Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Original Research Article

Delirium in Critically Ill Cancer Patients With COVID-19

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Background: *COVID-19 has been a devastating pandemic with little known of its neuropsychiatric complications. Delirium is 1 of the most common neuropsychiatric syndromes among hospitalized cancer patients with incidence ranging from 25% to 40% and rates of up to 85% in the terminally ill. Data on the incidence, risk factors, duration, and outcomes of delirium in critically ill cancer patients with COVID-19 are lacking.*
Objective: *To report the incidence, riaks and outcomes of critically ill cancer patients who developed COVID-19.*
Methods: *This is a retrospective single-center study evaluating delirium frequency and outcomes in all critically ill cancer patients with COVID-19 admitted between March 1 and July 10, 2020. Delirium was assessed by Confusion Assessment Method for Intensive Care Unit, performed twice daily by trained intensive care unit (ICU) nursing staff. Patients were considered to have a delirium-positive day if Confusion Assessment Method for Intensive Care Unit was positive at least once per day.* **Results:** *A total of 70 patients were evaluated. Of those 70, 53 (75.7%) were found to be positive for delirium. Patients with delirium were significantly older than patients without delirium (median age 67.5 vs 60.3 y,* $P = 0.013$*). There were no significant differences in demographic characteristics, chronic medical conditions, neuropsychiatric history, cancer type, or application of prone positioning between the 2 groups. Delirium patients were less likely to receive cancer-directed therapies (58.5% vs 88.2%,* $P = 0.038$*) but more likely to receive antipsychotics (81.1% vs 41.2%,* $P = 0.004$*), dexmedetomidine (79.3% vs 11.8%,* $P < 0.001$*), steroids (84.9% vs 58.8%,* $P = 0.039$*), and vasopressors (90.6% vs 58.8%,* $P = 0.006$*). Delirium patients were more likely to be intubated (86.8% vs 41.2%,* $P < 0.001$*), and all tracheostomies (35.9%) occurred in patients with delirium. ICU length of stay (19 vs 8 d,* $P < 0.001$*) and hospital length of stay (37 vs 12 d,* $P < 0.001$*) were significantly longer in delirium patients, but there was no statistically significant difference in hospital mortality (43.4% vs 58.8%,* $P = 0.403$*) or ICU mortality (34.0% vs 58.8%,* $P = 0.090$*).* **Conclusions:** *Delirium in critically ill cancer patients with COVID-19 was associated with less cancer-directed therapies and increased hospital and ICU length of stay. However, the presence of delirium was not associated with an increase in hospital or ICU mortality.*

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Key words: COVID-19, cancer, critically ill, CAM-ICU, delirium.

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INTRODUCTION

Delirium is a significant neuropsychiatric syndrome encountered among hospitalized patients with cancer.[1–4] It is characterized by an acute disturbance in awareness, attention, and cognition due to another medical condition, medications, substance intoxication/withdrawal, toxin, or multiple etiologies.[5] In patients admitted to the intensive care unit (ICU), delirium has been associated with increased length of stay (LOS), in-hospital mortality, and cognitive adverse outcomes.[6] The incidence rate ranges between 25% and 40% among cancer patients, with higher rates (up to 88%) among the terminally ill.[1,7] Early detection and management of delirium have the potential to improve clinical outcomes.[8] Cancer patients represent a unique population at risk for delirium and its worst outcomes.

In the advent of the COVID-19 pandemic, the primary research focus was on respiratory manifestations of the infection. With continued observation of clinical presentations, understanding of its neuropsychiatric complications became a paramount issue.[9,10] Data pertaining to delirium incidence in COVID-19 infections in critically ill patients are limited with recent estimates of 34%–80%.[11–13] Increased levels of C-reactive protein on admission has been associated with increased risk of delirium in COVID-19 patients.[14] Cancer has been documented as a significant risk factor for COVID-19 infection as well as higher rates of adverse clinical outcomes than in patients without cancer.[15–17] Chemotherapy, surgery, and immunotherapy have also been associated with increased morbidity and mortality in infected patients.[15,18–21] However, these risk factors have not been studied in critically ill cancer patients with COVID-19 infection.

