COVID-19 Outcomes in Hospitalized Patients With Active Cancer: Experiences From a Major New York City Health Care System

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BACKGROUND: The authors sought to study the risk factors associated with severe outcomes in hospitalized coronavirus disease 2019 (COVID-19) patients with cancer. METHODS: The authors queried the New York University Langone Medical Center’s records for hospitalized patients who were polymerase chain reaction–positive for severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) and performed chart reviews on patients with cancer diagnoses to identify patients with active cancer and patients with a history of cancer. Descriptive statistics were calculated and multivariable logistic regression was used to determine associations between clinical, demographic, and laboratory characteristics with outcomes, including death and admission to the intensive care unit. RESULTS: A total of 4184 hospitalized SARS CoV-2+ patients, including 233 with active cancer, were identified. Patients with active cancer were more likely to die than those with a history of cancer and those without any cancer history (34.3% vs 27.6% vs 20%, respectively; P < .01). In multivariable regression among all patients, active cancer (odds ratio [OR], 1.89; CI, 1.54-2.67; P < .01), older age (OR, 1.06; CI, 1.05-1.06; P < .01), male sex (OR for female vs male, 0.70; CI, 0.58-0.84; P < .01), diabetes (OR, 1.26; CI, 1.04-1.53; P = .02), and morbidly obese body mass index (OR, 1.87; CI, 1.24-2.81; P < .01), and elevated D-dimer (OR, 6.41 for value >2300; CI, 4.75-8.66; P < .01) were associated with increased mortality. Recent cancer-directed medical therapy was not associated with death in multivariable analysis. Among patients with active cancer, those with a hematologic malignancy had the highest mortality rate in comparison with other cancer types (47.83% vs 28.66%; P < .01). CONCLUSIONS: The authors found that patients with an active cancer diagnosis were more likely to die from COVID-19. Those with hematologic malignancies were at the highest risk of death. Patients receiving cancer-directed therapy within 3 months before hospitalization had no overall increased risk of death. Cancer 2021;127:3466-3475. © 2021 American Cancer Society.

LAY SUMMARY:
• Our investigators found that hospitalized patients with active cancer were more likely to die from coronavirus disease 2019 (COVID-19) than those with a history of cancer and those without any cancer history.
• Patients with hematologic cancers were the most likely among patients with cancer to die from COVID-19.
• Patients who received cancer therapy within 3 months before hospitalization did not have an increased risk of death.

KEYWORDS: active, cancer, chemotherapy, coronavirus, coronavirus disease 2019 (COVID-19), hospitalized, New York City, outcomes, risk.

INTRODUCTION
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread worldwide since its initial detection in Wuhan, China, at the end of 2019, setting off a global pandemic. The illness it causes, coronavirus disease 2019 (COVID-19), has been detected in over 200 countries or regions, with greater than 25 million cases currently recognized in the United States (US). In March 2020, New York State emerged as an epicenter of the disease in the US, at that time accounting for most cases and deaths nationally.1 Our institution, which includes 3 large tertiary care hospitals, located in the United States (US). In March 2020, New York State emerged as an epicenter of the disease in the US, at that time among the most affected by COVID-19. Brooklyn and Nassau County, where 2 of our hospitals are located, experienced some of the highest mortality rates from COVID-19 in the US.1
Increasing age has emerged as the risk factor, with the largest effect on severe complications from COVID-19. Early reports showed 80% of deaths occurred in those 65 years and older. Severe cases have also been associated with underlying medical conditions, and the combination of increased age and comorbidities leads to the highest rate of severe outcomes. Early case series and cohort studies identified hypertension, obesity, and diabetes as 3 of the most common comorbidities in hospitalized patients. Numerous studies have identified multiple other medical conditions associated with worsened outcomes from COVID-19. Outside of age, however, the contribution of specific comorbidities to severe outcomes remains unclear, because of heterogeneity in sampling and analysis between studies. One critical question is the risk posed to patients with cancer, and how cancer itself affects outcomes from COVID-19 in a population that is older and has more chronic medical conditions at baseline. For example, in 1 study of 423 patients with cancer that were positive for SARS-CoV-2 at a single-center, multiple comorbidities predicted for hospitalization and severe disease in univariate analysis, but not in multivariable analysis. A growing body of research suggests that patients with cancer are at increased risk of adverse outcomes from COVID-19. Within this population, determining the added risk of various cancer-directed therapies to developing serious outcomes from the disease is paramount. A limited number of studies suggest that recent treatment with chemotherapy or other antineoplastic medical therapies is not associated with worse outcomes from COVID-19, whereas others found a deleterious effect from recent use of checkpoint inhibitors. Our hard-hit centers in New York City have an important role in furthering the understanding of the pandemic, and specifically how the disease affects patients with cancer. Using one of the largest databases of hospitalized patients with cancer with COVID-19 to date, we studied the association of active cancer and antineoplastic therapy with outcomes in patients with COVID-19.

