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Health Outcomes and Economics of Cancer Care

Impact of Cancer History on Outcomes Among Hospitalized Patients with COVID-19

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Key Words. COVID-19 • Cancer • SARS-CoV-2 • Hospitalized patients • Matched cohort

Abstract

Background. Early reports suggested increased mortality from COVID-19 in patients with cancer but lacked rigorous comparisons to patients without cancer. We investigated whether a current cancer diagnosis or cancer history is an independent risk factor for death in hospitalized patients with COVID-19.

Patients and Methods. We identified patients with a history of cancer admitted to two large hospitals between March 13, 2020, and May 10, 2020, with laboratory-confirmed COVID-19 and matched them 1:2 to patients without a history of cancer.

Results. Men made up 56.2% of the population, with a median age of 69 years (range, 30–96). The median time since cancer diagnosis was 35.6 months (range, 0.39–435); 80% had a solid tumor, and 20% had a hematologic malignancy. Among patients with cancer, 27.8% died or entered hospice versus 25.6% among patients without cancer. In multivariable analyses, the odds of death/hospice were similar (odds ratio [OR], 1.09; 95% confidence interval [CI], 0.65–1.82). The odds of intubation (OR, 0.46; 95% CI, 0.28–0.78), shock (OR, 0.54; 95% CI, 0.32–0.91), and intensive care unit admission (OR, 0.51; 95% CI, 0.32–0.81) were lower for patients with a history of cancer versus controls. Patients with active cancer or who had received cancer-directed therapy in the past 6 months had similar odds of death/hospice compared with cancer survivors (univariable OR, 1.31; 95% CI, 0.66–2.60; multivariable OR, 1.47; 95% CI, 0.69–3.16).

Conclusion. Patients with a history of cancer hospitalized for COVID-19 had similar mortality to matched hospitalized patients with COVID-19 without cancer, and a lower risk of complications. In this population, patients with active cancer or recent cancer treatment had a similar risk for adverse outcomes compared with survivors of cancer. ***The Oncologist*** 2021;26:685–693

Implications for Practice: This study investigated whether a current cancer diagnosis or cancer history is an independent risk factor for death or hospice admission in hospitalized patients with COVID-19. Active cancer, systemic cancer therapy, and a cancer history are not independent risk factors for death from COVID-19 among hospitalized patients, and hospitalized patients without cancer are more likely to have severe COVID-19. These findings provide reassurance to survivors of cancer and patients with cancer as to their relative risk of severe COVID-19, may encourage oncologists to provide standard anticancer therapy in patients at risk of COVID-19, and guide triage in future waves of infection.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is causing a global pandemic. The resulting disease, COVID-19, can cause severe lower respiratory tract infection and systemic inflammatory response, requiring mechanical ventilation and frequently resulting in death [1]. In a large cohort of patients with COVID-19, the 5% who became

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critically ill had a 49% mortality rate [2]. These poor outcomes are more frequent in patients with various comorbidities, including diabetes, hypertension, and advanced age [3, 4]. Initial reports suggested that cancer may be an independent risk factor for severe COVID-19, and severe outcomes from COVID-19 are a major concern among patients with cancer and survivors of cancer [5–10]. To date, however, there is a paucity of rigorously controlled data to address whether people with active cancer or a history of cancer are more likely to experience severe complications and death as a consequence of COVID-19 compared with similar patients without cancer. Additionally, there are limited data available to guide oncologists regarding whether survivors of cancer who have completed active treatment and have no evidence of disease are at increased risk for adverse outcomes following a COVID-19 diagnosis. We therefore reviewed a series of patients admitted to two large teaching hospitals in Boston with confirmed COVID-19 to compare outcomes among patients with and without a history of cancer.

Materials and Methods

Participants

We identified all patients over 18 years of age admitted to any inpatient service at Brigham and Women's Hospital, Dana-Farber Cancer Institute, or Massachusetts General Hospital between March 13, 2020, and May 10, 2020, for management of symptomatic confirmed COVID-19 confirmed by reverse transcriptase-polymerase chain reaction respiratory tract specimens. Patients with a history of cancer were defined as those with a current diagnosis of, or a history of, invasive cancer or hematologic malignancy; patients with a history of noninvasive cancers, cutaneous squamous or basal cell carcinomas, or premalignant hematologic conditions were excluded. These cases were matched 1:2 to patients without a history of cancer accounting for age ($\pm$5 years, with two cases ≥90 years of age matched $\pm$7 years), admission date ($\pm$2 weeks), race, and gender. The current analysis represents follow-up through June 15, 2020. This study was determined to be exempt from full review and granted a waiver of informed consent by the Dana-Farber/Harvard Cancer Center institutional review board.

