Original Article

Mortality and prognostic factors in hospitalized COVID-19 patients with cancer: an analysis from a large healthcare system in the United States

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Background: To evaluate clinical outcomes in patients with malignancy who are SARS-CoV-2 (COVID-19) positive and investigate if factors such as age, gender, and race contribute to COVID-19 mortality in patients with malignancy.

Methods: Retrospective data was gathered from Memorial Healthcare System of COVID-19 patients hospitalized from March 1, 2020 to January 18, 2021. Active malignancy was defined as either receiving antineoplastic therapy or being under surveillance. The primary endpoint was in-hospital mortality. Descriptive statistics were used to summarize the characteristics and outcomes. Univariate and multivariate logistic analysis were performed to define baseline clinical characteristics potentially associated with mortality in cancer patients with COVID-19.

Results: A total of 4,870 COVID-19 patients were enrolled in the study, and 265 of those patients had a diagnosis of active malignancy. The study population was diverse which included non-Hispanic whites (NHW) 816 (16.8%), Hispanics 2,271 (46.6%) and Blacks 1,534 (31.5%). Of the cancer patients, 24.1% were NHW, 43% were Hispanic and 28.7% were Black. Amongst the races, 37.5% of in-hospital mortalities were NHW, while 18.4% were Hispanics and 19.7% were Black. The in-hospital mortalities amongst the two malignancy types, solid and hematological, accounted for 24.6% and 23.5% of deaths and they were not found to be statistically significant (P=0.845). After adjustments for age, gender and race were made, cancer was independently associated with an increased in-hospital mortality, with an adjusted odds ratio of 1.48 [95% confidence interval (CI): 1.08–2.01]. Increased age and elevated serum levels of creatinine and C-reactive protein (CRP) were associated with an increased risk of death in cancer patients with COVID-19.

Conclusions: COVID-19 in patients with cancer had poorer outcomes in comparison to those who were cancer-free. Both hematological and solid malignancies had similar in-hospital mortality rates. The highest in-hospital mortalities of cancer patients with COVID-19 were non-Hispanic whites in-comparison to Hispanics with the least. Age, elevated levels of creatinine and CRP were independently associated with increased risk of death in cancer patients hospitalized with COVID-19. The findings indicate the need for close surveillance and monitoring of these patients as they are more likely to have higher risk of death from COVID-19.

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Introduction

Coronavirus-19 (COVID-19), a novel coronavirus and culprit of the global pandemic, posed a challenge on healthcare systems around the world. As of now, there have been over 45 million verified COVID-19 cases globally, with 730,000 deaths in the United States (1). Patients with chronic co-morbidities including cancer were at elevated risk for severe COVID-19 (1) and robust data analysis has shown that patients with cancer who develop COVID-19 have increased morbidity and mortality (2,3). The global pandemic has increased the health disparities gap between different races/ethnic groups affecting disproportionately Black, Hispanic and Native American minorities (4). Black and Hispanic cancer patients were more likely to develop COVID-19 and had worse outcomes than Non-Hispanic whites (NHW) (5,6). Additionally, older frail adults are more likely to have increased morbidity and mortality from COVID-19 complications in comparison to the general population. In the United States, 8 out of 10 COVID-19 deaths were in adults aged greater than 65 years (7). Patients with cancer who are actively receiving treatment or in remission under active surveillance are at an increased risk for severe complications including mortality. This Florida-based institutional study enrolled patients with and without cancer who were hospitalized with laboratory-confirmed COVID-19. The primary objective was to evaluate clinical outcomes such as in-hospital mortality in COVID-19 patients with cancer. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-1667/rc).

Methods

Study population

Memorial Health Care System (MHS) is the third-largest public health care system in the US with six hospitals located in South Florida. In this cohort study, retrospective data was collected of adults patients (aged 18 years or older) with COVID-19 who were admitted consecutively to the health system between March 17, 2020, and January 18, 2021. Patients with presumptive COVID-19 who did not have a laboratory-confirmed SARS-CoV-2 infection were excluded. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by The Institutional Review Board of MHS (protocol No. MHS 2021.008). Written informed consent was waived as this was a retrospective analysis of existing data.

