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ORIGINAL ARTICLE

Hospitalization characteristics and outcomes of patients with cancer and COVID-19 at a comprehensive cancer center

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Abstract

Purpose Several studies have confirmed increased mortality among patients with both COVID-19 and cancer. It remains important to continue to report observations of morbidity and mortality from COVID-19 in this vulnerable population. The purpose of this study is to describe the hospitalization characteristics and outcomes of patients with both cancer and COVID-19 admitted to our comprehensive cancer center.

Methods This was a descriptive study of the first COVID-19-related hospitalization among adult patients with cancer admitted to our institution. Descriptive statistics were used to summarize patient demographics, clinical as well as hospitalization characteristics. Overall survival (OS) was estimated using the Kaplan–Meier method.

Results A total of 212 patients were included in our cohort with a mean age of 59 years. Fifty-four percent of patients had history of solid tumor malignancy and 46% had hematologic malignancies. Eighty-five percent of our cohort had active malignancy. The mean length of stay (LOS) for hospitalization was 11.2 days (median LOS of 6 days). Twenty-five percent had severe disease and 10.8% died during their initial hospitalization. Those who had severe disease had worse survival at the end of the observation period.

Conclusions COVID-19 among cancer patients causes significant morbidity and mortality as well as repeat hospitalizations. Continued study of COVID-19 in this vulnerable population is essential in order to better inform evolving treatment algorithms, public health policies, and infection control protocols, especially for institutions caring for patients with cancer.

Keywords COVID-19 · Cancer hospitalizations · COVID and cancer outcomes

Introduction

The coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is one of the most impactful public health emergencies that the current world has known. Within 3 months of its initial discovery among a cluster of patients in Wuhan, China, in December 2019, COVID-19 had spread significantly across the globe and was declared a global pandemic by March 2020 [1]. Over the course of 1 year, the microbiological profile, natural history, risk factors, treatment options, and clinical outcomes relating to COVID-19 have been described in the general population at large, and among specific vulnerable populations such as in patients with cancer. One of the earliest studies on COVID and cancer showed that patients with cancer had worse clinical outcomes and higher risk of COVID-19 [2]. Several studies had since confirmed increased mortality among patients with both COVID-19 and cancer (pooled case mortality rate, 25.6%) [3]. Much is still unknown about this novel virus and the disease it causes; however, and to date, it continues to rampage across the globe causing multiple case surges and upturning the public's health and way of living.

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As with other institutions caring for cancer patients, our comprehensive cancer center, 1 of 71 NCI-designated cancer centers in the USA, adapted to the evolving pandemic in order to care for its patients. Inpatient operations were modified in order to ensure enhanced protection and continued care for vulnerable immunocompromised patients. Over the course of several months, inpatient COVID units were set up at a designated area of the hospital in order to take care of patients either suspected or confirmed to have COVID-19. A dedicated team of oncology-hospitalists, intensivists, infectious disease specialists, nurses, respiratory therapists, physical and occupational therapists, social workers, case managers, and other healthcare subspecialties staffed these units. Unit-specific standard operating procedures were developed and implemented for all aspects of inpatient care. The aim of this study is to describe the hospitalization characteristics and outcomes of patients with both cancer and COVID-19, who were admitted to our comprehensive cancer center. The institutional review board at our institution approved this study.

Patients and methods

This was a retrospective study conducted within a single center from March 23 to September 30, 2020. The unit of analysis was the first COVID-19 hospitalization encounter of adult cancer patients who were admitted at our center with confirmed COVID-19 disease via positive nasopharyngeal RT-PCR test for the SARS-CoV-2 virus. All patient data were aggregated and analyzed in the Syntropy platform, as part of the Data-Driven Determinants of COVID-19 Oncology Discovery Effort (D3CODE) protocol at our institution.

