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Case Report

Impact of Covid19 on Cancer Patients: A Single Center Experience and Comparison to CDC Data

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Abstract

Purpose: The raging pandemic of SARS-CoV-2 has generated the need to address the epidemiological and disease patterns that identify higher risk populations. Cancer patients have been postulated to be at higher risk for mortality, although the current data is conflicting. We sought to compare the outcomes of cancer patients to the CDC cohort and identify high risk features within our cancer population.

Methods: We conducted a retrospective cohort study of patients with pre-existing cancer diagnosis and diagnosed with COVID-19 infection between 3/2020-6/2020 and analyzed risk factors leading to worse outcome. We also compared our data with the local population average from the Center for Disease Control (CDC), during the same time frame, to assess differences in mortality with special emphasis on comorbidities.

Results: When compared to CDC cohort, our study did not identify an increase in mortality in the cancer cohort, suggesting that cancer patients are not necessarily predisposed to worse outcomes from COVID-19. However, older age and diagnosis of a hematological malignancy was associated with increased mortality. Our study also identified that male sex and presence of comorbidities such as chronic kidney disease, coronary artery disease and hyperlipidemia were risk factors for requiring critical care. Higher hospitalization and readmission rates were noted in our cancer cohort when compared to CDC cohort highlighting the importance of close monitoring in cancer patients to keep mortality rates low. Reactive airway disease and Coronary artery disease were more common comorbidities in the cancer cohort whereas diabetes and hypertension were common in the CDC cohort.

Introduction

The pandemic of the Severe Acute Respiratory Syndrome (SARS)-CoV-2 virus has resulted in over 600000 deaths in the United States as of July 2021 and seemingly will continue to cause a significant disease burden in the countries across the world. The published literature postulates that the severity of the disease is associated with various comorbidities including, diabetes [1,2], cardiovascular disease [3,4], obesity [5], hyperlipidemia, asthma, COPD[6,7] and cancer. Fung et al summarize that patients with cancer are at higher risk of severe disease and those with lung cancer and hematological malignancies experience disproportionately higher mortality [8]. While our understanding of these associations continues to expand, there is limited data on the risk factors that predispose to severe disease from SARS-CoV-2 within the cohort of patients diagnosed with cancer. Kuderer et al utilized the COVID-19 and Cancer Consortium (CCC19) database to study patients with malignancies between March-April, 2020 and identified that increasing age, increased comorbidities, diagnosis of hematological malignancy and ECOG performance status of >=2 was associated with increased mortality [9]. We decided to further explore the risk factors for worse outcomes in patients with cancer in our single center experience with the disease.

Methods

IRB approval was obtained to create a registry of patients with solid/hematological malignancies with a PCR-based diagnosis of SARS CoV-2 who have been followed within the clinical system. This is a retrospective cohort study, the data for which was obtained from the aforementioned registry. The hospital

EMR was utilized for obtaining the following: demographics, cancer history including diagnosis and treatment received, ABO typing, comorbidities such as diabetes, hypertension, chronic kidney disease (CKD), reactive airway disease (including Chronic obstructive pulmonary disease and asthma), coronary artery disease (CAD), anemia, hyperlipidemia, atrial fibrillation (afib), seizures, drug abuse and obesity (above comorbidities were subsequently used to calculate the Charlson Comorbidity Index-CCI), presenting symptoms of COVID-19, radiological findings, hospitalization history that included the following: critical care needs, receipt of therapy including remdesivir, convalescent plasma, anticoagulation, steroids, levels of inflammatory markers (D-dimer, CRP, ferritin, platelets) and outcome. The primary outcomes analyzed were ICU admission and death rates. Secondary outcomes were hospitalization and readmission rates.

The data from our cohort was compared to the public data of 693 cases that was available at the Center for Disease Control (CDC) website for Worcester county Massachusetts during the same time frame of March to June 2020. The exact percentage of patients with cancer within the CDC cohort was not known. The data was subsequently analyzed using Stata version 16 (StataCorp LLC). All the categorical data was analyzed using logistic regression analyses to identify relationship between outcome variables and comorbidities and p-value<0.05 was considered significant.

