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ORIGINAL ARTICLE

Milano Policlinico ONCOVID modified Score for risk evaluation in oncology during the COVID-19 pandemic: a prospective monocentric study

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Abstract

Purpose Due to their immunosuppressed status, patients with cancer have been reported to be at increased risk of COVID-19 infection. We aimed to assess the prevalence of COVID-19 in patients with cancer and to identify its risk factors.

Methods A prospective study was conducted at the Department of Medical oncology of Sfax from November 2020 to February 2021. We analyzed data of 226 patients treated for solid cancer. We used the Milano Policlinico ONCOVID modified Score to quantify the risk of infection in patients with cancer.

Results Patients aged less than 70 years represented 85%. The most common primary tumors were breast cancer (37%) and colorectal cancer (22%). Comorbidities were observed in 39% of cases. Among 226 patients with cancer, 19 patients (8.4%) had COVID-19 disease. In 42% of cases, patients were under chemotherapy and 63% of them have a metastatic disease. Fifteen patients (79%) were symptomatic. A severe form of COVID-19 requiring hospitalization was seen in 4 patients (21%). Of 19 patients who tested positive for COVID-19, 47% had an intermediate and high risk of infection. COVID-19 infection was correlated with intermediate or high risk ($p=0.018$), age < 70 years ($p=0.035$), and chemotherapy treatment ($p=0.032$). In multivariable analysis, only the intermediate or high risk were correlated with COVID-19 infection in cancer patient ($p=0.025$).

Conclusion This study concluded that using the Milano Policlinico ONCOVID modified Score is very helpful for clinicians to identify vulnerable patients and to make the appropriate decision in the management of cancer patients.

Keywords COVID-19 · Cancer · Milano Policlinico ONCOVID Score

Introduction

The novel coronavirus disease 2019 (COVID-19), first reported in China in December 2019, is a worldwide health threat. It became a public health emergency of international concern because of its severity and rapid spread [1]. According to the World Health Organization (WHO), as of October 1, 2021, there have been 233,503,524 confirmed cases of COVID-19, including 4,777,503 deaths. As of 23 January 2022, over 346 million confirmed cases and over 5.5 million deaths have been reported worldwide. A slower increase in case incidence was observed at the global level, with only half of the regions reporting an increase in the number of new weekly cases, as compared to five out of six regions in the previous week. The Eastern Mediterranean Region reported the largest increase in the number of new cases (39%), followed by the South-East Asia Region (36%) and the European Region (13%).

In Tunisia, since the outbreak of the pandemic in March 2020, 788.012 cases of COVID-19 have been recorded, of which 25.803 have died and 704.030 have recovered. According to the same report, as of January 15, 51 new hospitalizations were recorded in public and private health establishments, of which 128 people were in intensive care and 26 were placed on artificial respirators. A total of 544 people with COVID-19 are currently hospitalized, according to the Ministry of Health. Several patients have been reported to be at increased risk of infection with high morbidity and mortality mostly elderly patients, males, and those with comorbidities, such as hypertension, chronic lung

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disease, diabetes, and cancer [2]. The present article focuses on the Milano Policlinico ONCOVID Score to weigh the risk of COVID-19 in Tunisian patients with cancer. The main issue raised by the pandemic is whether the risk of COVID-19 outweighs that of cancer treatment delay. In the present situation, oncologists need to decide which kind of patient should start (or continue) which kind of treatment and how much will this increase the risk of complications in case of COVID-19 in these vulnerable patients.

Materials and methods

Study design and participant

A prospective study was conducted at the department of medical oncology of Sfax, from November 2020 to February 2021. This was a consecutive cohort of all patients during this defined period. We had included in our study patients who have been followed for histologically proven cancer and who are undergoing adjuvant or palliative cancer treatment (chemotherapy or targeted therapy), over the age of 18, able to answer the questions, and who agreed to participate in the study.