Data collection and outcomes

All clinical data were extracted from patients' electronic medical records. Patients' baseline characteristics were recorded and included age, gender, race and ethnicity, and underlying conditions such as obesity (defined as a calculated body mass index ≥30 kg/m^2), smoking history, comorbidities, and history of malignancy (solid or hematologic). Laboratory data were collected within 24 hours of hospitalization, including neutrophilia, lymphocyte counts, and serum levels of C-reactive protein (CRP), D-dimers, interleukin-6 (IL-6), lactate dehydrogenase (LDH), creatinine, aspartate aminotransferase (AST), and alanine aminotransferase (ALT). All patients in the study were followed from admission to discharge/death from the hospital. The primary endpoint was in-hospital mortality in cancer patients who tested positive for COVID-19. We compared the mortality rates in COVID-19 patients with a cancer history to those without. Additionally, we evaluated potential risk factors for in-hospital mortality in cancer patients with COVID-19.

Statistical analysis

Descriptive statistics were used to summarize characteristics and outcomes from the study population. Continuous variables were presented using median and interquartile range (IQR) or mean ± standard deviation (SD), whereas categorical variables were presented using absolute number and frequencies (%). Comparisons between groups was

performed using independent sample *t*-tests, Mann-Whitney U-tests, χ^2 or Fischer's exact tests, as appropriate. Logistic regression analyses were performed to estimate the odds ratios (ORs) and adjusted ORs and their 95% confidence intervals (CIs) for association of cancer with COVID-19 in-hospital mortality adjusting for age, sex, and ethnicity. Univariate and multivariable logistic analysis were performed to define baseline clinical characteristics potentially associated with mortality in cancer patients with COVID-19. The following variables were evaluated in the univariate logistic regression: age, sex, race/ethnicity, hypertension, diabetes, chronic obstructive pulmonary disease, chronic kidney disease, coronary artery disease, obesity, smoking, and laboratory tests (neutrophilia, lymphopenia, D-dimer, creatinine, C-reactive protein, AST, and ALT). Variables with a P<0.05 in the univariate logistic regression were included in multivariate analysis. No imputation method was used for missing data. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS version 27; Chicago, IL, USA) and the GraphPad Prism (version 9.0, San Diego, CA, USA). A P value of less than 0.05 was considered statistically significant.

Results

A total of 4,870 patients with COVID-19 were included in the study cohort, of which 265 (5.4%) had a history of cancer (*Table 1*). Most common represented cancers included hematologic (26.0%), breast (16.2%), prostate (11.3%), gastrointestinal (GI) (9.8%) and lung (8.3%) respectively.

As shown in *Table 1*, the study population was diverse, with 2,271 (46.6%) of Hispanics, 816 (16.8%) of NHW and 1,534 (31.5%) of Blacks. Amongst the cancer patients, there were 24.1% NHW, 28.7% Blacks and 43% Hispanics. Patients with cancer were older and had more comorbidities including hypertension, chronic obstructive pulmonary disease (COPD), coronary heart disease, and chronic kidney disease (CKD), compared to patients without cancer (*Table 1*). Furthermore, smoking and the use of angiotensinconverting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) were more common in patients with cancer (*Table 1*). Lab findings revealed that COVID-19 patients with cancer had decreased lymphocytes and elevated levels of ALT compared to those without cancer (*Table 1*).