Data Collection

Data abstracted from the medical record included sociodemographics, body mass index (BMI), underlying comorbidities, immunosuppressed status (e.g., recent treatment with steroids, immunomodulatory therapy, chemotherapy, or history of allogenic or autologous bone marrow transplant [BMT]), COVID-19 clinical complications, outcomes, and treatments including chloroquine/hydroxychloroquine and COVID-19 clinical trials (e.g., remdesivir, tocilizumab). Heart rate, blood pressure, temperature, respiratory rate, oxygen saturation, and laboratory test results (white blood cell count, hematocrit, platelets, absolute neutrophils and lymphocytes, creatinine, alanine aminotransferase, aspartate aminotransferase, total bilirubin, ferritin, lactic acid dehydrogenase, C-reactive protein, troponin, erythrocyte sedimentation rate, D-dimer, interleukin-6, and procalcitonin) at admission were also extracted.

For all patients, preadmission medical history was used to calculate a Charlson comorbidity index [11], and comorbidities were also grouped: cardiovascular/vascular, neurologic, gastrointestinal/hepatic, renal, pulmonary, and diabetes. For patients with a history of cancer, cancer type and stage, date of diagnosis, current treatment or treatment in the last 6 months (chemotherapy, targeted therapy, immunotherapy, radiation), and history of BMT were documented. A group of patients with "active cancer" was defined to isolate a population with more significant cancer burden or undergoing potentially deleterious treatments. Thus, "active cancer" was defined as having metastatic disease, a current hematological malignancy, or cancer-directed systemic medical therapy (except endocrine therapy) within the last 6 months. Those without "active cancer" were categorized as "cancer survivors."

Statistical Analysis

Primary Analysis: Patients with or Without a History of Cancer

Descriptive statistics were used to compare patient and clinical characteristics and outcomes of patients with and without cancer. The primary endpoint was death or hospice admission during hospitalization for COVID-19. Secondary outcomes included intubation and admission to the intensive care unit (ICU). Conditional logistic regression was used to evaluate the association between having cancer and adverse clinical outcomes and complications (death/discharge to hospice, intubation, ICU hospitalization, shock, and acute respiratory distress syndrome [ARDS]). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated; p values ≤.05 were considered statistically significant. The primary multivariable model was adjusted for baseline immunosuppression and comorbidities (cardiovascular disease, pulmonary disease, and diabetes). We fit additional models stratified by "active cancer" status to identify whether having metastatic disease, a current hematological malignancy, or cancer-directed systemic medical therapy within the last 6 months differentially impacted mortality.

Analysis of Patients with a History of Cancer

Among patients with a history of cancer, logistic regression models (unadjusted for matching factors) were fit to identify predictors of death/hospice and ORs and 95% CIs calculated. Variables with p values ≤.20 in univariable analyses were included in the final multivariable model; p values ≤.05 were considered statistically significant. All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

Results

Study Population Characteristics

Between March 13, 2020, and May 10, 2020, 183 patients with a history of cancer were admitted with COVID-19. Of these 183, two matched control patients without a history of cancer were identified for 162 cases (88.5%). Table 1 includes demographic information and reported comorbidities at

