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Evaluation of COVID-19 Mortality and Adverse Outcomes in US Patients With or Without Cancer

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IMPORTANCE As the COVID-19 pandemic continues, understanding the clinical outcomes of patients with cancer and COVID-19 has become critically important.

OBJECTIVE To compare the outcomes of patients with or without cancer who were diagnosed with COVID-19 and to identify the factors associated with mortality, mechanical ventilation, intensive care unit (ICU) stay, and hospitalization.

DESIGN, SETTING, AND PARTICIPANTS This cohort study obtained data from the Optum de-identified COVID-19 electronic health record data set. More than 500 000 US adults who were diagnosed with COVID-19 from January 1 to December 31, 2020, were analyzed.

EXPOSURES The patient groups were (1) patients without cancer, (2) patients with no recent cancer treatment, and (3) patients with recent cancer treatment (within 3 months before COVID-19 diagnosis) consisting of radiation therapy or systemic therapy.

MAIN OUTCOMES AND MEASURES Mortality, mechanical ventilation, ICU stay, and hospitalization within 30 days of COVID-19 diagnosis were the main outcomes. Unadjusted rates and adjusted odds ratios (ORs) of adverse outcomes were presented according to exposure group.

RESULTS A total of 507 307 patients with COVID-19 were identified (mean [SD] age, 48.4 [18.4] years; 281 165 women [55.4%]), of whom 493 020 (97.2%) did not have cancer. Among the 14 287 (2.8%) patients with cancer, 9991 (69.9%) did not receive recent treatment and 4296 (30.1%) received recent treatment. In unadjusted analyses, patients with cancer, regardless of recent treatment received, were more likely to have adverse outcomes compared with patients without cancer (eg, mortality rate: 1.6% for patients without cancer, 5.0% for patients with no recent cancer treatment, and 7.8% for patients with recent cancer treatment). After adjustment, patients with no recent cancer treatment had similar or better outcomes than patients without cancer (eg, mortality OR, 0.93 [95% CI, 0.84-1.02]; mechanical ventilation OR, 0.61 [95% CI, 0.54-0.68]). In contrast, a higher risk of death (OR, 1.74; 95% CI, 1.54-1.96), ICU stay (OR, 1.69; 95% CI, 1.54-1.87), and hospitalization (OR, 1.19; 95% CI, 1.11-1.27) was observed in patients with recent cancer treatment. Compared with patients with nonmetastatic solid tumors, those with metastatic solid tumors and hematologic malignant neoplasms had worse outcomes (eg, mortality OR, 2.36 [95% CI, 1.96-2.84]; mechanical ventilation OR, 0.87 [95% CI, 0.70-1.08]). Recent chemotherapy and chemoimmunotherapy were also associated with worse outcomes (eg, chemotherapy mortality OR, 1.84 [95% CI, 1.51-2.26]).

CONCLUSIONS AND RELEVANCE This cohort study found that patients with recent cancer treatment and COVID-19 had a significantly higher risk of adverse outcomes, and patients with no recent cancer treatment had similar outcomes to those without cancer. The findings have risk stratification and resource use implications for patients, clinicians, and health systems.

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The COVID-19 pandemic has profoundly affected health care systems across the world. As of July 2021, more than 194 million infection cases and more than 4.1 million deaths associated with COVID-19 have been reported globally.[1] Comorbid conditions have been described as a main factor in COVID-19 outcomes.[2-6] Patients with cancer have been found to have an increased risk of SARS-CoV-2 infection and to have a more severe disease course.[7-9] Patients with cancer are often older and have more comorbidities than the general population. In addition, the immune system of patients with cancer is frequently compromised as a consequence of anticancer treatments, the disease itself, or both. Although evidence suggests that patients with cancer and COVID-19 are more likely to have adverse outcomes, most of the available information originates from relatively small studies, many of which report conflicting results, particularly regarding the association of cancer type and recent cancer treatment with outcomes.[9-16]

Cancer is a major public health problem worldwide. In the US alone, the number of cancer survivors was estimated to be 16 million as of January 2019.[17] As the COVID-19 pandemic continues, understanding the clinical outcomes of patients with cancer and COVID-19 become critically important. In this cohort study, we analyzed real-world electronic health record (EHR) data of more than 500 000 adults to compare the outcomes of patients with or without cancer who were diagnosed with COVID-19 and to identify the factors associated with mortality, mechanical ventilation, intensive care unit (ICU) stay, and hospitalization.

Key Points

Question What are the rates of death, mechanical ventilation, intensive care unit stay, and hospitalization among patients with COVID-19 with or without cancer?

Findings In this cohort study of 507 307 patients with COVID-19, those with cancer who received anticancer treatment within 3 months before COVID-19 diagnosis had an increased risk of death, intensive care unit admission, and hospitalization. Patients without recent cancer treatment had similar or better outcomes than patients without cancer.

Meaning The results of this study have risk stratification and resource use implications for patients, clinicians, and health care systems.

