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COVID-19 Outcomes Among Patients With Cancer: Observations From the University of California Cancer Consortium COVID-19 Project Outcomes Registry

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Abstract

Background: The risks associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its associated illness, coronavirus disease 2019 (COVID-19), among patients with a cancer diagnosis have not been fully characterized. This study leverages data from a multi-institutional cohort study, the University of California Cancer COVID Consortium, to evaluate outcomes associated with SARS-CoV-2 infection among patients with cancer.

Methods: Clinical data were collected from March to November 2020 and included patient demographics, cancer history and treatment, SARS-CoV-2 exposure and testing, and COVID-19 clinical management and outcomes. Multivariate ordinal logistic regression permitting unequal slopes was used to evaluate the impact of demographic, disease, and treatment factors on SARS-CoV-2 related hospitalization, intensive care unit (ICU) admission, and mortality.

Findings: Among all evaluated patients (*n* = 303), 147 (48%) were male, 118 (29%) were older adults (≥65 years old), and 104 (34%) were non-Hispanic white. A subset (*n* = 63, 21%) had hematologic malignancies and the remaining had solid tumors. Patients were hospitalized for acute care (*n* = 79, 26%), ICU-level care (*n* = 28, 9%), or died (*n* = 21, 7%) due to COVID-19. Patients with ≥2 comorbidities were more likely to require acute care (odds ratio [OR] 2.09 [95% confidence interval (CI), 1.23-3.55]). Cough was identified as a significant predictor of ICU hospitalization (OR 2.16 [95% CI, 1.03-4.57]). Importantly, mortality was associated with an active cancer diagnosis (OR 3.64 [95% CI, 1.40-9.5]) or advanced age (OR 3.86 [95% CI, 1.2-12.44]).

Interpretation: This study observed that patients with active cancer or advanced age are at an increased risk of death from COVID-19. These study observations can inform risk counseling related to COVID-19 for patients with a cancer diagnosis.

Key words: COVID-19; cancer; mortality.

Implications for Practice

This study leverages a multi-ethnic cohort to report on the clinical outcomes among patients with a confirmed positive severe acute respiratory syndrome coronavirus 2 test and an invasive cancer diagnosis. In this diverse and large clinical database, the authors observed that older adults or patients with an active cancer diagnosis requiring ongoing management are at an increased risk of death from coronavirus disease 2019 (COVID-19). These observations can inform risk counseling related to COVID-19 as well as guidance on vaccine prioritization for patients with a cancer diagnosis.

Introduction

The current global pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the associated illness coronavirus disease 2019 (COVID-19) have emerged as a leading cause of death in the US.[1] Research to date suggests that compared to the general population, patients with an active

cancer diagnosis may have higher risks of developing COVID-19 following SARS-CoV-2 infection[2] and increased morbidity and mortality associated with disease onset.[3-5] However active management of cancer can vary widely based on disease type, extent of disease, and patient comorbidities, and the relationship between an active cancer diagnosis, prior or current cancer therapy, and subsequent COVID-19 clinical outcomes remains poorly understood. COVID-19 outcomes research to date amongst patients with cancer has not fully accounted for identified non-cancer-specific risk factors including the scope of COVID-19 symptoms and comorbidity.[4,6,7] We sought to assess the impact of a cancer diagnosis as well as clinical- and disease-specific factors on COVID-19 clinical outcomes leveraging a racially/ethnically diverse, multi-institutional longitudinal cohort database. We hypothesized that among patients with cancer, unique clinical and demographic characteristics, as well as cancer treatment exposures may affect the risk of hospitalization, intensive care unit (ICU)-admission, and death following SARS-CoV-2 infection.