Results

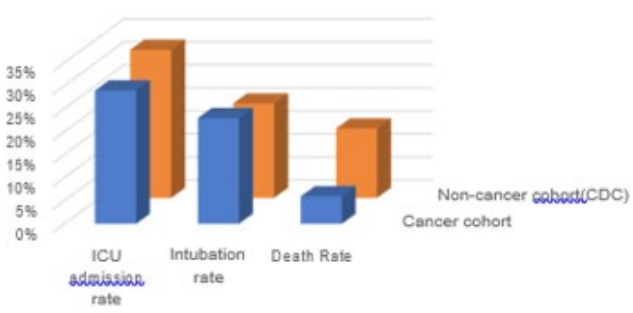
A total of 31 patients were identified with a cancer diagnosis who were diagnosed with SARS- CoV-2 from 3/2020- 6/2020. In this cohort, the median age was 64 years (IQR 58-70), 54% were males and 45% were females. 21/31 (67%) were Caucasians, 5/31(16%) were Hispanics, 4/31(12%) were African Americans and 1/31(3%) were Asians. Of the 31 patients, 7 had hematological malignancies and 23 had solid malignancies, 1 patient had been diagnosed with both solid and hematological malignancies (Table 1). A total of 22/31 patients (70%) were undergoing active treatment for their oncological diagnosis. Of the patients with hematological malignancies, 2 had undergone hematopoietic stem cell transplant (1 patient had undergone transplant in 2016 and the other in 2019) and 6/7 patients were undergoing active chemotherapy or immunotherapy (1 patient had declined treatment in the past). Of the 23 patients with solid malignancies, 3 were undergoing active chemotherapy, 4 were undergoing chemo-radiation, 4 were on immunotherapy and 4 on endocrine therapy. A total of 8 patients were not undergoing active chemo/immune/endocrine therapy of which 3 had undergone surgical intervention for their solid tumors. Of the 22 patients, 17 were found to have A or AB blood typing, 3/22 had O typing while 2/22 had B typing. We didn't have ABO typing results available on 9 patients.

Study ID	Age	Sex	Ethnicity	Cancer Type	Diagnosis	Stage	Cancer Treatment	Transplant	Blood Group
2	55	Male	Caucasian	Solid	SCC larynx	IV	Chemotherapy+ Radiation	No	A+
4	68	Female	Caucasian	Solid	Lung adenocarcinoma	IV	Immunotherapy	No	AB-
5	67	Female	Caucasian	Solid	GBM	NA	Chemotherapy+ Radiation	No	O+
6	84	Male	Caucasian	Solid	Cholangiocarcinoma	IV	Chemotherapy	No	A+
7	39	Female	Hispanic	Solid	Breast Cancer	II	Endocrine therapy	No	NA
10	80	Female	Caucasian	Solid	Breast Ca	IV	Chemotherapy	No	O+
11	58	Female	Caucasian	Solid	Lung adenocarcinoma	IV	Immunotherapy	No	A+
14	70	Male	Caucasian	Solid	RCC + Lung adenocarcinoma	IV	Immunotherapy	No	NA
16	57	Female	Caucasian	Solid	Breast Cancer	NA	Chemotherapy+ Radiation	No	AB+
17	45	Female	Caucasian	Solid	Breast Cancer	I	Endocrine therapy	No	NA