Methods

Data Source and Study Cohort

We conducted this cohort study using the Optum deidentified COVID-19 EHR data set to conduct this study. The data were obtained from Optum's longitudinal EHR repository, which includes data from more than 700 hospitals and 7000 clinics across the US and captures point-of-care diagnostic data that are specific to COVID-19, such as patient-level and clinical results from both inpatient and ambulatory settings. Race and ethnicity data were self-reported in the Optum EHR. This study was granted approval by the MD Anderson Cancer Center Institutional Review Board, which considered the study exempt from obtaining patient informed consent on the basis of its code of regulations. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Patients with COVID-19 were identified using *International Classification of Diseases, Ninth Revision* (*ICD-9*) and *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*) diagnosis codes; Healthcare Common Procedure Coding System codes; Logical Observation Identifiers Names and Codes; and laboratory test names[4] (eTable 1 in the Supplement). A COVID-19 diagnosis via polymerase chain reaction, antigen test, or serologic confirmation was required for inclusion in the study. We used the earliest specimen collection, test, or result date as the COVID-19 diagnosis date. The COVID-19 diagnosis dates ranged from January 1 to December 31, 2020, and the last follow-up date was January 28, 2021.

Patients with COVID-19 who had known age (≥18 years) and sex were included. We identified patients with cancer by using *ICD-9* and *ICD-10* codes. Patients without cancer were defined as individuals with no or at most 1 cancer diagnosis code any time before COVID-19 who did not receive any anticancer treatments within 1 year of COVID-19 diagnosis. Patients with cancer were defined as individuals with 4 or more cancer diagnosis codes of the same type; at least 2 of these codes had to be 30 days apart and within 1 year before COVID-19 diagnosis. We performed sensitivity analyses that used a more traditional definition with only 2 or more codes. Patients with cancer were further categorized according to recent (within 3 months before COVID-19 diagnosis) treatment (radiotherapy or systemic therapy) or no recent treatment (eFigure 1 in the Supplement).

Outcomes and Covariates

Mortality, mechanical ventilation, ICU stay, and hospital admission within 30 days of COVID-19 diagnosis were the outcomes of interest. Death data were obtained from the Social Security Administration Death Master File, including month and year of death; therefore, date of death was set as the 15th of the month. To better capture mortality, we performed sensitivity analyses that extended follow-up to the next month among patients who were diagnosed with COVID-19 after the 15th of the month. Mechanical ventilation was identified using Healthcare Common Procedure Coding System codes or *ICD-10* procedure codes.[18] Intensive care unit stay[19] was defined as hospitalization in an ICU that did not include mechanical ventilation (eTable 1 in the Supplement).

Demographic variables were extracted. Comorbidities,[20] including severe obesity (body mass index [calculated as weight in kilograms divided by height in meters squared] ≥40), and Charlson-Deyo[21] comorbidity index score (range: 0 to ≥2, with the highest score indicating a higher number of comorbidities) excluding cancer, were recorded.

Among patients with cancer, treatment was identified using *ICD-9* or *ICD-10* diagnosis and procedure codes as well as Healthcare Common Procedure Coding System codes[22]

(eTable 1 in the Supplement). Patients with cancer were categorized according to type of malignant neoplasm and extent of disease (nonmetastatic solid tumors, metastatic solid tumors, and hematologic malignant neoplasms) and according to recent administration of radiotherapy or systemic treatment (none or chemotherapy, immunotherapy, chemoimmunotherapy, targeted therapy, endocrine therapy, antilymphocyte therapy, or stem cell transplant).

Statistical Analysis

Variables were compared according to assigned exposure groups using χ^2 test or unpaired, 2-tailed *t* test. Outcomes were compared using χ^2 test, and unadjusted rates and 95% CIs were plotted. Temporal trends according to 2020 calendar quarters (January to March, April to June, July to September, and October to December) were assessed.

Logistic regression models were used to evaluate the association between patient group and outcome category using a forward step-by-step approach, with patients without cancer as the reference group. Variables in the final model included age, comorbidity, sex, race and ethnicity (which were self-reported in the Optum EHR), severe obesity, skilled nursing facility stay within 3 months before COVID-19 diagnosis, 2020 calendar quarters, insurance type, and region. Results were presented as odds ratios (ORs) with 95% CIs. All included patients had known age and sex. Patients who were missing data in other covariates were grouped into other or unknown categories (ie, other race included Asian, other regions were not specified in the data set, and other insurance included people without insurance). No imputation methods were used. Subgroup analyses of the outcomes among hospitalized patients were performed.

Logistic regression models were used to examine the association between cancer type (nonmetastatic solid tumors, metastatic solid tumors, and hematologic malignant neoplasms) and outcomes. Patients with nonmetastatic solid tumors were the reference group. In addition to the variables in the main model, history of multiple cancers and recent radiotherapy or systemic treatment were included in the model. The association between different individual tumor types and outcomes among patients with solid tumors and hematologic malignant neoplasms was evaluated separately.

Analyses were conducted using SAS, version 9.4 (SAS Institute), and R, version 4.0.5 (R Foundation for Statistical Computing). All tests were 2 sided, with a statistical significance level of $P = .05$.