MATERIALS AND METHODS

Study Design

In this case control study, we report data from patients admitted to the New York University (NYU) Langone Health System from March 1, 2020, to May 15, 2020. The study was approved by NYU Langone’s institutional review board. Data were then collected using EPIC’s Clarity reporting system and by additional chart review.

Participants

We identified all patients 18 years old or older who tested positive for SARS-CoV-2 by reverse transcription polymerase chain reaction and were admitted to 1 of the NYU Langone Hospitals during the study. All patients were screened for cancer on the basis of the presence of an International Classification of Diseases, Tenth Revision (ICD-10) diagnostic code in their medical records. Patients with an ICD-10 code present in their records were then chart-reviewed to identify those with active cancer, which was defined by any of the following: 1) a new diagnosis of cancer on or after March 1, 2019 (1 year before data collection), or 2) ongoing cancer-directed therapy on or after March 1, 2019. Cancer-directed therapy included systemic medical therapy, radiotherapy, and surgical resection. Within this group, recent treatment was defined as systemic medical therapy given within 3 months of hospitalization. Systemic medical therapy was defined as any of the following: chemotherapy, immune checkpoint inhibitors, small molecule targeted therapies, monoclonal antibodies (excluding checkpoint inhibitors), antibody-drug conjugates, and hormonal therapies.

A Consolidated Standards of Reporting Trials diagram detailing the chart review process for selecting patients with active cancer is shown in Figure 1. History of cancer was defined by an ICD-10 cancer diagnosis and chart review to confirm the cancer diagnosis, without the criteria above qualifying for active cancer. No history of cancer was defined by the absence of an ICD-10 cancer diagnosis at any time period. Solid tumors were defined as those originating from the following organs: lung, prostate, breast, liver, skin, gastrointestinal tract, and hepatic system.

Demographic and clinical characteristics were collected for all patients, including age, sex, ethnicity, body mass index (BMI), history of diabetes mellitus (DM), history of hypertension (HTN), and D-dimer level. We chose to gather data only on BMI, DM and HTN among all comorbidities because data capture was complete and they were early established risk factors for COVID-19 morbidity. Outcome data collected included intensive care unit (ICU) admission and death. For patients with active cancer, cancer type and treatment modality were determined by manual chart review (Supporting Table 2).

Outcomes and Statistical Analysis

The primary end point was death. Secondary end points were ICU requirement and combined death/or ICU requirement. Univariate analyses using the Pearson $\chi^2$
and t tests were conducted to identify associations between individual clinical/demographic characteristics and outcomes to determine significance. Two-sided P value of <.05 was considered statistically significant. Three multivariable logistic regression models were performed to examine associations between clinical and demographic characteristics among the entire COVID-19 cohort and the following outcomes: death, ICU, and death or ICU. Multivariable logistic regression was also conducted on the subset of patients with active cancer to identify associations between clinical and demographic characteristics and death. For this model, cancers of the central nervous system (CNS) and mesenchymal tumors were included in solid tumors in addition to those listed above. Odds ratios (OR) were calculated and considered statistically significant if the P value was <.05 and the 95% CI did not cross 1.0. Statistical analysis was performed in SAS (version 9.4).

RESULTS
In total, 233 patients with active cancer were identified. Patients with active cancer were older than those with a history of cancer and no cancer diagnosis (mean age, 71.2 years vs 62.2 years; P < .01) and less likely to be male (50.6% vs. 58.7%; P < .01). Among 233 patients with active cancer, 164 had solid tumors (70.4%), 69 had a hematologic cancer (29.6%). Demographics are summarized in Table 1 with additional detail in Supporting Table 1.

Of 233 patients with active cancer hospitalized with COVID-19, 80 died, 45 were treated in an ICU, and 92 died and/or required ICU care. In univariate analyses (Table 2), patients with active cancer died more frequently compared to those without cancer (34.33% vs 19.74%; P < .01), but there was no significant difference in death rate of patients with active cancer compared to those with history of cancer (34.33% vs 27.64%; P = .08). Compared to noncancer patients, patients with active cancer had a higher rate of the combined adverse outcome of ICU or death (31.36% vs 39.48%; P = .01). There was no difference in combined adverse outcome between patients with active cancer and those with a history of cancer (39.48% vs 37.20%; P = .61).

Patients with active cancer who had received cancer-directed medical therapy within 3 months of hospital admission had a higher rate of ICU admission (25.22% vs 13.56%; P = .04), and there was a nonsignificant numerically higher rate of death (40% vs 28.81%; P = .10).

