Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Characteristics and outcomes of cancer patients with covid-19 at a safety-net hospital

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ABSTRACT

Patients with cancer are a vulnerable population during the COVID-19 pandemic due to underlying immunosuppression, pre-existing comorbidities, and poor nutrition. There is a lack of data describing the disease course of cancer patients with COVID-19 disease. Therefore, we analyzed data from cancer patients with COVID-19 who were admitted to our hospital. Cancer patients were categorized into two groups as survivors and non-survivors of COVID-19. Among 68 cancer patients with COVID-19, 27% of patients were admitted to ICU, and 37% of the patients died. The median age was 72, and non-survivors were older than survivors ($p = 0.001$). Non-survivors had higher comorbidity scores, late-stage cancer, and worse ECOG performance status than survivors (all p values<0.005). Non-survivors also had significantly lower lymphocyte count and albumin level but higher lactate dehydrogenase, C-reactive protein, fibrinogen, troponin, and ferritin levels than survivors. On multivariable analysis, increased age and mechanical ventilation were associated with increased odds of death. We report no association between anti-cancer treatments and mortality from COVID-19 disease. In summary, cancer patients have higher mortality of COVID-19 infection than the general population. In addition to generally known risk factors, the high mortality rate in cancer patients with COVID-19 is associated with several cancer-specific factors.

Introduction

The novel severe acute respiratory syndrome coronavirus-2 (SARS–CoV-2) was first detected in December 2019 in Wuhan, China, then spread rapidly to almost every country globally, with United States, India, and Brasil as impacted the most [1]. The World Health Organization nominated SARS–CoV-2 as the cause of the Coronavirus Disease 2019 (COVID- 19) and has been formally declared a pandemic [2]. As of May 28, 2021, more than 170 million cases have been confirmed worldwide, leading to 3.5 million deaths [3].

Patients with cancer are a vulnerable population during the COVID-19 pandemic for many aspects, including underlying immunosuppression, pre-existing comorbidities, and poor nutrition. Especially critically ill cancer patients are more prone to having macro- and micro-nutrition deficits, leading to poorer outcomes [4]. Cancer patients often have high exposure to the healthcare system due to follow-up visits for treatment, surveillance, and supportive care. Liang et al. reported that cancer patients had poorer outcomes and higher incidence of COVID-19 than the general population [5]. They also reported a higher rate of serious adverse events such as intensive care unit admissions and requiring invasive ventilation. Another study found a 28.6% case-fatality rate of COVID-19 in patients with cancer [6]. Cancer patients might be immunocompromised due to antineoplastic therapy, some supportive medications including steroids, and the immunosuppressive nature of cancer itself [7]. Thus, patients with cancer seemed to be at high risk for developing unfavorable outcomes. To date, limited data exist describing the disease course of patients with cancer who infected with COVID-19. Current studies are limited by small sample sizes. The mortality outcomes of COVID-19 and either systemic antineoplastic treatment or immunotherapeutic drugs are mainly unknown, limited with small studies.

The clinical characteristics of cancer patients infected with COVID-

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19 largely remain obscure. Given the vulnerability of the cancer patients and potentially severe outcomes of COVID-19, an understanding of the factors related to clinical outcomes in patients with cancer is urgently needed. Therefore, we collected and analyzed data from cancer patients with COVID-19 who were admitted to our hospital. In this retrospective study, we aimed to describe clinical characteristics and outcomes of patients with cancer diagnosed with COVID-19 and identify risk factors associated with in-hospital mortality.

Materials and methods

In this retrospective study, we reported patients with COVID-19 who had a history of cancer. The patient data was collected in Capital Health Regional Medical Center between March 2020 and October 2020. This study was approved by the Institutional Ethics Committee of Capital Health Regional Medical Center. The need for informed consent was waived by the ethics committee due to the retrospective nature of the study and no identifiable patient information published. Two physicians (MO and MM) independently verified the data accuracy.