The overall mortality rate of COVID-19 cancer patients was significantly higher than those without cancer (23.8% versus 11.4%, P<0.001), with an odds ratio (OR) of 2.35 (95% CI: 1.74–3.16) (*Figure 1*). The mortality in COVID-19 cancer patients was significantly associated with older age and male gender, with the highest mortality of 37.5% for NHW and the least of 18.4% for Hispanics, respectively (*Figure 2*). After adjusting for age, gender, and race, cancer was an independent risk factor for in-hospital mortality amongst COVID-19 patients, with an adjusted OR of 1.48 (95% CI: 1.08–2.01; P=0.014) (*Figure 1*).

Among patients with cancer, hematologic malignancies accounted for 24.6% of COVID-19-related cancer deaths, in comparison to solid malignancies that accounted for 23.5%, but difference was found to be not statistically significant (P=0.845) (*Figure 3*).

Table 2 shows the comparison of comorbidities between patients who died and those who survived COVID-19 hospitalization. In COVID-19 patients without malignancy, those who died in the hospital (n=526) were more likely to have more comorbidities including diabetes, hypertension, COPD, coronary heart disease, CKD, obesity, smoking, and the use of ACEI and ARBs than those who survived COVID-19 hospitalization. However, the COVID-19 patients with malignancy who died in the hospital (n=63)

Table 1 Study cohort demographic, clinical, and lab findings of patients hospitalized with COVID-19

Variable	Total (n=4,870, %)	With cancer (n=265, %)	Without cancer (n=4,605, %)	P value
Age (years), median [IQR]	61 [47–73]	71 [62–81]	60 [46–72]	<0.001
Age group, years				<0.001
<50	1,430 (29.4)	23 (8.7)	1,407 (30.5)	
50–65	1,488 (30.5)	55 (20.8)	1,433 (31.2)	
>65	1,952 (40.1)	187 (70.5)	1,765 (38.3)	

Table 1 (*continued*)

Table 1 (*continued*)

Variable	Total (n=4,870, %)	With cancer (n=265, %)	Without cancer (n=4,605, %)	P value
Male	2,480 (50.9)	130 (49.1)	2,350 (51.1)	0.532
Race/Ethnic group				0.005
White	816 (16.8)	64 (24.1)	752 (16.3)	
Black	1,534 (31.5)	76 (28.7)	1,458 (31.7)	
Hispanic or Latino	2,271 (46.6)	114 (43.0)	2,157 (46.8)	
Other	249 (5.1)	11 (4.2)	238 (5.2)	
Comorbidity				
Hypertension	3,174 (65.1)	210 (79.2)	2,964 (64.4)	<0.001
Diabetes	1,947 (39.9)	118 (44.5)	1,829 (39.7)	0.12
COPD	400 (8.2)	50 (18.8)	350 (7.6)	<0.001
Coronary heart disease	741 (15.2)	77 (29.1)	664 (14.4)	<0.001
CKD	727 (14.9)	82 (30.9)	645 (14.0)	<0.001
Obesity	1,726 (35.4)	93 (35.1)	1,633 (35.5)	0.903
Smoking	1,167 (23.9)	92 (34.7)	1,075 (23.3)	<0.001
ACEIs	1,561 (32.1)	125 (47.2)	1,436 (31.2)	<0.001
ARBs	1,201 (24.7)	83 (31.3)	1,118 (24.3)	0.009
WBC ($\times 10^9$/L), median (IQR)	7.4 (5.4–10.3)	7.1 (5.1–10.2)	7.4 (5.3–10.3)	0.483
Missing data	3 (0.1)	0 (0)	3 (0.1)	>0.999
Lymphocyte ($\times 10^9$/L), median (IQR)	1.1 (0.7–1.5)	0.9 (0.6–1.4)	1.1 (0.7–1.5)	0.005
Missing data	325 (6.8)	27 (10.2)	298 (6.5)	0.018
D-dimer (>30 ng/mL), n (%)	80 (1.6)	5 (1.9)	75 (1.6)	0.747
Missing data	4,208 (86.4)	49 (18.5)	4,159 (90.3)	<0.001
CRP (mg/L), median (IQR)	6.6 (2.8–12.1)	6.6 (2.7–12.1)	6.6 (2.9–12.1)	0.900
Data missing	673 (13.8)	32 (12.1)	641 (13.9)	0.397
LDH (U/L), median [IQR]	319 [243–433]	305 [238–424]	320 [244–434]	0.253
Missing data	1,156 (23.7)	58 (21.9)	1,098 (23.8)	0.467
IL-6 (pg/mL), median (IQR)	36.1 (13.1–87.0)	25.9 (13.1–78.2)	36.4 (13.2–88.4)	0.602
Missing data	3,957 (81.3)	210 (79.3)	3,747 (85.4)	0.389
Creatinine (mg/dL), median (IQR)	0.9 (0.7–1.2)	0.9 (0.7–1.3)	0.9 (0.7–1.2)	0.079
Missing data	136 (2.8)	0 (0)	136 (3.0)	0.005
AST (U/L), median [IQR]	37 [25–56]	34 [23–52]	37 [25–57]	0.068
Missing data	328 (6.7)	18 (6.8)	310 (6.7)	0.969
ALT (U/L), median [IQR]	37 [25–62]	32 [22–49]	38 [25–62]	<0.001
Missing data	334 (6.9)	18 (6.8)	316 (6.9)	0.965