Figure 1. Consolidated Standards of Reporting Trials style diagram detailing classification of patients with active cancer. The initial patient pool included 4184 patients with positive severe acute respiratory syndrome coronavirus 2 nasopharyngeal polymerase chain reaction swabs. Two patients were immediately excluded because of young age (<18 years). A total of 3460 patients without an International Classification of Diseases, Tenth Revision (ICD-10) cancer diagnosis were excluded using an automated screen. The authors subsequently conducted individual chart review on the remaining patients to exclude patients without a cancer history in the chart, patients with documented remission or excision of cancer before March 2019, and patients with limited medical records.
We evaluated differences by treatment type and found that patients who received monoclonal antibodies were numerically more likely to require ICU care, but the difference did not reach statistical significance (38.90% vs 16.67%; *P* = .06). Those that received chemotherapy (41.27% vs 31.76%; *P* = .23), small molecule targeted therapies (52 vs 32.21%; *P* = .08), and hormone therapies (40% vs 33.50%; *P* = .62) within this time period had numerically but nonsignificant higher rates of death. There was no difference in adverse outcomes in patients who had received immune checkpoint inhibitors.

Patients with CNS malignancy had the highest rate of death (50%), but only 4 patients with CNS tumors were included. Patients with hematologic cancer had a higher rate of death compared to those with solid cancers (47.83% vs 28.66%; *P* < .01). Hematologic patients with cancer had a higher rate of ICU use compared to those with solid malignancies, but this difference was not significant (27.4% vs 16.0%; *P* = .07). Patients with hematologic cancer also had a significantly increased risk of experiencing the combined outcome of either death or ICU requirement compared to those with solid tumors (53.62% vs 33.54%; *P* = .01).

We conducted a sensitivity analysis in which we modeled associations of covariates with death as a primary outcome (Supporting Table 3). This was done separately for those with solid tumors and those with hematologic malignancies. We found similar results in the 2 models, although the power of the smaller subsets was limited. One notable exception was that among the hematologic malignancies, the associations of weight and outcomes were different from what was seen among solid tumors. These findings warrant further study among more patients.

Among the entire study population, by univariate analysis death occurred more frequently in men than women (23.54% vs 18.75%; *P* < .01), and men were more likely to require ICU care (26.46% vs 16.57%; *P* < .01). The mean age of patients who died was higher compared to those who did not (72.70% vs 58.80%; *P* < .01). There was no difference in age between those requiring ICU care and those who did not (61.79% vs 61.84%; *P* = .95). Patients with HTN were more likely to die (26.20% vs 18%; *P* < .01) and were more likely to require ICU care compared to those
without HTN (24% vs 21.18%; \( P = .03 \)). Patients with diabetes also were more likely to die (26.60% vs 19.10%; \( P < .01 \)) and require intensive care (25.95% vs 20.54%; \( P < .01 \)). BMI category was associated with death (\( P < .01 \)) and ICU requirement (\( P = .03 \)), with worse outcomes for the underweight and morbidly obese. Race was associated with mortality in univariate analysis, and hospitalized Black patients were less likely to die compared to White patients (15.32% vs 23.98%; \( P < .01 \)).

Although patients with cancer frequently have an elevated D-dimer at baseline, our models found that elevated D-dimer was a strong independent predictor of poor outcomes in all included patients and the percentage of patients experiencing poor outcomes correlated with increasing D-dimer level. In patients with D-dimer >2300 ng/mL, 65.46% died or required ICU care, as did 41.93% in patients with D-dimer 1151-2300 ng/mL, and 18.83% in those with D-dimer 231-1150 ng/mL. Comparatively, only 7.30% in those with D-dimer <230 ng/mL experienced the same outcomes.

In multivariable logistic regression analysis (Table 3), patients with active cancer were more likely to die (OR, 1.89; 95% CI, 1.33%-2.67%; \( P < .01 \)) (Figure 2A) but not more likely to have the combined end point of death or ICU (OR, 1.35; 95% CI, 0.96%-1.89%; \( P = .08 \)) (Figure 2B). History of cancer was not associated with an increased risk of any adverse outcome (for death: OR, 1.20; 95% CI, 0.92%-1.57%; \( P = 18 \); for death