Methods

In this cohort study, we report data from the University of California COVID Cancer registry database. The currently participating institutions include the University of California San Francisco (UCSF) and the University of California San Diego (UCSD). At UCSF, patients with a known cancer diagnosis were identified from a master dashboard of COVID-19 tested UCSF patients which were then filtered by primary Vizient clinical program assignment based on prior ICD-10 encounter diagnoses. All COVID-19 positive patients with cancer were identified at UCSF using the UCSF COVID-19 Research Data Mart. This data source includes extracts from the UCSF electronic health record (EHR) system for patients who were tested for COVID-19 with positive or negative results. At UCSD, a patient list was generated to identify all confirmed positive serologic or molecular SARS-CoV-2 tests from the UC COVID Research Data Set (CORDS), which utilizes the UC Health Data Warehouse to identify COVID-19 tested patients. For this study, tests were identified using the Logical Observation Identifiers Names and Codes (LOINC) codes 94500-6, 94309-2, 94531-1, 94310-0, 94306-8, 94533-7, and 94534-5. Among positive cases, a manual review was then performed to identify patients with concurrent invasive cancer diagnoses. Patients were eligible for inclusion if they either had at least 2 clinical encounters in an oncology clinical unit in the 12 months prior to a diagnosis of COVID-19, or a diagnosis of cancer was made within the 90 days following a diagnosis of COVID-19. In addition to a clinical diagnosis of COVID-19, eligible patients were required to have a positive serologic or molecular SARS-CoV-2 test result. De-identified data from eligible patients from both participating centers were manually extracted from the EHR between March 1 and November 30, 2020. Data was combined utilizing an electronic REDCap database.[8,9] Longitudinal follow-up data will be abstracted for this cohort at 6, 12, and 18 months following diagnosis and reported separately, once mature.

This study was deemed exempt from review by the UCSF institutional review board (IRB) review and received local IRB approval at UCSD.

Patient identified were classified as having active cancer or inactive cancer. Active cancer was defined as requiring current treatment or having evidence of cancer that was stable or progressing on or off treatment. All patients in remission or with no evidence of recurrent cancer were defined as having inactive disease. Baseline clinical data abstracted included general medical history such as comorbidities and concurrent medications, socio-demographics, cancer history and treatment, SARS-CoV-2 exposure and testing, and COVID-19 clinical management and outcomes. This study followed patients from initial COVID-19 diagnosis to 30-, 60-, or 90-days after to ensure follow-up information availability. The endpoints evaluated were restricted to within 90-days. The majority of patients (*n* = 275) had at least 90-days of follow-up data, while a subset (*n* = 28, 9%) had not reached 90-day follow-up.

Outcomes

We evaluated demographic, disease, and treatment factors for their effects on 3 primary endpoints attributed to a COVID-19 diagnosis: hospitalization, ICU admission, and mortality.

Statistical Analysis

Descriptive statistics were used to summarize the baseline demographic and clinical characteristics. A single ordinal response with 4 levels in increasing order of severity (outpatient visits/hospitalization non-ICU/hospitalization-ICU/death) was created by combining the 3 outcomes. A multivariate ordinal logistic regression was used to evaluate the relationship between preselected predictors and the primary endpoints of this study. A review of the current literature and current practice was used to establish a covariate list of demographic, disease, and treatment characteristics, including race, age, gender, cancer type, stage, treatment history, smoking history, and body mass index (BMI). In addition to the patient-level covariates, the per-facility 7-day average count of COVID-19 positive cases was included in the model to account for facility-level characteristics related to COVID-19 burden at the time the participant tested positive for SARS-CoV-2. The ordinal logistic regression considers the odds of more severe COVID-19 outcomes over less successively, that is, the odds of hospitalization or death over the outpatient visit, the odds of hospitalization resulting in ICU admission or death over hospitalization without ICU admission or outpatient visit, and the odds of death over the rest. We tested the common effect of each factor included in the model on all 3 odds and permitted different effects or so-called unequal slopes when the common effects assumption was rejected at 0.1 significance level. With unequal slopes, the odds ratio for hospitalization, ICU admission, and mortality were separately determined. Modeling of the ordinal response combining all 3 COVID-19 outcomes is less affected by the small numbers of death or ICU admissions than separately modeling each outcome using logistic regression and, hence, is more reliable.

