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Clinical characteristics and outcomes among critically ill patients with cancer and COVID-19-related acute respiratory failure

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Abstract

Background Coronavirus disease 2019 (COVID-19) has affected individuals worldwide, and patients with cancer are particularly vulnerable to COVID-19-related severe illness, respiratory failure, and mortality. The relationship between COVID-19 and cancer remains a critical concern, and a comprehensive investigation of the factors affecting survival among patients with cancer who develop COVID-19-related respiratory failure is warranted. We aim to compare the characteristics and outcomes of COVID-19-related acute respiratory failure in patients with and without underlying cancer, while analyzing factors affecting in-hospital survival among cancer patients.

Methods We conducted a retrospective observational study at Taipei Veterans General Hospital in Taiwan from May to September 2022, a period during which the omicron variant of the severe acute respiratory syndrome coronavirus 2 was circulating. Eligible patients had COVID-19 and acute respiratory failure. Clinical data, demographic information, disease severity markers, treatment details, and outcomes were collected and analyzed.

Results Of the 215 enrolled critically ill patients with COVID-19, 65 had cancer. The patients with cancer were younger and had lower absolute lymphocyte counts, higher ferritin and lactate dehydrogenase (LDH) concentrations, and increased vasopressor use compared with those without cancer. The patients with cancer also received more COVID-19 specific treatments but had higher in-hospital mortality rate (61.5% vs 36%, $P = 0.002$) and longer viral shedding (13 vs 10 days, $P = 0.007$) than those without cancer did. Smoking [odds ratio (OR): 5.804, 95% confidence interval (CI): 1.847–39.746], elevated LDH (OR: 1.004, 95% CI: 1.001–1.012), vasopressor use (OR: 5.437, 95% CI: 1.202–24.593), and new renal replacement therapy (OR: 3.523, 95% CI: 1.203–61.108) were independent predictors of in-hospital mortality among patients with cancer and respiratory failure.

Conclusion Critically ill patients with cancer experiencing COVID-19-related acute respiratory failure present unique clinical features and worse clinical outcomes compared with those without cancer. Smoking, elevated LDH, vasopressor use, and new renal replacement therapy were risk factors for in-hospital mortality in these patients.

Keywords Acute respiratory failure, Coronavirus disease 2019 (COVID-19), Malignancy, Vasopressor, Inflammatory marker

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Background

The COVID-19 pandemic posed a considerable global challenge. The pandemic resulted in up to 6.9 million deaths (till November 2023, according to the data from World Health Organization) [1] and placed substantial burdens on health-care systems worldwide. Individuals with certain pre-existing conditions are particularly susceptible to COVID-19, and the relationship between COVID-19 and cancer has become a crucial and concerning issue. Patients with cancer are more susceptible to severe illness from COVID-19 than are those without cancer, which may be due to the presence of concurrent comorbidities, the inherent immunosuppressive characteristics of cancer, and the immunosuppression induced by systemic cancer treatments [2], with mortality rates as high as 25% being reported for patients with solid organ malignancies [3]. Respiratory failure is a severe complication of COVID-19 that typically occurs approximately 1 week after the onset of symptoms. Respiratory failure is usually accompanied by thrombosis and acute renal failure [4]. Treatment strategies for COVID-19-related respiratory failure are similar to those established for acute respiratory distress syndrome (ARDS) [5], and include oxygen therapy; lung-protective ventilation; prone positioning; supportive care; and administration of specific medications, such as corticosteroids, antiviral agents, immunomodulators, and anticoagulants [4–6]. Treatment for COVID-19-related respiratory failure among patients with cancer requires a multidisciplinary approach. The risk of death from COVID-19 among cancer patients is influenced by age; male sex; performance status; comorbidities; and hematological malignancies [7–10]. Whether recent cancer treatment influence survival remains controversial [2, 11, 12]. Understanding the factors that increase the risk of death from COVID-19 is crucial for optimizing patient management and improving outcomes. This study aims to investigate and compare the characteristics and outcomes among patients experiencing COVID-19-related acute respiratory failure between individuals with and without underlying cancer, while further analyzing the factors influencing in-hospital survival among cancer patients.

