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Short communication

Cancer, transplant, and immunocompromising conditions were not significantly associated with severe illness or death in hospitalized COVID-19 patients

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ABSTRACT

Objective: Patients with cancer, transplant, and other immunocompromising conditions are at uncertain risk of severe COVID-19 illness. This study aimed to clarify whether patients with immunocompromising conditions were more likely to develop severe COVID-19 illness in a single urban academic medical center.
Methods: A retrospective chart review and electronic data extraction of the first 401 patients at the University of Chicago Hospitals with SARS-CoV-2 infection was performed. Patients met criteria for severe COVID-19 illness if they required ICU level care, high flow oxygen, positive pressure support, helmet non-invasive ventilation, mechanical ventilation, or ECMO, developed ARDS, or died.
Results: The mean age was 60 years, 52% were women, 90% were African American, and mortality at 30 days post discharge was 13%. Severe COVID-19 illness was found in 168 (40%) patients. Of the 56 patients with past or current cancer, 25 (45%) had severe illness (p=0.76). Of the 55 patients with other immunocompromised conditions, 24 (44%) had severe illness (p=0.89) After controlling for age, sex, and race, neither cancer (p=0.73) nor immunocompromised conditions (p=0.64) were associated with severe illness.
Conclusion: No association was found between severe COVID-19 illness and cancer, transplant, and other immunocompromising conditions in a cohort of mostly African American patients.

1. Background

As of February 12, 2021, COVID-19 is the leading cause of death in the United States [1]. Higher rates of morbidity and mortality have been found in men, and in patients with advanced age, hypertension, diabetes, chronic kidney disease (CKD), obesity, and chronic respiratory diseases [2]. Patients with cancer, transplantation, and other immunocompromising conditions have also been considered to be at higher risk for severe illness [3-6]. Conversely, it has been theorized that immunosuppression could protect patients from the cytokine release syndrome described in COVID-19 illness [7]. We aimed to clarify whether patients with immunocompromising conditions were more likely to develop severe COVID-19 illness in a single urban academic medical center.

2. Materials and methods

We conducted a retrospective chart review and electronic data extraction of the first 401 patients admitted to the University of Chicago Medical Center (UCMC) with a positive SARS-CoV-2 test from March 13, 2020 to April 18, 2020. All SARS-CoV-2 cases were confirmed from nasopharyngeal swab specimens using the Roche® cobas 6800 assay and the Xpert® Xpress SARS-CoV-2 assay.

Patients were defined as having a history of cancer if they had any past, current, solid, or hematologic cancer, and as in an immunocompromised state if they had a history of stem cell or solid organ transplant

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(SOT), HIV, chemotherapy within the past three months, or any autoimmune condition. Immunosuppressive therapies or steroids (≥ 10mg/day of prednisone) at admission were also defined as immunocompromising conditions. Patients met criteria for severe COVID-19 illness if they required ICU level care, high flow oxygen, positive pressure support, helmet non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation, developed acute respiratory distress syndrome, or died during admission.

Multivariate logistic regression, chi-squared test, and t-test were performed between demographics, co-morbidities, and the development of severe COVID-19 illness, and controlled for age, race, and gender. Significance was defined as two-sided p-value<0.05. Analyses utilized R version 3.6.3 (R Core Team).

This study received a formal Determination of Quality Improvement status according to UCMC institutional policy. As such, this initiative was not considered human subjects research and was therefore not reviewed by the institutional review board.

3. Results

Of the first 401 patients admitted to UCMC with COVID-19, 360 (90%) were African American, 209 (52%) were women, and 299 (75%) were residents of South Side Chicago. Mean age was 60 years (SD 17.3 years) and 128 (31%) patients were older than 70 years of age (Table 1). Of 401 patients, 168 (40%) had severe illness (Table 2) and 64 (50%) patients over age 70 had severe illness. In-hospital treatments included hydroxychloroquine with or without lopinavir (n=136, 34%), remdesivir (n=122, 31%), corticosteroids (n=26, 6%), and tocilizumab (n=83, 21%). Overall, 68 (17%) patients were intubated. At 30 days post-discharge, there were 51 (13%) deaths, including 4 (2%) patients with moderate illness. Of 122 patients who received remdesivir, 10 (8%) died, compared to 41 (15%) who died out of 275 patients who did not receive remdesivir (P=0.09).