### TABLE 1. Patient Demographics

|                      | COVID-19 Patients With Active Cancer (n = 233) | COVID-19 Patients Without Active Cancer (n = 3953) | \( P \) |
|----------------------|---------------------------------------------|--------------------------------------------------|--------|
| Age, mean, y         | 71.2                                        | 62.2                                             | <.001  |
| Sex                  |                                             |                                                  |        |
| Male                 | 118 (50.6%)                                 | 2320 (58.7%)                                    | <.001  |
| Female               | 115 (49.4%)                                 | 1633 (41.3%)                                    | <.001  |
| Comorbidities        |                                             |                                                  |        |
| HTN                  | 149 (63.8%)                                 | 1720 (43.5%)                                    | <.001  |
| DM                   | 84 (36.1%)                                  | 1380 (34.9%)                                    | .715   |
| Ethnicity            |                                             |                                                  | .552   |
| Asian                | 14 (6.0%)                                   | 296 (7.5%)                                       |        |
| Black                | 32 (13.7%)                                  | 601 (15.2%)                                      |        |
| Other                | 56 (24.0%)                                  | 1118 (28.2%)                                     |        |
| White                | 122 (52.4%)                                 | 1734 (43.9%)                                     |        |
| Unknown              | 9 (3.9%)                                    | 204 (5.2%)                                       |        |
| BMI                   |                                             |                                                  | .002   |
| Normal               | 80 (34.4%)                                  | 925 (23.4%)                                      | <.001  |
| Underweight          | 12 (5.2%)                                   | 95 (2.4%)                                        | .010   |
| Overweight           | 77 (33.0%)                                  | 1391 (35.2%)                                     | .614   |
| Obese                | 54 (23.1%)                                  | 1257 (31.8%)                                     | <.001  |
| Morbidly obese       | 9 (3.8%)                                    | 281 (7.1%)                                       | <.001  |
| D-dimer              |                                             |                                                  | .02    |
| <230 ng/mL           | 18 (7.6%)                                   | 893 (22.6%)                                      |        |
| 231-1150 ng/mL       | 104 (44.7%)                                 | 1593 (40.3%)                                     |        |
| 1151-2300 ng/mL      | 31 (13.2%)                                  | 332 (8.4%)                                       |        |
| >2300 ng/mL          | 80 (34.5%)                                  | 1135 (28.7%)                                     |        |
| Antineoplastic therapy within 3 months (n = 115) | | | |
| Immune checkpoint inhibitor | 12 (10.4%) | NA | |
| Small molecule       | 26 (22.6%)                                  | NA                                               |        |
| Monoclonal antibody  | 18 (15.7%)                                  | NA                                               |        |
| Antibody-drug conjugate | 1 (0.9%) | NA | |
| Chemotherapy         | 63 (55%)                                    | NA                                               |        |
| Hormonal therapy     | 30 (26%)                                    | NA                                               |        |
| Cancer type          |                                             |                                                  |        |
| Hematologic          | 69 (29.6%)                                  | NA                                               |        |
| Lung                 | 35 (15.0%)                                  | NA                                               |        |
| GI                   | 28 (12.0%)                                  | NA                                               |        |
| Prostate             | 25 (10.7%)                                  | NA                                               |        |
| Breast               | 23 (9.9%)                                   | NA                                               |        |
| CNS                  | 5 (2.1%)                                    | NA                                               |        |
| Other                | 48 (20.6%)                                  | NA                                               |        |

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; CNS, central nervous system; DM, diabetes mellitus; GI, gastrointestinal; HTM, hypertension; NA, not applicable.
or ICU: OR, 1.17; 95% CI, 0.91%-1.51%; \( P = .21 \).

Multivariable analysis among 233 patients with active cancer showed a higher risk of death in older patients with cancer (OR, 1.03; 95% CI, 1.00%-1.06%; \( P = .04 \)) and those with D-dimer \( \geq 1150 \) ng/dL (OR, 2.19; 95% CI, 1.09%-4.37%; \( P = .02 \)) (Figure 2C). There was no association of treatment type or tumor category with risk of death. Patients with hematologic malignancies experienced a nonsignificant increase in mortality rates when compared to patients with solid cancers (OR, 1.82; 95% CI, 1.03-3.23; \( P = .04 \)).