Methods

This retrospective observational study was conducted at Taipei Veterans General Hospital, a tertiary medical center in Taiwan, between May and September 2022. During this period, the omicron variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was circulating in Taiwan. Patients were included in this study if they were infected with SARS-CoV-2 and experienced acute respiratory failure, defined as requiring high-flow nasal cannula (HFNC), or noninvasive ventilation (NIV), or mechanical ventilation (MV). SARS-CoV-2 infection was confirmed through reverse transcription polymerase chain reaction (RT-PCR) by using the Roche Cobas 6800 system (Roche Diagnostics, Rotkreuz, Switzerland).

Electronic medical records were reviewed to collect clinical information. Patients with advanced stage or metastatic cancer and those without remission were included. Other demographic data, including age, sex, body mass index (BMI), smoking and vaccination history, underlying diseases, do not resuscitate (DNR) code status, laboratory results on admission, and severity, were also obtained. Severity was assessed on the day of respiratory failure, including sequential organ failure assessment (SOFA) scores, Mean arterial pressure (MAP) scores (derived from the SOFA score, accounted for the administration of vasoactive agents, rating as 0 (no hypotension), 1 (mean arterial pressure < 70 mmHg), 2 (dopamine ≤5 mcg/kg/min or any dose of dobutamine), 3 (dopamine > 5 mcg/kg/min, epinephrine ≤0.1 mcg/kg/min, or norepinephrine ≤0.1 mcg/kg/min), and 4 (dopamine > 15 mcg/kg/min, epinephrine > 0.1 mcg/kg/min, or norepinephrine > 0.1 mcg/kg/min) [13], Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II score [14], Glasgow coma scale [15], vasopressor usage, PaO_2/FiO_2 ratio (estimated as the ratio of arterial oxygen partial pressure [PaO_2 in mmHg] to fractional inspired oxygen) [16] were collected upon the day of respiratory failure. Treatment information, including receiving corticosteroids, tocilizumab, remdesivir, nirmatrelvir/ritonavir, molnupiravir, and enoxaparin; surgery; and new renal replacement therapy during admission, was also reviewed. Cytomegalovirus (CMV) infection, gastrointestinal bleeding, and thromboembolism were included as disease-related complications. Clinical courses and outcomes, such as the use of MV and ECMO, in-hospital mortality, and duration from the onset of symptoms until the day the cycle threshold (Ct) value exceeded 30, were also recorded [17]. Studies revealed a Ct value of 30 or higher to be non-infectious, with no virus isolated from culture [18]. In addition, a Ct value of at 30 or higher is the threshold for isolation release set by the Taiwan Center for Disease Control [19].

Statistical analysis

The baseline characteristics were summarized using descriptive statistics, and continuous variables were expressed as medians and interquartile ranges. The Mann-Whitney U test was employed to assess differences in distribution between two independent groups for non-normally distributed continuous variables. Pearson's chi-square test or Fisher's exact test were used to examine variations in the distribution of categorical variables across different groups. In-hospital survival time and

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time to reach Ct > 30 among the patients with and without cancer were plotted using the Kaplan-Meier method and compared using a log-rank test. Cox proportional hazard models were used to assess the factors associated with in-hospital mortality, and factors with $P < 0.1$ in univariable analysis were incorporated into multivariable analysis. Statistical significance was indicated by $P < 0.05$. Statistical analyses were performed using IBM SPSS Statistics, version 26.0 (IBM, Armonk, NY, USA).

Results

In total, 215 patients with COVID-19-related acute respiratory failure were enrolled. Among these patients, 65 had cancer. The patient characteristics, laboratory results, disease severity on the day of respiratory failure, treatment, complications, and outcomes are summarized in Table 1.

The patients with cancer were younger than those without cancer (median age 73 vs 82 years, $P = 0.001$). Furthermore, the patients with cancer had lower prevalence rates of cerebrovascular accidents (9.2% vs 20.7%, $P = 0.041$) and heart failure (1.5% vs 14%, $P = 0.003$) than did the patients without cancer.

The patients with cancer had lower absolute lymphocyte counts (median 546.8 vs 781.6 × 10^9/L, $P = 0.003$) and higher concentrations of ferritin (1035 vs 529 ng/mL, $P = 0.002$) and lactate dehydrogenase (LDH; median 423 vs 339 U/L, $P = 0.01$) on the day of respiratory failure than did the patients without cancer. The patients with cancer also had higher mean arterial pressure scores (median 1 vs 0.5, $P = 0.022$) and a higher prevalence of vasopressor use (43.1% vs 28%, $P = 0.03$) on the day of respiratory failure than did the patients without cancer.