Results

Patient Characteristics

The study cohort included 303 patients. The clinical and demographic characteristics of patients are summarized overall and by outcome in Table 1. Overall, 147 (48%) were identified as male and 118 (29%) were 65 years or older. With regards to ethnicity and race, 104 (34%) were non-Hispanic white, 21 (7%) were NH Black, 126 (42%) were Hispanic, 27

Table 1. Patient characteristics in the University of California Cancer Consortium COVID-19 Project Outcomes Registry from March to November 2020

| | Total | | COVID-19 outcomes | | | | | | | |
| | | | Outpatient | | Hospitalization non-ICU | | Hospitalization-ICU | | Death | |
	N	Row %	N	Row %	N	Row %	N	Row %	N	Row %
Total	303	100	175	57.8	79	26.1	28	9.2	21	6.9
Facility										
UC San Diego Health	139	100	92	66.2	26	18.7	12	8.6	9	6.5
UC San Francisco Health	164	100	83	50.6	53	32.3	16	9.8	12	7.3
Gender										
Female	156	100	97	62.2	40	25.6	12	7.7	7	4.5
Male	147	100	78	53.1	39	26.5	16	10.9	14	9.5
Age										
<65	185	100	116	62.7	42	22.7	18	9.7	9	4.9
≥65-100	118	100	59	50	37	31.4	10	8.5	12	10.2
Race										
Non-Hispanic (NH) White	104	100	67	64.4	21	20.2	9	8.7	7	6.7
NH Black	21	100	13	61.9	6	28.6	2	9.5		
Hispanic	126	100	68	54	35	27.8	13	10.3	10	7.9
Asian	27	100	12	44.4	11	40.7	1	3.7	3	11.1
Other/Unknown	25	100	15	60	6	24	3	12	1	4
BMI										
0-30	197	100	114	57.9	47	23.9	21	10.7	15	7.6
≥30	106	100	61	57.5	32	30.2	7	6.6	6	5.7
Insurance										
Medicaid	75	100	40	53.3	25	33.3	5	6.7	5	6.7
Medicare	104	100	51	49	34	32.7	8	7.7	11	10.6
Commercial	95	100	65	68.4	18	18.9	10	10.5	2	2.1
Other	29	100	19	65.5	2	6.9	5	17.2	3	10.3
Cancer type										
Solid tumor	240	100	145	60.4	60	25	21	8.8	14	5.8
Malignant hematologic cancer	63	100	30	47.6	19	30.2	7	11.1	7	11.1
Smoking history										
Never smoker	210	100	129	61.4	52	24.8	18	8.6	11	5.2
Prior or current smoker	93	100	46	49.5	27	29	10	10.8	10	10.8
Active cancer status										
Yes—active/stable/progressive	154	100.0	90	58.4	40	26.0	17	11.0	7	4.5
No—remission/no evidence of disease	149	100.0	85	57.0	39	26.2	11	7.4	14	9.4
Influenza vaccine status										
Not vaccinated	94	100	54	57.4	21	22.3	14	14.9	5	5.3
Prior vaccination	143	100	85	59.4	37	25.9	9	6.3	12	8.4
Unknown	66	100	36	54.5	21	31.8	5	7.6	4	6.1
Primary language										
English	219	100	137	62.6	53	24.2	18	8.2	11	5
Spanish	71	100	34	47.9	21	29.6	8	11.3	8	11.3
Other	13	100	4	30.8	5	38.5	2	15.4	2	15.4
Marital status										
Single/legally separated/divorced/widowed	124	100	68	54.8	32	25.8	15	12.1	9	7.2
Married/in relationship/significant other	172	100	101	58.7	47	27.3	13	7.6	11	6.4
Unknown/declined	7	100	6	85.7					1	14.3
Employment status										
Unemployed	132	100	52	39.4	48	36.4	16	12.1	16	12.1
Currently employed	79	100	57	72.2	17	21.5	4	5.1	1	1.3
Unknown	92	100	66	71.7	14	15.2	8	8.7	4	4.3

