LETTERS
https://doi.org/10.1038/s41591-020-0979-0

nature medicine

Determinants of COVID-19 disease severity in patients with cancer

Elizabeth V. Robilotti[1,2,3], N. Esther Babady[1,4], Peter A. Mead[1,3], Thierry Rolling[1], Rocio Perez-Johnston[5], Marilia Bernardes[1], Yael Bogler[1], Mario Caldararo[1], Cesar J. Figueroa[1,3], Michael S. Glickman[1,3], Alexa Joanow[1], Anna Kaltsas[1,3], Yeon Joo Lee[1,3], Anabella Lucca[1,6], Amanda Mariano[1], Sejal Morjaria[1,3], Tamara Nawar[1], Genovefa A. Papanicolaou[1,3], Jacqueline Predmore[1], Gil Redelman-Sidi[1,3], Elizabeth Schmidt[1], Susan K. Seo[1,3], Kent Sepkowitz[1,3], Monika K. Shah[1,3], Jedd D. Wolchok[3,7], Tobias M. Hohl[1,3], Ying Taur[1,3,8] and Mini Kamboj[1,2,3,8] ✉

As of 10 April 2020, New York State had 180,458 cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and 9,385 reported deaths. Patients with cancer comprised 8.4% of deceased individuals[1]. Population-based studies from China and Italy suggested a higher coronavirus disease 2019 (COVID-19) death rate in patients with cancer[2,3], although there is a knowledge gap as to which aspects of cancer and its treatment confer risk of severe COVID-19[4]. This information is critical to balance the competing safety considerations of reducing SARS-CoV-2 exposure and cancer treatment continuation. From 10 March to 7 April 2020, 423 cases of symptomatic COVID-19 were diagnosed at Memorial Sloan Kettering Cancer Center (from a total of 2,035 patients with cancer tested). Of these, 40% were hospitalized for COVID-19, 20% developed severe respiratory illness (including 9% who required mechanical ventilation) and 12% died within 30 d. Age older than 65 years and treatment with immune checkpoint inhibitors (ICIs) were predictors for hospitalization and severe disease, whereas receipt of chemotherapy and major surgery were not. Overall, COVID-19 in patients with cancer is marked by substantial rates of hospitalization and severe outcomes. The association observed between ICI and COVID-19 outcomes in our study will need further interrogation in tumor-specific cohorts.

The characterization of COVID-19 in patients with cancer remains limited in published studies and nationwide surveillance analyses. Reports from outside the United States raise the possibility that patients with cancer on active therapy have a higher risk of COVID-19-related severe events[4–7]. In the current study, we report on the epidemiology of COVID-19 experienced at our tertiary care cancer center during the height of incident cases in New York City and offer an analysis of risk factors for severe infection that is pertinent to populations of patients with cancer. From 10 March until 7 May 2020, SARS-CoV-2 was detected in 946 patients at Memorial Sloan Kettering Cancer Center. In comparison with New York City COVID-19 data, the age-stratified rates of hospitalization and death among 946 laboratory-confirmed cases from 10 March until 7 May 2020 are shown in Supplementary Fig. 1. Clinical characteristics were abstracted for a final study population consisting of 423 case patients diagnosed from 10 March until 7 April 2020, with a follow-up period of at least 30 d or death (Fig. 1).

Table 1 shows the demographic and clinical characteristics of the 423 cases. Most patients were adults over the age of 60 years (234, 56%). The most frequent cancer types included solid tumors such as breast (86, 20%), colorectal (37, 9%) and lung (35, 8%). Lymphoma was the most common hematologic malignancy (48, 11%). Over half of the cases were metastatic solid tumors (238, 56%). At least one of the specified comorbid conditions was present in 248 (59%) individuals: diabetes, hypertension, chronic kidney disease and cardiac disease. Of the presenting symptoms examined, fever (78%) and cough (82%) were the most common, whereas shortness of breath (44%) and diarrhea (26%) were less common but not rare. Chest radiographic findings were varied and are summarized in Supplementary Table 1. In the cohort, 168 (40%) of 423 patients were hospitalized, and 87 (20%) developed severe respiratory illness, including 47 (11%) who required high-flow oxygen and 40 (9%) who required mechanical ventilation. In the absence of approved therapy for COVID-19 during this period, several investigational treatments were administered, including hydroxychloroquine, azithromycin, remdesivir, tocilizumab, convalescent plasma and corticosteroids (Supplementary Table 2). Illness in seven pediatric patients was mild and without complications. The overall case fatality rate was 12% (51 of 423). Case fatality for hospital and intensive care unit (ICU) admittance were 24% (41 of 168) and 35% (17 of 48), respectively.

