown). At the time of COVID-19 infection, almost two-thirds of the subjects in our cohort were undergoing cancer-related therapy, particularly conventional chemotherapy, followed by hormone therapy and targeted agents including immunotherapy. In a similar study, almost all of the patients who tested positive for COVID-19 had received anticancer treatment within 4 weeks before infection, particularly chemotherapy in more than half

of the cases (Fillmore et al 2021). While chemotherapy causes immunosuppression, immunotherapy gives a booster to the immune system to fight against cancer cells. In several studies cytotoxic chemotherapy did not seem to worsen the course of COVID-19 infection. However, lymphopenia at COVID-19 diagnosis and/or baseline neutropenia proved to be risk factors for more severe forms of illness (Jee et al 2020). There are also previous studies that imply that patients who underwent chemotherapy or surgery a month before the COVID-19 diagnosis, had worse prognosis in terms of severe events related to infection (Yarza et al 2020; Hanna et al 2020). Another report from U.K., U.S. and Sweden, showed that subjects undergoing chemotherapy or immunotherapy had a higher risk of testing positive for COVID-19 and also an increased risk of hospitalization due to COVID-19 (Lee et al 2021).

Apart from hormone therapy, in our cohort all other treatments required postponement due to COVID-19 infection, with an average of 20 to 27 days for patients receiving chemotherapy or targeted therapies, respectively. The first oncological evaluation performed after COVID-19 infection resolution showed that most of the patients had stable disease, whereas 11.4% had progressive disease. Persistence of symptoms after COVID-19 infection was significantly correlated with cancer progression. Moreover, mortality rate was higher among patients admitted for hospital care and those presenting dyspnea. A review of the studies addressing this topic state that cancer patients under active oncologic therapy show a higher mortality rate due to COVID-19 (Saini et al 2019; Madan et al 2020; Pathania et al 2021). There are also reports that showed that the frequency of COVID-19 infection was lower in patients receiving cancer related therapy, perhaps out of more caution and less exposure, and the mortality rate was not statistically significantly different in comparison with patients under no treatment (Fillmore et al 2021). However, mortality rates are higher than the mortality rates reported in the global population (Kuderer et al 2020; De Azambuja et al 2020). Professional medical oncology societies have been providing updated guidelines to support health care professionals with the management, treatment and supportive care needs of the patients with cancer in the circumstances of COVID-19 pandemic (Aapro et al 2021). Mainly, treatment decisions should be discussed for each patient, balancing the risks and benefits depending on treatment setting (neo-/adjuvant or metastatic), disease prognosis, patient comorbidities, patient preferences, probability and risks of COVID-19 infection (Aapro et al 2021).

Conclusion

In our study, type of cancer therapy influenced the delays of oncologic treatment. There was a significant association between persistence of symptoms after SARS-CoV-2 infection and cancer progression. Mortality rate due to SARS-CoV-2 infection was correlated with dyspnea and the need for hospital admission.

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