Table 1. Continued

	Total		COVID-19 outcomes							
			Outpatient		Hospitalization non-ICU		Hospitalization-ICU		Death	
	N	Row %	N	Row %	N	Row %	N	Row %	N	Row %
Additional comorbidities										
Immunosuppressed	84	100	41	48.8	28	33.3	9	10.7	6	7.1
History of pulmonary disease	71	100	34	47.9	24	33.8	7	9.9	6	8.5
History of cardiovascular disease	150	100	77	51.3	46	30.7	14	9.3	13	8.7
History of renal disease	39	100	18	46.2	14	35.9	3	7.7	4	10.3
Autoimmune disease	13	100	7	53.8	2	15.4	3	23.1	1	7.7
Comorbidity										
0-1	121	100	85	70.2	18	14.9	12	9.9	6	5
≥2	182	100	90	49.5	61	33.5	16	8.8	15	8.2
Concomitant medications										
0	26	100	16	61.5	4	15.4	5	19.2	1	3.8
1 to 3	159	100	102	64.2	35	22	12	7.5	10	6.3
4 to 6	106	100	53	50	34	32.1	9	8.5	10	9.4
7+	12	100	4	33.3	6	50	2	16.7		
Concomitant medications										
Corticosteroids	53	100	25	47.2	12	22.6	9	17	7	3.2
ACE inhibitors	45	100	27	60	14	31.1	3	6.7	1	2.2
Angiotensin receptor blockers	32	100	23	71.9	9	28.1				
Anti-virals	58	100	30	51.7	15	25.9	8	13.8	5	8.6
Aspirin	54	100	35	64.8	14	25.9	1	1.9	4	7.4
Ibuprofen, naproxen, or other NSAIDs	70	100	41	58.6	22	31.4	4	5.7	3	4.3
Treatment history										
Surgical treatment	171	100	104	60.8	47	27.5	12	7	8	4.7
Radiation therapy	77	100	42	54.5	20	26	9	11.7	6	7.8
Systemic therapy	207	100	117	56.5	55	26.6	18	8.7	17	8.2
Myelosuppressive therapy	128	100	73	57	35	27.3	10	7.8	10	7.8
Hormone therapy	48	100	33	68.8	9	18.8	4	8.3	2	4.2
Targeted therapy	61	100	25	41	22	36.1	6	9.8	8	13.1

Abbreviation: ACE, angiotensin-converting enzyme; BMI, body mass index; NSAID nonsteroidal anti-inflammatory drugs.

(9%) were Asian, and 25 (8%) were other/unknown. Nearly one-quarter (*n* = 71, 23%) were primarily Spanish-speaking.

In this cohort, 104 (34%) were Medicare insured, 75 (25%) were Medicaid insured, 95 (31%) had commercial insurance, and 29 (10%) had other insurance status. Among patients for whom marital status was known, 124 (41%) were single and 172 (57%) were married or in a relationship. A total of 79 (26%) patients were documented as employed. Overall, 106 (35%) had a BMI ≥ 30. Ninety-three (31%) had a prior or current history of smoking tobacco and 143 (47%) were vaccinated for seasonal influenza.

Regarding cancer history, a total of 63 (21%) patients had hematologic malignancies. Among patients with solid tumors, the most commonly identified malignancies were prostate cancer (*n* = 33; 11%) and breast cancer (*n* = 58; 19%). The full distribution of cancer types is presented in Supplementary Table S1. There were 149 patients (49%) in remission from cancer, and 154 (51%) with active cancer, 80 (26%) of whom were on anti-cancer treatment with response or stable disease, and 54 (18%) of whom had disease progression in the setting

of active therapy. A total of 84 patients (28%) were on systemic treatments that are known to cause immunosuppression or increased susceptibility to infection. Prior treatment history included surgery in 171 (56%), radiation in 77 (25%), systemic treatment in 207 (68%), hormone therapy in 48 (16%), and targeted therapy in 61 (20%) patients since cancer diagnosis. A small subset of patients had received immunotherapy (*n* = 17, 5.6%).

The distribution of time from diagnosis to COVID-19 outcome is presented in Supplementary Fig. S1A-D. The mean time between initial cancer diagnosis and COVID-19 infection was 1742.8 days (standard deviation [SD] = 2755.9) overall. The mean time between surgery, radiation, and systemic treatment and COVID-19 outcome was 1493.9 (SD = 3001.5), 1631.7 (SD = 1766.4), and 1027.1 (SD =1273.5) days, respectively. Cumulative COVID-19 positivity in each facility and amongst cancer and non-cancer patients is shown in Figure 1.