Descriptive statistics were used to summarize patient demographics, clinical as well as hospitalization characteristics. Continuous variables were reported as means with standard deviations (SD), and/or medians with range of data. We used frequency counts and corresponding proportions for categorical variables. Distribution of overall survival (OS) was estimated using the Kaplan–Meier method [4]. Log-rank test was performed to test the difference in survival between groups [5]. Patient outcomes described include disease severity, inpatient mortality, overall survival (OS), 30-day mortality, and 30-day all-cause readmission. We defined severe disease as anyone requiring at least non-invasive ventilation or high-flow oxygen per our institutional treatment algorithm for COVID-19.

Results

Patient and clinical characteristics

There were 212 *first* COVID hospitalization encounters observed during the initial 6 months of the COVID pandemic response at our comprehensive cancer center. The mean age of admitted patients was 59 years (min = 18, max = 91, SD = 15.1). Fifty-four percent of the patients were female ($n = 114$). Fifty-two percent of the patients were White ($n = 110$), 24% were African American ($n = 51$), and 19% classified themselves as "other." The most common primary language spoken was English (87%, $n = 185$), followed by Spanish (12%, $n = 25$).

Fifty-four percent of patients ($n = 115$) had clinical history of solid tumor malignancies, and the remaining 46% ($n = 97$) had hematologic malignancies regardless of disease activity. The most common site for solid tumor malignancy observed was breast ($n = 27$), followed by gastrointestinal (GI) cancers ($n = 21$). Among hematologic malignancies, the most common was lymphoma ($n = 34$), followed by leukemia ($n = 32$) (Fig. 1). Eighty-five percent of patients ($n = 181$) were determined to have active cancer (defined as not in remission, receiving some form of cancer treatment, or with evidence of disease).

Hospitalization characteristics

The mean length of stay (LOS) observed among patients' first COVID hospitalization was 11.2 days (SD = 12.6, median = 6 days). Twenty-four percent of patients ($n = 50$) were admitted to the intensive care unit (i.e., followed by intensivists in the COVID unit). Within this subgroup, 35% were mechanically ventilated ($n = 18$). The mean LOS among patients with an ICU stay was 21 days (SD = 14.2). Majority of the patients in our total cohort were discharged home, with or without home health services (80.6%, $n = 171$).

Table 1 shows the values of common laboratory evaluations at the time of admission. Of the key inflammatory markers taken, the mean ferritin level was 1684, C-reactive protein 81, and sedimentation rate 56. The mean value for NT pro B-type natriuretic peptide (NT pro BNP) was elevated at 1451; however, this is likely affected by outlier upper values. The mean procalcitonin level was 1.0.

The most common COVID-19-directed treatment given was corticosteroids (dexamethasone administered in 32.2% of encounters; methylprednisolone in 24.9%, prednisone in 10.6%; hydrocortisone in 9.2%). It should be noted that some patients may have been switched from one type of corticosteroid to another throughout their hospitalization. A total of 30.9% of patients received remdesivir, 21.7% received tocilizumab, and 14.3% received convalescent plasma. Azithromycin and hydroxychloroquine were given in 13.8% and 9.7% of patients respectively although most administrations were given within the first few months of the study period.