Results

We identified 507 307 patients with COVID-19, including 493 020 patients (97.2%) without cancer and 14 287 patients (2.8%) with cancer, of whom 9991 (69.9%) did not receive recent treatment and 4296 (30.1%) received recent treatment. The full cohort had a mean (SD) age of 48.4 (18.4) years and comprised 281 165 women (55.4%) and 226 142 men (44.6%). Patient characteristics are shown in **Table 1**. Among patients with recent cancer treatment, the distribution according to therapy received is shown in eTable 3 in the Supplement. Patients with cancer vs those without cancer were significantly older (median [IQR] age, 67 [58-76] years vs 48 [32-61] years; $P < .001$) and had a higher Charlson-Deyo Comorbidity Index score (≥2: 7389 [51.7%] vs 71 950 [14.6%]; $P < .001$).

Patients with cancer, and particularly those who received recent treatment, were significantly more likely to have adverse outcomes in all unadjusted analyses (eFigure 2 in the Supplement). For example, the mortality rate was 1.6% for patients without cancer, 5.0% for patients with no recent cancer treatment, and 7.8% for patients with recent cancer treatment. For these 3 groups, the rates of mechanical ventilation were 2.2%, 3.7%, and 6.8%; ICU stay were 3.3%, 7.7%, and 12.3%; and hospitalization were 14.6%, 25.2%, and 33.7%; the rates were highest among patients with recent cancer treatment. A decrease in the 2020 quarterly rates of all outcomes was observed (eFigure 3 in the Supplement). For example, among patients with recent treatment, the mortality rate was 11.5% during the first quarter of 2020 and 8.4% during the last quarter. The decrease in the rates of mechanical ventilation (17.1% to 5.7%), ICU stay (14.4% to 12.8%), and hospitalization (58.4% to 23.9%) was evident. Adverse outcomes by cancer type are shown in eFigure 4 in the Supplement.

Independent factors associated with adverse outcomes included older age, male sex, Hispanic ethnicity or Black race, severe obesity, and higher comorbidity index score. The multivariable models in the entire cohort (n = 507 307) are shown in **Table 2**. Compared with patients without cancer, patients with recent cancer treatment had a significant increase in the risk of death (OR, 1.74; 95% CI, 1.54-1.96), ICU stay (OR, 1.69; 95% CI, 1.54-1.87), and hospitalization (OR, 1.19; 95% CI, 1.11-1.27) (Table 2). In contrast, patients with no recent cancer treatment had a lower risk of mechanical ventilation (OR, 0.61; 95% CI, 0.54-0.68) and hospitalization (OR, 0.79; 95% CI, 0.75-0.83), and they had no significant differences in mortality (OR, 0.93; 95% CI, 0.84-1.02) or ICU stay (OR, 0.98; 95% CI, 0.91-1.06). Subgroup analyses among hospitalized 75 792 patients revealed similar results (eTable 2 in the Supplement). For example, patients with recent cancer treatment had a significant increase in the risk of death (OR, 1.34; 95% CI, 1.14-1.57) and ICU stay (OR, 1.21; 95% CI, 1.07-1.38).

Among 14 287 patients with cancer, those with metastatic solid tumors and hematologic malignant neoplasms vs those with nonmetastatic solid tumors had worse outcomes (**Table 3**). Patients with metastatic solid tumors had higher mortality (OR, 2.36; 95% CI, 1.96-2.84) and hospitalization (OR, 1.37; 95% CI, 1.24-1.52) compared with patients with nonmetastatic solid tumors. The same pattern was observed for patients with hematologic malignant neoplasms (mortality OR, 1.72 [95% CI, 1.42-2.08]; mechanical ventilation OR, 1.42 [95% CI, 1.17-1.73]; ICU stay OR, 1.29 [95% CI, 1.11-1.49]; and hospitalization OR, 1.44 [95% CI, 1.30-1.59]). Recent radiotherapy or systemic therapy was associated with an increased risk of adverse outcomes. Specifically, the recent administration of chemotherapy or chemoimmunotherapy increased the risk of all adverse outcomes. Compared with patients with no recent systemic therapy, patients with recent chemoimmunotherapy (OR, 2.31; 95% CI, 1.45-3.66) and chemotherapy (OR,

Table 1. Characteristics of Patients Diagnosed With COVID-19 in the Optum Data Set