### TABLE 2. Univariate Analyses

|                   | Died Alive | \( P \) | Died or ICU Alive, No ICU | \( P \) |
|-------------------|------------|--------|---------------------------|--------|
| Age, mean (SD), y | 72.7 (13.8) | 58.8 (18.9) | <.01 | 67.0 (17.3) | 59.3 (19.0) | <.01 |
| Sex, No. (%)      |            |        |                           |        |
| Male              | 572 (23.5) | 1858 (76.5) | <.01 | 877 (36.1) | 1553 (63.9) | <.01 |
| Female            | 327 (18.8) | 1417 (81.3) |        | 483 (27.7) | 1261 (72.3) |        |
| Comorbidities, No. (%) |        |        |                           |        |
| HTN               | 486 (26.2) | 1368 (73.8) | <.01 | 703 (37.9) | 1151 (62.1) | <.01 |
| No HTN            | 413 (18.0) | 1886 (82.0) |        | 657 (28.6) | 1642 (71.4) |        |
| DM                | 384 (26.6) | 1061 (73.4) | <.01 | 561 (38.8) | 884 (61.2) | <.01 |
| No DM             | 515 (19.1) | 2177 (80.9) |        | 795 (29.9) | 1897 (70.5) |        |
| Ethnicity, No. (%)|            |        |                           |        |
| Asian             | 80 (25.8)  | 230 (74.2) | <.01 | 119 (38.4) | 191 (61.6) | <.01 |
| Black             | 97 (15.3)  | 536 (84.7) |        | 157 (24.8) | 476 (75.2) |        |
| Other             | 241 (20.5) | 933 (79.5) |        | 372 (31.7) | 802 (68.3) |        |
| White             | 445 (24.0) | 1411 (76.0) | <.01 | 644 (31.7) | 1212 (68.3) | <.01 |
| Unknown           | 36 (17.9)  | 165 (82.1) |        | 67 (33.3)  | 134 (66.7) |        |
| BMI, No. (%)      |            | <.01   |                           |        |
| Normal            | 216 (23.9) | 688 (76.1) | <.01 | 309 (34.2) | 595 (65.8) | <.01 |
| Underweight       | 25 (26.0)  | 71 (77.4) | <.01 | 36 (37.5)  | 60 (62.5)  | <.01 |
| Overweight        | 290 (22.0) | 1030 (78.0) | <.01 | 439 (33.3) | 881 (66.7) | <.01 |
| Obese             | 212 (18.0) | 967 (82.0) | <.01 | 362 (30.7) | 817 (69.3) | <.01 |
| Morbidly obese    | 48 (18.5)  | 212 (81.5) | <.01 | 92 (35.4)  | 168 (64.8) | <.01 |
| D-dimer, No. (%)  |            | <.01   |                           |        |
| <231 ng/mL        | 15 (3.3)   | 910 (96.7) | <.01 | 33 (7.3)   | 417 (92.7) | <.01 |
| 231-1150 ng/mL    | 212 (12.8) | 1445 (87.2) | <.01 | 312 (18.8) | 1345 (81.2) | <.01 |
| 1151-2300 ng/mL   | 98 (27.8)  | 255 (72.2) | <.01 | 148 (42.0) | 205 (58.0) | <.01 |
| >2300 ng/mL       | 510 (43.0) | 677 (57.0) | <.01 | 777 (65.5) | 410 (34.5) | <.01 |
| Cancer status, No. (%) |        |        |                           |        |
| Active            | 80 (34.3)  | 153 (65.7) | <.01 | 92 (39.5)  | 141 (60.5) | <.01 |
| Non-active        | 136 (27.6) | 356 (72.4) | <.01 | 183 (37.2) | 309 (62.8) | <.01 |
| Never             | 683 (19.7) | 2777 (80.3) | <.01 | 1085 (31.4) | 2375 (68.6) | <.01 |
| Active cancer type, No. (%) | |        |                           |        |
| Hematologic      | 33 (47.8)  | 36 (52.2) | <.01 | 37 (53.6)  | 32 (46.4)  | <.01 |
| Solid            | 47 (28.7)  | 117 (71.3) | <.01 | 55 (33.5)  | 109 (66.5) | <.01 |
| Treatment in active cancer, No. (%) |        |        |                           |        |
| Any therapy      | 46 (40.0)  | 69 (60.0) | <.10 | 50 (43.4)  | 65 (56.5)  | <.27 |
| Treatment type, No. (%) |        |        |                           |        |
| Chemotherapy      | 26 (41.3)  | 37 (58.7) | <.19 | 29 (46.0)  | 34 (54.0)  | <.36 |
| No treatment     | 36 (29.0)  | 88 (71.0) | <.19 | 44 (35.5)  | 80 (64.5)  | <.19 |
| Treatment, not chemotherapy |        |        |                           |        |
| Drug type, No. (%) |        |        |                           |        |
| Checkpoint inhibitor | 4 (33.3)   | 8 (66.7) | <.08 | 5 (41.7)   | 7 (58.3)   | <.10 |
| No checkpoint inhibitor | 76 (34.4) | 145 (65.6) | <.23 | 87 (39.4)  | 134 (60.6) | <.48 |
| Monoclonal antibody | 9 (50.0)   | 9 (50.0) | <.23 | 9 (50.0)  | 9 (50.0)   | <.48 |
| No monoclonal antibody | 71 (33.0) | 144 (67.0) | <.23 | 83 (38.6)  | 132 (61.4) | <.12 |
| Small molecule    | 13 (52.0)  | 12 (48.0) | <.08 | 14 (56.0)  | 11 (44.0)  | <.12 |
| No small molecule | 67 (32.2)  | 141 (67.8) | <.08 | 78 (37.5)  | 130 (62.5) | <.09 |
| Antibody-drug conjugate | 1 (100.0) | 0 (0.0) | <.39 | 1 (100.0) | 0 (0.0) | <.39 |
| No antibody-drug conjugate | 79 (34.1) | 153 (66.0) | <.39 | 91 (39.2) | 141 (60.8) | <.39 |
| Chemotherapy      | 26 (41.3)  | 37 (58.7) | <.23 | 29 (46.0)  | 34 (54.0)  | <.27 |
| No chemotherapy   | 54 (31.8)  | 116 (68.2) | <.23 | 63 (37.1)  | 107 (62.9) | <.79 |
| Hormone           | 12 (40.0)  | 18 (60.0) | <.62 | 13 (43.3)  | 17 (56.7)  | <.79 |
| No hormone        | 68 (33.5)  | 135 (66.5) | <.62 | 79 (38.9)  | 124 (61.1) | <.62 |