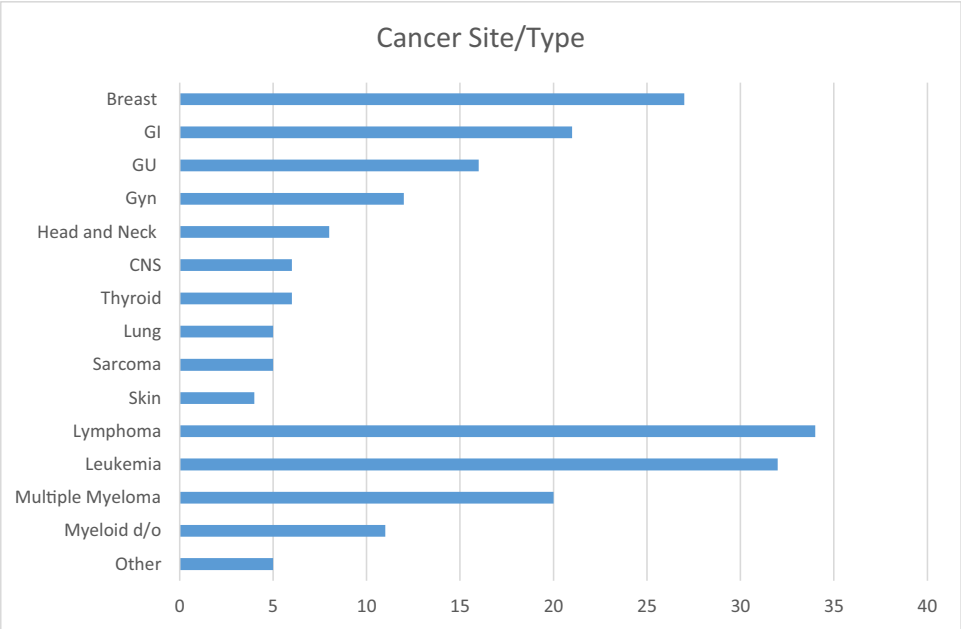

Fig. 1 Distribution of patients by cancer site or type

Table 1 Summary statistics of laboratory evaluations on admission

Laboratory component (reference range)	Mean value (SD)	Median (min, max)
Albumin (3.3–5.4 gm/dL)	3.5 (0.6)	3.6 (1.7, 4.9)
Creatinine (0.67–1.17 mg/dL)	1.1 (0.9)	0.9 (0.3, 6.9)
CRP (≤ to 10.00 mg/L)	80.5 (67.8)	65.4 (0.2, 261.7)
D-dimer (0.10–0.50 mcg/ml)	1.8 (2.3)	1.0 (0.3, 19.2)
Ferritin (30–400 ng/mL)	1684.5 (5491.7)	569.0 (27.0, 64,909.0)
Hct (40.0–54.0%)	32.4 (6.6)	32.3 (15.9, 51.0)
Hgb (14.0–18.0 gm/dL)	10.6 (2.2)	10.7 (5.6, 16.9)
IL-6 (0–5 pg/mL)	54.0 (149.0)	20.0 (3.0, 1698.0)
NT ProBNP (≤ 125 pg/mL)	1451.2 (3681.1)	387.0 (13.0, 22,519.0)
Platelet count (140–440 K/uL)	172.3 (119.3)	149.0 (5.0, 687.0)
Procalcitonin (≤ 0.08 ng/mL)	1.0 (4.9)	0.1 (0.0, 43.4)
Sed rate (0–9 mm/hr)	56.0 (31.6)	54.0 (7.0, 134.0)
Sodium level (136–145 mEq/L)	136.9 (5.2)	137.0 (118.0, 150.0)
Troponin-T (≤ 18 ng/L)	34.8 (46.5)	17.0 (6.0, 280.0)
WBC (4.0–11.0 K/uL)	9.0 (21.6)	5.1 (0.1, 199.1)

COVID-19 outcomes

Among our patients with cancer who were hospitalized with COVID-19, 25% had severe respiratory disease. We observed a 10.8% inpatient mortality rate among our patients. The 30-day mortality rate was 15.3% and the 30-day all-cause readmission rate was 32.8% among the 189 patients who were discharged alive. Of the readmitted encounters, 35.5% were due to cancer or treatment-related complications; 32.2% were related to COVID-19; 14.5% were readmissions to receive cancer treatment; and 17.7% were related to other medical issues not related to cancer or COVID-19. Overall survival by the end of follow up period (September 30, 2021) was worse for patients who were classified as having severe disease, compared to those who had mild or moderate disease ($p < 0.001$) (Fig. 2). One-year OS rates were 50.0% and 73.4% for those having severe disease vs mild or moderate disease, respectively. When we compared survival between hematologic and solid tumor patients, we found no significant difference between the 2 groups ($p = 0.39$) (Fig. 3).