Variable	No. (%)			*P* value
		Patient with cancer		
	Patient without cancer	With no recent treatment	With recent treatment	
No. of patients (N = 507 307)	493 020	9991	4296	
Diagnosis period in 2020, calendar quarters				
January-March	27 391 (5.6)	627 (6.3)	445 (10.4)	<.001
April-June	139 390 (28.3)	3468 (34.7)	1723 (40.1)	
July-September	124 409 (25.2)	2297 (23.0)	838 (19.5)	
October-December	201 830 (40.9)	3599 (36.0)	1290 (30.0)	
Age, y				
Median (IQR)	48 (32-61)	68 (59-77)	66 (57-75)	<.001
18-39	181 888 (36.9)	482 (4.8)	208 (4.8)	
40-49	81 532 (16.5)	645 (6.5)	371 (8.6)	
50-54	45 147 (9.2)	609 (6.1)	331 (7.7)	
55-59	45 555 (9.2)	960 (9.6)	406 (9.5)	
60-64	41 818 (8.5)	1343 (13.4)	553 (12.9)	
65-69	31 454 (6.4)	1435 (14.4)	702 (16.3)	
70-74	23 582 (4.8)	1407 (14.1)	636 (14.8)	
75-79	16 174 (3.3)	1303 (13.0)	459 (10.7)	
80-84	11 398 (2.3)	965 (9.7)	347 (8.1)	
≥85	14 472 (2.9)	842 (8.4)	283 (6.6)	
Sex				
Female	273 727 (55.5)	5041 (50.5)	2397 (55.8)	<.001
Male	219 293 (44.5)	4950 (49.5)	1899 (44.2)	
Race and ethnicity[a]				
Hispanic	58 013 (11.8)	625 (6.3)	321 (7.5)	<.001
Non-Hispanic				
Black	74 440 (15.1)	1696 (17.0)	726 (16.9)	
White	295 733 (60.0)	7145 (71.5)	2961 (68.9)	
Other or unknown	64 834 (13.2)	525 (5.3)	288 (6.7)	
Severe obesity: BMI ≥40				
No	442 905 (89.8)	8901 (89.1)	3839 (89.4)	.03
Yes	50 115 (10.2)	1090 (10.9)	457 (10.6)	
Charlson-Deyo Comorbidity Index score[b]				
0	342 637 (69.5)	2890 (28.9)	1060 (24.7)	<.001
1	78 433 (15.9)	2131 (21.3)	817 (19.0)	
≥2	71 950 (14.6)	4970 (49.7)	2419 (56.3)	
SNF stay				
No	489 736 (99.3)	9713 (97.2)	4103 (95.5)	<.001
Yes	3284 (0.7)	278 (2.8)	193 (4.5)	
Insurance type				
Commercial	274 397 (55.7)	4731 (47.4)	2115 (49.2)	<.001
Medicare	55 672 (11.3)	3374 (33.8)	1409 (32.8)	
Medicaid	35 733 (7.2)	417 (4.2)	289 (6.7)	
Uninsured or unknown	127 218 (25.8)	1469 (14.7)	483 (11.2)	
Region				
Midwest	264 363 (53.6)	5801 (58.1)	2349 (54.7)	<.001
Northeast	104 328 (21.2)	2478 (24.8)	1327 (30.9)	
South	80 146 (16.3)	1221 (12.2)	315 (7.3)	
West	22 697 (4.6)	290 (2.9)	200 (4.7)	
Other or unknown[c]	21 486 (4.4)	201 (2.0)	105 (2.4)	

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); SNF, skilled nursing facility.

[a] Race and ethnicity were self-reported in the Optum EHR, and other category included Asian, other, or unknown. Further detail on other category was unavailable.

[b] Score range: 0 to ≥2, with the highest score indicating a higher number of comorbidities.

[c] Other category was not defined in the Optum EHR.

Table 2. Logistic Regression Models of Adverse Outcomes Among Patients Diagnosed With COVID-19[a]

	30-d Mortality		30-d Mechanical ventilation		30-d ICU stay		30-d Hospitalization	
Variable	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Patient group								
Without cancer	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
With no recent treatment	0.93 (0.84-1.02)	.12	0.61 (0.54-0.68)	<.001	0.98 (0.91-1.06)	.61	0.79 (0.75-0.83)	<.001
With recent treatment	1.74 (1.54-1.96)	<.001	1.00 (0.88-1.13)	.94	1.69 (1.54-1.87)	<.001	1.19 (1.11-1.27)	<.001
Age, y								
18-39	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
40-49	2.83 (2.37-3.39)	<.001	2.22 (2.02-2.45)	<.001	1.71 (1.60-1.82)	<.001	1.11 (1.07-1.14)	<.001
50-54	4.59 (3.83-5.49)	<.001	3.19 (2.89-3.53)	<.001	2.1 (1.95-2.25)	<.001	1.39 (1.34-1.44)	<.001
55-59	6.10 (5.15-7.23)	<.001	4.20 (3.82-4.61)	<.001	2.62 (2.45-2.81)	<.001	1.71 (1.66-1.77)	<.001
60-64	9.86 (8.40-11.57)	<.001	5.30 (4.84-5.81)	<.001	2.89 (2.70-3.08)	<.001	2.03 (1.97-2.10)	<.001
65-69	15.90 (13.58-18.61)	<.001	6.80 (6.19-7.46)	<.001	3.48 (3.25-3.73)	<.001	2.67 (2.58-2.76)	<.001
70-74	22.52 (19.23-26.37)	<.001	7.44 (6.75-8.20)	<.001	4.15 (3.86-4.47)	<.001	3.28 (3.16-3.41)	<.001
75-79	33.88 (28.92-39.69)	<.001	8.31 (7.50-9.21)	<.001	4.65 (4.30-5.02)	<.001	4.11 (3.94-4.28)	<.001
80-84	52.07 (44.43-61.02)	<.001	7.09 (6.34-7.94)	<.001	5.31 (4.89-5.76)	<.001	5.10 (4.87-5.34)	<.001
≥85	94.65 (81.10-110.48)	<.001	4.84 (4.31-5.44)	<.001	6.69 (6.19-7.22)	<.001	6.50 (6.22-6.78)	<.001
Sex								
Female	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Male	1.70 (1.62-1.78)	<.001	1.98 (1.90-2.06)	<.001	1.51 (1.46-1.56)	<.001	1.25 (1.23-1.28)	<.001
Race and ethnicity[b]								
Hispanic	1.20 (1.10-1.31)	<.001	1.78 (1.67-1.9)	<.001	1.56 (1.48-1.64)	<.001	1.92 (1.87-1.97)	<.001
Non-Hispanic								
Black	0.98 (0.92-1.05)	.56	1.33 (1.27-1.4)	<.001	1.39 (1.33-1.45)	<.001	1.66 (1.62-1.70)	<.001
White	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Other	1.36 (1.27-1.47)	<.001	1.81 (1.70-1.92)	<.001	1.12 (1.06-1.18)	<.001	1.29 (1.26-1.33)	<.001
Severe obesity: BMI ≥40								
No	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Yes	1.61 (1.50-1.73)	<.001	1.82 (1.72-1.92)	<.001	1.41 (1.35-1.48)	<.001	1.64 (1.60-1.68)	<.001
Charlson-Deyo Comorbidity Index score[c]								
0	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
1	1.91 (1.78-2.05)	<.001	2.30 (2.17-2.44)	<.001	2.39 (2.28-2.49)	<.001	1.97 (1.92-2.01)	<.001
≥2	3.49 (3.29-3.70)	<.001	4.83 (4.59-5.09)	<.001	3.86 (3.70-4.02)	<.001	3.22 (3.15-3.29)	<.001
Region								
Midwest	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Northeast	1.21 (1.14-1.28)	<.001	0.98 (0.93-1.02)	.32	0.56 (0.54-0.59)	<.001	1.48 (1.44-1.51)	<.001
South	1.86 (1.75-1.96)	<.001	1.03 (0.97-1.09)	.39	0.85 (0.81-0.89)	<.001	1.55 (1.51-1.59)	<.001
West	1.50 (1.34-1.67)	<.001	1.26 (1.15-1.38)	<.001	2.77 (2.62-2.93)	<.001	1.38 (1.33-1.44)	<.001
Other[d]	1.25 (1.10-1.42)	<.001	1.01 (0.91-1.12)	.92	1.03 (0.95-1.12)	.46	1.10 (1.05-1.15)	<.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ICU, intensive care unit; OR, odds ratio.