The patients with cancer were more likely to receive remdesivir (90.8% vs 73.3%, $P = 0.004$), tocilizumab (46.2% vs 30.7%, $P = 0.029$), and corticosteroids (93.8% vs 82%, $P = 0.023$) than were the patients without cancer. In terms of outcomes, the patients with cancer were significantly more likely to die in hospital (in-hospital mortality rate 61.5% vs 36%, $P = 0.002$) and took longer to reach Ct > 30 (median 13 vs 10 days, $P = 0.007$) than did the patients without cancer. The in-hospital survival and time to reach Ct > 30 in patients with and without cancer are illustrated in Fig. 1.

The characteristics of the 65 patients with cancer are summarized in Table 2 and Fig. 2.

Most (87.7%) patients with cancer had solid tumors, with lung cancer (24.6%) and gastrointestinal tumors (15.4%) being the most common, followed by hematological malignancies (12.3%). In total, 34 (52.3%) patients received cancer-related treatment within 4 weeks before receiving a COVID-19 diagnosis, with approximately half receiving cytotoxic chemotherapy.

In-hospital mortality among the patients with cancer was 61.5%, with 25 survivors and 40 nonsurvivors (Table 3). The nonsurvivors were more likely to be smokers (42.5% vs 12%, $P = 0.024$) than were the survivors. Furthermore, the nonsurvivors had higher white blood cell counts (median 12,450 vs 8500 × 10^9/L, $P = 0.006$) and concentrations of ferritin (median 3220 vs 673.5 ng/mL, $P < 0.001$), LDH (median 534.5 vs 256 U/L, $P < 0.001$), lactate (median 33 vs 15.7 mg/dL, $P = 0.005$), and D-dimer (median 4.605 vs 1.570 µg/mL, $P = 0.007$) than did the survivors. Additionally, the nonsurvivors had a higher incidence of vasopressor use on the day of respiratory failure (55% vs 24%, $P = 0.014$) and new renal replacement therapy during admission (22.5% vs 4%, $P = 0.044$) than did the survivors. The difference in survival status was not statistically significant based on whether patients had undergone systemic treatment or received cytotoxic chemotherapy within the 4 weeks preceding their COVID-19 diagnosis.

The comparison of the characteristics, laboratory data, treatment, complications, and outcomes between cancer patients who have undergone recent systemic treatment and those who have not received it was summarized in Supplemental Table 1. The patients who have underwent cancer treatment were younger (median 71.5 vs 79 years old, $P = 0.029$), had lower absolute lymphocyte count on the day of respiratory failure (median 657.6 vs 440.28 × 10^9/L, $P = 0.030$), higher LDH level (median 536 vs 342 U/L, $P = 0.016$), and took shorter to reach Ct > 30 (median 8.5 vs 17 days, $P = 0.033$) than did the patients without treatment.

According to multivariable analysis (Table 4), smoking (OR: 5.804, 95% CI: 1.847−39.746, $P = 0.043$), an elevated concentration of LDH (OR: 1.004, 95% CI: 1.001−1.012, $P = 0.025$), vasopressor use on the day of respiratory failure (OR: 5.437, 95% CI: 1.202−24.593, $P = 0.028$), and new renal replacement therapy during admission (OR: 3.523, 95% CI: 1.203−61.108, $P = 0.034$) were significantly associated with in-hospital mortality among patients with cancer and COVID-19-related respiratory failure.

Discussion

This study revealed the characteristics and factors that influence in-hospital mortality among patients with cancer and COVID-19-related respiratory failure during the period in which the omicron variant of SARS-CoV-2 was circulating in Taiwan. The patients with cancer and COVID-19-related respiratory failure exhibited distinct clinical characteristics, including lower lymphocyte counts, higher ferritin and LDH concentrations, and increased vasopressor use than did the patients without cancer. Additionally, the patients with cancer received COVID-19-related treatments more frequently than did

Table 1 Characteristics between COVID-19 patients with respiratory failure with and without cancer