Next, we assessed risk factors for hospitalization and severe respiratory illness, the latter defined as the requirement for high-flow oxygen supplementation or mechanical ventilation. In the multivariate analysis, the following risk factors were independently associated with hospitalization: non-white race, hematologic malignancy, a composite measure of chronic lymphopenia and/or corticosteroid use and treatment with ICI therapy (Table 2). Age older than 65

[1]Infectious Diseases, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA. [2]Infection Control, Memorial Sloan Kettering Cancer Center, New York, NY, USA. [3]Department of Medicine, Joan and Sanford Weill Medical College of Cornell University, New York, NY, USA. [4]Clinical Microbiology Service, Department of Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA. [5]Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, USA. [6]Employee Health and Wellness Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA. [7]Human Oncology and Pathogenesis Program, Department of Medicine, Ludwig Center and Parker Institute for Cancer Immunotherapy at Memorial Sloan Kettering Cancer Center, New York, NY, USA. [8]These authors contributed equally: Ying Taur, Mini Kamboj. ✉e-mail: kambojm@mskcc.org

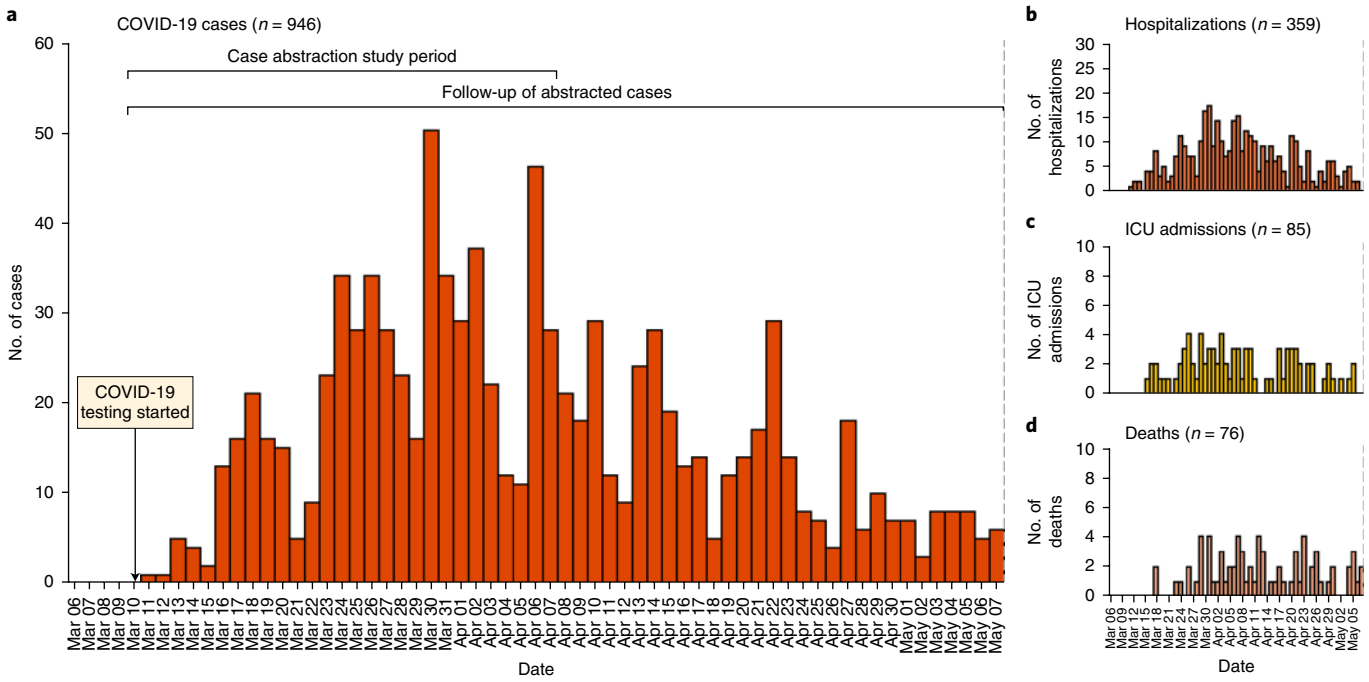

Fig. 1 | Number of SARS CoV-2-positive cases (a), hospitalizations (b), ICU admissions (c) and deaths (d) from 10 March to 7 May 2020. Case abstraction study period was from 10 March to 7 April 2020. Follow-up of abstracted cases was until 7 May 2020.