We had excluded from these study patients who do not have cancer, those under 18 years old, those with backwardness or major cognitive impairment, and patients who refused to participate in the study. All procedures performed in this study were in accordance with the ethical standards of the institutional and the local national research committee of Habib Bourguiba and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Our study was approved by the local Habib Bourguiba committee. We used the Milano Policlinico ONCOVID modified Score to assess the risk of COVID-19 infection in patients with cancer. This score includes patient characteristics such as sex, performance status, age, *body mass index* (*BMI*), comorbidities such as hypertension, cardiovascular disease, diabetes, chronic obstructive pulmonary disease and chronic systemic infections, and concomitant steroid treatment including continuous therapy with a dose of > 10 mg daily of prednisone equivalent, lasting for more than the 1-month period and history of respiratory infection. In addition, this score includes disease characteristics with thoracic tumor and history of thoracic radiotherapy only for patients with extrathoracic tumors. Furthermore, it includes treatment characteristics with the precision of the lines and type of treatment. Finally, the neutrophil–lymphocyte ratio impacted this score. According to the Milano Policlinico ONCOVID Score, we were able to define 3 groups of risk, low (< 4) intermediate (4–6), and high risk (> 6). At the end of the study, we evaluated the prevalence of COVID19 infection in this population (Table 1).

Table 1 The Milano Policlinico ONCOVID modified Score

Variables	Score
Patients characteristics	
Sex	Female = 0 Male = 1
ECOG PS	0–1 = 0 ≥ 2 = 1
Age	> 70 = 0 ≥ 70 = 1
BMI	< 30 = 0 ≥ 30 = 1
Comorbidities[a]	No = 0 Yes = 1 Yes > 1 = 2
Concomitant steroid treatment [b]	No = 0 Yes = 1
Disease characteristics	
Thoracic tumor	No = 0 Yes = 1
History of thoracic radiotherapy [c]	No = 0 Yes = 1
Treatment characteristics	
Line of treatment	Adjuvant = 0 > 1 = 1
Type of treatment	HT/TKIs/TT/mAB = 0 CT = 1 IT/IT + CT = 2
History of IrAEs [d]	No = 0 Yes = 1 Yes, pneumonitis = 2
Laboratory values	
NLR	< 5 = 0 ≥ 5 = 1

BMI, body mass index; *CT*, chemotherapy; *ECOG*, Eastern Cooperative Oncology Group; *F*, female; *HT*, hormonal therapy; *irAEs*, immune-related adverse events; *IT*, immunotherapy; *M*, male; *mAb*, monoclonal antibody; *NLR*, neutrophil-to-lymphocyte ratio; *PS*; performance status; *TKIs*, tyrosine kinase inhibitors; *TT*, targeted therapy

[a]Comorbidities include hypertension, cardiovascular disease, diabetes, chronic obstructive pulmonary disease, and chronic systemic infections

[b]Concomitant steroid treatment includes continuous therapy with a dose of > 10 mg daily of prednisone equivalent, lasting for more than the 1-month period

[c]Only for patients with extrathoracic tumors

[d]Only for patients treated with IT or IT + CT

Statistical study

Descriptive statistics (frequencies, percentage) were calculated. The study of the associations between the variables was made by the hypothesis tests. The chi-square chi2 (χ^2) was useful for analyzing such differences in categorical variables, especially those nominals in nature. The comparison of proportions was made by Pearson's "chi2 (χ^2)" test when the theoretical size is greater than 5 and by the