Of the 401 patients, 56 (14%) had a past or current diagnosis of cancer, and 55 (14%) were immunocompromised due to transplantation (n=13, 3%), HIV (n=8, 2%), or other conditions (Table 2). All HIV patients were on anti-retroviral therapy with an undetectable viral load and CD4 cell counts >200 cells/ml. The immunosuppressive agents used were mycophenolate (n=2), tacrolimus (n=2), cyclosporine (n=1), and azathioprine (n=1). Of the 56 patients with past or current cancer, 31 (55%) had moderate COVID-19 illness and 25 (45%) had severe illness (p=0.76). Of the 55 patients with other immunocompromised conditions, 31 (56%) had moderate COVID-19 illness and 24 (44%) had severe illness (p=0.89) (Table 2). After controlling for age, sex, and race, neither cancer (p=0.73) nor immunocompromised conditions (p=0.64) were associated with severe illness (Table 2).

Following univariate analysis, age (p=0.002), hypertension (p=0.004), diabetes (p=0.02), CKD (p=0.003), and congestive heart failure (p=0.04) were all associated with severe COVID-19 illness (Table 2). After controlling for age, sex, and race, diabetes was the only comorbidity that was significantly associated with severe illness (p=0.03), and hypertension and CKD approached significance (p=0.05 and 0.07, respectively) (Table 2).

Table 1
Demographic characteristics of first 401 patients admitted to University of Chicago Hospital with COVID-19.

Demographic characteristic	Number of patients (%)
Age	
<18	3 (1)
18-29	15 (4)
30-39	35 (9)
40-49	49 (12)
50-59	84 (21)
60-69	88 (22)
70-79	69 (17)
80+	58 (14)
Female sex	209 (52)
Race	
Asian/Middle-Eastern/Indian	4 (1)
African-American	360 (90)
More than once race	7 (2)
Unknown	5 (1)
White	25 (6)
Ethnicity	
Hispanic/Latino	9 (2)
Not Hispanic/Latino	388 (97)
Unknown	4 (1)
Zip code located on Chicago's South Side[a]	299 (75)

[a] Includes zip codes 60637,60615,60653,60649,60617, 60619, 60620,60628,60621, 60636,60629, 60638, 60632,60609, and 60632.

Table 2
Associations between co-morbid conditions and severe COVID-19 illness.

Co-morbid Condition	All Patients, n (%) 401	Moderate Illness, n (%) 233 (60)	Severe Illness, n (%) 168 (40)	p-value[a]	Adjusted p-value[b]
HTN	276 (69)	147 (63)	129 (77)	0.004	0.05
DM	152 (38)	76 (33)	76 (45)	0.02	0.03
Class I or II obesity	133 (34)	75 (33)	58 (25)	0.74	0.39
Class III obesity	69 (17)	41 (18)	28 (17)	0.89	0.14
CKD	96 (24)	43 (18)	53 (32)	0.003	0.07
CHF	65 (16)	30 (13)	35 (21)	0.04	0.11
Cancer	56 (14)	31 (13)	25 (15)	0.76	0.73
Immunocompromised	55 (14)	31 (13)	24 (14)	0.89	0.64
Autoimmune condition[c]	27 (7)	15 (6)	12 (7)	0.93	
Immunosuppressive therapy[d]	21 (5)	11 (5)	10 (6)	0.74	
Steroid use[e]	17 (4)	7 (3)	10 (6)	0.23	
Recent chemotherapy	13 (4)	7 (3)	6 (4)	1.0	
SOT recipient	9 (2)	3 (1)	6 (4)	0.17	
HIV	8 (2)	7 (3)	1 (1)	0.15	
Stem cell transplant	4 (1)	2 (1)	2 (1)	1.0	
CAD	53 (13)	27 (12)	26 (16)	0.33	0.99
Liver Disease	16 (4)	10 (4)	6 (4)	0.92	
Hemoglobinopathy	5 (1)	3 (1)	2 (1)	1.0	