IQR, interquartile range; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; WBC, white blood cell; CRP, C-reactive protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; n, number.

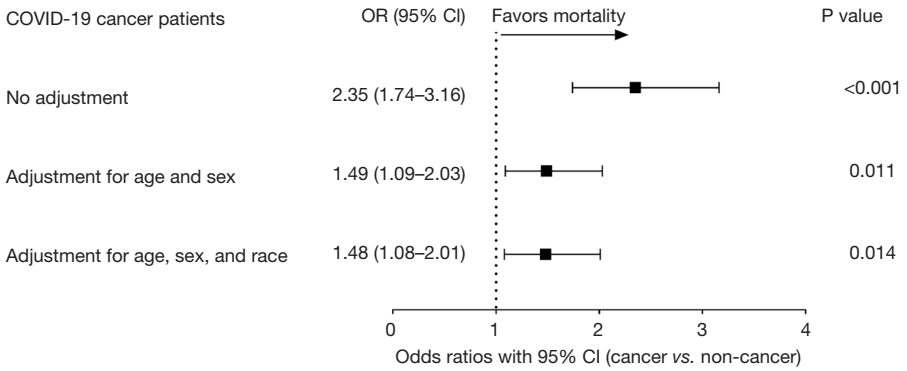

Figure 1 The odds ratio for mortality in patients with cancer with adjustments for age, sex and race. OR, odds ratio; CI, confidence interval.