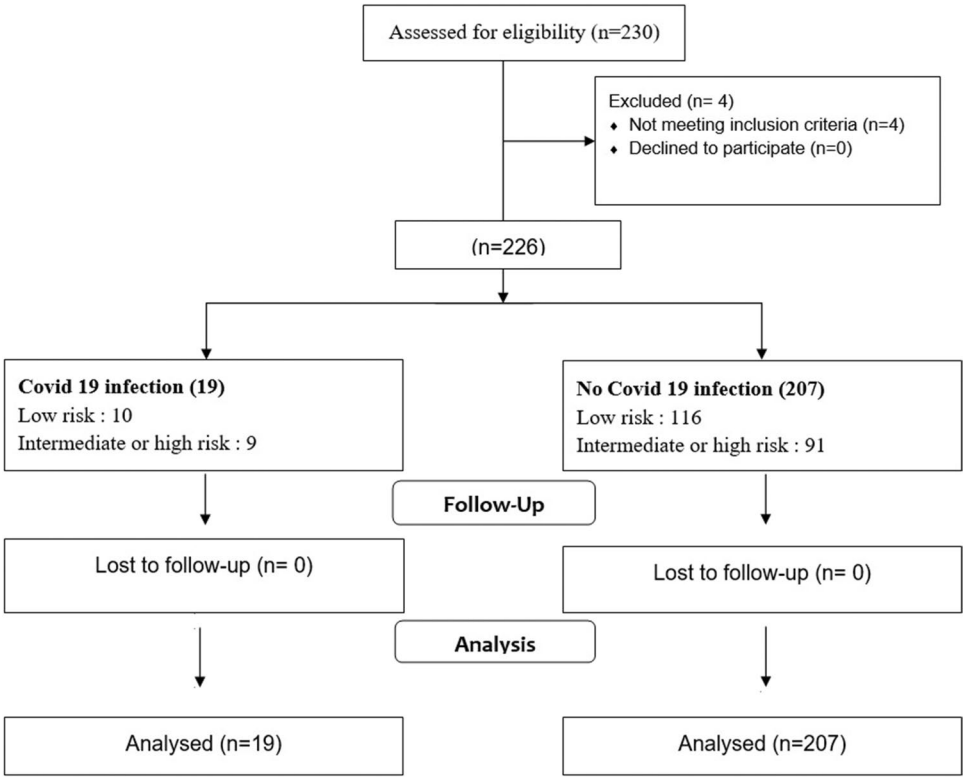

Fig. 1 Patient recruitment consort flowchart

"Fisher (*F*)" exact test when one of the theoretical numbers is less than 5 for independent samples. The correlation between risk factors of COVID-19 infection and the occurrence of COVID-19 infection was also calculated. A p-value < 0.05 was considered statistically significant.

Results

1. Patients characteristics

   Among 226 patients included (Fig. 1), patients under 70 years presented 85%. The sex ratio was 0.5 with a female predominance. The most common primary tumor subtypes were breast cancer (37%), colorectal cancers (22%), ovarian (7.5%), and lung cancer (5.5%). A metastatic disease was observed in 58% of patients. Comorbidities such as diabetes, hypertension, cardiovascular disease, and chronic obstructive pulmonary disease were observed in 39% of cases (Table 2).

   Among our patients, coronavirus disease was detected in 19 patients (8.4%). The incidence of COVID-19 infection in female was 10.7% and 4% in men (Table 3). Two of them had a poor performance status (> 2) and four patients (21%) were obese. Among 34 patients aged more than 70 years old, 6 patients (31%) had confirmed positive COVID-19 test. Comorbidities such as diabetes, hypertension, cardiovascular disease, and chronic obstructive pulmonary disease were observed in 31% of cases ($n = 6$). Patients with metastatic tumor presented 63% of all infected patients. In 42% of cases, patients were under chemotherapy. Clinically, 15 patients (79%) presented with symptoms such as fever, dyspnea, caught, myalgia, and ageusia/anosmia. A severe form of COVID19 requiring hospitalization was seen in 4 patients (21%).
2. Factors correlated with COVID-19 infection

   In our study, among all patients, the risk of COVID-19 infection was estimated as low in 56% of cases and intermediate or high in 44% of patients. Among our patients, coronavirus disease was detected in 19 patients (8.4%). Of 19 patients tested positive for COVID19, 47% had an intermediate and high risk of infection. COVID-19 infection was correlated with age < 70 years ($p = 0.035$, $\chi^2 = 4.437$, ddl = 1), chemotherapy treatment ($p = 0.032$, $\chi^2 = 4.613$, ddl = 1), and intermediate or high risk ($p = 0.018$, $\chi^2 = 4.892$, ddl = 1) (Table 4). In multivariable analysis, only the intermediate or high risk were correlated with COVID-19 infection in cancer patient ($p = 0.025$). Symptomatic COVID was correlated with stage IV ($p = 0.041$, $\chi^2 = 4.156$, ddl = 1), chemotherapy ($p = 0.004$, $\chi^2 = 7.367$, ddl = 1), and intermediate or high risk ($p = 0.04$, $\chi^2 = 3.754$, ddl = 1). Only the intermediate or high risk were correlated with COVID-19 infection in cancer patient ($p = 0.03$).