Discussion

By the end of study follow up (September 2021), the US government SARS-CoV-2 Interagency Group (SIG) had recorded 10 SARS-CoV-2 variants that are being monitored [6]. Many of these have, over time, been designated as variants of concern or variants of interest, depending on transmissibility or presence of genetic attributes that could impact public health and clinical care such as diagnostics,

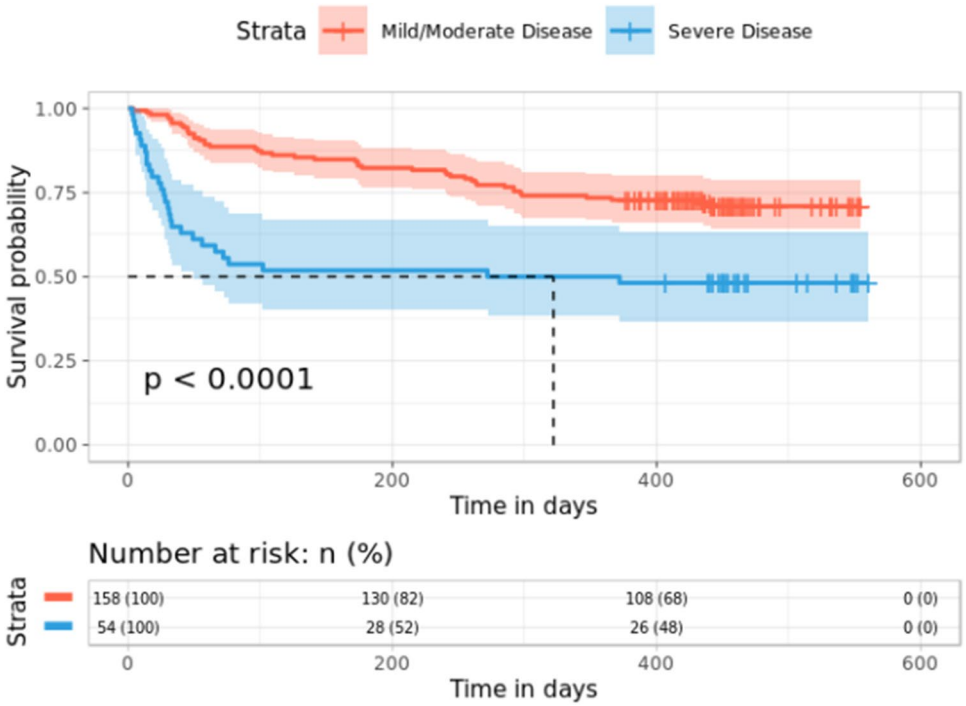

Fig. 2 Kaplan–Meier curve comparing patients with mild or moderate disease with severe disease