years, former or current smoker, hypertension and/or chronic kidney disease and history of cardiac disorder were significant predictors in univariate but not in multivariate analysis. The risk factors for severe respiratory illness due to COVID-19 were similar to those for hospitalization but not identical (Table 2). Severe respiratory illness was significantly more common with age older than 65 years. Of note, treatment with ICI also remained an independent predictor of severe respiratory illness. Age and ICI are illustrated by the Kaplan–Meier estimator for this endpoint in Supplementary Figure 2. Notably, metastatic disease, recent chemotherapy or major surgery within the previous 30 d did not show a significant association with either hospitalization or severe respiratory illness. Given the apparent association of ICI with COVID-19 severity, we explored this further by calculating stratum-specific rates of hospitalization and severe respiratory illness (Table 3). Because PD-1 blockade, a type of ICI, is commonly used to treat lung cancer, we examined the occurrence of outcomes by ICI use and underlying cancer (lung versus non-lung) and observed higher frequencies of hospitalization and severe respiratory illness in both ICI-treated groups. Further, we incorporated lung cancer as a covariate with immune checkpoint blockade in a post hoc analysis and found separate, distinct effects of lung cancer and ICI treatment on hospital admission and severe respiratory illness (Supplementary Table 3).

In two separate models, we evaluated the symptoms and laboratory markers as predictors of clinical outcomes of interest. Fever, cough, new onset dyspnea and diarrhea at the time of clinical presentation were associated with a higher risk of hospitalization and severe respiratory illness (Supplementary Table 4), but only dyspnea and diarrhea were independently predictive of severe outcomes. For laboratory biomarkers, evaluated longitudinally and coded as time-dependent predictors, procalcitonin, lymphopenia, interleukin-6, D-dimer and lactate dehydrogenase correlated with subsequent severe respiratory illness (Supplementary Table 5). Finally, we assessed the distribution of first cycle threshold (Ct) values at the time of laboratory diagnosis for both analytic targets of the SARS CoV-2 PCR assay and found no significant association between Ct values and severe respiratory illness (Supplementary Figure 3).

Patients with cancer are among those most vulnerable to severe illness from respiratory viral infections[8]. Our early experience with COVID-19 at a large tertiary care cancer center demonstrated severe disease in 20% of patients diagnosed with COVID-19, with an overall case fatality rate of 12%. Similarly to other studies in the general population, we found that age, non-white race, cardiac disease, hypertension and chronic kidney disease correlated with severe outcomes[9,10]. Contrary to early reports, receipt of chemotherapy within 30 d before COVID-19 diagnosis was not associated with a higher risk of complications[6]. Recent major surgery and metastatic disease also did not confer a significant risk of severe COVID-19. Treatment with ICI predicted both hospitalization and severe disease, although there was considerable heterogeneity in ICI-treated tumor types, and disease-specific factors could not be individually addressed. COVID-19 among children with cancer exhibited a milder course, consistent with early reports in children without cancer, but represented a small portion of the evaluated population (7, 2%).

A raw comparison with New York City cases during the same time period shows that patients with cancer at Memorial Sloan Kettering in the age range of 0–64 years were hospitalized at higher rates than the general New York City COVID-19 population (Supplementary Fig. 1). Crude death rates were similar across age groups at Memorial Sloan Kettering and citywide, except the elderly (≥75 years of age), in which we observed lower rates at Memorial Sloan Kettering. Beyond cancer, it is plausible that competing mortality risks, functional status and socioeconomic disparities contribute to the age-specific differences observed between the Memorial Sloan Kettering and citywide populations.

Very recently, other groups have reported their observations of COVID-19 in cancer-wide patient populations. These include the COVID-19 and Cancer Consortium (CCC19), a multi-institution registry including centers across the United States, Canada and Spain[11]; the United Kingdom Coronavirus Cancer Monitoring

Table 1 | Patient demographics and clinical characteristics ($n = 423$)

Characteristic	No. (%)
Age (years)	
<18	7 (2)
18–29	11 (3)
30–39	19 (4)
40–49	51 (12)
50–59	101 (24)
60–69	134 (32)
≥70	100 (24)
Sex	
Male	212 (50)
Female	211 (50)
Race	
White	263 (62)
Black	68 (16)
Asian	36 (9)
Other	56 (13)
Body mass index (BMI, kg/m^2)	
<18.5 (underweight)	13 (3)
18.5–24.9 (normal)	135 (32)
25.0–29.9 (overweight)	146 (35)
30.0–39.9 (obese)	109 (26)
≥40 (severely obese)	20 (5)
Smoking status	
Current	10 (2)
Former	157 (37)
Never	249 (59)
Unknown	7 (2)
Underlying cancer[a]	
Hematologic	
Leukemia	32 (8)
Lymphoma	48 (11)
Myeloma	22 (5)
Solid tumor	
Breast	86 (20)
Colorectal	37 (9)
Lung	35 (8)
Prostate	26 (6)
Other	137 (32)
Metastatic disease	238 (56)
Major surgery (30 d)[b]	31 (7)
Asthma	43 (10)
COPD	29 (7)
Diabetes	84 (20)
Cardiac dysfunction[c]	84 (20)
Chronic kidney disease	36 (9)
Hypertension	214 (51)
Systemic chemotherapy (within 30 d)[d]	191 (45)
Chronic corticosteroid[e]	66 (16)
Chronic lymphopenia[f]	9 (2)
ICI[g]	31 (7)
Symptoms at onset	
Fever	331 (78)
Shortness of breath	186 (44)
Cough	347 (82)
Diarrhea	109 (26)
Outcomes (30 d)	
Hospitalization status	
Not admitted	243 (57)
Admitted	168 (40)
Already hospitalized	12 (3)
Oxygen requirements[h]	
None[i]	279 (66)
Low-flow oxygen	57 (13)
High-flow oxygen[j]	47 (11)
Mechanical ventilation	40 (9)
Death	51 (12)