Clinical characteristics related to COVID-19 are summarized in Table 2. Among the study cohort, 175 (58%) did not
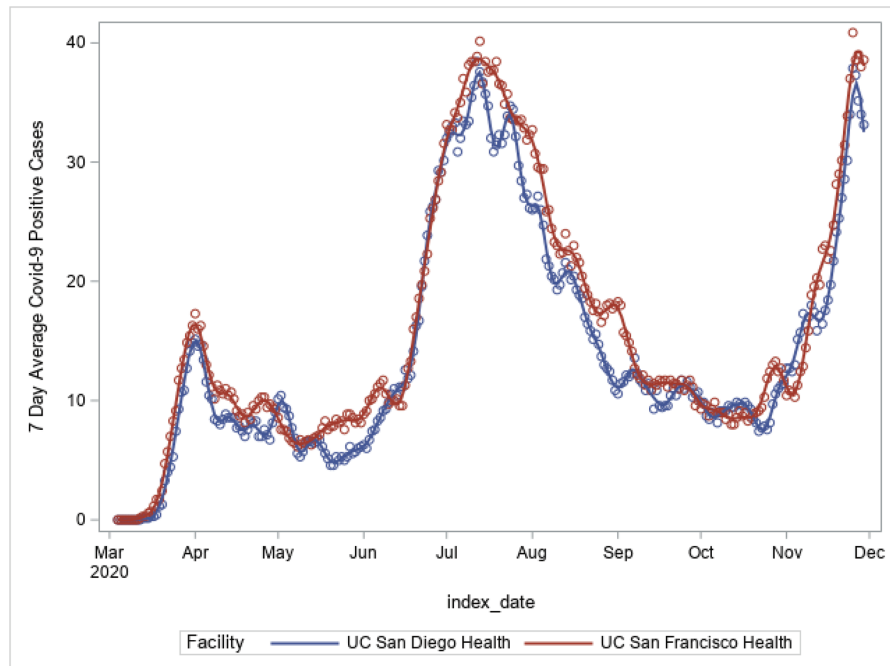
Figure 1. SARS-CoV-2: 7 days average positive cases between March and November 2020 for UCSF and UCSD.

require hospitalization, 79 (26%) were hospitalized, 28 (9%) required ICU admission, and death attributed to COVID-19 occurred in 21 (7%). A total of 137 (45%) patients had fever, 176 (58%) had cough, and 204 (67%) were symptomatic. Fifty-seven (19%) had a known exposure to SARS-CoV-2.

Table 3 summarizes the results of a multivariable ordinal logistic regression model assessing predictors of hospitalization, ICU admission, or death. Patients with 2 or more comorbidities had a higher odd of hospitalization (non-ICU) (odds ratio [OR] 2.09 [95% confidence interval (CI), 1.23-3.55]). Importantly, mortality was associated with having an active cancer diagnosis (OR 3.64 [95% CI, 1.40-9.5]) or being an older adult (≥65 years old) (OR 3.86 [95% CI, 1.2-12.44]). Cough was significantly associated with hospitalization (OR 1.83 [95% CI, 1.07-3.13]) and ICU admission (OR 2.16 [95% CI, 1.03-4.56]), however, not with mortality.

Discussion

This study leveraged a multi-institutional, racially/ethnically diverse clinical registry to analyze outcomes among patients with an invasive cancer diagnosis. The analysis suggests that patients with active disease receiving ongoing anti-cancer treatment have a higher odd of death from COVID-19 compared to patients with without evidence of active disease. In addition, we also observed that other patient factors such as number of comorbidities are associated with hospitalization at time of SARS-CoV-2 infection.

The literature to date has reported variable outcomes following SARS-CoV-2 infection among patients with cancer. A meta-analysis performed by ElGohary et al. observed a mortality rate of up to 21% and an ICU admission rate of 14% among patients with cancer and confirmed COVID-19 infection, suggesting an added risk for patients with cancer compared to the general population.[10] On the other hand, Barlesi et al examined 7251 patients with cancer and observed that COVID-19 was no more lethal among the study sample compared to the general population.[6] Our study observation adds

to the emerging literature in elucidating that the additional risk for hospitalization may be driven by the presence of active cancer requiring ongoing clinical management or being an older adult.

These data also inform healthcare utilization among vulnerable populations such as patients with active cancer. Interestingly, the current literature reports on decreased engagement with healthcare professionals, higher odds of canceling an outpatient oncology appointment, and reduced healthcare utilization among patients with cancer.[11] We did not observe a relationship between active cancer and risk of hospitalization, however, a significant association between active cancer and mortality. Future research will need to uncover factors that may reduce risk of mortality in this patient population.