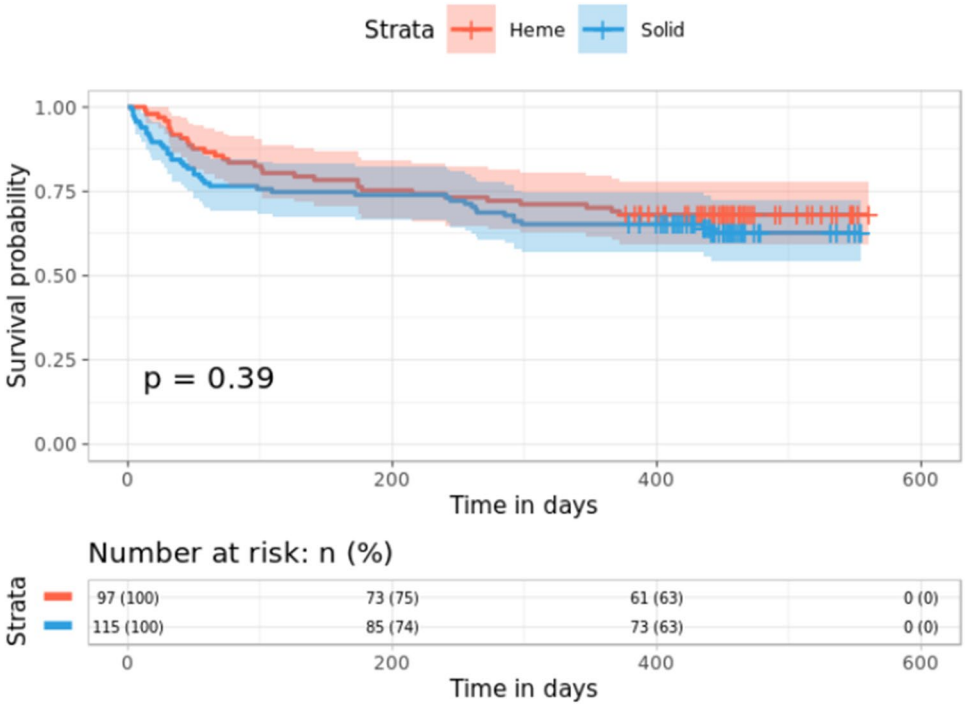

Fig. 3 Kaplan–Meier curve comparing survival of patients with hematologic vs solid tumor

treatments, and vaccination. The USA has experienced at least 3 COVID-19 waves to date, corresponding with extreme surges in the number of cases [7]. Because of the evolving nature of the COVID-19 pandemic, host behavior, public policy, and the virus itself, it continues to be important to describe the trends and patterns of COVID-19 cases, including COVID-19 hospitalization outcomes. This is especially true for the immunocompromised and hence most vulnerable patient populations such as those dealing with cancer.

During the first 6 months of the COVD-19 pandemic, the USA had registered 6.9 million cases and 200,000 deaths [8]. The COVID-19 hospitalization rate was 170 per 100,000 with people ages 65 years and older, and those between 60

and 64 years having the highest hospitalization rates (460 per 100,000 and 255 per 100,000, respectively) [9]. Within the Texas Medical Center where our hospital is situated, there have been 24,805 COVID-19 hospitalizations during the same time period regardless of cancer status, and regardless of whether the encounter was a readmission for the same patient or not [10]. In contrast, we saw 261 total COVID-19 hospitalizations which included initial and subsequent hospitalizations among 212 unique patients during this same period. The median age of our patients was 59 years but patients as young as 18 and as old as 91 years old were hospitalized to our COVID unit, reflecting the age spectrum of COVID-19 morbidity which is not limited to the elderly alone among patients with cancer. There was not much difference in gender distribution in our study, and the race distribution is comparable to other large scale studies within the USA on cancer and COVID-19, although this could also possibly reflect the cancer distribution by race in the state of Texas, with patients identifying as White making up majority of patients [11–13].

Among our patients who had solid tumor malignancies, breast was the most common cancer site, followed by GI cancers. This was consistent with the findings of Wang et al. in their study, which included data on 73 million patients from hospitals and clinicians across the USA through August 2020 [14]. Notably, the most common cancer in Texas based on the latest state cancer profile was also breast cancer [11]. Also similar to our study findings, Wang et al. noted slightly more cases of lymphoma compared to leukemia in their subgroup of patients with both cancer and COVID-19. While we did not explore association of specific cancer types with mortality, our survival analysis did not note a difference in OS between hematologic and solid tumor malignancies. Other collaborative studies in the USA with bigger sample size however have noted that hematologic malignancies were associated with increased all-cause mortality and poorer outcomes [12, 13].

In our cohort, our mean LOS of 11.2 days was likely affected by outlier cases (maximum LOS = 87 days). The median LOS for our hospitalized patients was 6 days and these findings were similar to other studies looking at hospitalizations for this patient population [15, 16]. The average LOS for our hospitalized patients without COVID-19 during the same time period was 7.6 days. It is possible that the COVID-19 treatments available during the study period could have driven the LOS for some of our patients. Within the USA, remdesivir, a 5-day course antiviral drug, was one of the few medications given emergency use authorization and eventually approved by the US Food and Drug Administration (FDA) for COVID-19 needing hospitalization [17]. The pattern and frequency of other treatments given, such as hydroxychloriquine, azithromycin, dexamethasone, and convalescent plasma, correlate with the evolution of evidence from various studies on COVID-19 and FDA guidance throughout the first year of the pandemic. Many of these treatments are no longer recommended.