Patients with laboratory-confirmed SARS-CoV-2 were included. Patients with only clinically and radiologically diagnosis of COVID-19 were excluded from the study.

Cancer patients were categorized into two groups as survivors and non-survivors of COVID-19. We included demographics (age at diagnosis, gender, race/ethnicity, insurance status), clinical findings (obesity status, comorbidity score, smoking status, type of malignancy, stage of disease, performance status, therapies, oxygen requirement, admission to intensive care unit (ICU), and laboratory findings. Obesity status was defined as overweight (BMI 25–29.9) and obese (BMI $\geq$ 30). The comorbidity score was calculated using the Charlson Comorbidity Index and categorized as $\leq$ 3 and >3. Smoking status was divided into three groups: Never smoker, a former smoker, and a current smoker. Functional status was evaluated using the Eastern Cooperative Oncology Group (ECOG) performance status scale. The staging was described as early-stage (I-II) and late-stage (III-IV) for solid malignancies. We defined active anti-cancer therapy if patients received systemic chemotherapy or others within four weeks of COVID-19 diagnosis. COVID-19 treatment information was also collected: Remdesivir, convalescent plasma, tocilizumab, dexamethasone, methylprednisolone, hydroxychloroquine, azithromycin. Time to ICU admission was defined as the number of days from ward admission to ICU admission.

Statistics

We used the *t*-test, chi-square, or Fisher's exact test as appropriate to compare the baseline characteristics between survivor and non-survivor patients with COVID-19. The multivariable logistic regression model was performed to assess the association between variables and death. The odds ratio (OR) and 95% confidence interval (CI) were calculated with the logistic regression model. All analyses were performed using the SPSS version 22, and $p < 0.05$ was considered statistically significant.

Results

We identified 562 patients with COVID-19; 68 (12%) patients had a history of cancer. Among 68 cancer patients with COVID-19, 25 (37%) patients had died of COVID-19. The median age was 72 (23–91), and non-survivors were older than survivors (median age 67 vs. 77, $p = 0.001$). Thirty-seven (54%) patients were male, and 36 (53%) patients were Black. Non-survivors were more likely to be male (68% vs. 32%) and Black. Twenty-five (37%) patients were overweight, and 19 (28%) patients were obese. Forty-four (65%) patients had never smoked. Thirty-nine (57%) patients had comorbidity scores> 3, and non-survivors had higher comorbidity scores compared to survivors (80% vs. 44%, $p = 0.004$). The most common cancer type was breast cancer (22%), following by prostate cancer (18%), lung cancer (12%), hematological cancers (12%), and colon cancer (10%). The most common insurance type was Medicare MGD insurance (49%) which was higher in non-survivors compared to survivors (64% vs. 40%, $p = 0.002$). Non-survivors had worse ECOG performance status than survivors ($p<0.001$). Nineteen (76%) patients had an ECOG performance status of 3, and 6 (24%) patients had ad ECOG performance status of 4 among non-survivors. Twenty-two (32%) patients received anti-cancer therapy within four weeks of COVID-19 diagnosis, including systemic chemotherapy (19%), radiotherapy (3%), hormonotherapy (9%), and others (2%). The most common treatment of COVID-19 was methylprednisolone (29%), followed by dexamethasone (25%) and azithromycin (25%). Twenty (29%) patients required oxygen therapy via high-flow nasal cannula, 15 (22%) patients required non-invasive mechanical ventilation or invasive mechanical ventilation with a median time of 5 days. Mechanic ventilation was more frequently applied in non-survivors (40% vs. 7%, $p<0.001$). A total of 27% of patients were admitted to ICU with a median time of 5.5 days. Twenty-five (37%) patients had the late-stage disease, and it was more frequently in non-survivors than in survivors (60% vs. 23%, $p = 0.002$). Baseline characteristics of the cancer patients were summarized in Table 1.