	All cases (n = 215)	Cancer (n = 65)	No Cancer (n = 150)	*P* value***
Demographics				
Age, year, median	80	73	82	0.001
Male	145(67.4)	43(66.2)	102(68)	0.791
Body mass index, kg/m^2, median	21.9	22.84	21.71	0.521
BMI[a] < 18	36(18.3)	18.5(20.3)	24(16)	0.624
BMI > 24	62(31.5)	23(35.4)	39(26)	0.138
Vaccination doses, median	2	2	2	0.392
Ever vaccinated	143(66.5)	45(69.2)	98(65.3)	0.730
Fully vaccinated (> = 3 doses)	93(43.3)	32(49.2)	61(40.7)	0.244
Smoker	53(24.7)	20(30.8)	33(22)	0.171
DNR[a]	146(67.9)	47(72.3)	99(66)	0.363
Comorbidity				
Cerebrovascular disease	37(17.2)	6(9.2)	31(20.7)	0.041
Dementia	21(14.4)	5(7.7)	26(17.3)	0.065
Heart failure	22(10.2)	1(1.5)	21(14%)	0.003
Myocardial infarction	3(1.4)	0	3(2)	0.338
Peripheral vascular disease	11(5.1)	2(3.1)	9(6)	0.372
Diabetes mellitus	86(40)	22(33.8)	64(42.7)	0.225
Chronic kidney disease	50(23.3)	12(19.5)	34(24)	0.539
End stage renal disease	24(11.2)	5(7.7)	19(12.7)	0.287
Peptic ulcer	8(3.7)	0	8(5.3)	0.057
Hepatobiliary disease	21(9.8)	11(16.9)	10(6.7)	0.051
Chronic obstructive pulmonary disease	14(6.5)	4(6.2)	10(6.7)	0.889
Bronchiectasis	1(0.5)	0	1(0.7)	0.696
Interstitial lung disease	2(0.9)	1(1.5)	1(0.7)	0.516
Chronic oxygen use	9(4.2)	3(4.6)	6(4)	0.546
Laboratory data on the day of respiratory failure (median)				
White blood cells, 10^9/L	11,150	10,060	11,640	0.800
Absolute lymphocyte count, 10^9/L	708	546.8	781.6	0.003
Albumin, g/dL	3.05	3.1	3	0.795
C-reactive protein, mg/dL	6.1	6.89	5.91	0.331
Procalcitonin, ng/mL	0.72	0.68	0.75	0.909
Ferritin, ng/mL	668	1035	529	0.002
Lactic dehydrogenase, U/L	363	423	339	0.010
Lactate, mg/dL	23.3	26.4	23.15	0.274
D-dimer, ug/mL	2.472	2.35	2.62	0.600
Fibrinogen, mg/dL	381	378.1	390.7	0.453
Platelet count, /uL	182,000	159,000	186,500	0.090
Severity on the day of respiratory failure				
PaO2/FiO2 ratio, median	140	134.9	144	0.437
SOFA[a] score, median	8	8	8	0.705
APACHE II[a] score, median	24	24	24	0.612
MAP score[b], median	1	1	0.5	0.022
Vasopressor use	70(32.6)	28(43.1)	42(28)	0.030
GCS[a], median	7	8	7	0.286
Treatment				
Mechanical ventilation	131(60.9)	42(64.6)	89(59.3)	0.466
Surgery	60(27.9)	16(24.6)	44(29.3)	0.479
New renal replacement therapy during admission	21(9.8)	10(15.4)	11(7.3)	0.068

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Table 1 (continued)

	All cases (n = 215)	Cancer (n = 65)	No Cancer (n = 150)	P value***
Extracorporeal membrane oxygenation	8(3.7)	5(7.7)	3(2)	0.056
Tocilizumab	76(35.3)	30(46.2)	46(30.7)	0.029
Remdesivir	169(78.6)	59(90.8)	110(73.3)	0.004
Nirmatrelvir/ritonavir	6(2.8)	4(6.2)	2(1.3)	0.117
Molnupiravir	11(5.1)	2(3.1)	9(6)	0.511
Enoxaparin	72(33.5)	22(33.8)	50(33.3)	0.942
Corticosteroid	184(85.6)	61(93.8)	123(82)	0.023
Complications				
CMV[a] infection	38(17.7)	16(24.6)	22(14.7)	0.198
Gastrointestinal bleeding	62(28.8)	17(26.2)	45(30)	0.567
Thromboembolism	13(6.0)	7(10.8)	6(4)	0.084
Outcomes				
ICU[a] admission	159(77.6)	48(73)	111(74)	0.987
Hospital length of stay, days, median	27	28	25	0.971
In-hospital mortality	94(43.7)	40(61.5)	54(36)	0.002
28 days mortality	69(30.7)	24(36.9)	42(28)	0.193
Time from symptoms onset to 1st Ct[a] > 30, days, median	11	13	10	0.007