Abbreviations: BMI, body mass index; DM, diabetes mellitus; HTM, hypertension; ICU, intensive care unit.
TABLE 3. Multivariable Logistic Regression Models Among All Patients

| Variable                      | OR Estimate | 95% CI      | P     |
|-------------------------------|-------------|-------------|-------|
| **(A) Mortality**             |             |             |       |
| Age                           | 1.06        | 1.05-1.06   | <.01  |
| Sex                           |             |             |       |
| Male                          | 1.00        | —           | —     |
| Female                        | 0.70        | 0.58-0.84   | <.01  |
| Race                          |             |             |       |
| White                         | 1.00        | —           | —     |
| Asian                         | 1.18        | 0.83-1.67   | .35   |
| Black                         | 0.61        | 0.46-0.81   | <.01  |
| Other                         | 1.29        | 1.03-1.61   | .03   |
| Unknown                       | 0.85        | 0.54-1.34   | .48   |
| Comorbid conditions           |             |             |       |
| No diabetes                   | 1.00        | —           | —     |
| Diabetes                      | 1.26        | 1.04-1.53   | .02   |
| No hypertension               | 1.00        | —           | —     |
| Hypertension                  | 0.91        | 0.74-1.10   | .31   |
| Weight class                  |             |             |       |
| Normal BMI                    | 1.00        | —           | —     |
| Underweight                   | 1.99        | 1.08-3.65   | .03   |
| Overweight                    | 1.15        | 0.91-1.15   | .24   |
| Obese                         | 1.20        | 0.92-1.55   | .18   |
| Morbidly obese                | 1.87        | 1.24-2.81   | <.01  |
| Cancer status                 |             |             |       |
| No history of cancer          | 1.00        | —           | —     |
| Active cancer                 | 1.89        | 1.34-2.67   | <.01  |
| Non-active cancer             | 1.20        | 0.92-1.57   | .18   |
| D-dimer                       |             |             |       |
| ≤230 ng/mL                    | 1.00        | —           | —     |
| 231-1150 ng/mL                | 1.02        | 0.74-1.40   | .90   |
| 1151-2300 ng/mL               | 2.82        | 1.94-4.10   | <.01  |
| >2300 ng/mL                   | 6.41        | 4.75-8.66   | <.01  |
| **(B) ICU/mortality combined**|             |             |       |
| Age                           | 1.02        | 1.01-1.02   | <.01  |
| Sex                           |             |             |       |
| Male                          | 1.00        | —           | —     |
| Female                        | 0.75        | 0.63-0.89   | <.01  |
| Race                          |             |             |       |
| White                         | 1.00        | —           | —     |
| Asian                         | 1.07        | 0.78-1.47   | .69   |
| Black                         | 0.49        | 0.38-0.63   | <.01  |
| Other                         | 0.95        | 0.78-1.17   | .64   |
| Unknown                       | 0.99        | 0.67-1.44   | .94   |
| Comorbid conditions           |             |             |       |
| No diabetes                   | 1.00        | —           | —     |
| Diabetes                      | 1.34        | 1.13-1.60   | <.01  |
| No hypertension               | 1.00        | —           | —     |
| Hypertension                  | 1.17        | 0.98-1.39   | .09   |
| Weight class                  |             |             |       |
| Normal BMI                    | 1.00        | —           | —     |
| Underweight                   | 2.39        | 1.41-4.02   | <.01  |
| Overweight                    | 1.01        | 0.81-1.25   | .95   |
| Obese                         | 1.08        | 0.86-1.35   | .53   |
| Morbidly obese                | 1.70        | 1.20-2.41   | <.01  |
| Cancer status                 |             |             |       |
| No history of cancer          | 1.00        | —           | —     |
| Active cancer                 | 1.35        | 0.96-1.89   | .08   |
| Non-active cancer             | 1.17        | 0.91-1.15   | .21   |
| D-dimer                       |             |             |       |
| ≤230 ng/mL                    | 1.00        | —           | —     |
| 231-1150 ng/mL                | 1.24        | 0.96-1.60   | .10   |
| 1151-2300 ng/mL               | 4.05        | 2.96-5.53   | <.01  |
| >2300 ng/mL                   | 11.95       | 9.28-15.38  | <.01  |

Abbreviations: BMI, body mass index; CI, confidence interval; ICU, intensive care unit; OR, odds ratio.