Non-survivors had lower lymphocyte count (8.2 vs. 13 109/L, $p = 0.03$), albumin level (2.8 vs. 3.5 g/dL, $p = 0.003$), but higher lactate dehydrogenase (501 vs. 371 U/L, $p = 0.04$), C-reactive protein (21.6 vs. 7.9 mg/dL, $p = 0.01$), fibrinogen (736 vs. 587 mg/dL, $p = 0.02$), troponin (0.15 vs. 0.01, $p = 0.009$), and ferritin (697 vs. 531.5 ng/mL, $p = 0.03$) levels compared to survivors. Laboratory findings were summarized in Table 2.

On multivariable logistic regression analysis, increasing age (OR 1.20 [95% CI 1.04–1.38], $p = 0.01$), and mechanical ventilation (OR 32.2 [95% CI 3.73–307.5], $p = 0.003$) were associated with increased odds of death (Table 3). There was no association between gender, obesity status, comorbidity score, anti-cancer therapy, stage of disease, and death.

Discussion

In this retrospective, single-center cohort study, we reported demographic, clinical, and laboratory findings, as well as treatments and outcomes, for 68 patients with cancer and laboratory-confirmed COVID-19 infection. Patients with cancer appear to have an increased risk of mortality or severe disease course in the ongoing COVID-19 pandemic regardless of cancer type and antineoplastic treatment. In our cohort, a total of 27% of patients were admitted to ICU, and 37% of the patients died, which is higher than the reported mortality rate in the general population. Similarly, in the literature, few studies reported increased mortality in a cancer patient with COVID-19 disease. In their cohort, Miyashita et al. reported a 28.4% case fatality rate [8]. Another study from Italy reported 20% of the deceased patients with COVID-19 had an active cancer history within the past five years [9]. Similarly, few studies reported increased mortality in cancer patients compared to the general population [10-12]. Although underlying mechanisms are not clearly explained, these findings suggest that patients with cancer are more susceptible to a poor prognosis of COVID-19. Both cancer and patients' specific risk factors play a vital role in this matter, including impaired immune function and the fragility of cancer patients [13].

Age, gender, and comorbidities are previously reported factors related to mortality in patients with cancer and COVID-19 infection. Similarly, in our study, non-survivors were more likely to be older, male, and black. Additionally, higher comorbidity scores and increased oxygen requirement with NIVM and MV were associated with increased mortality (p values <0.004 and <0.001, respectively). Also, we determined several cancer-specific factors that are related to increased mortality in cancer patients with COVID-19. ECOG performance status of 3 or higher and advanced stage of cancer (Stage 3 and 4) were significantly associated with increased mortality (p values <0.02 and <0.001, respectively). On multivariable logistic regression analysis, only

Table 1
Baseline characteristics of cancer patients with COVID-19.