Table 1. Patient characteristics

Characteristics	Total ($n = 486$), *n* (%)	Current or prior cancer history ($n = 162$), *n* (%)	No history of cancer ($n = 324$), *n* (%)
Median age (range), yr	69 (30–98)	69.0 (30–98)	68.5 (30–96)
Age, yr			
<65	173 (35.6)	55 (34.0)	118 (36.4)
65–74	135 (27.8)	50 (30.9)	85 (26.2)
≥75	178 (36.6)	57 (35.2)	121 (37.4)
Sex			
Male	273 (56.2)	91 (56.2)	182 (56.2)
Female	213 (43.8)	71 (43.8)	142 (43.8)
Race			
Asian	11 (2.4)	4 (2.5)	7 (2.3)
Black	92 (20.0)	29 (18.4)	63 (20.8)
White	299 (64.9)	102 (64.5)	197 (65.0)
More than one race or other	59 (12.8)	23 (14.6)	36 (11.9)
Unknown/not reported	25	4	21
Hispanic			
Yes	64 (13.2)	22 (13.5)	42 (15.1)
No	373 (76.8)	137 (84.6)	236 (84.9)
Unknown/not reported	49 (10.0)	3 (1.9)	46
First language other than English			
Yes	123 (25.3)	40 (24.7)	83 (25.6)
No	363 (74.7)	122 (75.3)	241 (74.4)
BMI			
<18.5	13 (2.7)	6 (3.7)	7 (2.2)
18.5–24.9	114 (23.6)	46 (28.4)	68 (21.2)
25–29.9	158 (32.7)	50 (30.9)	108 (33.6)
≥30	198 (41.0)	60 (37.0)	138 (43.0)
Missing	3	—	3
Median Charlson score (range)	5 (0–19)	7 (2–19)	4 (0–14)
Presence of comorbidities			
Cardiovascular/vascular	159 (32.7)	48 (29.6)	111 (34.3)
Neurologic	58 (11.9)	10 (6.2)	48 (14.8)
GI/hepatic	25 (5.1)	13 (8.0)	12 (3.7)
Renal	132 (27.2)	49 (30.3)	83 (25.6)
Pulmonary	92 (18.9)	33 (20.4)	59 (18.2)
Diabetes	188 (38.7)	56 (34.6)	132 (40.7)
Immunosuppressed	80 (16.5)	52 (32.1)	28 (8.6)

Abbreviations: —, no data; BMI, body mass index; GI, gastrointestinal.

presentation for the cases ($n = 162$), matched noncancer controls ($n = 324$), and total study population ($n = 486$). Median age of the population was 69 years (range, 30–98), 56.2% were men, and 35.5% were non-White. Diabetes (38.7%), cardiovascular/vascular (32.7%), and renal (27.2%) disease were the most prevalent comorbidities. A higher proportion of patients with cancer (32.1%) were immunosuppressed than patients without a history of cancer (8.6%).

Case and Treatment Characteristics

Cancer and treatment characteristics for cases are presented in Table 2. The majority (79.6%) had a history of a solid tumor malignancy, and hematologic malignancies accounted for 20.4% of cases (supplemental online Table 1). Cancer diagnosis had occurred a median of 35.6 months (range, 0.39–435.4) prior to admission. At the time of admission for COVID-19, nearly one third (31.7%) of all cases were currently receiving or had received cancer-directed systemic therapy within the last 6 months. Of cases, most (21.6%) were receiving cytotoxic chemotherapy, 13.6% targeted therapy (not including hormonal therapy), and 8.0% immunotherapy. At the time of admission for COVID-19, 19% (31/162) had metastatic disease and 15.4% (25/162) had active hematologic malignancy. Overall, 47.5%

Table 2. Cancer and treatment characteristics for cases ($n = 162$)

Characteristic	*n* (%)
Cancer type	
Solid tumor	129 (79.6)
Hematologic malignancy	33 (20.4)
Median months since diagnosis (range)[a]	35.6 (0.39–435.4)
Stage at diagnosis	
Local/local with nodes	101 (62.3)
Distant metastases	23 (14.2)
Hematologic	33 (20.4)
Unknown	5 (3.1)
Status of cancer at COVID diagnosis	
Active treatment/metastatic disease	77 (47.5)
NED	85 (52.5)
Any current systemic treatment	
Yes	43 (26.5)
No	119 (73.5)
Any systemic treatment in the last 6 months	
Yes	51 (31.7)
No	110 (68.3)
Unknown	1
Any active (current and/or in last 6 months)	
Systemic treatment	
Yes	51 (31.5)
No	111 (68.5)
Active (current and/or in last 6 months)	
Chemotherapy	
Yes	35 (21.6)
No	127 (78.4)
Active (current and/or in last 6 months)	
Targeted therapy	
Yes	22 (13.6)
No	140 (86.4)
Active (current and/or in last 6 months)	
Immunotherapy	
Yes	13 (8.0)
No	149 (92.0)
Prior radiation	
Yes	68 (43.6)
No	88 (56.4)
Unsure	6

[a]Excludes three patients for whom date of cancer diagnosis was not available and one patient who was diagnosed during COVID-19 hospitalization.
Abbreviation: NED, no evidence of disease.

of cases were defined as ‘‘active cancer,’’ having either metastatic or hematologic malignancy at COVID-19 admission and/or received cancer-directed systemic therapy within the last 6 months. The remaining cases (52.5%) were classified as ‘‘survivors.’’