In our cohort, we also observed that having 2 or more comorbidities is significantly associated with an increased risk of hospitalization. This observation has been noted across tumor types and in the general population. For example, Vuagnat et al examined COVID-19 outcomes among patients with breast cancer and observed that non-cancer comorbidities were associated with mortality in the study sample.[12] Specifically Vuagnat et al reported an increase in mortality rate among patients with cancer driven by the number of comorbidities rather than current treatment or receipt of radiation.[12] A literature review by Sanyaolu et al found that comorbidities of hypertension and diabetes mellitus were associated with the development of a more severe course of COVID-19 among the study population.[13] Therefore, patients with multiple comorbidities, regardless of cancer status, will require more aggressive preventive measures and vaccine access to mitigate risk of severe illness from SARS-CoV-2.

In our multivariate model, Hispanic ethnicity was not associated with a higher risk of hospitalization. The COVID-19 pandemic has dramatically accentuated health disparities across the US.[14-16] While racial/ethnic minorities have been observed to have higher rates of infection, likely driven by social determinants of health,[14,17] this analysis did not observe

Table 2. COVID-19 presentation characteristics among patients in the University of California Cancer Consortium COVID-19 Project Outcomes Registry from March to November 2020

| | Total | | COVID-19 Outcomes | | | | | | | |
| | | | Outpatient | | Hospitalization non-ICU | | Hospitalization-ICU | | Death | |
	N	Row %	N	Row %	N	Row %	N	Row %	N	Row %
Total	303	100	175	57.8	79	26.1	28	9.2	21	6.9
Fever										
Afebrile	166	100	109	65.7	35	21.1	13	7.8	9	5.4
Fever	137	100	66	48.2	44	32.1	15	10.9	12	8.8
Cough										
No cough	127	100	89	70.1	25	19.7	6	4.7	7	5.5
Cough	176	100	86	48.9	54	30.7	22	12.5	14	8
Month of confirmed infection (2020)										
March	25	100	10	40	9	36	4	16	2	8
April	21	100	13	61.9	2	9.5	3	14.3	3	14.3
May	25	100	15	60	8	32			2	8
June	51	100	28	54.9	9	17.6	7	13.7	7	13.7
July	71	100	46	64.8	16	22.5	4	5.6	5	7
August	56	100	30	53.6	22	39.3	4	7.1		
September	32	100	21	65.6	7	21.9	2	6.3	2	6.3
October	19	100	12	63.2	6	31.6	1	5.3		
November	3	100					3	100		
Symptomatic infection										
Asymptomatic	99	100	72	72.7	17	17.2	3	3	7	7.1
Symptomatic	204	100	103	50.5	62	30.4	25	12.3	14	6.9
Known exposure										
Not known	246	100	140	56.9	64	26	23	9.3	19	7.7
Known	57	100	35	61.4	15	26.3	5	8.8	2	3.5
Daily average of positive cases in the last 7 days prior to index date										
0-10 cases	105	100	60	57.1	27	25.7	12	11.4	6	5.7
11-20 cases	80	100	42	52.5	22	27.5	9	11.3	7	8.8
21-30 cases	52	100	32	61.5	14	26.9	3	5.8	3	5.8
31-40 cases	66	100	41	62.5	16	24.2	4	6.1	5	7.6
Daily average of positive cases in the last 7 days prior to index date, Mean (SD)	18.5 (11.1)		19.4 (11.1)		17.7 (11.21)		15.2 (12.3)		18.9 (12.3)	
Received COVID-19-directed therapy										
Yes	227	100	108	47.6	75	33	26	11.5	18	7.9
No	76	100	67	88.2	4	5.3	2	2.6	3	3.9
Number of COVID-19-directed therapies received										
0	76	100	67	88.2	4	5.3	2	2.6	3	3.9
1	81	100	55	67.9	20	24.7	4	4.9	2	2.5
2	72	100	35	48.6	22	30.6	9	12.5	6	8.3
3	42	100	15	35.7	18	42.9	4	9.5	5	11.9
4	17	100	2	11.8	7	41.2	3	17.6	5	29.4
5+	15	200	1	8.3	8	91.6	6	100	0	0
COVID-19-directed therapy type										
Hydroxychloroquine	7	100			4	57.1	2	28.6	1	14.3
Anti-virals	42	100	22	52.4	8	19	6	14.3	6	14.3