[a] Variables in the model also included COVID-19 2020 diagnosis period, skilled nursing facility stay within 3 months before COVID-19 diagnosis, and insurance type.

[b] Race and ethnicity were self-reported in the Optum EHR, and other category included Asian, other, or unknown. Further detail on other category was unavailable.

[c] Score range: 0 to ≥2, with the highest score indicating a higher number of comorbidities.

[d] Other category was not defined in the Optum EHR.

1.84; 95% CI, 1.51-2.26) had the highest mortality risk. No increased risk of death was observed among patients with recent immunotherapy (OR, 0.88; 95% CI, 0.63-1.25) or endocrine or targeted therapy (OR, 1.08; 95% CI, 0.81-1.45). Increase in the risk of death was observed among patients who received antilymphocyte or stem cell transplant (OR, 1.51; 95% CI, 0.97-2.35).

Outcomes among patients with different solid tumors (n = 10 966) and hematologic malignant neoplasms (n = 3291) were analyzed separately (eTables 4 and 5 in the Supplement). For solid tumors, compared with patients with breast cancer, those with digestive noncolorectal and lung cancer had higher risks of mortality. For hematologic malignant neoplasms, compared with patients with leukemia, those with

Table 3. Logistic Regression Models of Adverse Outcomes Among Patients With Cancer Diagnosed With COVID-19[a]