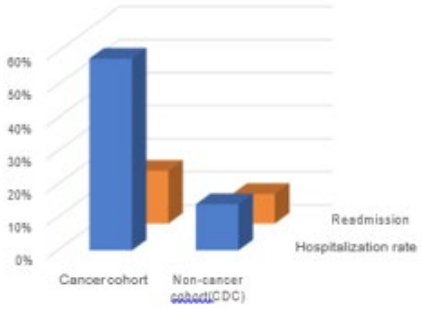
18	59	Female	Caucasian	Solid	Breast Cancer + SCC tongue	NA	Immunotherapy	No	NA
19	39	Female	Caucasian	Solid	Breast cancer		Endocrine therapy	No	NA
21	66	Female	Caucasian	Solid	Pancreatic adeno-carcinoma	IV	Not received	No	NA
22	64	Male	African American	Solid	RCC	I/II	Surgery	No	AB-
23	69	Male	Hispanic	Solid	Prostate Cancer	T3N1	Endocrine therapy	No	NA
24	74	Male	Hispanic	Solid	SCC Lung	III	Not received	No	A+
25	86	Male	Caucasian	Solid	Squamous cell cancer	I	Not received	No	AB-
26	74	Male	African American	Solid	Ampullary cancer	pT2N1M0	Surgery	No	A-
27	58	Male	Caucasian	Solid	Rectal adenocarci-noma	II	Not received	No	AB-
28	58	Female	African American	Solid	Lung adenocarci-noma	IV	Chemotherapy	No	NA
29	62	Male	Hispanic	Solid	SCC anal canal	LA	Chemotherapy+ Radiation	No	AB-
30	33	Female	Hispanic	Solid	Goblet cell tumor of the appendix	II	Surgery	No	O+
31	67	Male	Caucasian	Solid	Pancreatic adeno-carcinoma	IV	Not received	No	AB-
1	71	Male	Caucasian	Hematological	AML		Chemotherapy	Yes	B+
3	60	Female	Caucasian	Hematological	Multiple Myeloma		Immunotherapy	Yes	A+
8	79	Male	Caucasian	Hematological	Low grade lym-phoma		Chemotherapy	No	A+
9	53	Male	Caucasian	Hematological	AML		Chemotherapy	No	A+
12	69	Female	Caucasian	Hematological	DLBCL + CLL		Chemotherapy	No	A+
13	69	Male	Caucasian	Hematological	B-cell lymphoma		Not received	No	NA
20	62	Male	African American	Hematological	CML		Immunotherapy	No	B-
15	64	Male	Asian	Hematological +Solid	CML and SCLC	NA	Immunotherapy	No	A+

Table 1: Demographic characteristics of the cancer cohort at our Institution.

We compared the characteristics between our cohort (cancer cohort) to the data from CDC (local population) (Table 2 and Figure 1) we found a statistically significant lower death rate (6% vs 15%, p<0.05) in our cohort despite a comparable ICU admission rate (29% vs 32%) and intubation rate (23% vs 21%) between the two cohorts. The hospitalization and readmission rates were significantly different between our cohort and CDC cohort at 58% vs 15% and 16% vs 9% respectively (p<0.05). The proportion of males and females was fairly consistent among the two cohorts. For the ethnic distribution of the patients, Caucasians formed the majority in our population vs the CDC cohort (67% vs 38%, p<0.05), followed by Hispanics (16% vs 22%, p=0.21), African Americans (12% vs 29%, p<0.05) and Asians (3% vs 6%, p =0.19). While the comparison of the CCI scores could not be directly compared between the two cohorts, a higher percentage of diabetes (36% vs 22%, p<0.05) and hypertension (58% vs 41%, p<0.05) was seen in the CDC cohort compared to our cancer cohort. However, the incidence of CKD (20% vs 16%, p=0.30), reactive airway disease (26% vs 11%, p<0.05), coronary artery disease (23% vs 12%, p<0.05) and obesity (58% vs 46%, p=0.08) was higher in our cancer cohort vs CDC cohort.



Primary out comes



Secondary out comes

Characteristics	Subclasses	Cancer cohort	CDC cohort	p-Value
		(n=31)		
Primary outcome(s)				
	ICU admission rate	29%	32%	0.57
	Intubation rate	23%	21%	0.58
	Death Rate	6%	15%	0.02
Secondary outcomes(s)				
	Hospitalization rate	58%	14%	0
	Readmission	16%	9%	0.02
Age (years)				
	Median	64	NA	
Sex				
	Male	54%	51%	0.63
	Female	45%	49%	0.53
Ethnicity				
	Caucasian	67%	38%	0
	Hispanic	16%	22%	0.21
	African American	12%	29%	0
	Asian	3%	6%	0.19
Cancer type				
	Hematological	26%	NA	-
	Solid	74%	NA	-

Comorbidities				
	CCI score(median)	6	NA	-
	CCI %(median)	2%	NA	-
	Diabetes(I/II)	22%	36%	0.02
	Hypertension	41%	58%	0.02
	CKD	20%	16%	0.3
	Reactive airway disease	26%	11%	0
	CAD	23%	12%	0
	Obesity	58%	46%	0.08

Figure 1 and Table 2: Comparison of characteristics between the cancer cohort and the county cohort (Data: CDC).