COPD, chronic obstructive pulmonary disease. [a] In patients with multiple malignancies, the most active and recently treated malignancy was used to define the underlying cancer. [b] Defined as any surgical procedure requiring general anesthesia. [c] Heart failure, myocardial infarction, valvular replacement or cardiomyopathy. [d] Systemic, parenteral chemotherapy. [e] Corticosteroids (equivalent of prednisone 20 mg or higher) for at least 10 d. [f] Absolute lymphocyte count <500 per microliter over five previous consecutive measurements. [g] ICI therapy consisted of the following, given within 90 d: pembrolizumab (18), nivolumab (5), atezolizumab (3), avelumab (1), durvalumab (1), ipilimumab (1), nivolumab + ipilimumab (1) and pembrolizumab followed by nivolumab (1). [h] Highest oxygen requirement over 30 d is shown. [i] Note: two patients had chronic tracheostomy because of prior medical issues but did not require supplemental oxygen during COVID-19 infection. [j] Includes the following oxygen delivery routes: non-rebreather mask, high-flow nasal oxygen and bilevel positive airway pressure.

Project (UKCCMP), a registry spanning the United Kingdom[12]; and two studies from large healthcare systems in New York City, one at Montefiore[13] and another at Mount Sinai[14].

Our reported case fatality rate of 12% was similar to those reported by CCC19 (13%) and Mount Sinai (11%). Interestingly, Montefiore and UKCCMP both reported a 28% case fatality rate in their populations of patients with cancer. The reasons for this finding are unclear, but these two studies might have had patients who were both older (both reported a median age of 69) and sicker. In the Montefiore study, most patients with cancer who died were residents of nursing homes or shelters (36%), not on active cancer therapy, and had prominent comorbid conditions (69% of the deceased had at least one other severe comorbid disease). It is possible that differences in the use of critical care resources might have contributed to variation in outcomes in patients with cancer. Socioeconomic and racial disparities described in study populations add further complexity to the interpretation of the relationship between cancer and COVID-19 outcomes. Similar to our findings, these studies found no increased risk with chemotherapy treatment or with metastatic disease.

A notable finding of our study is the association of checkpoint inhibitor immunotherapy as a risk factor for severe outcomes in patients treated with ICI, which was independent of age, cancer type, and other comorbid conditions. Although we observed more severe COVID-19 in ICI recipients with underlying lung cancer, patients

Table 2 | Predictors of hospitalization and severe respiratory illness for COVID-19