	30-d Mortality		30-d Mechanical ventilation		30-d ICU stay		30-d Hospitalization	
Variable	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Cancer type								
Nonmetastatic solid tumors	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Metastatic solid tumors	2.36 (1.96-2.84)	<.001	0.87 (0.70-1.08)	.20	1.16 (0.99-1.35)	.06	1.37 (1.24-1.52)	<.001
Hematologic malignant neoplasms	1.72 (1.42-2.08)	<.001	1.42 (1.17-1.73)	<.001	1.29 (1.11-1.49)	<.001	1.44 (1.30-1.59)	<.001
Age, y								
18-39	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
40-49	1.97 (0.83-4.71)	.13	0.80 (0.40-1.58)	.51	0.93 (0.59-1.46)	.75	0.90 (0.70-1.16)	.42
50-54	2.35 (1.01-5.51)	.048	0.98 (0.51-1.88)	.96	1.16 (0.75-1.79)	.51	0.78 (0.60-1.01)	.06
55-59	2.06 (0.90-4.71)	.09	1.53 (0.86-2.72)	.15	1.51 (1.01-2.26)	.04	1.04 (0.82-1.32)	.76
60-64	3.15 (1.43-6.93)	.004	1.75 (1.01-3.02)	.04	1.26 (0.85-1.86)	.25	0.99 (0.78-1.24)	.91
65-69	3.65 (1.66-8.01)	.001	1.47 (0.84-2.55)	.17	1.67 (1.14-2.46)	.008	1.32 (1.05-1.66)	.02
70-74	3.73 (1.70-8.19)	.001	1.20 (0.68-2.10)	.53	1.25 (0.84-1.85)	.27	1.20 (0.95-1.51)	.13
75-79	6.19 (2.82-13.56)	<.001	1.78 (1.02-3.11)	.04	1.72 (1.16-2.55)	.007	1.59 (1.26-2.01)	<.001
80-84	7.33 (3.33-16.11)	<.001	1.24 (0.69-2.23)	.47	1.54 (1.03-2.32)	.04	1.94 (1.52-2.48)	<.001
≥85	11.29 (5.13-24.81)	<.001	1.07 (0.59-1.95)	.82	2.58 (1.73-3.86)	<.001	2.23 (1.74-2.86)	<.001
Race and ethnicity[b]								
Hispanic	0.91 (0.63-1.30)	.59	1.26 (0.89-1.78)	.19	1.32 (1.03-1.68)	.03	1.45 (1.24-1.70)	<.001
Non-Hispanic								
White	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Black	0.97 (0.79-1.20)	.81	1.55 (1.27-1.89)	<.001	1.04 (0.88-1.22)	.66	1.41 (1.27-1.57)	<.001
Other	1.30 (0.93-1.82)	.12	1.32 (0.93-1.87)	.12	1.30 (1.00-1.68)	.05	1.07 (0.90-1.28)	.44
Sex								
Female	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Male	1.37 (1.18-1.60)	<.001	1.60 (1.35-1.89)	<.001	1.40 (1.24-1.59)	<.001	1.32 (1.21-1.43)	<.001
Severe obesity: BMI ≥40								
No	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Yes	1.27 (1.00-1.62)	.05	1.77 (1.41-2.23)	<.001	1.08 (0.89-1.31)	.44	1.24 (1.09-1.41)	.001
Charlson-Deyo Comorbidity Index Score[c]								
0	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
1	1.84 (1.32-2.57)	<.001	2.87 (1.96-4.19)	<.001	1.48 (1.18-1.85)	<.001	1.48 (1.30-1.68)	<.001
≥2	3.89 (2.93-5.16)	<.001	5.43 (3.86-7.62)	<.001	2.87 (2.38-3.47)	<.001	2.62 (2.34-2.92)	<.001
Region								
Midwest	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Northeast	1.14 (0.94-1.38)	.17	1.10 (0.90-1.34)	.37	0.65 (0.55-0.76)	<.001	1.43 (1.30-1.58)	<.001
South	2.16 (1.76-2.66)	<.001	1.46 (1.12-1.91)	.005	0.77 (0.62-0.95)	.01	1.48 (1.30-1.69)	<.001
West	0.91 (0.59-1.41)	.69	1.79 (1.23-2.60)	.002	2.39 (1.86-3.08)	<.001	1.08 (0.86-1.35)	.50
Other[d]	1.38 (0.86-2.24)	.19	1.29 (0.78-2.13)	.32	0.89 (0.59-1.34)	.58	1.04 (0.79-1.37)	.78
Radiotherapy[e]								
No	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Yes	1.72 (1.28-2.31)	<.001	1.36 (0.96-1.93)	.08	1.47 (1.15-1.89)	.002	1.59 (1.32-1.92)	<.001
Systemic treatment[e]								
None	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Chemotherapy	1.84 (1.51-2.26)	<.001	1.74 (1.39-2.17)	<.001	2.21 (1.89-2.59)	<.001	1.40 (1.24-1.58)	<.001
Immunotherapy	0.88 (0.63-1.25)	.49	1.54 (1.07-2.22)	.02	1.15 (0.87-1.51)	.32	1.02 (0.85-1.22)	.83
Chemoimmunotherapy	2.31 (1.45-3.66)	<.001	3.64 (2.24-5.93)	<.001	3.29 (2.27-4.78)	<.001	2.22 (1.62-3.03)	<.001
Endocrine therapy or targeted therapy	1.08 (0.81-1.45)	.60	1.47 (1.09-1.97)	.01	0.80 (0.61-1.04)	.10	1.06 (0.91-1.23)	.47
Antilymphocyte/anti-CD20/SCT	1.51 (0.97-2.35)	.07	1.37 (0.87-2.15)	.18	1.25 (0.86-1.81)	.25	1.52 (1.18-1.95)	.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ICU, intensive care unit; OR, odds ratio; SCT, stem cell transplant.

[a] Variables in the model also included COVID-19 2020 diagnosis period, history of multiple cancers, skilled nursing facility stay within 3 months before COVID-19 diagnosis, and insurance type.

[b] Race and ethnicity were self-reported in the Optum EHR, and other category included Asian, other, or unknown. Further detail on other category was unavailable.

[c] Score range: 0 to ≥2, with the highest score indicating a higher number of comorbidities.

[d] Other category was not defined in the Optum EHR.

[e] Received within 3 months before COVID-19 diagnosis.

lymphoma had lower risks of mortality, ICU stay, and hospitalization. Patients with myeloma had lower risks of ICU stay.

Matched analysis showed consistent results (eTable 6 in the Supplement). For example, the 30-day mortality matched by age, sex, and comorbidity was 3.6% for patients without cancer, 4.7% for patients with no recent treatment, and 8.6% for patients with recent cancer treatment. Sensitivity analyses using a less restrictive definition to identify patients with cancer and a modified mortality follow-up showed consistent results.