In terms of COVID outcomes, majority of our patients were discharged home after initial hospitalization (80.6%) despite 25% having severe disease. Our inpatient mortality (10.8%) is better than the pooled in-hospital mortality rate in a systematic review of clinical outcomes among patients with COVID-19 and cancer published by Zarifkar et al. [18]. This systematic review, however, only included studies through April 2020 which may account for the difference. Data from the National COVID Cohort Collaborative (NC3) registry also noted a 14.5% inpatient mortality among 19,515 patients who had COVID-10 and cancer through March 2021. In terms of 30-day mortality, the COVID-19 and Cancer Consortium (CCC-19) which included information on 4966 patients with COVID-19 and cancer observed 14% of patients died within 30 days [12]. This is not very different from our own findings of 15.5% 30-day mortality. When looking at overall survival, not surprisingly, patients with severe disease had worse outcomes. The high all-cause 30-day readmission rate observed in our cohort potentially reflects the combined complexity of COVID-19 and cancer illness and necessary ongoing oncologic care for some of these patients. In the general population, a *Morbidity and Mortality Weekly* (MMWR) report showed that 1 in 11 patients hospitalized with COVID-19 get readmitted within 2 months of discharge, with 45% of these readmissions being due to COVID-19 [19]. This and our findings support close follow up, in-person or via telemedicine, to ensure continued critical care for vulnerable patients.

Our study aimed to present specific data on COVID hospitalizations including outcomes of patients admitted to a comprehensive cancer center. COVID-19, unfortunately, is a disease that will remain until the world gets adequate control of the pandemic. Pooled data such as that curated from multi-institution collaboratives [20] and single-center data like ours should continue to be collected and patterns of hospitalization and outcomes should continue to be described to inform healthcare providers, health systems, researchers, and policy makers. This becomes more important especially as we see variation in characteristics of transmissibility and risk for causing severe disease across different strains of SARS CoV-2. Future studies should look into variations in treatment and hospitalization patterns, as well as clinical outcomes in relation to the dominant strains in a particular region.

Our study has several limitations. First, we presented hospitalization characteristics and outcomes of the first COVID-19 hospitalization only. Secondly, our data only extends to hospitalizations through September 2020, and hence, our findings may not be reflective of COVID-19 outcomes caused by SARS coV-2 variants that have gained

epidemiologic dominance after our study period. Follow-up studies will be needed to further characterize the course of COVID-19 among cancer patients as new variants of the virus are identified.

In conclusion, COVID-19 among cancer patients causes significant morbidity and mortality as well as repeat hospitalizations. Moreover, those who had severe disease seemed to have worse overall survival by the end of our observation period. Continued study of COVID-19 in this vulnerable population is essential in order to better inform evolving treatment algorithms, public health policies, and infection control protocols, especially for institutions caring for patients with cancer.

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Data analysis and interpretation: JM, MM, EK, AM, JH, KD, NA, CL, KK, DR, OO, MS, ME, KW, HL, MG
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Final approval of manuscript: JM, MM, EK, AM, JH, KD, NA, CL, KK, DR, OO, MS, ME, KW, HL, MG

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Declarations

Ethics approval The institutional review board at The University of Texas MD Anderson Cancer Center approved this study.

Consent to participate Not applicable. A waiver of informed consent has been granted by the institutional review board at The University of Texas MD Anderson Cancer Center.

Consent for publication Not applicable. There is no patient identifiable data in this publication.

Competing interests Marina George is a consultant and part-owner of Marvin Health and has the following additional disclosures: spouse consults for UptoDate and Daichi-Sankyo. All other authors declare that they have no competing interests regarding this work.

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