We compared the patients who required critical care with those who were admitted to the hospital but did not require admission to the ICU (Table 3). The median age was 64 years for both the cohorts (p=0.14). Males were more likely to require critical care ($p<0.05$). No significant ethnic differences were noted in the cohort requiring critical care vs those who were hospitalized. There was no difference between the diagnoses of solid or hematological malignancies in ICU admission rate. Similarly, no difference in comorbidities reflected in the CCI score was noted in the admission to the ICU vs hospitalization without ICU admission (p=0.13). However, on further analysis of the individual comorbidities, patients with CKD, CAD and hyperlipidemia were more likely to require critical care and this difference was statistically significant. There was no difference among the two cohorts when comparing the co-existing diagnoses of diabetes, hypertension, reactive airway disease, anemia, atrial fibrillation, seizures, drug abuse and obesity. Radiological and hematological (elevation of inflammatory markers) evidence was also uniformly distributed between the cohorts.

Characteristics	**Subclasses**	**Critical Care**	**Hospitalization**	**p value**
		(n=9)	(n=9)	
Age (years)				
	Median	64	64	0.14
Sex				
	Male	8	0	0
	Female	1	1	0.61
Ethnicity				
	Caucasian	6	5	0.65
	Hispanic	2	1	0.32
	African American	1	2	0.48
	Asian	0	1	0.32
Cancer type				
	Hematological	6	6	1
	Solid	3	3	1
Comorbidites				
	CCI score(median)	6	6	0.13
	CCI %(median)	2	2	0.13
	Diabetes(I/II)	4	2	0.16
	Hypertension	3	5	0.37
	CKD	3	1	0.05
	Reactive airway disease	3	2	0.48

	CAD	3	1	0.05
	Anemia	2	3	0.56
	Hyperlipidemia	3	1	0.05
	A-fib	1	1	1
	Seizures	2	1	0.32
	Drug abuse	4	2	0.16
	Obesity	5	5	1
Presentation				
	Asymptomatic	2	1	0.32
	Symptomatic	7	8	0.72
Radiological evidence				
	Present	8	8	1
	Absent	1	1	1
Therapy administered				
	Remdesivir	3	0	0
	Convalescent plasma	4	1	0
	Steroids	4	1	0
	Therapeutic anticoagulation	2	3	0.56
Inflammatory markers				
	D-dimer	7	4	0.13
	Ferritin	6	5	0.65
	CRP	7	6	0.68

Table 3: Comparison of characteristics of critically ill patients vs non-critical hospitalized patients in the cancer cohort.

We further analyzed the differences within the cohort in reference to the primary outcomes (Table 4). A total of 9 patients were admitted to the ICU, 7 were intubated and mechanically ventilated. A total of 5 patients died of COVID-related complications (acute hypoxic respiratory failure, cardiovascular events). The median age was similar across the 2 cohorts (ICU admission and deceased) and ranged from 64-66 years. In the ICU cohort, age (OR 1.10, 95% CI 0.969-1.251), sex (OR 0.1, 95% CI 0.008-1.17), ethnicity, cancer type (OR 1, 95% CI 0.14-7.099) was not statistically significant. However, in the deceased cohort, increasing age (OR 1.136, 95% CI 1.002 - 1.288) and the diagnosis of hematological malignancy (OR 8.25, 95% CI 1.028-66.192) was statistically associated with higher mortality (Figure 2). The CCI score was not significant in the ICU or the deceased cohorts (OR 1.39, 95% CI 0.908-2.130: OR 1.07, 95% CI 0.799-1.455 respectively). Though CCI score did not appear to be independent risk factors to predict mortality in our patient cohort, the patients that died from COVID -19 disease were noted to have higher CCI scores.