In March 2020, New York City became the epicenter of the U.S. COVID-19 experience. Memorial Sloan Kettering Cancer Center, a 470-bed academic tertiary cancer center in New York City, cared for cancer patients with COVID-19. The critical care and psychiatry teams closely collaborated for assessment and management of delirium in patients admitted to ICU with COVID-19. Institutional sedation and delirium management guidelines were established in anticipation of medication shortages.[22] Based on the emergence of anecdotal evidence, there was concern of a need for high-dose sedation with multiple agents and potentially a high incidence of delirium among critically ill COVID-19 patients. The aim of this retrospective study is to determine the incidence of delirium in critically ill cancer patients with COVID-19 infection, potential risk factors associated with the development of delirium, usage of narcoanalgesic and sedative agents, and outcomes.

STUDY DESIGN AND METHODS

Study Design

This is a retrospective, single-center observational study analyzing all cancer patients ≥18 years of age who required ICU care for COVID-19 infection at the Memorial Sloan Kettering Cancer Center from March 1, 2020, to July 10, 2020. Patients were either directly admitted to ICU upon presentation or transferred from other floors to the ICU. COVID-19 infection was confirmed by reverse transcriptase polymerase chain reaction testing on nasopharyngeal swabs. We excluded patients without cancer and those who were admitted to ICU for <72 hours. The study was granted a waiver of informed consent by the institutional review board. All data were kept in a secure local Research Electronic Data Capture server.[23]

Treatment Guidelines

Early experiences from China, Italy, and the United States warned of the need for high sedation requirements along with polypharmacy to achieve adequate comfort and ventilator synchrony.[24] Additionally, with a high number of patients, many centers had to deal with shortages of commonly used ICU sedatives. In this setting, the critical care team at MSK collaborated with psychiatry colleagues to manage the needs for prolonged sedation among critically ill cancer patients with COVID-19. The protocol allowed for judicious use of medications which were short in supply while supplementing with nonstandard medications to manage potential delirium during the weaning process.[22]

Demographics, Clinical, and Oncological Data

Demographic, clinical, and outcome data included age, gender, race, cancer types and subtypes, medical and neuropsychiatric comorbidities, service type (medical or surgical), Mortality Probability Model II score on ICU admission, use of mechanical ventilation (MV) and vasopressor agents, steroids, prone positioning, physical

restraints and tracheostomy, need for maximum FiO_2 and positive end-expiratory pressure levels, COVID-19-directed therapies, dates of intubation and extubation, dates of hospital and ICU admission and discharge, and survival status.[25] Laboratory values were obtained within the first 7 days of ICU admission and included C-reactive protein, interleukin 6, ferritin, and absolute lymphocyte count. Oncologic data included cancer type and subtype, presence of metastatic disease, history of hematopoietic stem cell transplantation, and time of last cancer intervention. Last cancer-related treatment or intervention before COVID-19 infection included any chemotherapy, radiation, surgery, hematopoietic stem cell transplantation, or invasive procedure that were performed with curative or palliative intent within 30 days of hospital admission. Cancer types were divided into solid or hematologic (leukemia, lymphoma, multiple myeloma, or hematopoietic stem cell transplantation) while subtype classification included gastrointestinal, genitourinary, head and neck, thoracic, or other.