Clinical Presentation

Vital signs and summary laboratory values at the time of admission are detailed in supplemental online Table 2. Presenting vitals and laboratory values were similar between cases and matched controls; notable differences include a lower absolute lymphocyte count (0.73 vs. 0.83; $p = .004$).

Clinical Course and Outcomes: Cases Versus Noncancer Controls

In-hospital treatments, complications, and outcomes are shown in Table 3. Among all patients, the majority (75%) received antibiotics and nearly half (44.5%) were treated with chloroquine or hydroxychloroquine. Enrollment in a remdesivir (16%) or tocilizumab clinical trial was less common (10%). The most prevalent complication over the course of hospitalization was pneumonia (87.9%), followed by ARDS (39.1%). Approximately 40% of patients were admitted to the ICU and 36.6% were intubated. As of last follow-up, 46 cases (28.4%) and 82 controls (25.3%) had either died in the hospital or been discharged to hospice; a total of 10 patients were still hospitalized (4 cases and 6 controls). The mean duration of hospitalization was identical (median, 9 days) among cases and controls.

Results from univariable and multivariable conditional logistic regression, including model results stratified by cancer status, are shown in Tables 4 and 5. In univariable analyses, cases and noncancer controls had similar odds of death or hospice during their hospitalization (OR, 1.21; 95% CI, 0.77–1.92); the odds of death or discharge to hospice (OR, 1.09 95% CI, 0.65–1.82) remained similar between cases and noncancer controls after adjusting for baseline comorbidities and immunosuppression at the time of admission (Table 4). There was a trend toward higher odds of death or hospice among patients with active cancer versus matched noncancer controls in univariable analyses (OR, 1.98; 95% CI, 0.99–3.96) that was nonsignificant in the multivariable model that adjusted for immunosuppression and baseline comorbidities, (OR, 2.18; 95% CI, 0.82–5.77).

In both univariable and multivariable analyses (Table 5), patients with cancer were less likely to experience complications of COVID-19, including intubation (univariable OR, 0.57; 95% CI, 0.36–0.88; multivariable OR, 0.46, 95% CI; 0.28–0.78), shock (univariable OR, 0.61; 95% CI, 0.38–0.98; multivariable OR, 0.54; 95% CI, 0.32–0.91), and ICU admission (univariable OR, 0.55; 95% CI, 0.36–0.83; multivariable OR, 0.51; 95% CI, 0.32–0.81) and a trend toward a lower risk of ARDS that did not reach statistical significance (univariable OR, 0.67; 95% CI, 0.45–1.01; multivariable OR, 0.64; 95% CI, 0.41–1.01). Results were similar in models stratified by active cancer status.

Risk Factors for Mortality Among Patients with a History of Cancer

Analysis of factors associated with mortality or hospice among all cases is shown in Table 6. In unadjusted analysis, mortality or hospice was associated with older age (age ≥ 75 vs. <65; OR, 3.83; 95% CI, 1.52–9.64) and a higher Charlson score reflecting the inclusion of cancer diagnosis into this scoring system (OR, 1.18; 95% CI, 1.05–1.33). Older

Table 3. Clinical course and complications

Complication	Total ($n = 486$), *n* (%)	Current or prior cancer history ($n = 162$), *n* (%)	No history of cancer ($n = 324$), *n* (%)
Antibiotics	364 (74.9)	126 (77.8)	238 (73.5)
(Hydroxy)chloroquine	216 (44.4)	61 (37.7)	155 (47.8)
Remdesivir clinical trial	79 (16.3)	40 (24.7)	39 (12.0)
Tocilizumab	46 (9.5)	21 (13.0)	25 (7.7)
Pneumonia	427 (87.9)	134 (82.7)	293 (90.4)
CV complications	116 (23.9)	33 (20.4)	83 (25.6)
ARDS	190 (39.1)	54 (33.3)	136 (42.0)
CV shock/shock	123 (25.3)	32 (19.8)	91 (28.1)
DVT	8 (1.7)	2 (1.2)	6 (1.9)
Renal failure	59 (12.1)	11 (6.8)	48 (14.8)
Intubation	168 (36.6)	44 (27.2)	124 (38.3)
ICU admission	198 (40.7)	52 (32.1)	146 (45.1)
Median duration of hospitalization (range)[a], days	9 (0–76)	9 (1–73)	9 (0–76)
Disposition			
Discharged home	189 (39.7)	69 (42.6)	120 (37.0)
Discharged to facility	159 (33.3)	43 (26.5)	116 (35.8)
Discharged to hospice	3 (0.6)	1 (0.6)	2 (0.6)
Deceased	125 (26.3)	45 (27.8)	80 (24.7)
Still hospitalized	10 (2.1)	4 (2.5)	6 (1.9)