[a] P-values calculated using chi-squared test.
[b] Adjusted p-values calculated by controlling for age, sex, and race.
[c] Autoimmune conditions included but were not limited to multiple sclerosis, collagen vascular diseases, systemic lupus erythematous, rheumatoid arthritis, multiple sclerosis, Sjojgren's syndrome, inflammatory bowel disease, celiac disease, ankylosing spondylitis, psoriatic arthritis, dermatomyositis, scleroderma, and polymyalgia rheumatica.
[d] Immunosuppressive therapies included methotrexate, azathioprine, mTOR inhibitors (tacrolimus, serolimus, everolimus), cyclosporine, mycophenolate, and immunosuppressive monoclonal antibodies.
[e] Included use of ≥10mg prednisone or the equivalent corticosteroid.Abbreviations: HTN = hypertension; DM = diabetes mellitus; CKD = chronic kidney disease; CHF = congestive heart failure; SOT = solid organ transplant; CAD = coronary artery disease

4. Discussion

In a predominately African American population of hospitalized patients with COVID-19, we found that 111 (28%) were immunocompromised hosts due to cancer, transplantation, HIV, or other immunocompromised states, and these conditions were not significantly associated with severe COVID-19 illness or death. However, 49 out of 111 immunocompromised patients developed severe illness or died, highlighting the severity of COVID-19 outcomes among all hospitalized patients. Our findings suggest that if cancer or other immunocompromising conditions do predict a greater risk of severe COVID-19 illness, it is not likely to be a very large effect size. As has been reported in many COVID-19 cohorts, we found a high mean age (60 years),

a higher risk of severe disease among patients >70, and high rates of co-morbidities such as hypertension (69%), diabetes (38%), obesity (36%), and CKD (24%) [8,9].

The intubation rate of 17% and the overall 30-day mortality rate of 13% are lower than hospital cohorts in New York City and Detroit, which reported mortality rates of 20-21% in the first several thousand patients with COVID-19 admitted in Spring 2020 [8, 9]. The use of remdesivir in almost one third of patients, as well as positive pressure devices, high flow oxygen, and negative pressure ICU units may have contributed to these differences [10].

The Chicago Health Department has reported a three-fold greater risk of mortality from COVID-19 among African American patients compared to whites [11]. Our findings argue against a biological cause of the greater mortality among African American individuals in Chicago and suggest that a lower COVID-19 mortality rate may be achievable in such patients in the United States with access to effective treatment and supportive care.

Previous studies have examined the risk of severe COVID-19 illness in patients with immunocompromising conditions with mixed results. In a study of 10,926 COVID-19-related deaths, those with a hematologic malignancy in the last five years had an at least 2.5-fold increased risk of mortality compared to patients without cancer, but this decreased slightly after five years [5]. For non-hematologic cancers, hazard ratios were smaller and increased risks were associated mainly with recent diagnoses in comparison to patients without cancer [5].

One large study of SOT recipients with COVID-19 in New York City found higher rates of severe disease and mortality compared to non-transplant patients with COVID-19 in China [6]. However, other studies have shown that SOT recipients early in their post-transplant course are not at increased risk [12, 13].

In the largest multi-center study to date, there was a significantly greater risk of COVID-19-related hospitalizations in people living with HIV (PLHIV) (21%), SOT recipients (55%), and both conditions (69%) after adjustment for age and co-morbidities ($P \leq 0.03$). They also found a 50% greater risk of mechanical ventilation in PLHIV, a two-fold greater risk in SOT, and a three-fold greater risk with both conditions [14].

Our limitations include the single study site with a modest case number, and the broad, inclusive definition of immunocompromised states (justified by the novelty of the pandemic and the need to cast a wide net for more severe disease).

In sum, this study found no association between severe COVID-19 illness and death in patients with cancer, transplant, and other immunocompromising conditions in a cohort of mostly African American patients in Chicago during Spring 2020. This study contributes further to the understanding of the course of COVID-19 among a heterogeneous group of immunosuppressed patients and is the first to explore disease severity among a predominantly African American patient population.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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