Delirium Assessment

Delirium was determined via the Confusion Assessment Method (CAM) for ICU, a validated scale for the diagnosis of delirium in the ICU.[26] Patients were followed up sequentially with twice-daily CAM-ICU screenings until resolution, death, or discharge. Assessment was performed by Memorial Sloan Kettering Cancer Center critical care nurses, who undergo extensive delirium and CAM-ICU training comprising biannual in-person didactics and audits. Competency is determined both via test scores as well as in-person evaluation by nurses that have been designated as "*Delirium Champions*". In-person evaluation is also dependent on bi-annual audits (clinician-based chart reviews contrasted with CAM-ICU scores) to assess reliability and accuracy. CAM-ICU was reported as either positive or negative and "unable to assess" for paralyzed or comatose patients. Patients were assessed to have delirium if they had at least 1 positive CAM-ICU over a 24-hour period. Unable-to-assess fields prompted independent chart review of the psychiatry, critical care medicine, and nursing notes by 2 study staff to confirm the accuracy of the recorded finding or a concurrent diagnosis of delirium. Consensus was sought from several other study authors if the independent chart review was inconclusive.

Richmond Agitation Sedation Scale (RASS) scores were recorded twice daily by nursing staff to determine delirium subtype.[27] For patients with positive CAM-ICU, RASS scores of −5 to 0 were classified as "not hyperactive," and RASS scores of +1 or above were classified as hyperactive. RASS was summarized for each patient using the average across all available RASS values for each patient.

Outcomes

The primary outcome was to determine the frequency of delirium in critically ill COVID-19 patients with cancer and potential risk factors associated with the development of delirium. Positive delirium was defined as any positive CAM-ICU assessment or notes entered by psychiatry or ICU staff supporting a diagnosis of delirium for patients with unable-to-assess results. Any patient with 1 or more days of delirium was considered as a positive delirium patient. Secondary outcomes included hospital and ICU mortality, hospital and ICU LOS, duration of intubation, and requirement for tracheostomy.

Statistical Analysis

Categorical variables are described using count and percent and compared between delirium positive and negative groups using Fisher's exact test. Continuous variables are described using median and interquartile range (IQR) and compared using Wilcoxon rank sum test. SAS version 9.4 (SAS institute Inc., Cary, NC) was used for all analysis. All tests were 2-sided, and $P < 0.05$ was considered significant.

RESULTS

During the study period, there were 103 ICU admissions for COVID-19 of which 70 patients met the inclusion criteria. Of the included patients, 53 (75.7%) were found to have delirium. Delirium was present for a median of 10 days (IQR 5–18) with a range of 1–78 days. For the entire study group, the median age was 65.9 (IQR 60.3–71.2), and the minority were female (45.7%). The predominant cancers were thoracic with 12 cases (17.1%), lymphoma 12 (17.1%), and leukemia 12 (17.1%). Overall, there were few comorbid conditions, but the most common was hypertension (41.4%) followed by diabetes (28.6%) (Table 1). The median hospital LOS was 30 days (IQR 16–55), and median