Table 2 Characteristics of patients

Parameter	Number	Percentage
Gender		
Male	77	34%
Female	149	66%
Age		
< 70	192	85%
> 70	34	15%
Performance status		
0–1	201	89%
> 2	25	11%
Obesity (BMI > 30)		
Yes	35	16%
No	191	84%
Comorbidities		
Yes	88	39%
No	138	61%
Concomitant steroid treatment	38	17%
Thoracic tumor (primary tumor/lung metastases)		
Yes	36	16%
No	190	84%
History of thoracic radiation therapy		
Type of treatment	50	22%
Chemotherapy	171	76%
HT/TT/TKI*	44	19%
Line of treatment		
Adjuvant	73	33%
Non adjuvant	153	67%
NLR**		
< 5	199	88%
> 5	27	12%

*Hormone therapy/targeted therapy/ tyrosine kinase inhibitors

**Neutrophile to lymphocyte ratio

Table 3 Characteristics of COVID-19-positive and -negative cancer patients

Variable	COVID-19 status (226 patients)	
	Positive ($n = 19$) %	Negative ($n = 207$) %
Sex: male	3 (15%)	73 (35%)
Age > 70 years	6 (31%)	28 (13.5%)
Performance status > 2	2 (10.5%)	23 (11.5%)
Comorbidities	6 (31%)	82 (39%)
Stage IV disease	12 (63%)	119 (57%)
Chemotherapy	8 (42%)	163 (78%)
NLR > 5	2 (10.5%)	25 (12%)
Risk of infection		
-Low	10 (53%)	116 (56%)
-Intermediate	9 (47%)	85 (41%)
-High	0	6 (3%)

Table 4 Factors correlated with COVID infection

	Cases	Rate %	p*	χ^2
Stage				
Non-metastatic	7	0.36	0.633	0.229
Metastatic	12	0.63		
Sex				
Male	3	0.15	0.08	3.073
Female	16	0.84		
PS				
0–1	17	0.89	0.93	0.006
≥ 2	2	0.1		
Age				
< 70	13	0.68	**0.035**	**4.437**
≥ 70	6	0.31		
Stage				
Metastatic	12	0.63	0.623	0.230
Localized	7	0.36		
BMI				
< 30	15	0.78	0.484	0.489
≥ 30	4	0.21		
Comorbidities				
Yes	6	0.31	0.493	0.470
No	13	0.68		
Chemotherapy				
Yes	10	0.52	**0.032**	**4.613**
No	9	0.47		
Milano Policlinico ONCOVID modified Score				
Intermediate and high risk	9	0.47	**0.018**	**4.892**
	10	0.52		
Low risk				

*p significant if < 0.05

Discussion

Through this prospective study, we demonstrated that using the Milano Policlinico ONCOVID modified Score is very helpful for clinicians to identify vulnerable patients and to make the appropriate decision in the management of cancer patients. COVID-19 infection was correlated with age < 70 years, chemotherapy treatment, and intermediate or high risk. However, in multivariable analysis, only the intermediate or high risk were correlated with COVID-19 infection in cancer patient ($p = 0.025$). In fact, in case of a high-risk score, treatment schedules can be maintained only if safe administration is guaranteed. Treatment administration should be tailored depending on the type of treatment and disease response. Unnecessary procedures should be avoided to reduce hospital access.