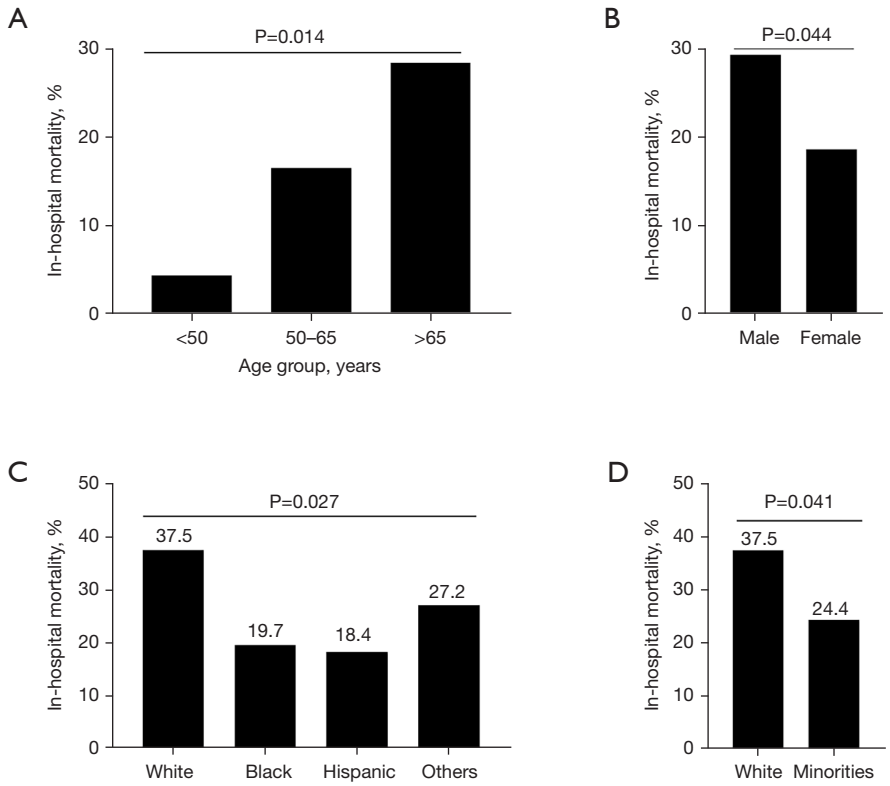

Figure 2 In-hospital mortalities amongst different age groups, genders, races and minorities. (A) Age (years) *vs.* IHM (%). (B) Gender *vs.* IHM (%). (C) Races *vs.* IHM (%). (D) Minorities *vs.* IHM (%). IHM, in-hospital mortality.

were more likely to have diabetes, coronary heart disease or CKD than patients who survived COVID-19 hospitalization but were otherwise comorbid similar (*Table 2*).

Univariate and multivariate logistic regression models were constructed to estimate the association of clinical factors with the risk of in-hospital mortality in COVID-19 patients with cancer (*Table 3*). By univariate analyses, older age, male gender, diabetes, CKD, coronary heart disease, increased CRP, creatinine, and AST were associated with increased risk of in-hospital mortality. We then modeled a multivariable logistic regression including age, gender, race, and history of hypertension, diabetes, chronic obstructive

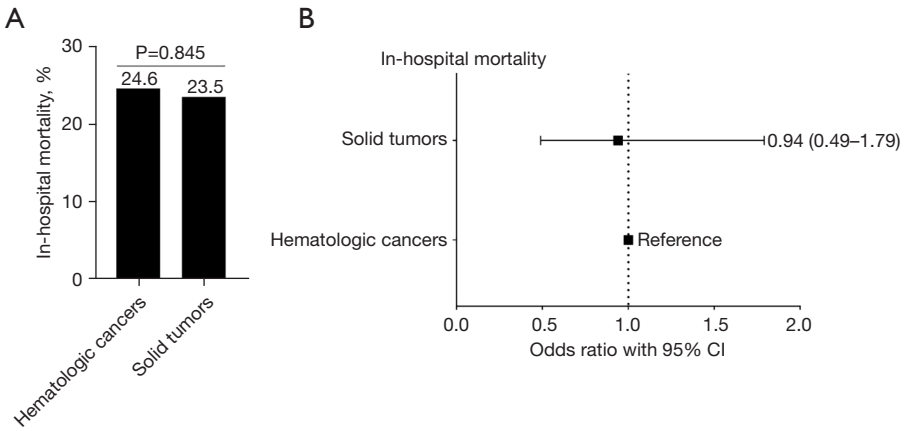

Figure 3 In-hospital mortalities amongst the two sub-categories of malignancy: solid and hematological malignancy. (A) Patients with solid malignancies or hematological malignancies had similar odds ratios of experiencing in-hospital mortalities. (B) Patients with solid malignancies had decreased odds ratios of experiencing in-hospital mortality, while hematological malignancies experienced no difference in mortality. CI, confidence interval.