P values and ORs are shown for mortality as a single outcome (A) and mortality or ICU use as a combined outcome (B).

CI, 0.88%-3.77%; P = .11) as did patients who received chemotherapy within the past 3 months (OR, 1.70; 95% CI, 0.77%-3.76%; P = .20) or patients who received any other medical anti-neoplastic therapy within the past 3 months (OR, 2.02; 95% CI, 0.83%-4.93%; P = .12) when compared to patients who received no treatment. Race was not associated with death among patients with active cancer.

Among the entire study population, older patients were more likely to die (OR, 1.06 per increased year of age; 95% CI, 1.05%-1.06%; P < .01) and more likely to have the combined adverse outcome of death or ICU care (OR, 1.02; 95% CI, 1.01%-1.02%; P < .01). Compared to men, women had a lower risk of death (OR, 0.7; 95% CI, 0.58%-0.84%; P < .01) and of the combined adverse outcome (OR, 0.7; 95% CI, 0.63%-0.89%; P < .01). Relative to White patients, Black patients had a lower risk of death (OR, 0.61; 95% CI, 0.46%-0.81%; P < .01) and combined adverse outcome (OR, 0.49; 95% CI, 0.38%-0.63%; P < .01). Patients with DM had an increased risk of death (OR, 1.26; 95% CI, 1.04%-1.52%; P = .02) and combined adverse outcome (OR, 1.34; 95% CI, 1.13%-1.60; P < .01). Patients at extremes of low and high BMI had worse outcomes: underweight BMI was associated with an increased risk of death (OR, 1.99; 95% CI, 1.08%-3.65%; P = .03) and combined adverse outcome (OR, 2.39; 95% CI, 1.41%-4.02%; P < .01). The same was true for morbidly obese BMI (OR, for death 1.87; 95% CI, 1.24%-2.81%; P < .01; OR, for combined outcome 1.70; 95% CI, 1.20%-2.41%; P < .01). There was no significant difference in either outcome for those with obese BMI.

D-dimer >2300 ng/mL was associated with a high risk of death (OR, 6.41; 95% CI, 4.75%-8.66%; P < .01) and combined adverse outcome (OR, 11.95; 95% CI, 9.28%-15.38%; P < .01), relative to the normal value of <230 ng/mL. Patients with a D-dimer of 1151-2300 ng/mL also had a higher risk of death (OR, 2.82; 95% CI, 1.94%-4.10%; P < .01) and combined adverse outcome (OR, 4.05; 95% CI, 2.96%-5.53%; P < .01). Those with D-dimer <230-1150 ng/mL did not have an increased risk of death or ICU requirement.

DISCUSSION

In this retrospective study of patients hospitalized with confirmed SARS-CoV-2 infection at a large multicenter single institution in New York City, we found that patients with active cancer had a higher risk of death independent of other risk factors. Patients with hematologic malignancy had the highest rate of death within this
group. Among patients with active cancer, receiving cancer-directed medical therapy within 3 months of hospital admission did not increase the risk of death, and there was no specific therapy type that led to increased risk of death. To our knowledge, this is the largest sample of patients with active cancer from a single center to date, and 1 of only 2 studies to incorporate D-dimer, an essential control to discern the independent effects of cancer and thrombosis.

Prior data have suggested worse outcomes form COVID-19 in patients with active cancer, but these studies have important limitations. Dai et al., 12 in a case-control study, found that patients with cancer had a higher risk of ICU requirement and need for mechanical ventilation and a nonsignificant trend toward increased death; however, 45% of the 105 patients with cancer had been diagnosed more than 1 year before hospital admission, and only 21 patients had received chemotherapy and/or immunotherapy. Other studies included small samples of patients with cancer, such as the analysis by Liang et al. 15 that evaluated 18 patients with cancer, the study by Zhang et al. 16 that included 28 of these patients, and the analysis by Yu et al. 19 that included 6 patients with active cancer. Studies with smaller numbers of patients with cancer, 19, 20 as well those with larger samples, 13, 21, 22 have reported rates of adverse outcomes in cohorts of patients with cancer without comparison to a control group and used population level outcome data for comparison. Kuderer et al., 14 in a prospective cohort of patients with cancer, found that those with active cancer had inferior outcomes compared to those with a history of cancer; however, these definitions appear to be subjective without prespecified definitions. Miyashita et al. 23 found that there was a higher point estimate, but no significant difference, of relative risk of death in patients with cancer, although this numerically higher risk appears to be driven by 3 deaths out of 53 patients with cancer under 51 years old.