Table 2. Continued

	Total		Outpatient		Hospitalization non-ICU		Hospitalization-ICU		Death	
	N	Row %	N	Row %	N	Row %	N	Row %	N	Row %
Lopinavir/Ritonavir	2	100			2	100				
Oseltamivir (Tamiflu)	3	100	1	33.3	2	66.7				
Remdesivir	45	100			25	55.6	14	31.1	6	13.3
Azithromycin	29	100	10	34.5	10	34.5	3	10.3	6	20.7
Corticosteroids	57	100	19	33.3	19	33.3	12	21.1	7	12.3
Statins	89	100	53	59.6	26	29.2	6	6.7	4	4.5
Convalescent plasma	12	100			7	58.3	4	33.3	1	8.3
Anticoagulation	104	100	19	18.3	55	52.9	19	18.3	11	10.6
Aspirin	57	100	38	66.7	14	24.6	4	7	1	1.8
Other	36	100	10	27.8	12	33.3	8	22.2	6	16.7

Abbreviation: COVID-19, coronavirus disease 2019.

Table 3. Ordinal logistic regression to evaluate factors that increase the cumulative odds of hospitalization, ICU admission, and mortality (partial proportional odds model)

Covariates with different slopes	(Hospitalization with or without ICU or death) versus outpatient		(ICU admission or death) versus outpatient and/or non-ICU hospitalization		Mortality versus (outpatient and/or any hospitalization)	
	Odds ratio (OR) (95% confidence interval [CI]	P	Odds ratio (OR) (95% confidence interval [CI]	P	Odds ratio (OR) (95% confidence interval [CI]	P
Malignant hematologic cancer	1.29 (0.74-2.25)	.3704	1.29 (0.74-2.25)	.3704	1.29 (0.74-2.25)	.3704
Active cancer[a]	1.14 (0.69-1.89)	.609	1.14 (0.6-2.19)	.6843	**3.64 (1.4-9.5)**	**.0082**
Male	1.45 (0.9-2.34)	.1239	1.45 (0.9-2.34)	.1239	1.45 (0.9-2.34)	.1239
Hispanic	1.69 (0.96-2.99)	.0703	1.69 (0.96-2.99)	.0703	1.69 (0.96-2.99)	.0703
Other/un-known race	1.21 (0.64-2.3)	.5515	1.21 (0.64-2.3)	.5515	1.21 (0.64-2.3)	.5515
Age 65+[a]	1.53 (0.89-2.63)	.1271	1.32 (0.66-2.65)	.4364	**3.86 (1.2-12.44)**	**.0239**
BMI 30+	0.85 (0.51-1.41)	.5281	0.85 (0.51-1.41)	.5281	0.85 (0.51-1.41)	.5281
Fever	1.58 (0.96-2.61)	.0744	1.58 (0.96-2.61)	.0744	1.58 (0.96-2.61)	.0744
Cough[a]	**1.83 (1.07-3.13)**	.0281	**2.16 (1.03-4.57)**	**.0428**	1.01 (0.34-2.96)	.9904
2+ Comorbidities[a]	**2.09 (1.23-3.55)**	.0066	0.88 (0.43-1.8)	.7247	1.78 (0.56-5.65)	.3296

[a]Common effect of each factor across the odds of more severe covid-19 outcomes over less successively was tested. Different effects were included only when necessary. Emboldened values all meet statistical significance.
Abbreviation: BMI, body mass index; ICU, intensive care unit.

differences in clinical outcomes after infection by race/ethnicity. While these data did not identify a clear difference in healthcare utilization by race/ethnicity, these findings will need to be further evaluated on a population level.

We observed that clinical factors informed risk for patients with cancer and a COVID-19 diagnosis. Specifically, the presentation with cough symptoms increased the odds of requiring ICU admission. While cough and fever are commonly observed in symptomatic COVID-19,[7] the presence of fever did not appear to have a significant association with requiring ICU-level care. The observation of initial cough being associated with ICU admission in the present cohort suggests that initial pulmonary symptoms likely require early intervention

to mitigate risk of requiring critical care. Zhao et al generated a prediction model and risk for ICU admission and mortality and COVID-19 and noted that pulse oxygen saturation was a variable that predicted ICU admission.[18] Our observation builds on the growing evidence of data that respiratory symptoms are a major factor that predicts critical care needs among patients with COVID-19.