TABLE 1. Demographic and Clinical Data Among All Patients

Characteristic	Delirium negative *n* = 17 (24.3)	Delirium positive *n* = 53 (75.7)	All patients *n* = 70 (100)	*P* value
Age, y	60.3 (49.5–65.6)	67.5 (62.0–71.5)	65.9 (60.3–71.2)	0.013
Gender				
Female	9 (52.9)	23 (43.4)	32 (45.7)	0.580
Race				0.315
Asian	2 (12.5)	5 (9.8)	7 (10.5)	
Black	1 (6.3)	12 (23.5)	13 (19.4)	
White	12 (75)	33 (64.7)	45 (67.2)	
Other	1 (6.3)	1 (2)	2 (3)	
Missing	1 (5.9)	2 (3.8)	3 (4.3)	
Oncologic data				
Solid	11 (64.7)	27 (50.9)	38 (54.2)	0.406*
Breast	3 (17.7)	3 (5.7)	6 (8.6)	
Gastrointestinal	2 (11.8)	2 (3.8)	4 (5.7)	
Genitourinary	1 (5.9)	7 (13.2)	8 (11.4)	
Thoracic	2 (11.8)	10 (18.8)	12 (17.1)	
Neurologic	2 (11.8)	1 (1.9)	3 (4.3)	
Other	1 (5.9)	4 (7.6)	5 (7.1)	
Hematologic	6 (35.3)	26 (49.1)	32 (45.7)	
Leukemia	3 (17.7)	09 (16.9)	12 (17.1)	
Lymphoma	1 (5.9)	11 (20.6)	12 (17.1)	
Multiple myeloma	2 (11.8)	4 (7.6)	6 (8.6)	
Other	0 (0)	2 (3.8)	2 (2.9)	
Oncologic treatment				
All treatments	15 (88.2)	31 (58.5)	46 (65.7)	0.038†
Systemic treatment‡	12 (70.6)	29 (54.7)	41 (58.6)	
Radiotherapy	2 (11.8)	0 (0)	2 (2.9)	
Surgery	1 (5.9)	2 (3.8)	3 (4.3)	
No treatment	2 (11.8)	22 (41.5)	24 (34.3)	
Medical comorbidities				
Alcoholism	0 (0)	0 (0)	0 (0)	
CAD	1 (5.9)	6 (11.3)	7 (10)	1.000
CHF	0 (0)	0 (0)	0 (0)	
Cirrhosis	0 (0)	1 (1.9)	1 (1.4)	1.000
Hepatitis	1 (5.9)	0 (0)	1 (1.4)	0.243
Chronic oxygen use	0 (0)	0 (0)	0 (0)	
Dementia	0 (0)	0 (0)	0 (0)	
Diabetes	4 (23.5)	16 (30.2)	20 (28.6)	0.761
Organ transplant Hx.	0 (0)	0 (0)	0 (0)	
HIV/AIDS	0 (0)	1 (1.9)	1 (1.4)	1.000
Hypertension	6 (35.3)	23 (43.4)	29 (41.4)	0.587
Immunosuppressed	0 (0)	1 (1.9)	1 (1.4)	1.000
IBS	1 (5.9)	0 (0)	1 (1.4)	0.243
Pulmonary disease	4 (23.5)	3 (5.7)	7 (10)	0.4054
Renal disease	1 (5.9)	1 (1.9)	2 (2.86)	0.429
Autoimmune disease	0 (0)	1 (1.9)	1 (1.4)	1.000
Neuropsychiatric comorbidities				
Psychotic disorder	0 (0)	1 (1.9)	1 (1.4)	1.000
Bipolar disorder	0 (0)	0 (0)	0 (0)	
Substance use disorder	0 (0)	1 (1.9)	1 (1.4)	1.000
Depressive disorder	3 (17.7)	5 (9.4)	8 (11.4)	0.392
Anxiety disorder	2 (11.8)	5 (9.4)	7 (10)	1.000
Cognitive disorder§	1 (5.9)	4 (7.6)	5 (7.1)	1.000

Data are *n* (%) or median (IQR).

CAD = coronary artery disease; CHF = congestive heart failure; IBS = inflammatory bowel disease; IQR = interquartile range.

* Comparison is between solid vs hematologic.

† Comparison is between any treatment vs none.

‡ Included cytotoxic chemotherapy, endocrine therapy, targeted therapy, immunotherapy, and others—see Supplemental Material.

§ Includes prior diagnosis of major neurocognitive disorder or delirium.

ICU LOS was 12.5 days (IQR 8–25). A significant number of patients (53, 75.7%) required intubation with median duration of 15 days (8–23). Overall hospital and ICU mortality were 33 (47.4%) and 28 (40.0%), respectively (Table 4).

Group Comparisons

Patients with delirium were significantly older (67.5 vs 60.3, $P = 0.013$), were less likely to receive cancer-directed therapies (58.5% vs 88.2%, $P = 0.038$), and more likely to receive antipsychotics (81.1% vs 41.2%, $P = 0.004$) or dexmedetomidine (79.3% vs 11.8%, $P < 0.001$). The use of various medications was longer in patients with delirium: antipsychotics (median 6 vs 2 d, $P < 0.001$), opioids (5.5 vs 3.0, $P = 0.033$), benzodiazepines (6 vs 2, $P < 0.001$), and propofol (4 vs 2, $P < 0.045$) (Table 3). There was no significant difference between the 2 groups regarding race, gender, comorbid conditions, underlying neuropsychiatric disorders, and cancer type or subtype (Table 1). Similarly, there were no statistically significant differences among the COVID-19-specific therapeutics based on delirium status. Laboratory data, including absolute lymphocytes and C-reactive protein, did not show any statistically significant difference between the 2 groups (Table 3).