[a]Excludes $n = 10$ still hospitalized as of last follow-up.
Abbreviations: ARDS, acute respiratory distress syndrome; CV, cardiovascular; DVT, deep vein thrombosis; ICU, intensive care unit.

age remained significantly associated with mortality or hospice in multivariable analyses (OR, 3.05; 95% CI, 1.02–9.14). Compared with survivors, patients with active cancer were not more likely to die or be discharged to hospice (univariable OR, 1.31; 95% CI, 0.66–2.60; multivariable OR, 1.40 95% CI, 0.66–2.97). Other sociodemographic, cancer-related, and COVID treatment–related covariates were similarly not associated with an increased risk of death or hospice following hospitalization among patients with a history of cancer.

Discussion

Patients with a history of cancer who are hospitalized with COVID-19 are at high risk of death, but among a cohort of patients hospitalized at two large, urban, academic medical centers, we found that the risk of hospital death or discharge to hospice was similar for patients with and without a history of cancer. Importantly, patients with and without a cancer history both presented with similar laboratory values and vital signs, suggesting similar severity of COVID-19 at hospital admission. Additionally, among patients with a cancer history, those with current cancer, with advanced cancer, or who had recently received cancer-directed medical therapy had a similar risk of death compared with survivors of cancer. Results from earlier studies that have compared COVID-19 outcomes between patients with and without a history of cancer have suggested that cancer is a risk factor for mortality from COVID-19 [12]. A single institution study from New York City reported a case fatality rate of 28%, approximately twice the rate of controls without cancer from the same institution (14%) and more than

Table 4. Association of cancer and COVID-19 mortality or discharge to hospice in all patients, patients with active cancer, and patients with a prior cancer history

	Death/discharge to hospice[a]			
Cancer history	Unadjusted OR (95% CI)	*p* value	Adjusted[b] OR (95% CI)	*p* value
All patients with a current or prior cancer history	1.21 (0.77–1.92)	.41	1.09 (0.65–1.82)	.75
Patients with active cancer	1.98 (0.99–3.96)	.053	2.18 (0.82–5.77)	.12
Patients with a prior cancer history but currently NED	0.82 (0.44–1.52)	.53	0.75 (0.38–1.46)	.39

[a]Excludes 10 patients still hospitalized as of last follow-up.
[b]Adjusted for immunosuppressive status, cardiovascular comorbidities, pulmonary comorbidities, and diabetes.
Abbreviations: CI, confidence interval; NED, no evidence of disease; OR, odds ratio.

Table 5. Association between cancer and adverse COVID-19 clinical outcomes in all patients, patients with active cancer, and patients with a prior cancer history

Cancer history	Intubation				ICU				ARDS				Shock			
	Unadjusted OR (95% CI)	*p* value	Adjusted[a] OR (95% CI)	*p* value	Unadjusted OR (95% CI)	*p* value	Adjusted[a] OR (95% CI)	*p* value	Unadjusted OR (95% CI)	*p* value	Adjusted[a] OR (95% CI)	*p* value	Unadjusted OR (95% CI)	*p* value	Adjusted[a] OR (95% CI)	*p* value
All patients with a current or prior cancer history	0.57 (0.36–0.88)	.01	0.46 (0.28–0.78)	.004	0.55 (0.36–0.83)	.005	0.51 (0.32–0.81)	.004	0.67 (0.45–1.01)	.06	0.64 (0.41–1.01)	.06	0.61 (0.38–0.98)	.04	0.54 (0.32–0.91)	.02
Patients with active cancer	0.52 (0.27–1.00)	.05	0.27 (0.10–0.78)	.02	0.53 (0.29–0.96)	.03	0.39 (0.17–0.89)	.03	0.63 (0.34–1.16)	.14	0.54 (0.23–1.24)	.15	0.65 (0.33–1.29)	.22	0.52 (0.21–1.28)	.15
Patients with a prior cancer history but currently NED	0.61 (0.33–1.10)	.10	0.52 (0.27–1.01)	.052	0.57 (0.32–1.02)	.06	0.52 (0.28–0.96)	.04	0.71 (0.41–1.24)	.23	0.64 (0.35–1.17)	.15	0.57 (0.30–1.11)	.10	0.53 (0.27–1.06)	.07