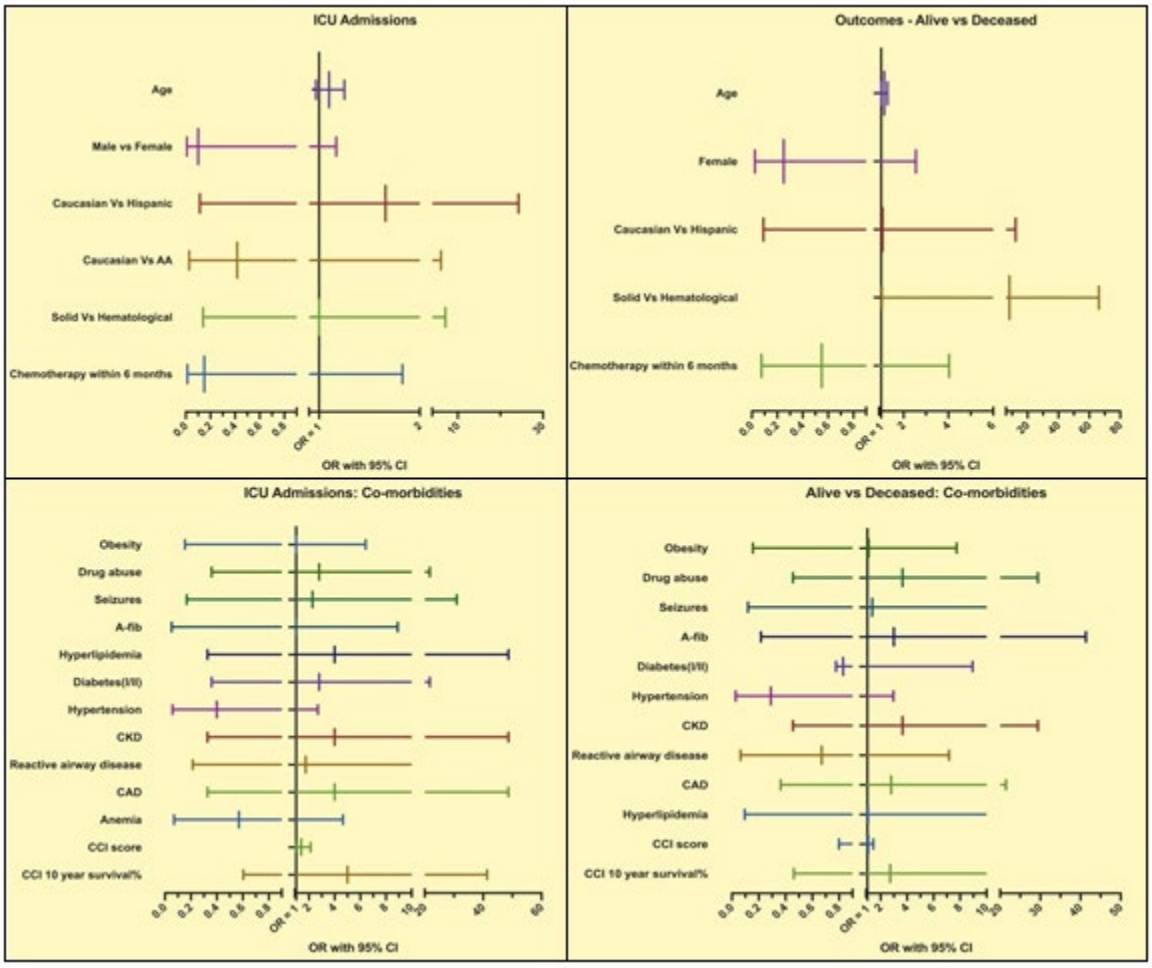


Figure 2: Forest plots comparing demographics and comorbidities among the two major primary outcomes.