Delirium patients were more likely to be intubated (86.8% vs 41.2%, $P < 0.001$) and to require tracheostomy (35.9% vs 0%, $P = 0.003$). Duration of MV was significantly longer in the delirium group (16 vs 6, $P = 0.001$), but there was no statistically significant difference in prone positioning (56.6% vs 47.1%, $P = 0.580$), maximal positive end-expiratory pressure (14 cm H_2O vs 10 cm H_2O, $P = 0.456$), or maximal FiO_2 requirements (100% vs 100%, $P = 0.630$). Physical restraints were used on 32.1% of delirium-positive patients (32.1% vs 0%, $P < 0.007$) (Table 2). Patients with delirium had significantly higher ICU (19 vs 8 d, $P < 0.001$) and hospital (37 vs 12 d, $P < 0.001$) LOS. There was no significant difference in hospital (43.4% vs 58.8%, $P = 0.403$) or ICU (34.0% vs 58.8%, $P = 0.090$) mortality between patients with delirium and those without (Table 4).

TABLE 2. Delirium Data

Delirium	53 (75.7)
Duration, d	10 (5–18)
RASS	−2.5 (−3.2 to −1.5)
Hyperactive	
Ever	36 (67.9)
Never	17 (32.1)

Data are *n* (%), median (IQR).

IQR = interquartile range; RASS = Richmond Agitation Sedation Scale.

DISCUSSION

Our study of critically ill cancer patients with COVID-19 at a tertiary cancer center during the first wave of the pandemic showed several important findings. First, the rate of delirium was similar to that of the general critically ill populations[11,14]; however, mortality did not differ between groups. As previously noted, the presence of delirium was associated with increased duration of MV as well as LOS. Surprisingly, receipt of cancer-directed therapies within the last 30 days was associated with a lower rate of delirium. Early intubation and sedation practices at the beginning of the pandemic may have impacted the development of delirium. The novelty of the disease, anecdotal experience from critical care providers communicating throughout the world, and the basic pathophysiological knowledge from respiratory insufficiency led to the initial treatment of COVID-19 with early intubation, MV, and deep sedation. With more experience, COVID-19 management has dramatically evolved.[28] For instance, only 78% of our study population received steroids, whereas dexamethasone would now be a standard therapy.[29,30]

In our study, hospital LOS was about 3 times higher, and the ICU LOS was 2 and a half times higher for the delirium group than that for the nondelirium group. Higher hospital and ICU LOS and mortality in delirium patients have been reported in the literature.[6,31] The mortality patterns in our cohort were similar to those of critically ill cancer patients suffering from acute respiratory failure but significantly lower than the pooled mortality of critically ill cancer patients who developed COVID-19.[32–34] One explanation of the lower hospital mortality in our cohort is the small sample size. Our institutional efforts of immersing a psychiatry consultant to each ICU team and having specific guidelines for sedation practices for the critically ill patients with COVID-19 may have also contributed to lower mortality.[35] Emerging data have shown a potential protective factor against mortality