[a] BMI, Body mass index; DNR, Do not resuscitate; SOFA, Sequential Organ Failure Assessment; APACHE, Acute Physiology and Chronic Health Evaluation; MAP, Mean arterial pressure; GCS, Glasgow coma scale; CMV, Cytomegalovirus; ICU, Intensive Care Unit; Ct, cycle threshold

[b] MAP score is defined from the calculation of SOFA score, with inotropic doses as mcg/kg/min: 0, No hypotension; 1, MAP < 70 mmHg; 2, Dopamine ≤5 or Dobutamine (any dose); 3, Dopamine > 5, Epinephrine ≤0.1, or norepinephrine ≤0.1; 4, Dopamine > 15, Epinephrine > 0.1, or Norepinephrine > 0.1
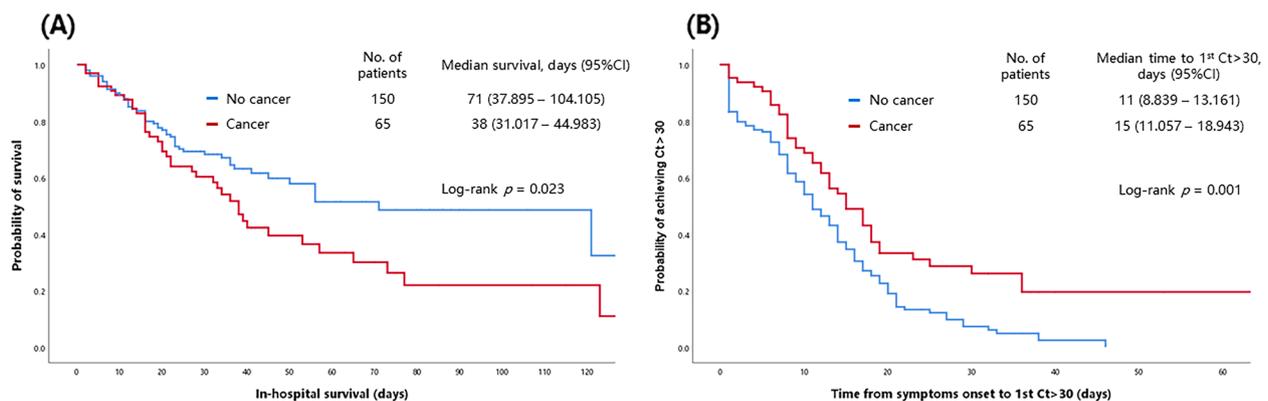
*** Between patients with and without malignancy

Fig. 1 The in-hospital survival and time to reach Ct > 30 in patients with and without cancer. CI, confidence interval; Ct, cycle threshold

the patients without cancer; however, in-hospital mortality was higher among the patients with cancer than among those without cancer. Smoking, an elevated LDH concentration, vasopressor use, and new renal replacement therapy were independent predictors of in-hospital mortality among this population.

The patients with cancer were generally younger and less likely to have histories of cerebrovascular accidents and heart failure than were the patients without cancer. This finding indicates that comorbidities other than cancer contributed to the development of severe disease. The patients with cancer had lower absolute lymphocyte counts and higher ferritin and LDH concentrations on the day of respiratory failure than did the patients without cancer. Other biomarkers, such as C-reactive protein (CRP), lactate, fibrinogen, D-dimer, and procalcitonin, did not significantly differ between the patients with and without cancer. In Cai et al., among patients with COVID-19, those with cancer had higher concentrations of inflammatory markers and cytokines