Table 2 Comparison of comorbidities between non-survivors and survivors in COVID-19 patients with and without cancer

Comorbidities	With cancer (N=265)			Without cancer (N=4,605)		
	Non-survivors (n=63, %)	Survivors (n=202, %)	P value	Non-survivors (n=526, %)	Survivors (n=4,079, %)	P value
Diabetes	35 (55.6)	83 (41.1)	0.044	291 (55.5)	1,538 (37.7)	<0.001
Hypertension	55 (87.3)	155 (76.7)	0.081	464 (88.2)	2,500 (61.3)	<0.001
COPD	12 (19.1)	38 (18.8)	0.967	88 (16.7)	262 (6.4)	<0.001
CKD	32 (50.8)	50 (24.8)	<0.001	180 (34.2)	465 (11.4)	<0.001
Coronary heart disease	25 (39.7)	52 (25.7)	0.033	151 (28.7)	513 (12.6)	<0.001
Obesity	24 (38.1)	69 (34.2)	0.568	208 (39.5)	1,425 (34.9)	0.038
Smoking	21 (33.3)	71 (35.2)	0.792	184 (34.9)	891 (21.8)	<0.001
ACEIs	34 (53.9)	91 (45.1)	0.216	201 (38.2)	1,235 (30.3)	<0.001
ARBs	21 (33.3)	62 (30.7)	0.693	169 (32.1)	949 (23.3)	<0.001

COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; n, number.

pulmonary disease, chronic kidney disease, coronary artery disease, obesity, smoking, using of ACEI or ARBs, and biochemical parameters (WBC, lymphocyte, CRP, LDH, creatinine, AST, and ALT) as covariates. Results revealed that age, CKD, CRP, and AST were independently associated with increased risk of death in COVID-19 patients with cancer, with multivariable-adjusted ORs of 1.05 (95% CI: 1.02–1.09; P=0.004), 2.21 (95% CI: 1.05–4.65; P=0.036), 1.06 (95% CI: 1.02–1.11; P=0.004), and 1.01 (95% CI: 1.0–1.01; P=0.049) respectively (*Table 3*).

Discussion

Initially, there were worries regarding COVID-19's deleterious effects in cancer patients, owing to an immunosuppressive state generated by anticancer drugs and disease itself (8). COVID-19's implications have been studied before, but the precise implications in cancer patients are restricted, and the effect on cancer treatment is unknown (9). The goal of this study was to assess the consequences of COVID-19 infection in cancer patients

Table 3 Clinical factors associated with in-hospital mortality among COVID-19 patients with cancer

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Demographics						
Age	1.05	1.02–1.08	<0.001	1.05	1.02–1.09	0.004
Male	1.82	1.02–3.23	0.042			
Race						
Black	0.41	0.19–0.88	0.021			
Hispanic	0.38	0.18–0.75	0.006			
Other	0.63	0.15–2.58	0.517			
White (reference)						
Obesity	1.19	0.66–2.13	0.568			
Smoking	0.92	0.51–1.67	0.792			
Comorbidities						
Diabetes	1.79	1.01–3.17	0.045			
Hypertension	2.08	0.93–4.68	0.076			
COPD	1.02	0.49–2.08	0.967			
CKD	3.14	1.74–5.65	<0.001	2.21	1.05–4.65	0.036
Coronary heart disease	1.89	1.05–3.44	0.035			
ACEIs	1.43	0.81–2.52	0.217			
ARBs	1.13	0.62–2.06	0.693			
Biochemical parameters						
WBC	1.02	0.99–1.04	0.06			
Lymphocyte	1.16	0.98–1.36	0.077			
CRP	1.06	1.02–1.11	0.002	1.06	1.02–1.11	0.004
D-dimer	2.17	0.36–13.3	0.401			
Creatinine	1.34	1.09–1.63	0.004			
AST	1.01	1.0–1.01	0.031	1.01	1.0–1.01	0.049
ALT	0.99	0.99–1.01	0.605			

COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; WBC, white blood cell; CRP, C-reactive protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; OR, odds ratio; CI, confidence interval.

in terms of care and, ultimately, clinical outcomes, such as death and ethnic or racial differences.