[a]Adjusted for immunosuppressive status, cardiovascular comorbidities, pulmonary comorbidities, and diabetes.
Abbreviations: ARDS, acute respiratory distress syndrome; CI, confidence interval; ICU, intensive care unit; NED, no evidence of disease; OR, odds ratio.

fourfold higher than the New York City–wide rate (6%) [6]. Similarly, a multi-institutional Chinese study reported higher mortality (OR, 2.34; 95% CI, 1.15–4.77) among cancer cases compared with controls, although the proportion of cases who died (11.4%) was substantially lower than in our population [7]. Possible explanations for these divergent findings may include differences between study populations including selection of controls, as well as definitions and assessments of key risk factors and outcomes.

A recent meta-analysis that examined outcomes among patients with cancer found that in a subgroup analysis of studies that was restricted to patients older than 65, mortality between individuals with and without cancer was in fact similar [12], supporting the findings of our study, where nearly two thirds of patients were ≥ 65 years of age. Additionally, a recent matched cohort study comparing outcomes between admitted patients with cancer and matched controls showed no statistically significant difference in mortality, suggesting that a history of cancer and cancer-directed therapies alone may not confer a higher risk of the most severe COVID-19 outcomes in hospitalized patients [13].

In our study population, patients with metastatic or hematologic malignancy or who had undergone treatment within the last 6 months were not at increased risk for poor outcomes compared with survivors of cancer. These results are largely consistent with a prospective study based in the U.K. that included 800 patients with cancer with COVID-19 where the majority (88%) of patients were hospitalized. Overall, 28% of patients died; however, recent systemic treatment and having metastatic disease were not associated with an increased risk of death [14]. In contrast, only half of patients with cancer enrolled in the international COVID and Cancer Consortium (CCC) registry were hospitalized, suggesting that the substantially lower 30-day mortality observed—13%—among this cohort of more than 900 patients with cancer is attributable to the heterogeneity in COVID-19 severity [8]. In the CCC, those with stable or progressive disease (vs. remission or no evidence of disease) had higher odds of death, and chemotherapy within the last month was not associated with increased mortality [8]. Other studies have documented an increased risk of mortality associated with receipt of chemotherapy, including a study from China inclusive of 205 patients diagnosed with cancer, the majority of whom (80%) were ≥ 1 year from diagnosis [5].

Cancer and its associated treatment modalities would seem likely to contribute to SARS-CoV-2 infection and poor outcomes. Patients are in frequent contact with the health care system, have a serious comorbidity, and are often receiving immunosuppressive treatments. This has prompted more conservative cancer treatment from many oncologists, and in some cases, discussions of deprioritizing patients with cancer for receipt of scarce resources during COVID-19 surge periods [15–17]. Given our finding that systemic cancer treatment may not adversely impact outcomes, withholding systemic cancer therapy and refusing scarce resources to patients with cancer may not be warranted. Furthermore, survivors of cancer can be reassured that their risks do not appear to be

Table 6. Univariable and multivariable factors associated with mortality/discharge to hospice in patients with cancer ($n = 158$)