Our study observed a lower death rate than has been previously reported by Kuderer et al and Jee et al.[4,19] The study period examined was from March to November 2020 (compared to Kuderer et al in March to May 2020 and Jee et al in March to April 2020). Therefore, it is reasonable to expect that treatment for COVID-19 quickly evolved during this

time which may explain the lower death rate in this current analysis. However, this analysis did not adjust or control for the COVID-19 directed therapies which is a limitation. This analysis did control for COVID-19 disease burden in each facility at the time of COVID-19 positive diagnosis as a *proxy* for healthcare capacity.

This analysis has additional limitations worth noting. There are insufficient numbers to report clinical outcomes by cancer type, and variation in the COVID-19 disease phenotype based on cancer type and treatment history has been reported.[3] For example, a population-based study in Italy observed that patients with cancer had an increased risk of SARS-CoV-2 infection compared to the general population, however a protective effect was observed among men with prostate cancer on androgen deprivation therapy.[20] As our study sample increases over time, we will be powered to determine the impact of both cancer type, and cancer-specific treatments on COVID-19 outcomes. Facilities relied on confirmation of COVID-19 positivity in the EHR, which may lead to under-ascertainment of the true study population. Additionally, this was a retrospective analysis that relied on documented clinical data in the EHR. We did not incorporate variables that reflect functional/performance status in the analysis as it was missing in a large proportion of patients proximal to the date of diagnosis with COVID-19. Given that functional status is a major predictor of outcomes for patients with cancer,[21] this is a current limitation of the analysis. This analysis also did not allow us to distinguish cause of death therefore we were unable to perform a competing risk analysis. Future research will need to capture cause of death and also be a sufficient sample to add additional covariates in the model.

Despite these limitations, this study has several strengths. We leveraged a multi-institutional, geographically diverse dataset and incorporated facility characteristics into our analytical model. The utilization of COVID-19 positivity rate at each participating site served as a facility-level surrogate of potential resource constraints.

Conclusion

Our study has 3 key observations. First, we observed that non-cancer-related clinical factors such as number of comorbidities is associated with hospitalization amongst patients with cancer who tested positive for SARS-CoV2. We also identified cough symptoms at presentation as a factor that is significantly associated with requiring ICU-level care among our study cohort. Lastly, a diagnosis of active cancer is significantly associated with increased mortality after COVID-19 infection.

Funding

Conflict of Interest

Julian C. Hong: Pending patent for prediction of acute care during cancer therapy, unrelated to manuscript (IP). **Rana R. McKay:** Dendreon, Vividion, Myovant (C/A); Bayer, Pfizer, Tempus (RF); serves on Advisory Board for AstraZeneca, Bayer, Bristol Myers Squib, Calithera, Exelixis, Janssen, Merck, Novartis, Pfizer, Sanofi, Tempus (SAB); Caris (Other—molecular tumor board); **Hope Rugo:** Pfizer, Merck, Novartis, Lilly, Roche, Odonate, Daiichi, Seattle Genetics, Macrogenics, Sermonix, Boehringer Ingelheim, Polyphor, Astra Zeneca, OBI and Gilead, Ayala Honoraria: Puma, Mylan, Samsung, Napo (RF—inst); **Eric J. Small:** Janssen, Fortis, Teon Therapeutics, Ulragenyx, Beigene, Tolero (C/A); Janssen, Johnson and Johnson (H); Fortis Therapeutics, Harpoon Therapeutics (OI). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

Author Contributions

Conception/design: H.T.B., E.J.S. Provision of study material/patients: H.T.B., S.Z., A.B., E.J.S. Collection and/or assembly of data: H.T.B., J.C.H., S.Y., A.L., S.Z., R.R.M., O.H., M.R., C.W., E.J.S. Data analysis and interpretation: H.T.B., M.-O.K., J.C.H., S.Y., A.L., I.T., S.Z., R.R.M., O.H., P.C., H.R., V.S.K., M.R., C.W., A.B., E.J.S. Manuscript writing: H.T.B., M.-O.K., J.C.H., S.Y., A.L., I.T., S.Z., R.R.M., O.H., P.C., H.R., V.S.K., M.R., C.W., A.B., E.J.S. Final approval of manuscript: All authors.

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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