Variable	Univariate		Multivariate	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Predictors of hospitalization, by logistic regression (*n* = 411[a])				
Age (>65 years)	1.81 (1.20–2.72)	0.004	1.53 (0.96–2.43)	0.072
Sex (female)	0.89 (0.60–1.32)	0.575		
Race (non-white)	1.36 (0.91–2.04)	0.135	1.62 (1.05–2.51)	0.029
BMI (≥30 kg/m^2)	0.89 (0.58–1.36)	0.585		
Smoking (current/former)	1.60 (1.07–2.40)	0.022	1.37 (0.88–2.13)	0.169
Asthma/COPD	1.39 (0.81–2.37)	0.226	1.07 (0.59–1.92)	0.828
Cancer (non-metastatic solid)	1.00 (Ref)	-	1.00 (Ref)	
Cancer (metastatic solid)	0.89 (0.53–1.50)	0.647	0.76 (0.43–1.34)	0.338
Cancer (hematologic)	2.24 (1.25–4.06)	0.007	2.49 (1.35–4.67)	0.003
Major surgery (within 30 d)	1.24 (0.53–2.84)	0.612		
Diabetes	1.20 (0.73–1.96)	0.467		
Cardiac disorder	1.86 (1.13–3.07)	0.015	1.35 (0.77–2.36)	0.297
HTN/chronic kidney disease	1.84 (1.24–2.75)	0.003	1.51 (0.96–2.39)	0.077
Systemic chemotherapy (within 30 d)	1.04 (0.70–1.54)	0.845		
Chronic lymphopenia or corticosteroids	1.86 (1.11–3.15)	0.019	1.85 (1.06–3.24)	0.030
ICI	2.53 (1.18–5.67)	0.017	2.84 (1.24–6.72)	0.013
Predictors of severe respiratory illness, by Cox proportional hazard (*n* = 423)				
Variable	**Univariate**		**Multivariate**	
	HR (95% CI)	***P* value**	**HR (95% CI)**	***P* value**
Age (>65 years)	2.02 (1.33–3.08)	0.001	1.67 (1.07–2.60)	0.024
Sex (female)	1.04 (0.68–1.58)	0.859		
Race (non-white)	1.20 (0.79–1.84)	0.394		
BMI (≥30 kg/m^2)	1.01 (0.64–1.59)	0.965		
Smoking (current/former)	1.78 (1.17–2.72)	0.007	1.39 (0.89–2.17)	0.148
Asthma/COPD	1.63 (0.98–2.71)	0.059	1.24 (0.72–2.13)	0.436
Cancer (non-metastatic solid)	1.00 (Ref)	-	1.00 (Ref)	-
Cancer (metastatic solid)	0.87 (0.48–1.59)	0.658	0.75 (0.40–1.41)	0.371
Cancer (hematologic)	1.69 (0.92–3.10)	0.092	1.79 (0.97–3.32)	0.063
Major surgery (within 30 d)	1.31 (0.63–2.71)	0.464		
Diabetes	1.09 (0.65–1.83)	0.745		
Cardiac disorder	2.02 (1.28–3.19)	0.002	1.44 (0.88–2.37)	0.147
HTN/chronic kidney disease	1.68 (1.09–2.58)	0.020	1.18 (0.73–1.89)	0.505
Systemic chemotherapy (within 30 d)	1.19 (0.78–1.82)	0.407		
Chronic lymphopenia or corticosteroids	1.59 (0.97–2.59)	0.066	1.42 (0.86–2.34)	0.165
ICI	2.38 (1.29–4.38)	0.005	2.74 (1.37–5.46)	0.004

CI, confidence interval; COPD, chronic obstructive pulmonary disease; HTN, hypertension; HR, hazard ratio; OR, odds ratio. [a]12 patients were excluded from the hospitalization endpoint; they were already hospitalized for other reasons before testing positive for SARS-CoV-2 with RNA PCR testing.

with non-lung cancer who were treated with ICI also demonstrated severe outcomes (Table 3). A possible explanation for this observation is an exacerbation of ICI-related lung injury or ICI-triggered immune dysregulation by T cell hyperactivation, which in turn might facilitate acute respiratory distress syndrome, a dreaded COVID-19 complication[15,16]. The association of ICI treatment with other severe infections is influenced by the use of corticosteroids for control of immune-mediated adverse events[17]. In this study, only one of 31 patients treated with ICI received corticosteroid therapy before the severe illness endpoint, and none had immune-mediated pneumonitis at the time of COVID-19 diagnosis. Thus, corticosteroids and immune-mediated adverse events were highly unlikely to influence the association of ICI treatment with COVID-19 severity reported in this study. The findings in our current study should be interpreted with caution due to the limitations of our ICI data set in evaluating tumor-specific risk.

Other studies have examined cancer immunotherapy as a risk factor, and, unlike our study, these did not find an association with poor outcomes[12,13,18]. However, these studies had few patients on immunotherapy and examined death as an endpoint. In this work, we examined an endpoint based on significant oxygen needs, which was more common than death. A disease-specific

Table 3 | Stratum-specific point estimates of outcomes by ICI treatment and underlying solid cancer (lung versus non-lung) ($n = 275$)

Cancer	Endpoint	Non-ICI no./ total no. (%)	ICI[a] no./total no. (%)
Lung cancer—	Hospitalization[b]	12/23 (52)	10/12 (83)
	Severe respiratory illness	8/23 (35)	7/12 (58)
Other solid cancers[c]	Hospitalization[b]	82/216 (38)	8/17 (47)
	Severe respiratory illness	34/221 (15)	5/19 (26)

[a] Includes the following non-lung malignancies where ICI was given as therapy: breast (86), lymphoma (48), colorectal (37), prostate (26), kidney (11), genitourinary (9), skin (9), brain (6), uterus (5) and cervix (3). [b] For hospitalization endpoint, seven patients already admitted to the hospital at the time of COVID-19 diagnosis were excluded from calculation. [c] Within 90 d.

analysis of PD-1 blockade in patients with lung cancer from our institution with COVID-19, but treated at multiple hospitals, did not suggest a discernible association[18]. It is unclear whether that study had the statistical power to uncover the effect size reported in this manuscript. It is important to note that these two studies had distinct endpoints and small overlapping study populations. It is possible that patients with lung cancer or other malignancies have confounding effects from other factors that were not fully evaluable in our population. Specifically, in lung cancer, global consortium efforts are underway to understand the observed effect of COVID-19[19]. Until further evidence is available, it is prudent not to alter treatment decisions but to consider increased vigilance with SARS CoV-2 testing in patients initiating or continuing treatment with ICIs, irrespective of symptoms.