Our findings show an increased risk of in-hospital mortality among patients with a cancer history and COVID-19, irrespective of whether the patient is on active antineoplastic treatment or surveillance. Consistent with our findings, a meta-analysis of 32 studies involving 46,499 patients (1,776 patients with cancer) with COVID-19 suggested that cancer patients are associated to have a higher risk of severe events compared with patients without cancer (10). These findings demonstrate the need for continued necessity of stratifying patients with cancer according to the risk of unfavorable outcomes. The search for determinants of severe COVID-19 in patients with

cancer still of supreme importance. Finally, all efforts should be directed toward protecting cancer patients through vaccinations (11-13) or using treatments that may improve survival or reduce intensive care unit admissions through the use of steroids (14) or even IV monoclonal antibodies as treatment (15).

Present study had a good representation of all age groups including ages 18 to >65 years old, with the median age group being 61. Co-morbid conditions such as obesity, hypertension, pulmonary, cardiovascular, renal, and diabetes were significantly higher amongst the cancer cohort in comparison to others. Consistently, a large study in the United Kingdom evaluated 800 COVID-19 positive cancer patients and amongst them, 226 died from COVID-19 related complications; it clearly showed that the probability of death was significantly increased in patients that were older, male sex and had comorbidities such as hypertension [1.95 (1.36–2.80)] and cardiovascular disease [2.32 (1.47–3.64)] (8). In consequence, conditions such as cardiovascular disease and diabetes are both pro-inflammatory conditions that may lead to a decreased immune response and ultimately, a poorer outcome (9,16,17).

Obesity in the United States has been increasing over the years and has led to a substantial increase in many diseases, including heart disease, diabetes mellitus, and most importantly cancer. Previous study in New York linked obesity in cancer patients with an increased need for invasive mechanical ventilation which showed a worse prognosis and increased rates of hospitalization due to COVID-19 with BMIs >25 kg/m^2 (18). Although obesity is considered pro-inflammatory and has been linked in the past to various diseases, it did not indicate a worse prognosis or increased in-hospital mortality in our study.

Certain abnormal lab findings were associated with a higher risk of adverse outcomes. Labs such as elevated CRP, elevated creatinine, and lymphopenia were all seen in COVID-19 positive cancer patients and contributed to their poor outcomes. In a large cohort study in Brazil, lymphopenia [2.20 (1.26–3.84)], creatinine elevation [2.86 (1.40–5.84)] and CRP elevation [2.86 (1.40–5.84)] were associated with an increased risk of death and worse prognosis, likely due to an increased inflammatory state and diminished immune response (19). In our study, the findings demonstrated that older individuals, elevated CRP and creatinine are independently associated with increased risk of in-hospital mortality in cancer patients with COVID-19. Being of Hispanic or black descent with co-morbid conditions, including cancer, were significant independent predictors of increased morbidity and mortality (in-hospital death) and contributed to an overall worse outcome, but NHW still had the highest mortality compared to both Hispanics or blacks.

To our knowledge, this is the largest South Florida cohort to assess in-hospital mortality and asses clinical characteristics potentially associated with mortality in hospitalized patients with cancer who were diagnosed with COVID-19. Among the limitations of retrospective nature of the study and the accrual in only one state largest public health care system in the US may limit the generalization of our clinical findings. Finally, the impact of COVID-19 on cancer needs to be evaluated with long-term follow-up of survivors.

In summary, COVID-19 infection in patients with malignancies carries a worse prognosis, including death, in comparison to those that are cancer free. Thus, we should devote all the available resources to try to decrease mortality amongst COVID-19 cancer patients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-1667/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-1667/dss

Peer Review File: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-1667/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-1667/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki

(as revised in 2013). The study was approved by The Institutional Review Board of MHS (protocol No. MHS 2021.008). Written informed consent was waived as this was a retrospective analysis of existing data.

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