Factor	Discharged home or to facility ($n = 112$)	Deceased/Discharged to hospice ($n = 46$)	Unadjusted OR (95% CI)	*p* value	Adjusted[a] OR (95% CI)	*p* value
Age, yrs						
<65	44 (39.3)	8 (17.4)	Reference		Reference	
65–74	35 (31.3)	15 (32.6)	2.36 (0.90–6.19)	.08	2.10 (0.75–5.91)	.16
≥75	33 (29.5)	23 (50.0)	3.83 (1.52–9.64)	.004	3.05 (1.02–9.14)	.05
BMI						
<18.5	4 (3.6)	1 (2.2)	0.43 (0.04–4.14)	.46		
18.5–24.9	29 (25.9)	17 (37.0)	Reference			
25–29.9	36 (32.1)	12 (26.1)	0.57 (0.23–1.38)	.21		
≥30	43 (38.4)	16 (34.8)	0.64 (0.28–1.46)	.28		
Race						
Asian	3 (2.7)	1 (2.2)	0.86 (0.09–8.59)	.90	0.40 (0.04–4.62)	.46
Black	18 (16.1)	9 (19.6)	1.29 (0.52–3.20)	.59	1.50 (0.57–3.94)	.42
White	72 (64.3)	28 (60.9)	Reference			
More than one race/ other/unknown	19 (17.0)	8 (17.4)	1.08 (0.43–2.76)	.87	1.26 (0.47–3.36)	.65
Gender						
Male	60 (53.6)	30 (65.2)	Reference		Reference	
Female	52 (46.4)	16 (34.8)	0.62 (0.30–1.25)	.18	0.67 (0.32–1.41)	.29
Cancer type						
Hematologic malignancy	20 (17.9)	11 (23.9)	Reference			
Solid tumor	92 (82.1)	35 (76.1)	0.69 (0.30–1.59)	.39		
Median months since diagnosis (range)[b]	32.0 (0.39–435.4)	56.3 (0.79–382.4)	1.00 (1.00–1.01)	.30		
Status of cancer at COVID-19 diagnosis						
Active disease/treatment	51 (45.5)	24 (52.2)	1.31 (0.66–2.60)	.45	1.40 (0.66–2.97)	.38
Survivor (No evidence of disease)	61 (54.5)	22 (47.8)	Reference		Reference	
Median Charlson score (range)	7 (2–19)	8 (4–14)	1.18 (1.05–1.33)	.006	1.10 (0.95–1.28)	.21
Immunosuppression						
Yes	35 (31.3)	14 (30.4)	0.96 (0.46–2.03)	.92		
No	77 (68.8)	32 (69.6)	Reference			
Presenting with respiratory complaint						
Yes	88 (78.6)	34 (73.9)	0.77 (0.35–1.72)	.53		
No	24 (21.4)	12 (26.1)	Reference			
Receipt of (hydroxy) chloroquine						
Yes	40 (35.7)	19 (41.3)	1.27 (0.63–2.56)	.51		
No	72 (64.3)	27 (58.7)	Reference			

Total ($n = 158$) excludes $n = 4$ still hospitalized.
Data are presented as *n* (%) unless otherwise noted.
[a]Multivariable model adjusted for age, race, gender, status of cancer diagnosis, and other variables with a *p* value <.20 in univariable modeling.
[b]Excludes $n = 3$ ($n = 1$ still deceased/discharged to hospice, $n = 2$ discharged home or to facility).
Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.

substantially higher by virtue of their cancer history. Interventions such as ICU admission and intubation were less common in patients with cancer, which might be due to either less severe disease or less aggressive care. Severe complications of COVID-19 (ARDS, shock, and renal failure) were also less common in patients with cancer than without cancer. Although the cause of this is unclear, it is possible that the immunosuppressive impact of cancer and its

associated treatments may protect against the more severe immune-mediated complications of COVID-19 [18]. Indeed, steroids can improve outcomes of patients with severe COVID-19 [19, 20]. We found that patients with cancer were more likely to be enrolled on a remdesivir clinical trial, perhaps improving upon their true outcomes. However, remdesivir is only known to shorten the duration of illness, without a statistically significant impact on mortality, which was the primary outcome in our study [21].

Strengths of our study include the systematic identification of cases, with controls matched on known risk factors for poor outcomes, as well as minimal missing data for both risk factors and key outcomes. Importantly, our patient population was treated at two major teaching hospitals where ventilators and medications to treat COVID-19 were consistently available, even during the surge in COVID-19 cases in this region.

The findings from our study should be interpreted in the context of several limitations. First, our study may not be sufficiently powered to detect small differences between patients with and without cancer. In particular, the number of patients with active disease or who were currently undergoing cancer treatment was relatively small and subgroup analyses may have been underpowered to identify significant associations among these patients. Cancer, its associated treatments, and the patients impacted are highly heterogenous; there are likely malignancies, anticancer therapies, and patient populations not represented in our study that might confer a greater risk of severe COVID-19. For example, recent studies have shown that specific high-intensity cytotoxic regimens, such as platinum with etoposide, are associated with worse COVID-19 outcomes [22]. All patients were treated at large, urban, academic hospitals and our results may not be generalizable to patients treated in other settings. There is also the potential for misclassification of our primary outcome because we did not conduct additional follow-up following hospital discharge. Thus, it is possible patients discharged home or to another facility may have subsequently died and this would not have been captured. In addition, we cannot exclude the potential for unmeasured confounding by factors that may impact COVID-19 complications and outcomes that we were unable to robustly capture with chart abstraction, such as smoking. Nonetheless, we were able to capture several well-characterized risk factors, including age, race, BMI, and comorbidities, and account for these characteristics in our analyses. It is possible that patients without cancer presented to the hospital with more severe COVID-19 than patients with cancer; however, similar presenting laboratory values and vitals between the two groups argue they had similar severity of disease at presentation. Finally, because COVID-19 testing is not universal, and many patients are treated in the outpatient setting, hospitalized patients represent only a subgroup of those with COVID-19.