Discussion

In this large cohort of patients with COVID-19, we found that patients with recent cancer treatment had significantly higher rates of adverse outcomes compared with patients with COVID-19 without cancer. In the fully adjusted models, patients with recent cancer treatment had a statistically significant increase in the 30-day risk of death, ICU stay, and hospitalization. Patients with no recent cancer treatment had a similar risk of mortality and ICU stay and a lower risk of mechanical ventilation and hospitalization compared with patients without cancer. This finding suggests that patients with cancer represent a heterogenous group, and risk stratification according to recent treatment and the treatment administered has important implications for patients, clinicians, and health care systems.

To our knowledge, this study is one of the largest reports to date to evaluate the diverse outcomes among patients with cancer and COVID-19. The large sample size allowed us to evaluate the implications of specific cancer treatments and cancer type. In addition, by including patients diagnosed with COVID-19 between January and December 2020, we were uniquely positioned to evaluate the temporal trends that likely reflect the benefits associated with new therapeutics, detailed treatment guidelines, and increased expertise by clinicians.[2]

We found that patients with cancer tended to be older and have more comorbidities than the general population. Older age, male sex, comorbidities, race and ethnicity, and severe obesity were all associated with adverse outcomes in this study. This observation is consistent with reports that identified the risk factors associated with adverse outcomes among patients with COVID-19 with or without cancer, in which biological and socioeconomic disadvantages and lifestyle factors likely play a role.[4,6,12,14,15,23-27] Consistent with the large, recently published EHR-based study by Sharafeldin et al,[27] we did not observe an increased risk of death among non-Hispanic Black patients. Such an observation could be attributed to the fully adjusted models, but the results will likely differ in a more diverse patient population, in which the social determinants of health may be more pronounced.

The unadjusted rates of the outcomes of interest were much lower among patients without cancer vs patients with cancer. However, in the fully adjusted models, although the risk of death was higher for patients with recent cancer treatment, we observed similar or better outcomes in patients without cancer and patients with no recent cancer treatment. Some studies have reported comparable mortality rates between patients with cancer and those without cancer after adjusting for age and comorbidities. The LEOSS (Lean European Open Survey on SARS-CoV-2 Infected Patients) registry reported a mortality rate of 22.5% among patients with cancer and 15% for patients without cancer; however, after adjusting for potential confounders, both groups had similar mortality rates.[28] Likewise, Miyashita et al[29] reported no difference in the risk of death between patients with or without cancer and COVID-19 (relative risk, 1.15; 95% CI, 0.84-1.57).

In addition to demonstrating that anticancer treatment within 3 months before COVID-19 diagnosis served as a risk-stratification variable, we were able to quantify the increased risk of adverse outcomes associated with radiotherapy and with different systemic therapies individually. Specifically, the increased risk seemed to be associated with the recent administration of chemotherapy or chemoimmunotherapy. The increased risk of adverse outcomes was of notable magnitude in contrast with the use of immunotherapy, targeted therapy, or endocrine therapy alone, which were associated with a higher risk of mechanical ventilation but not mortality, ICU stay, or hospitalization. Although the mechanisms of this association are not completely clear, the immunosuppression that is associated with chemotherapy likely plays a crucial role. Alternatively, the outcome for patients who received endocrine therapy likely reflected a healthier patient population who were treated in the adjuvant setting with agents that did not affect the immune system. We cannot exclude that active treatment was a proxy for not only active disease but also disease severity that could not be fully accounted for in the multivariable analyses.

Data regarding the implications of cancer therapies for outcomes in patients with COVID-19 have been inconsistent. Several studies have identified an association between recent treatment and adverse outcomes,[9-11,13,16,24] whereas others have not.[12,30,31] Using data from 29 studies, Zhang et al[12] reported no association between cancer treatment and risk of death, mechanical ventilation, or ICU stay in patients with COVID-19. Similarly, the UK Coronavirus Cancer Monitoring Project (N = 800) reported no association between chemotherapy and mortality from COVID-19.[15] Early data from the COVID-19 and Cancer Consortium study (N = 928) showed no association between cancer treatment and adverse outcomes, except for an increased risk in mortality among patients with hematologic malignant neoplasms who were treated with chemotherapy.[14] However, in a follow-up analysis with more than 4000 patients, anticancer therapies, particularly chemotherapy and antilymphocyte therapy, were found to be associated with high 30-day mortality.[16] The results of the present study are consistent with those of the large National COVID Cohort Collaborative, which found that recent (within 30 days) chemotherapy was associated with an increased risk of mortality, whereas the use of immunotherapy or targeted therapy did not have such an association.[27] Although we were not able to evaluate specific laboratory results, the COVID-19 and Cancer Consortium investigators reported that low or high absolute lymphocyte count and high absolute neutrophil count were associated with adverse outcomes.[16] Lymphopenia and neutropenia have been associated with an increased risk of

adverse outcomes[31]; however, the specific association between treatment, blood counts, and outcomes is not clear.