Characteristics	Overall*n* = 68	Survivors*n* = 43	Non-survivors*n* = 25	*p-value*
Age at diagnosis				***0.001***
Median	72 (23–91)	67 (23–88)	77 (56–91)	
< 75	40 (58.8)	32 (74.4)	8 (32.0)	
≥ 75	28 (41.2)	11 (25.6)	17 (68.0)	
Gender				*0.086*
Male	37 (54.4)	20 (46.5)	17 (68.0)	
Female	31 (45.6)	23 (53.5)	8 (32.0)	
Race/Ethnicity				*0.54*
White	23 (33.8)	15 (34.9)	8 (32.0)	
Black	36 (52.9)	21 (48.8)	15 (60.0)	
Other	9 (13.2)	7 (16.3)	2 (8.0)	
Obesity status				*0.52*
Normal	24 (35.3)	13 (30.2)	11 (44.0)	
Overweight (BMI 25–29.9)	25 (36.8)	17 (39.5)	8 (32.0)	
Obese (≥ 30)	19 (27.9)	13 (30.2)	6 (24.0)	
Comorbidity Score				***0.004***
≤ 3	29 (42.6)	24 (55.8)	5 (20.0)	
> 3	39 (57.4)	19 (44.2)	20 (80.0)	
Smoking status				*0.057*
Never smoked	44 (64.7)	32 (74.4)	12 (48.0)	
Former smoker	20 (29.4)	10 (23.3)	10 (40.0)	
Current smoker	4 (5.9)	1 (2.3)	3 (12.0)	
Type of malignancy				*0.74*
Breast	15 (22.1)	12 (27.9)	3 (12.0)	
Prostate	12 (17.6)	8 (18.6)	4 (16.0)	
Lung	8 (11.8)	4 (9.3)	4 (16.0)	
Colon	7 (10.3)	5 (11.6)	2 (8.0)	
Renal	5 (7.4)	2 (4.7)	3 (12.0)	
CNS	4 (5.9)	3 (7.0)	1 (4.0)	
Melanoma	3 (4.4)	2 (4.7)	1 (4.0)	
Hematologic	8 (11.8)	4 (9.3)	4 (16.0)	
Others	6 (8.8)	3 (7.0)	3 (12.0)	
Insurance status				***0.002***
Medicare Original	15 (22.1)	7 (16.3)	8 (32.0)	
Medicare MGD	33 (48.5)	17 (39.5)	16 (64.0)	
Others	20 (29.4)	19 (44.2)	1 (4.0)	
Self-pay/Charity	2 (2.9)	2 (4.7)	0 (0.0)	
Medicaid	4 (5.9)	3 (6.9)	1 (4.0)	
Commercial	8 (11.8)	8 (18.6)	0 (0.0)	
Managed care	6 (8.8)	6 (14.0)	0 (0.0)	
ECOG performance status				***<0.001***
0–2	35 (51.5)	35 (81.4)	0 (0.0)	
3	25 (36.8)	6 (14.0)	19 (76.0)	
4	8 (11.8)	2 (4.7)	6 (24.0)	
Anti-cancer therapy				*0.097*
None in the 4 weeks before COVID-19 diagnosis	46 (67.6)	26 (60.5)	20 (80.0)	
Within 4 weeks before COVID-19 diagnosis	22 (32.4)	17 (39.5)	5 (20.0)	
Systemic chemotherapy	*13 (19.1)*	*9 (20.9)*	*4 (16.0)*	
Radiotherapy	*2 (2.9)*	*2 (4.7)*	*0 (0)*	
Hormonotherapy	*6 (8.8)*	*5 (11.6)*	*1 (4.0)*	
Immunotherapy	*1 (1.5)*	*1 (2.3)*	*0 (0)*	
Treatment of COVID-19				
Remdesivir	16 (23.5)	13 (30.2)	3 (12.0)	*0.087*
Conv plasma	15 (22.1)	11 (25.6)	4 (16.0)	*0.35*
Toculizimab	3 (4.4)	2 (4.7)	1 (4.0)	*0.90*
Dexamethasone	17 (25.0)	16 (37.2)	1 (4.0)	***0.002***
Methylprednisolone	20 (29.4)	10 (23.3)	10 (40)	*0.14*
Hydroxychloroquine	10 (14.7)	4 (9.3)	6 (24.0)	*0.09*
Azithromycin	17 (25.0)	9 (20.9)	8 (32.0)	*0.30*
Oxygen requirement				***<0.001***
Room air or Up to 6 L	33 (48.5)	30 (69.8)	3 (12.0)	
High flow	20 (29.4)	10 (23.3)	10 (40.0)	
NIVM or MV	15 (22.1)	3 (7.0)	12 (40.0)	
Mechanic ventilation, days (median)	5 (1–37)	5 (5–5)	3 (1–37)	*0.48*
Hospital stay, days	6.5 (1–57)	6 (1–48)	7 (1–57)	*1.0*
Admission to ICU	5.5 (1–48)	7 (6–37)	3 (1–37)	*0.62*
Stage				***0.002***
I-II	43 (63.2)	33 (76.7)	10 (40.0)	
III-IV	25 (36.8)	10 (23.3)	15 (60.0)	

increased age (OR 1.20 [95% CI 1.04–1.38], $p = 0.01$) and mechanical ventilation (OR 32.2 [95% CI 3.73–307.5], $p = 0.003$) were associated with increased odds of death (Table 3).