Characteristics	Subclasses	ICU Admission	OR(CI)	p-Value	Death	OR(CI)2	p-Value2
		(n=9)			(n=5)		
Age (years)							
	Median	64	1.10 (0.969 - 1.251)	0.14	66	1.136 (1.002 - 1.288)	0.04
Sex							
	Male	8	ref		4		
	Female	1	0.1 (0.008 - 1.170)	0.07	1	0.25 (0.024 - 2.549)	0.24

Ethnicity							
	Caucasian	6	ref		4	ref	
	Hispanic	2	1.66 (0.114 - 24.255)	0.7	1	1.06 (0.091-12.276)	0.96
	African American	1	0.417 (0.028 - 6.063)	0.52	0	-	-
	Asian	0			0		
Cancer type							
	Solid	6	ref		2	ref	
	Hematological	3	1 (0.140 - 7.099)	1	3	8.25 (1.028 - 66.192)	0.04
Chemotherapy within 6 months		5	0.15(0.013-1.828)	0.14	3	0.552 (0.075 - 4.034)	0.56
Comorbidites							
	Diabetes(I/II)	4	2.8 (0.360 - 21.727)	0.32	1	0.83 (0.776 - 8.946)	0.88
	Hypertension	3	0.4 (0.059-2.702)	0.34	1	0.29 (0.028 - 2.976)	0.29
	CKD	3	4 (0.328 - 48.655)	0.27	2	3.66 (0.456 - 29.418)	0.22
	Reactive airway disease	3	1.75 (0.215 - 14.223)	0.6	1	0.67 (0.064 - 7.161)	0.74
	CAD	3	4 (0.328 - 48.655)	0.27	2	2.8 (0.364 - 21.485)	0.32
	Anemia	2	0.57 (0.070 - 4.644)	0.6	0	-	-
	Hyperlipidemia	3	4 (0.328 - 48.655)	0.27	1	1.05 (0.095 - 11.557)	0.97
	A-fib	1	1 (0.052 - 8.914)	1	1	3 (0.217 - 41.350)	0.41
	Seizures	2	2.28 (0.168 - 30.958)	0.53	1	1.37 (0.120 - 15.721)	0.79
	Drug abuse	4	2.8 (0.360 - 21.727)	0.32	2	3.66 (0.456 - 29.418)	0.22
	Obesity	5	1 (0.155 - 6.419)	1	3	1.1 (0.156 - 7.739)	0.92

CCI							
	CCI score(median, IQR)	6 (4,10)	1.39 (0.908 - 2.130)	0.13	6	1.07 (0.799 - 1.455)	0.62

Table 4: Comparison of characteristics when classified by ICU admission versus death.

Discussion

The association of severity of COVID-19 with various comorbid conditions has been a matter of great debate. Several studies have unanimously associated diabetes, hypertension, obesity, smoking with worse outcomes in patients with COVID-19. However, the jury on patients with cancer and SARS-CoV-2 infection seems to be divided. Initial studies suggested a probable worse outcome among cancer patients. Dai et al, Moro et al, Tian et al and He et al demonstrated in their studies a higher mortality rate among patients with malignancies when compared to the general population, particularly among hematological malignancies and stage IV metastatic cancers [10-13]. On the other hand, Shoumariyeh et al demonstrated that COVID-19 disease severity was not increased when comparing the cancer patients with their age matched cohort with no diagnosis of cancer [14]. Most of the aforementioned studies represent non-US populations.

Our study hoped to address 2 major questions:

i. Identifying characteristics which predispose cancer patients to worse outcomes. Compare between the adverse outcomes (hospitalization, ICU admission and mortality) and identify if a statistically significant difference exists among the characteristics.

ii. Compare the difference in outcomes of cancer patients diagnosed with COVID-19 to the standard population data of the local (Worcester) county during the same time frame of March to June 2020 (publicly available data from CDC)

Increasing age and a diagnosis of hematological cancer was observed to be significantly associated with higher mortality within our cancer cohort. This has also been supported by the data from other studies. On comparing cancer patients who required critical care vs those who were hospitalized (but had no critical care requirements) significantly higher proportion of male patients, and patients with comorbidities of CKD, CAD and hyperlipidemia was observed in the critically ill cohort. Given the importance of vascular risk factors in the pathogenesis of COVID-19 complications, it is not surprising that CKD, CAD and hyperlipidemia were identified in our study as risk factors for severe COVID 19 infection requiring critical care.

Our study also confirms, the high incidence of COVID 19 complications in male patients as shown in other studies [15].