There are several other limitations to our study. First, we describe a single-center retrospective analysis in a heterogeneous group of patients with cancer. Second, the effectiveness of experimental therapeutics used for the management of COVID-19 was not explicitly evaluated. With the postponement of all non-essential cancer care during the study period, COVID-19 testing practices were targeted toward symptomatic patients who needed medical evaluation, potentially overestimating the overall severity of COVID-19. Finally, with our study population and design, we are unable to provide a reliable comparison of COVID-19-related outcomes between cancer and non-cancer populations. Such an analysis should be conducted in homogenous cohorts with adequate adjustment for comorbidities, inclusion of patients with cancer on active therapy, a similar testing strategy and the ability to measure the effects of interrupting oncologic care.

Our study has the distinct strength of reporting the most extensive single-institution experience in patients with cancer from the epicenter of the US outbreak. Although we had a high number of COVID-19-related hospitalizations, critical care resources were never in short supply. Further, we describe outcomes on COVID-19-associated respiratory compromise and include a full 30-d follow-up for reporting primary study outcomes and death rates.

In summary, the outcome of COVID-19 is worse among individuals with underlying conditions, including cancer. Our group of 423 patients with cancer had substantial rates of severe respiratory outcomes (20%) and death (12%) with COVID-19 [3,13,20–22]. In addition, as was seen with the SARS epidemic in 2003, the ongoing risk of contracting the illness and indirect consequences of treatment disruptions are expected to have a lasting effect on the health and safety of patients undergoing treatment for cancer[23]. Continuous preparedness is paramount as routine cancer care is resumed in the coming weeks and months amidst the unpredictable threat posed by COVID-19. Informed approaches with universal screening, aggressive testing and rigorous control measures will be essential for the safe ongoing delivery of oncologic care.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-020-0979-0.

Received: 30 April 2020; Accepted: 11 June 2020;
Published online: 24 June 2020

References

1. New York State Department of Health. COVID-19 Tracker (2020); https://covid19tracker.health.ny.gov/views/NYS-COVID19-Tracker/NYSDOHCOVID-19Tracker-Map.
2. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) (16–24 February 2020); https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf.
3. Onder, G., Rezza, G. & Brusaferro, S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* https://doi.org/10.1001/jama.2020.4683 (2020).
4. Yu, J., Ouyang, W., Chua, M. L. K. & Xie, C. SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncol.* https://doi.org/10.1001/jamaoncol.2020.0980 (2020).
5. Liang, W. et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol.* **21**, 335–337 (2020).
6. Dai, M.-Y., et al. Patients with cancer appear more vulnerable to SARS-CoV-2: a multi-center study during the COVID-19 outbreak. *Lancet* **10**, 783–791 (2020).
7. Garassino, M. C. TERAVOLT (Thoracic cancERs international coVid 19 cOLlaboraTion): first results of a global collaboration to address the impact of COVID-19 in patients with thoracic malignancies. Data presented at the 2020 virtual meeting of the American Association for Cancer Research, 27–28 April 2020.
8. Hijano, D. R., Maron, G. & Hayden, R. T. Respiratory viral infections in patients with cancer or undergoing hematopoietic cell transplant. *Front. Microbiol.* **9**, 3097 (2018).
9. Garg, S. K. L., Whitaker, M. & O'Halloran, A. et al. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 - COVID-NET, 14 states, March 1–30, 2020. *MMWR Morb. Mortal. Wkly. Rep.* **69**, 458–464 (2020).
10. CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 — United States, February 12–March 28, 2020. *MMWR Morb. Mort. Wkly. Rep.* **69**, 382–386 (2020).
11. Kuderer, N. M., et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* https://doi.org/10.1016/S0140-6736(20)31187-9 (2020).
12. Lee, L. Y. W., et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet* https://doi.org/10.1016/S0140-6736(20)31173-9 (2020).
13. Mehta, V., et al. Case fatality rate of cancer patients with COVID-19 in a New York Hospital system. *Cancer Discov.* https://doi.org/10.1158/2159-8290.CD-20-0516 (2020).
14. Miyashita, H., et al. Do patients with cancer have a poorer prognosis of COVID-19? An experience in New York City. *Ann. Oncol.* https://doi.org/10.1016/j.annonc.2020.04.006 (2020).
15. Xu, Z. et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir. Med.* **8**, 420–422 (2020).
16. Vardhana, S. A. & Wolchok, J. D. The many faces of the anti-COVID immune response. *J. Exp. Med.* **217**, e20200678 (2020).
17. Del Castillo, M. M. et al. The spectrum of serious infections among patients receiving immune checkpoint blockade for the treatment of melanoma. *Clin. Infect. Dis.* **63**, 1490–1493 (2016).
18. Luo, J., et al. Impact of PD-1 blockade on severity of COVID-19 in patients with lung cancers. *Cancer Discov.* https://doi.org/10.1158/2159-8290.CD-20-0596 (2020).
19. Whisenant, J. G., et al. TERAVOLT: Thoracic Cancers International COVID-19 Collaboration. *Cancer Cell* **37**, 742–745 (2020).
20. Guan, W. J. & Zhong, N. S. Clinical characteristics of Covid-19 in China. Reply. *N. Engl. J. Med.* **382**, 1861–1862 (2020).