Cancer patients under active anti-cancer treatments have been generally considered a higher risk of worse outcomes than those who are not receiving anti-cancer treatment. The evidence to support these ideas is obscure and generally limited to retrospective studies with small sample sizes [5, 11, 14]. Our data do not demonstrate that chemotherapy or other anti-cancer treatments are related to increased mortality from COVID-19 disease. In their prospective cohort study of 800 cancer patients with COVID-19 disease, Lee et al. reported that recent anti-cancer treatment was not significantly associated with increased mortality [15]. Similarly, in their cohort of 938 patients, Kuderer et al. reported an absence of relation between mortality and anti-cancer treatments [16]. Therefore, the American Society of Clinical Oncology suggested that effective anti-cancer treatments could continue during the COVID-19 pandemic to spare our patients from increased cancer morbidity and mortality [17]. Also, recipients of hematopoietic stem cell transplantation patients remain at high risk and need special attention [18]. We highly encourage to conclude further studies with higher numbers of patients to confirm or negate these findings.

The most common cancer type in our study was breast cancer, following by prostate cancer and lung cancer. Cancer type was not associated with mortality. Also, race and ethnicity, obesity status, type of anti-cancer therapies, and smoking status were not associated with mortality. Several previous studies reported lung cancer was associated with a higher pneumonia rate and a more severe disease course [10, 19]. Our results demonstrated that several laboratory values were significantly associated with mortality. It's known that increased inflammatory markers are closely related to the inflammatory storm and unfavorable outcomes [20]. In our study, non-survivors had lower lymphocyte count and albumin level ($p = 0.03$, $p = 0.003$, respectively), but higher lactate dehydrogenase, C-reactive protein, fibrinogen, troponin, and ferritin level than survivors (all p values < 0.005) compared to survivors, These findings were similar to previous reports [10, 21, 22].

Our findings are important in supporting the limited evidence of susceptibility of cancer patients in the current pandemic. However, our study also has some limitations. First, the study was retrospective and non-randomized; therefore, it's a matter of recall bias and incomplete documentation. The sample size was not large enough to derive any firm conclusions. Tumor types were diverse; thus, heterogeneity could be possible. Additionally, we could not compare the characteristics, treatment strategies, and outcomes of cancer patients against a control group of patients without cancer. Finally, prospectively designed studies with larger sample sizes are needed to investigate the risk factors and outcomes in cancer patients with COVID-19.

Conclusion

In summary, patients with cancer are susceptible to more severe disease course and increased mortality of COVID-19 infection compared to the general population. In addition to generally known risk factors, the high mortality rate in cancer patients with COVID-19 disease is associated with cancer-specific factors such as stage and performance score. This study emphasizes the urgent need for more data, especially in

Table 2
Laboratory findings of cancer patients with COVID-19.