In this prospective study, we investigated the prevalence of COVID-19 infection in cancer patients which was found to be 8.4%. The same prevalence was reported by Fillmort et al. [3] who analyzed electronic health records of the US Veterans Affairs Healthcare System. Of 22 914 cancer patients tested for COVID-19, 1794 (7.8%) were positive.

In another study including 2152 patients, 190 patients (9%) were tested positive for COVID-19 [4].

This high prevalence may be explained by the susceptibility of patients with cancer to COVID-19 infection. In fact, in several studies, authors reported that patients with cancer were more prone to infection with severe events and an increased risk of death. This might be related to the systemic immunosuppressive state caused directly by tumor growth and indirectly by the effects of anti-cancer treatment [5]. In the current analysis, we used a personalized score to evaluate the risk of infection in cancer patients. In the Policlinico ONCOVID modified Score, clinical, biological, and therapeutic parameters have been analyzed together to define 3 groups of risk. We found that patients with intermediate or high risk were more exposed to infection. Consequently, using such scores may be helpful to identify the vulnerable population among cancer patients.

Males and elderly patients have been identified as more exposed to COVID-19 infection, which was not founded in the current study. This could be explained by the fact of the female predominance in the included patients. Paradoxically, the risk of infection was higher in patients aged less than 70 years, probably because they need to regularly visit hospitals for anti-cancer therapy.

In terms of cancer characteristics, in a cohort study of 105 cancer patients with COVID-19, Dai et al. [6] reported that lung cancer was the most common cancer histology in affected patients (20.95%), followed by gastrointestinal cancer (12.38%), and breast cancer (10.48%). However, in the present study, breast cancer (53%) and colorectal cancer (16%) were the two most frequent primary tumors found in infected patients unlike lung cancer (5%). This might be explicated by the heterogeneity in the characteristics of included patients.

In a cohort study conducted by Zhang et al. [7], 28 cancer patients with COVID-19 infection were included. It has been founded that a high percentage of infected patients (35.7%) suffered from a metastatic disease. Additionally, in the current study; the percentage of infected patients with a stage IV disease was high and presented 63% of all infected patients which highlights the susceptibility of this subgroup of patients to COVID-19 infection.

In COVID-19, clinical manifestations can vary from mild flu-like symptoms to life-threatening respiratory insufficiency [8].

In a cohort study in China, Liang et al. [9] showed an increased risk of severe clinical events in the case of COVID-19 infection in cancer patients. Likewise, in a meta-analysis published in 2021, about 43.26% of cancer patients with COVID-19 experienced severe events [10]. In our study, the majority of patients were symptomatic (79%) and 21% of them required hospitalization due to a severe disease course. We found that symptomatic.

COVID-19 infection was correlated to chemotherapy, stage IV disease, and intermediate or high risk according to the score calculated. In this study, most of the patients who tested positive for COVID-19 had active disease and were under chemotherapy (42%). We founded also that receiving chemotherapy was correlated to the risk of infection. Hence, the question of delaying the treatment in patients at risk of infection remains. A meta-analysis involving 15 studies demonstrated that chemotherapy could increase the risk of death from COVID-19 in cancer patients [11]. A recent meta-analysis composed of 52 cohorts involving 9231 cancer patients with COVID-19 was so far the largest scale investigation with respect to the impact of antitumor approaches on clinical outcomes of cancer patients with COVID-19, indicating that cancer patients with recent anti-tumor therapy (especially chemotherapy) were generally susceptible to develop into severe COVID19 or even death [12].

Our study has some limitations with a relatively small sample size, heterogeneity in patient's characteristics, tumor stages, and cancer types. However, through this prospective study, we demonstrated the utility of such risk scores to further help clinicians in making the appropriate actions to alleviate this risk in the cancer patient.

Author contribution W. B. K.: idea, conception, analysis, writing; M. L.: data collection, writing; S. K.: data collection; A. K.: supervision, revision.

Data availability Yes.

Code availability n/a.

Declarations

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and the national research committee of Habib Bourguiba and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Consent to participate Yes.

Consent for publication Yes.

Conflict of Interest The authors declare no competing interests.

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