TABLE 3. Medication and Laboratory Values

Characteristic	Delirium negative (*n* = 17)	Delirium positive (*n* = 53)	All patients (*n* = 70)	*P* value
Antipsychotics*	7 (41.2)	43 (81.1)	50 (71.4)	0.004
Duration, d	2 (1–2)	6 (3–8)	5 (3–8)	<0.001
Opioids*	12 (70.6)	48 (90.6)	60 (85.7)	0.055
Duration, d	3 (1.5–4.5)	5.5 (3–8)	4 (2–8)	0.033
Benzodiazepines*	11 (64.7)	46 (86.8)	57 (81.4)	0.069
Duration, d	2 (1–4)	6 (3–10)	5 (2–7)	<0.001
Paralytics*	10 (58.8)	39 (73.6)	49 (70)	0.361
Duration, d	3 (1–4)	5 (2–7)	4 (2–6)	0.120
Dexmedetomidine	2 (11.8)	42 (79.3)	44 (62.9)	<0.001
Duration, d	4.5 (2–7)	2 (1–3)	2 (1.5–3)	0.351
Ketamine	1 (5.9)	16 (30.2)	17 (24.3)	0.053
Duration, d	1 (1–1)	4.5 (2–7)	4 (2–6)	0.217
Propofol	9 (52.9)	42 (79.3)	51 (72.9)	0.057
Duration, d	2 (1–3)	4 (2–6)	3 (2–6)	0.045
Clonidine	0 (0.0)	3 (5.7)	3 (4.29)	1.000
Duration, d	NA (NA–NA)	1 (1–2)	1 (1–2)	
Steroids	10 (58.8)	45 (84.9)	55 (78.6)	0.039
Duration, d	2 (1–3)	4 (3–7)	3 (2–6)	0.007
Vasopressors	10 (58.8)	48 (90.6)	58 (82.9)	0.006
Duration, d	2 (1–3)	3.5 (2–6)	3 (2–6)	0.083
COVID medications				
Remdesivir	1 (5.9)	12 (22.6)	13 (18.6)	0.165
Hydroxychloroquine	8 (47.1)	25 (47.2)	33 (47.1)	1.000
Tocilizumab	1 (5.9)	8 (15.1)	9 (12.9)	0.438
Azithromycin	6 (35.3)	23 (43.4)	29 (41.4)	0.587
Laboratory values				
Absolute lymphocytes (k/mcl)	0.6 (0.3–1.3)	0.6 (0.4–1)	0.6 (0.3–1.0)	0.955
Missing	0	1	1	
C-reactive protein (mg/dL)	11.8 (8.2–24.7)	15.6 (10.9–23.7)	14.4 (10.6–23.7)	0.460
Missing	0	1	1	
Ferritin (ng/mL)	598 (425–1633)	1127 (396.5–2395.5)	855 (423–2073)	0.256
Missing	0	1	1	
IL-6 (pg/mL)	86.4 (58–174.2)	111.3 (56.9–239.1)	95.3 (57.3–224.5)	0.491
Missing	0	1	1	

Data are *n* (%) or median (IQR).

NA = not applicable; IL-6 = interleukin 6; IQR = interquartile range.

* For in-depth characteristics of medications used, please refer to the Supplemental Material.

that strengthens with increasing doses of haloperidol among critically ill patients when used immediately after delirium diagnosis.[36] This cohort was involved in a treatment algorithm that recommended low threshold of antipsychotic use upon ICU admission. A third of our cohort used haloperidol as their standard antipsychotic (see Supplemental Material). The lack of differences between the group mortality rates could potentially be explained by this protective effect. However, this finding requires further prospective studies.

We observed a lower rate of delirium in patients with COVID-19 who received cancer-related therapies within 30 days of hospital admission. Cancer therapies have been associated with increased morbidity and mortality in past studies although this is not a consistent finding.[15,18–20,37] Chemotherapies have been associated with the development of delirium although there are significant gaps in this research area, and most of the data come from cytotoxic agents.[38] Our cohort's systemic treatment involved cytotoxic drugs only 34% of the time (see Supplemental Material). It is possible that hormone-targeted therapies and immunotherapies may offer a protection toward cancer-related deliriogenic effects, without the additional neurotoxic effects that cytotoxic agents have shown to produce. Such an association merits further consideration through prospective or larger cohort studies. The limited number of comorbidities and the small sample size in this study may have also played a role in this result.