Findings (normal range)	Overall$n = 68$ Median levels	Survivors$n = 43$	Non-survivors$n = 25$	*p-value*
White blood cell count (4.0–10.10)	7.6 (0.8–24.2)	7.3 (0.82–21.0)	8.2 (2.0–24.2)	0.61
Neutrophils (1.6–6.1 × 10^9/L)	67.1 (0–95.0)	66 (0.38–90.0)	75 (0–95.0)	0.61
Lymphocytes (1.2–3.8 × 10^9/L)	11.0 (0.1–80.0)	13 (0.01–35.0)	8.2 (1.0–80.0)	***0.03***
Neutrophil–lymphocyte ratio	5.7 (0–90.0)	4.4 (0.03–90.0)	8.4 (0–78.0)	0.13
Total protein (6.5–8.5 g/dL)	6.8 (4.5–9.6)	6.9 (5.4–9.6)	6.3 (4.5–8.7)	0.07
Albumin (3.5–5.0 g/dL)	3.2 (2.1–4.8)	3.5 (2.3–4.8)	2.8 (2.1–4.1)	***0.003***
Lactate (0.7–1.9)	1.5 (0.2–7.2)	1.3 (0.2–7.2)	2.3 (1.1–5.6)	0.15
Lactate dehydrogenase (120–246 U/L)	415 (152.0–1971.0)	371.0 (152.0–865.0)	501 (291–1971)	***0.04***
Creatine kinase (30–135 U/L)	60 (24.0–1431.0)	55.0 (24.0–1431.0)	197 (33–486)	0.06
D-dimer (0–0.45 mg/L)	2.4 (0.5–20.0)	2.3 (0.5–14.0)	2.8 (0.6–20.0)	0.53
C-reactive protein (< 1 mg/dL)	16.2 (0.06–59.0)	7.9 (0.06–33.9)	21.6 (2.0–59.0)	***0.01***
Procalcitonin (0.00–0.08)	0.25 (0–80.0)	0.2 (0–5.0)	0.64 (0–80.0)	0.07
Fibrinogen (214–453 mg/dL)	669.0 (71–1539)	587 (71–833)	736 (280–1539)	***0.02***
BNP (0–899)	1585.0 (33.0–176,510.0)	800 (33–176,510)	2162 (75–16,442)	0.21
Troponin (0.000–0.034)	0.037 (0–1.29)	0.01 (0–0.36)	0.15 (0–1.29)	***0.009***
Sodium (137–145 mmol/L)	137.5 (128.0–164.0)	137 (128–164)	140 (131–157)	0.61
AST (14–36 U/L)	60.5 (17.0–629.0)	54.0 (17.0–153.0)	74 (26–629)	0.20
ALT (0–34 U/L)	34.5 (4.0–263.0)	32.5 (4.0–212.0)	42 (11–263)	0.44
Ferritin (11.1–264 ng/mL)	606.5 (32.4–3912.0)	531.5 (32.4–3912.0)	697 (180–3162)	***0.03***

Table 3
Multivariable logistic regression analysis to assess the relationship between death and other variables.

Characteristics	OR (95% CI)	*p*-value
Age at diagnosis (continuous)	1.20 (1.04–1.38)	***0.01***
Gender		
Male	Ref	
Female	1.19 (0.15–9.38)	*0.86*
Obesity status		
Normal	Ref	
Overweight (BMI 25–29.9)	2.87 (0.32–25.6)	*0.34*
Obese (≥ 30)	0.97 (0.10–8.9)	*0.98*
Comorbidity Score		
≤ 3	Ref	
> 3	2.95 (0.43–20.4)	*0.27*
Anti-cancer therapy		
None in the 4 weeks before COVID-19 diagnosis	Ref	
Within 4 weeks before COVID-19 diagnosis	0.44 (0.06–3.44)	*0.43*
Oxygen requirement		
Room air or Up to 6 L	Ref	
High flow	6.54 (0.90–46.2)	*0.06*
NIVM or MV	32.2 (3.73–307.5)	***0.003***
Stage		
I-II	Ref	
III-IV	3.74 (0.73–19.0)	*0.11*

OR: Odds ratio, CI: Confidence interval

terms of developing anti-cancer treatment strategies.

Conflict of interest

There is no conflict of interest to declare.

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CRediT authorship contribution statement

Muhammet Ozer: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Writing - original draft, Writing - review & editing. **Suleyman Yasin Goksu:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Writing - original draft, Writing - review & editing. **Mohammed Mahdi:** Conceptualization, Data curation, Investigation, Resources, Writing - original draft. **Neel Gandhi:** Methodology, Project administration, Resources, Supervision, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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