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Table 2 Additional characteristics among COVID-19 cancer patients with respiratory failure. (*n* = 65)

	n (%)
Cancer site	
Hematological	8 (12.3)
Lymphoma	7 (10.8)
Myeloproliferative neoplasm	1 (1.5)
Solid tumors	57 (87.7)
Breast	4 (6.2)
Prostate	5 (7.7)
Gastrointestinal	10 (15.4)
Hepatocellular carcinoma	4 (6.2)
Biliary tract	1 (1.5)
Pancreas	1 (1.5)
Lung	16 (24.6)
Gynecological	4 (6.2)
Head and neck	3 (4.6)
Genitourinary	5 (7.7)
Musculoskeletal	1 (1.5)
Central nervous system	2 (3.1)
Malignancy of unknown origin	1 (1.5)
Cancer treatment within 4 weeks of COVID-19 diagnosis	34 (52.3)
ICI* combination	4 (6.2)
ICI + chemotherapy	3 (4.6)
ICI + TKI*	1 (1.5)
Cytotoxic chemotherapy	16 (24.6)
Intravenous chemotherapy	12 (18.5)
Oral chemotherapy	4 (6.2)
Endocrine therapy	1 (1.5)
TKI	9 (13.8)
Monoclonal antibody	3 (4.6)
Anti-VEGF* agents	1 (1.5)

ICI immune checkpoint inhibitor, *TKI* tyrosine kinase inhibitor, *VEGF* vascular endothelial growth factor

(high-sensitivity C-reactive protein, procalcitonin, interleukin (IL)-2 receptor, IL-6, and IL-8) and fewer immune cells than did those without cancer, indicating that patients with cancer are more susceptible to immune dysregulation [17]. Lymphopenia is a marker of COVID-19 severity and may be used to detect respiratory failure [20–22]. Patients with COVID-19 who are critically ill often exhibit hyperferritinemia; however, ferritin concentration is not a reliable predictor of patient outcomes [23–25]. An elevated LDH concentration has also been associated with mortality among patients with COVID-19 with severe disease and acute respiratory distress syndrome [22, 26–28].

In the present study, we discovered that the patients with cancer were more frequently treated with remdesivir, tocilizumab, and corticosteroids than were those without cancer. Use of enoxaparin and oral antivirals (nirmatrelvir/ritonavir and molnupiravir) did not significantly differ between the patients with and without cancer. Interleukin (IL)-6, known to be associated with adverse clinical outcomes in patients with COVID-19 [29], is also a key cytokine in the tumor microenvironment. IL-6, present in high concentrations in various cancer types, correlates with cancer progression and therapeutic resistance [30, 31]. IL-6 deregulation participates in the systemic hyperactivated immune response commonly referred to as the cytokine storm. Corticosteroids modulate inflammation-mediated lung injury and thereby reduce the likelihood of short-term mortality and the need for mechanical ventilation [6, 32]. Tocilizumab, a monoclonal antibody against IL-6 receptor, reduces the likelihood of progression to mechanical ventilation or death in patients hospitalized with COVID-19 and is effective among patients with COVID-19 with various cancer types [33–35]. We propose that corticosteroids and tocilizumab were used more frequently among the patients with cancer than among those without cancer due to the hyperinflammatory status of the patients with cancer, whose inflammatory status was confirmed by their elevated concentrations of inflammatory markers (ferritin and LDH). The immunocompromised status of the patients with cancer may have led to active viral replication; therefore, although remdesivir was used more frequently among the patients with cancer than among those without cancer, the patients with cancer took longer to reach Ct > 30. The patients with cancer exhibited prolonged nasopharyngeal viral RNA shedding. Longer viral shedding is associated with older age, distant metastasis, and more severe COVID-19 disease [36].

The patients with cancer had higher MAP scores and a greater likelihood of vasopressor use on the day of respiratory failure than did those without cancer, indicating greater hemodynamic instability among these patients. The patients with cancer were also demonstrated a significantly higher in-hospital mortality rate compared to those without cancer, which is consistent with the finding of another study [37].

Among the patients with cancer in our study, in-hospital mortality was associated with smoking; a higher white blood cell count; and elevated concentrations of ferritin, LDH, lactate, and D-dimer. These factors indicate that an active inflammatory process may have contributed to a poor prognosis. The nonsurvivors with cancer were also significantly more likely to use vasopressors and receive new renal replacement therapy during their admission than were the survivors.