TABLE 4. ICU Data and Outcomes

Characteristic	Delirium negative (n = 17)	Delirium positive (n = 53)	All patients (n = 70)	P value
ICU LOS	8 (5–9)	19 (10–33)	12.5 (8–25)	<0.001
Hospital LOS	12 (9–18)	37 (26–58)	30 (16–55)	<0.001
Hospital mortality	10 (58.8)	23 (43.4)	33 (47.4)	0.403
ICU mortality	10 (58.8)	18 (34)	28 (40)	0.090
RRT	1 (5.9)	9 (17)	10 (14.3)	0.432
Intubation	7 (41.2)	46 (86.8)	53 (75.7)	<0.001
Intubation duration, d	6 (4–10)	16 (11–23)	15 (8–23)	0.001
ICU admission to intubation, d	0 (0–3)	1 (0–1)	0 (0–1)	0.858
Tracheostomy	0 (0)	19 (35.9)	19 (27.1)	0.003
ICU to trach days	NA (NA–NA)	26 (21–31)	26 (21–31)	
Max PEEP	10 (8–16)	14 (12–15)	14 (10–16)	0.456
Missing	10	6	16	
Max FiO_2	100.0 (100.0–100.0)	100.0 (100.0–100.0)	100.0 (100.0–100.0)	0.630
Missing	11	8	19	
Physical restraints	0 (0)	17 (32.1)	18 (24.3)	0.007
Prone ≥6 h	8 (47.1)	30 (56.6)	38 (54.3)	0.580
MPM_0-II	28 (22.5–56)	43 (28–70)	40 (26–64)	0.105
Psychiatry consult	4 (23.5)	31 (58.5)	35 (50)	0.024

Data are n (%), median (IQR).

FiO_2 = fraction of inspired oxygen; ICU = intensive care unit; IQR = interquartile range; LOS = length of stay; MPM_0-II = Mortality Probability Model II score on ICU admission; NA = not applicable; PEEP = positive end-expiratory pressure; RRT = renal replacement therapy.

The frequency of delirium among mechanically ventilated patients was twice that of patients who were not intubated. Additionally, patients with delirium had increased number of MV days and were the exclusive recipients of tracheostomy. These 2 variables may be indicative of illness severity and of the combined impact of delirium, COVID-19, and cancer. The severity of COVID-19 infection in intubated patients is also suggested by the increased use of steroids and vasopressors in this group. Vasopressors, older age, and MV have been demonstrated to be risk factors for the development of delirium.[3,39–41] The above findings in the setting of similar incident rates to the general critically ill population suggests that COVID-19 does not necessarily present with an added severity risk compared to other infectious causes of respiratory failure. Similarly, the incidence and outcomes of delirium may be very different with each variant of COVID throughout the pandemic. Our data are limited to the initial wave of the ancestral strain of COVID.

Our retrospective study has several limitations. This was a retrospective comparison of a single cohort. Having a non-COVID cohort could lead to potentially different results. It would have also been informative to consistently obtain electroencephalogram, brain imaging, and cerebrospinal fluid analysis data to better understand the unique neurological manifestations of COVID-19, but these data were not collected in the beginning to avoid transportation and invasive procedures. We erred on the side of safety and sparingly ordered ancillary tests unless clinically indicated to reduce the transmission of the virus. The diagnosis of hypoactive delirium was not included due to the ambiguity in establishing this diagnosis retrospectively in patients who were heavily sedated.[42] We were unable to provide long-term follow-up data and how the presence of delirium may have impacted quality of life, further cancer therapy, or return to pre-COVID cognitive function.

CONCLUSION

In a cohort of critically ill patients with cancer who were hospitalized for COVID-19, delirium had a high incidence and was associated with higher hospital and ICU stay and ventilation days, with similar rates to the general non-COVID-19 critically ill population. Administration of cancer-directed therapies appears to be a potential protective factor for delirium in this unique population. We also found that antipsychotic use in our study population with incident delirium was associated with a lower mortality. However, these findings warrant further observational or intervention-based studies

assessing antipsychotic dosing in incident delirium and cancer-directed therapies in this population.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jaclp.2022.05.005.

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