When compared to the data from the COVID-19 and Cancer Consortium (CCC-19) database (which combines populations from USA, Canada, Spain and anonymous health care practitioners from Argentina, Canada, EU, UK and USA, that concluded higher probability of severe disease and mortality among patients with cancer) our data did not show higher mortality among patients with malignancies when compared to the general population in the local county during the same three month time frame. While no COVID-specific therapies have been proven to show benefit so far, our institution emphasized awake proning and incentive spirometry in our patients hospitalized to the wards. High-flow nasal canula was used to support the population that does not require intubation but had increasing oxygen requirements. A dedicated prone team was created in the intensive care units which would prone ventilated patients for 16 hours each day with close monitoring of P/F ratios to guide further management. Ventilator-associated pneumonia prophylaxis with elevation of head-end of the bed and good oral care was aggressively pursued. Remdesivir, convalescent plasma and steroids were available and used in patients who met treatment criteria (used preferentially in critically ill patients. See table 3). Existing data however has not shown a clear beneficial role of these therapies in the management of patients with COVID-19 [16-20] and our data is not intended to contribute to further knowledge about these therapies and hence their role was not deeply investigated.

Despite the similar prevalence of comorbidities within our cancer cohort to the CDC average, our cohort had a statistically significant lower mortality rate (6% vs 15%, $p<0.05$). The hospitalization rates were however significantly higher in our cohort. At our institution, patients with a dual diagnosis of cancer and COVID-19 were presumed to be sicker than the general population with COVID-19 and early admission to the hospital was prompted by the treating oncologist's assessment and level of hypoxia. Typically, any supplemental oxygen requirement in the cancer cohort warranted admission. Closer follow up of these patients while outpatient and low threshold to hospitalize, as shown by the increased hospitalization and readmission rates in our cancer cohort, could have contributed towards the decreased mortality rates despite comparable comorbidities.

Our study identified that the characteristics between the cancer and local CDC cohort were mostly comparable except for statistically significant differences in ethnicity and some of the

individual comorbidities. We had a higher number of Caucasians and lower percentage of African Americans in our cancer cohort. The CDC data reflects a higher mortality among Caucasians than their counterpart African Americans and Hispanics. Despite the higher number of Caucasians in our cancer cohort, the mortality in our cohort was still lower than the CDC average, further strengthening our conclusion that the diagnosis of cancer does not necessarily entail a worse outcome compared to the average population when controlling for ethnic variability. Our cancer cohort had significantly lower rates of diabetes and hypertension but higher rates of reactive airway disease and CAD when compared to the CDC cohort. Our study shows that the presence and impact of comorbidities associated with COVID-19 in cancer patients tends to be different from what is typically seen in the general population. This has potential impact on the risk assessment and management of cancer patients diagnosed with COVID-19. Our study also highlights the importance of close monitoring and early hospitalization in cancer patients.

Limitations of our study include small sample size, data from a single center and lack of an internal control. However, it does provide for a dataset which identifies that despite the prior reporting of worse outcomes among cancer patients with COVID-19, only a subset of cancer patients, have poor outcomes.

Conclusion

The COVID-19 pandemic has generated an unmet need for identifying risk factors that lead to a higher risk of dying from the disease. Existing research has noted that patients with comorbidities including cancer are particularly susceptible to worse outcomes. We decided to study our population of cancer patients at University of Massachusetts and assess risk factors for Covid-19 related complications and compare it to the local Worcester county CDC population data during the same time frame. Our study did not observe a higher mortality rate in cancer patients diagnosed with covid-19 when compared to the CDC population cohort. However, we identified increasing age and a diagnosis of hematological cancer as risk factors for higher mortality within our cancer cohort. Future studies will help further the understanding of whether only certain subsets of cancer, predict worse disease outcomes in COVID-19 and whether early hospitalization and rigorous management including antibody treatments would allow for improved survival in this cohort.

All three authors contributed towards conceptualization, data acquisition, interpretation and critical revision for intellectual content. All authors have given final approval of the version to be published and agree to be accountable for all aspects of the work. In addition, first author Disha Dalela contributed towards formal analysis and interpretation of data and writing the original draft, Middle author Tzafra Tessier contributed towards primary acquisition of data, Senior/corresponding author Dr. Muthalagu Ramanathan provided primary conceptualization and supervision of the project.

Conflict of interest: No relevant conflict of interest for each of the authors.

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