21. CDC COVID-19 Response Team. Severe outcomes among patients with coronavirus disease 2019 (COVID-19) — United States, February 12–March 16, 2020. *MMWR Morb. Mortal. Wkly. Rep.* **69**, 343–346 (2020).
22. Wu, Z. & McGoogan, J. M. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* **323**, 1239–1242 (2020).
23. Hwang, S. W., Cheung, A. M., Moineddin, R. & Bell, C. M. Population mortality during the outbreak of severe acute respiratory syndrome in Toronto. *BMC Public Health* **7**, 93 (2007).

Methods

Memorial Sloan Kettering Cancer Center is a 514-bed tertiary cancer center in New York City with approximately 25,000 admissions and 173,000 patient days annually. Memorial Sloan Kettering maintains 19 ambulatory sites across New York State and New Jersey, with in excess of 1 million combined yearly outpatient visits. Approximately 23,000 individuals per year are under active treatment. During February and March 2020, a total of 14,067 individuals received parenteral chemotherapy at Memorial Sloan Kettering. Critical care resource allocation was determined by patient-expressed advanced directives and was not subject to shortage during the study period.

Study population. From 10 March until 7 April 2020, all consecutive adult and pediatric cases of symptomatic and laboratory-confirmed SARS-CoV-2 infection were included. The only exceptions were asymptomatic patients who were tested before surgery or before receipt of select myeloablative chemotherapy regimens ($n=30$). Thirty-three patients included in this study cohort were also included in Luo et al.[18]. Identification of case patients and their medical background and clinical course during COVID-19 illness were abstracted from electronic medical records. The Memorial Sloan Kettering Cancer Center Institutional Review Board granted a Health Insurance Portability and Accountability Act waiver of authorization to conduct this study.

Laboratory methods. Nasopharyngeal swab samples were collected using flocked swabs (Copan Diagnostics) and placed in viral transport media. SARS-CoV-2 RNA was detected using the Centers for Disease Control and Prevention protocol targeting two regions of the nucleocapsid gene (N1 and N2), with the following modifications: nucleic acids were extracted from specimens using the NUCLISENS EasyMag (bioMérieux) following an off-board, pre-lysis step[24,25]. Real-time reverse transcription PCR was performed on the ABI 7500 Fast (Applied Biosystems) in a final reaction volume of 20 µl, including 5 µl of extracted nucleic acids. Samples were reported as positive if both the N1 and N2 targets were detected.

Statistical analysis. We first assessed patient risk factors for hospitalization as part of the management for COVID-19, using logistic regression. Patients with nosocomial infection ($n=12$) were excluded from this analysis. Next, we assessed risk factors for severe respiratory illness, defined as the requirement for high-flow oxygen supplementation or mechanical ventilation. Cause-specific Cox proportional hazard modeling was applied for this. Analysis time began at the time of COVID-19 diagnosis and was censored at 30 d after diagnosis or death, in the absence of the endpoint beforehand. The proportional hazards assumption was verified by examining Schoenfeld residuals for all predictors.

For the outcomes described above, the following clinical variables were assessed: age, sex, race, diabetes, hypertension cardiovascular disease (myocardial infarction, heart failure, heart valve replacement or cardiomyopathy), chronic obstructive pulmonary disease, asthma, chronic kidney disease, obesity (body mass index $\geq$30 kg/m^2), smoking status, underlying cancer, major surgery (surgery requiring general anesthesia), chronic lymphopenia (absolute lymphocyte count <500 per microliter for at least five measurements, immediately preceding positive COVID-19 PCR test), chronic corticosteroid use (prednisone of 20 mg per day or equivalent, for at least 10 d), systemic parenteral chemotherapy within 30 d, major surgery within 30 d and treatment with an ICI within 90 d. In addition to past underlying conditions, new symptoms at the time of testing were assessed: fever, cough, shortness of breath and diarrhea.