Vaccination status, comorbidities, recent systemic cancer treatment, whether admitted due to COVID-19, whether infected during hospitalization, SOFA score and APACHE II score on the day of respiratory failure,
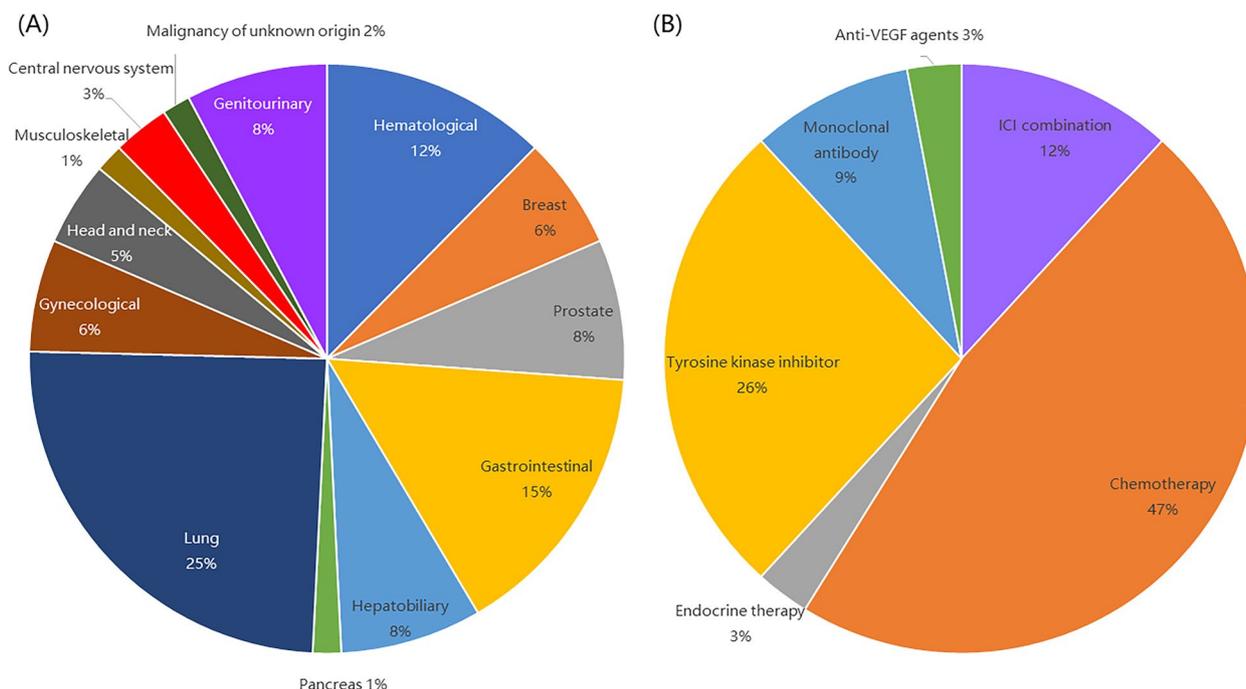
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Fig. 2 Cancer sites and recent treatment category among COVID-19 cancer patients with respiratory failure. VEGF, vascular endothelial growth factor

and specific treatments for COVID-19 (including those involving corticosteroids, antiviral and anticoagulation agents, and tocilizumab) did not significantly affect mortality.

In multivariable analysis, we identified several factors that were associated with in-hospital mortality among the patients with cancer and COVID-19-related respiratory failure. These factors included smoking, elevated LDH concentrations on the day of respiratory failure, requiring vasopressor use on the day of respiratory failure, and undergoing new renal replacement therapy during admission.

Active smoking is considered as an independent predictor of severe disease and mortality among patients with COVID-19 [9, 38–40]. Current smokers had significantly increased ACE2 expression in airway epithelial cells compared with nonsmokers, which provided more entry points for the SARS-CoV-2 virus and potentially increased susceptibility to infection [41]. However, in one study, active smoking was not associated with COVID-19 severity [42]. Elevated LDH concentration has been identified as an independent risk factor for disease severity and mortality among patients with COVID-19 [27, 28, 43]. The requirement for mechanical ventilation, vasopressors, and renal replacement therapy were reported to be poor prognostic factors among patients with cancer who were admitted to the intensive care unit [44].

Patients with COVID-19 who are admitted to the intensive care unit frequently receive continuous vasopressor support [45], highlighting the importance of hemodynamic monitoring and fluid management.