We were uniquely positioned to evaluate the implications of cancer type in patients with COVID-19. Compared with patients with nonmetastatic solid tumors, those with metastatic solid tumors, and particularly patients with hematologic malignant neoplasms, had an increased risk of adverse outcomes. This observation is consistent with previous reports.[14,15,27] In the meta-analysis by Zhang et al,[12] the fatality rate in the general population was 22.5% compared with 34.2% among patients with hematologic malignant neoplasms and COVID-19. In a European study that assessed COVID-19 severity and morality in 697 patients with hematologic malignant neoplasms, a 33% mortality rate was observed and higher rates of severe disease and death in patients with leukemia were reported.[32] In the present study, among patients with solid tumors, those with lung, gastrointestinal (noncolorectal), and central nervous system tumors had worse outcomes. Higher mortality and increased risk of severe COVID-19 infection have been reported in patients with lung cancer. The high prevalence of current and former smokers among patients with lung cancer and less pulmonary reserve have been suggested as possible factors.[9,12-15,23] In the TERAVOLT (Thoracic Cancers International COVID-19 Collaboration), a multinational registry of patients with thoracic malignant neoplasms and COVID-19, the hospitalization rate was 76% and the mortality rate was 33%.[23]

Patients with cancer and COVID-19 have higher rates of mortality than patients without cancer,[9,11,12,14,33,34] but the mortality estimates vary widely. In 1 of the largest EHR-based US studies to date, higher rates of death among patients with COVID-19 and cancer vs those without cancer (14.9% vs 5.26%) were reported.[7] A large Belgian study reported a 30-day in-hospital mortality rate of 31.7% for patients with COVID-19 and cancer compared with 20% among patients without cancer.[8] A large pooled analysis reported a 30-day mortality rate of 30% in studies with inpatient settings and a rate of 15% in studies with both outpatient and inpatient data,[35] emphasizing the importance of the clinical setting. Mortality rates in hospitalized patients have been consistently higher given that hospitalization itself is a marker of disease severity.

Mortality estimates should be interpreted with caution. Some studies report overall mortality, whereas others (such as this analysis) report 30-day outcomes. Most studies report all-cause mortality, and few include COVID-19–specific mortality, which could be relevant to patients with cancer. Furthermore, the impact of the COVID-19 pandemic and health care system constraints have not been uniform across the world; therefore, specific consideration should be given when interpreting results from Asia, Europe, and the US.

In this study, the unadjusted rates of mechanical ventilation and ICU stay were the highest among patients with recent cancer treatment. Similar to mortality estimates, reports on ICU stay and mechanical ventilation vary widely. A small study of patients with breast cancer reported no patients requiring ICU or mechanical ventilation.[36] An early COVID-19 and Cancer Consortium report described a mechanical ventilation rate of 12% and an ICU stay rate of 14%,[14] but more recent estimates with longer follow-up and a larger number of patients had much lower rates of 5% and 6%, respectively.[16] This change highlights the dynamism of the COVID-19 pandemic, in which improved treatments and availability of resources likely play a role. A study of outcomes among hospitalized patients reported higher rates of 18.1% for mechanical ventilation and 23.4% of ICU stay.[4] One of the highest rates of ICU stay was observed in the LEOSS registry in which 23.4% of the patients required ICU stay[28]; in the TERAVOLT study, 67% of the patients met ICU admission criteria, but only 9% were admitted to an ICU and 6% were on mechanical ventilation.[23]

Limitations

This study has some limitations. Despite the natural strengths of this study owing to its large sample size and scope, the study was EHR-based; therefore, COVID-19 diagnostic tests that were not reported within this EHR system could not be identified, potentially leading to ascertainment bias. Similarly, patients with cancer, particularly those with recent cancer treatment, were more likely to undergo COVID-19 testing regardless of their symptoms. Because we did not obtain data on symptoms at presentation, we could not calculate the proportion of asymptomatic patients with COVID-19. Information regarding important risk factors such as smoking, performance status, laboratory results, COVID-19–directed treatment, or recent surgical procedures was not included. Although we evaluated various outcomes of interest, our mortality ascertainment using Social Security Administration Death Master File could be an underestimation. Furthermore, despite the large sample size and robust multivariable regression models in this study, we could not exclude residual confounding. Although a proportion of uninsured patients were included in the EHR, caution should be applied if extrapolating the findings to an uninsured patient population, whose outcomes would likely be severely affected given the implications of social determinants of health for patients with COVID-19 and patients with cancer. The findings reflect the outcomes of adult patients who were treated in the US, and the outcomes may differ in settings with fewer resources or in areas of the world with health care capacity constraints.

Conclusions

This cohort study found that patients with cancer who received anticancer treatment within 3 months before COVID-19 diagnosis had worse outcomes compared with patients with COVID-19 without cancer. After adjusting for potential confounders, we observed that patients with no recent cancer treatment had similar or better outcomes than patients without cancer. Patients with metastatic solid tumors, and particularly those with hematologic malignant neoplasms, had worse outcomes. Recent systemic therapy, particularly chemotherapy and chemoimmunotherapy, were associated with adverse outcomes. The results of this study have risk stratification and resource use implications for the unprecedented challenges currently being experienced by patients, clinicians, and health care systems.

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Acquisition, analysis, or interpretation of data: All authors.
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