Conclusion

COVID-19 is an unprecedented challenge to the medical community, straining health care resources and requiring diagnosis, triage, and treatment of those with a novel, poorly characterized disease. A deeper knowledge of the comorbidities and patient characteristics that portend a severe outcome from COVID-19 can improve patient care and guide the use of scarce resources in future waves of infection. Our study contributes to the evolving knowledge base of how COVID-19 impacts patients with cancer and survivors of cancer, further informing clinical care and enhancing our understanding of outcomes in this population. We find that active cancer, systemic cancer therapy, and a history of cancer are not independent risk factors for death from COVID-19 among the hospitalized patients studied here, and hospitalized patients without cancer are more likely to have severe COVID-19 marked by intubation, ICU admission, ARDS, and shock.

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Disclosures

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References

1. Berlin DA, Gulick RM, Martinez FJ. Severe COVID-19. N Engl J Med 2020;383:2451–2460.

2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72,314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020; 323:1239–1242.

3. Goyal P, Choi JJ, Pinheiro LC et al. Clinical characteristics of COVID-19 in New York City. N Engl J Med 2020;382:2372–2374.

4. Guan W, Ni Z, Hu Y et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708–1720.

5. 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.

6. Mehta V, Goel S, Kabarriti R et al. Case fatality rate of cancer patients with COVID-19 in a New York hospital system. Cancer Discov 2020; 10:935–941.

7. Dai M, Liu D, Liu M et al. Patients with cancer appear more vulnerable to SARS-CoV-2: A multicenter study during the COVID-19 outbreak. Cancer Discov 2020;10:783–791.

8. 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.

9. Liang W, Guan W, Chen R et al. Cancer patients in SARS-CoV-2 infection: A nationwide analysis in China. Lancet Oncol 2020;21:335–337.

10. Desai A, Sachdeva S, Parekh T et al. COVID-19 and cancer: Lessons from a pooled meta-analysis. JCO Glob Oncol 2020;6:557–559.

11. Charlson ME, Pompei P, Ales KL et al. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis 1987;40:373–383.

12. Giannakoulis VG, Papoutsi E, Siempos II. Effect of cancer on clinical outcomes of patients with COVID-19: A meta-analysis of patient data. JCO Glob Oncol 2020;6:799–808.

13. Brar G, Pinheiro LC, Shusterman M et al. COVID-19 severity and outcomes in patients with cancer: A matched cohort study. J Clin Oncol 2020;38:3914–3924.

14. Lee LYW, Cazier JB, Starkey 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.

15. European Society for Medical Oncology (ESMO). Cancer patient management during the COVID-19 pandemic. Available at https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic. Accessed June 28, 2020.

16. El-Shakankery KH, Kefas J, Crusz SM. Caring for our cancer patients in the wake of COVID-19. Br J Cancer 2020;123:3–4.

17. Schrag D, Hershman DL, Basch E. Oncology practice during the COVID-19 pandemic. JAMA 2020;323:2005–2006.

18. Zhong J, Tang J, Ye C et al. The immunology of COVID-19: Is immune modulation an option for treatment? Lancet Rheumatol 2020;2:e428–e436.

19. Horby P, Lim WS, Emberson J et al. Effect of dexamethasone in hospitalized patients with COVID-19: Preliminary report. N Engl J Med. doi: 10.1101/2020.06.22.20137273

20. RECOVERY Collaborative Group, Horby P, Lim WS et al. Dexamethasone in hospitalized patients with COVID-19. N Engl J Med 2021;384: 693–704.

21. Rivera DR, Peters S, Panagiotou OA et al. Utilization of COVID-19 treatments and clinical outcomes among patients with cancer: A COVID-19 and Cancer Consortium (CCC19) cohort study. Cancer Discov 2020;10:1514–1527.

22. Grivas P, Khaki AR, Wise-Draper TM et al. Association of clinical factors and recent anticancer therapy with COVID-19 severity among patients with cancer: A report from the COVID-19 and Cancer Consortium. Ann Oncol 2021 [Epub ahead of print].

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