For comparison with New York City data, we derived cases, hospitalization rates and deaths for specified age strata from publicly available data sources maintained by the New York City Department of Health (https://www1.nyc.gov/site/doh/covid/covid-19-data.page) and compared frequencies with Memorial Sloan Kettering counts for the same age groups. Additional evaluation of risk factors was done for symptoms present at the time of diagnosis (fever, cough, dyspnea and diarrhea) and monitoring of clinical laboratory biomarkers (procalcitonin, absolute lymphopenia, interleukin-6, D-dimer and lactate dehydrogenase). The laboratory biomarkers were monitored over the course of analysis time and encoded as a time-dependent predictor in the time-to-event model.

For both outcomes, predictors were first analyzed separately in a univariate analysis. Predictors with a univariate P value of less than 0.25 were incorporated into a multivariate model[26,27]. The Kaplan–Meier estimator was calculated and shown for the cumulative probability of severe respiratory illness, for independent predictors. Details of sample population and statistical tests are provided in the Life Sciences Reporting Summary. All study analyses were performed using R version 3.5 (R Development Core Team).

Reporting Summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability

All data generated or analyzed during this study are included in this published article (and its supplementary information files).

References

24. Centers for Disease Control and Prevention. Real-Time RT–PCR Panel for Detection 2019-Novel Coronavirus (2020); https://www.fda.gov/media/134922/download.
25. Centers for Disease Control and Prevention. 2019-Novel Coronavirus (2019-nCoV) Real-time rRT–PCR Panel Primers and Probes (2020); https://www.cdc.gov/coronavirus/2019-ncov/downloads/rt-pcr-panel-primer-probes.pdf.
26. Hosmer, D. W. & Lemeshow, S. *Applied Survival Analysis: Regression Modeling of Time-to-Event Data* (Wiley, 1999).
27. Hosmer, D. W. & Lemeshow, S. *Applied Logistic Regression* (Wiley, 2000).

Acknowledgements

This study was supported by the Memorial Sloan Kettering Cancer Center core grant (P30 CA008748), the Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Diseases Award (to T.M.H.), the Ludwig Collaborative and Swim Across America Laboratory (to J.D.W.), the Parker Institute for Cancer Immunotherapy (to J.D.W.), the Memorial Sloan Kettering Cancer Center Department of Medicine and Weill Cornell Medicine.

Author contributions

E.V.R., M.K., Y.T. and M.S.G. made substantial contributions to the study conception and design. Y.T., E.V.R., P.A.M., T.R. and M.K. made substantial contributions to the acquisition of data. Y.T. and T.R. conducted statistical analysis. T.M.H., M.S.G., M.K., Y.T. and E.V.R. made substantial contributions to the interpretation of data. M.K. drafted the first version of the manuscript. E.V.R., N.E.B., P.A.M., T.R, R.P.-J., M.B., Y.B., M.C., C.J.F., M.S.G., A.J., A.K., Y.J.L., A.L., A.M., S.M., T.N., G.A.P., J.P., G.R.-S., E.S., S.K.S., K.S., M.K.S., J.D.W., T.M.H., Y.T. and M.K. contributed to critical revisions and approved the final version of the manuscript. M.K., Y.T., T.M.H. and E.V.R. take responsibility for the integrity of the work.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information is available for this paper at https://doi.org/10.1038/s41591-020-0979-0.

Correspondence and requests for materials should be addressed to M.K.

Peer review information Javier Carmona was the primary editor on this article and managed its editorial process and peer review in collaboration with the rest of the editorial team.

nature research

Corresponding author(s): Mini Kamboj, MD

Last updated by author(s): Jun 2, 2020

Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data was collected from the electronic health record and laboratory informatics system through manual extraction and automated processing.
Data analysis	All study analyses were performed on R version 3.5 (R Development Core Team, Vienna, Austria)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Clinical data subject to HIPPA restrictions; public data accessed for NYS https://covid19tracker.health.ny.gov/views/NYS-COVID19-Tracker/NYSDOHCOVID-369 19Tracker-Map

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No sample size was calculated because this was a retrospective study
Data exclusions	Outpatients with missing clinical information and asymptomatic individuals tested as part of diagnostic screening protocols before surgery or myeloablative chemotherapy were excluded.
Replication	Non-experimental study design in humans. Replication not feasible
Randomization	No randomization was performed on a retrospective cohort
Blinding	Data and sample collection of clinical specimens occurred before the conception of this study and was therefore blinded.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☐	☒ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Human research participants

Policy information about studies involving human research participants

Population characteristics	Study population was patients with cancer receiving care at our institution from March 10 through May 7th 2020.
Recruitment	This was a retrospective clinical study.
Ethics oversight	The MSKCC Institutional Review Board granted a HIPAA waiver of authorization to conduct the study.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	Not a clinical trial
Study protocol	Not a clinical trial
Data collection	Clinical parameters were extracted from the institutional database and the electronic health record.
Outcomes	Among COVID-19 patients outcomes included hospitalization and severe COVID-19 illness, defined as the need for high-flow oxygen or ventilator support.