We found that receiving cancer-directed medical therapy within 3 months of hospital admission was not associated with increased risk of death in multivariable analysis. This finding is consistent with a growing body of evidence. For example, Kuderer et al. 14 showed a trend that was not significant toward higher death rates in patients on active treatment. Lee et al. 28 found no increased rate of death in those receiving antineoplastic therapy within 1 month of COVID-19 diagnosis; these authors concluded that cancer therapy did not increase the risk of mortality from COVID-19. In the analysis by Jee et al there was no increased risk of severe outcomes in those receiving cancer therapy within 35 days of COVID-19 diagnosis. 17 These data, along with our findings, can begin to reassure patients and providers that medical cancer therapy does not significantly increase risk of serious outcomes from COVID-19.

Among patients with active cancer, those with a hematologic malignancy had the highest rate of death and combined adverse outcome, consistent with findings from multiple other studies. 12, 17, 21, 24 Risk of death was not significantly different in multivariable analysis for hematologic patients with cancer, although this model may be limited by small sample size. Recent data show that patients with hematologic malignancies hospitalized with COVID-19 had higher SARS-CoV-2 viral load compared to those with other cancer types, and higher viral load was a predictor for mortality. 25 Further research is needed to understand why these patients are at higher risk of death from COVID-19. The rate of ICU use in this group was disproportionately low, relative to the death rate, suggesting that escalation of care in this group specifically may have been avoided because of apparent futility or patient preference. It is possible this had the effect of artificially increasing the death rate in this group, because life-sustaining measures were not used that would prevent the death event from occurring before the data time cutoff.

D-dimer was the strongest predictor of death and ICU requirement. This is consistent with other work demonstrating the independent relationship of elevated D-dimer and serious outcomes from COVID-19 4, 26, 27 and highlights the role of micro- and macrovascular thrombosis in the pathogenesis of severe disease. 28-31 The most robust studies of patients with cancer with COVID-19 14, 17, 18 did not include D-dimer in their multivariable analyses. Our finding is relatively novel: to our knowledge, only Mehta et al. 24 have shown that elevated D-dimer independently predicts mortality in patients with cancer. Because active cancer was also independently associated with a higher risk of death, this suggests that active cancer plays a role in the pathogenesis of severe COVID-19 in distinct ways apart from thrombosis.

Among those hospitalized with COVID-19, we found that Black patients had a lower risk of death and combined adverse outcome compared to White patients. At the national level, there are higher rates of infections, hospitalization, and death in Black compared to White patients. 32 Higher rates of infection and death from COVID-19 in Black patients have been shown in both more and less affluent communities. 33 For hospitalized patients, this same signal has not emerged from
existing data. In a study of 3262 patients examined at a large medical center in New Orleans, a city where 75% of deaths from COVID-19 occur in Black residents, Price-Haywood et al. showed that Black race was independently associated with higher mortality. Petrilli et al. showed that Black patients had a similar rate of admission and lower risk of critical illness compared to Whites. Gold et al. found that although a higher percentage of Black patients were hospitalized, clinical outcomes were similar to White patients. Yehia et al. demonstrated that out of 11,210 patients with COVID-19 presenting at 92 hospitals across 12 states, there was no difference in in-hospital morality between White and Black patients. Taken together, these data suggest that Black patients are dying nationwide at a high rate relative to White counterparts but once hospitalized, there is not increased risk for an adverse outcome. Further study and resources are urgently needed to determine why disproportionately high rates of Black patients in the United States are infected with SARS-CoV-2 and dying from COVID-19.

Among the limitations of our study, selection bias of patients who were treated at this single institution may limit generalizability. However, NYU Langone is a single institution with 3 hospitals in demographically different areas of New York City and the NYC suburbs. Only those admitted to the hospital were included in our analysis, allowing for the possibility that outcomes among non-hospitalized patients with cancer could be better or worse than patients without cancer. Our analysis, nonetheless, likely captures the majority of critically ill, non-hospice-enrolled patients with cancer with COVID-19, because these patients continue to receive hospital-based care. An additional potential limitation of our study is that there is no established definition for active cancer. It is possible that our cutoff at 1 year included some patients who no longer had cancer. We hope, however, to create a new reference point for the definition of active cancer that can help to standardize future studies in this population. We also recognize that there may be unmeasured comorbid conditions that we did not include in our analysis that may influence outcomes. Finally, small sample size, particularly within the specific antineoplastic therapy groups, makes it difficult to draw conclusions regarding these patients.

In summary, we found that patients with active cancer had an increased risk of death from COVID-19 independent of age, peak D-dimer levels, and other covariates. Within this group, patients with hematologic malignancy had the highest rate of adverse outcome. Receiving cancer-directed therapy within the past 3 months did not increase the risk of death, and we found no differences in outcomes based on the types of antineoplastic therapy received. We also found that patients with cancer were more likely to die from COVID without entering the ICU, which likely reflects different goals of care among these 2 patient populations. Our finding that both D-dimer levels and active cancer independently predict worse outcomes suggests that cancer likely affects outcomes through mechanisms beyond just its prothrombotic effects.

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