Our study has several limitations. First, this was a single-center retrospective cohort study with a limited sample size. Second, the laboratory data and SARS-CoV-2 PCR follow-up intervals were not uniform, which potentially introduced bias. Third, some inflammatory biomarkers such as IL-6, IL-2R, IL-8 and antibody titers are either not routinely tested or have no available exam in our hospital, thus we do not have sufficient data to incorporate into our analysis. Treatment strategies may have also varied considerably by patient clinical status and clinician practice.

Conclusion

Patients with cancer who develop COVID-19-related respiratory failure exhibit distinct clinical characteristics and have a higher likelihood of receiving specific COVID-19 treatments, such as remdesivir and corticosteroids, than those without cancer do. Patients who develop COVID-19-related respiratory failure with cancer also experience unfavorable outcomes, including higher in-hospital mortality and longer duration of viral shedding, compared with those without cancer. Smoking, elevated LDH concentrations, vasopressor use, and

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Table 3 Comparison of patient characteristics between COVID-19 survivors and non-survivors among patients with cancer during hospital stay. (*n* = 65)

	Survivor (*n* = 25)	Nonsurvivor (*n* = 40)	*P* value
Demographics			
Age, years, median	75	72.5	0.212
Male	13(52)	30(75)	0.057
Body mass index, kg/m^2, median	21.04	23.17	0.229
BMI* < 18	7(28)	5(14.7)	0.210
BMI* > 24	9(36)	14(41.2)	0.687
Vaccination doses, median	2	2	0.890
Ever vaccinated	17(68)	28(70)	0.865
Full vaccination (> = 3 doses)	12(48)	12(48)	0.875
DNR*	15(60)	32(80)	0.080
Smoker	3(12)	17(42.5)	0.024
Cerebrovascular disease	4(16)	2(5)	0.194
Dementia	2(8)	3(7.5)	0.941
Heart failure	1(4)	0(0)	0.202
Peripheral vascular disease	1(4)	1(2.5)	0.733
Diabetes mellitus	9(36)	13(32.5)	0.772
Chronic kidney disease	3(12)	9(22.5)	0.288
End stage renal disease	1(4)	4(10)	0.377
Chronic obstructive pulmonary disease	2(8)	2(5)	0.624
Chronic oxygen use	2(8)	1(2.5)	0.304
Admitted due to COVID-19	12(48)	20(50)	0.875
Infected during hospitalization	3(12)	9(22.5)	0.344
Hematological malignancy	1(4)	6(15)	0.235
Laboratory data on the day of respiratory failure (median)			
White blood cells, 10^9/L	8500	12,450	0.006
Absolute neutrophil count, 10^9/L	6318.7	7105.45	0.345
Hemoglobin, g/dL	11.5	10.5	0.153
Absolute lymphocyte count, 10^9/L	639.58	531.40	0.571
Albumin, g/dL	3.1	3.1	0.349
C-reactive protein, mg/dL	4.78	7.16	0.157
Procalcitonin, ng/mL	0.51	1.42	0.375
Ferritin, ng/mL	673.5	3220	< 0.001
Lactic dehydrogenase, U/L	256	534.5	< 0.001
Lactate, mg/dL	15.7	33	0.005
D-dimer, ug/mL	1.570	4.605	0.007
Fibrinogen, mg/dL	435.6	358	0.188
Platelet count, /uL	159,000	154,000	0.422
Severity on the day of respiratory failure			
PaO2/FiO2 ratio, median	148	125.39	0.364
SOFA* score, median	7	10	0.071
APACHE* II score, median	22	25.5	0.160
MAP score**, median	1	3	0.048
GCS*, median	9	7.5	0.995
Vasopressor use	6(24)	22(55)	0.014
Treatment			
Cancer treatment in 4 weeks prior to COVID-19 diagnosis	12(48)	22(55)	0.583
Cytotoxic chemotherapy in 4 weeks prior to COVID-19 diagnosis	8(32)	11(27.5)	0.698
Mechanical ventilation	18(72)	24(60)	0.325

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Table 3 (continued)

	Survivor (*n* = 25)	Nonsurvivor (*n* = 40)	*P* value
Re-application of MV* after weaning	2(8)	2(5)	0.624
Tracheostomy	3(12)	1(2.5)	0.121
New renal replacement therapy during admission	1(4)	9(22.5)	0.044
Extracorporeal membrane oxygenation	0(0)	5(12.5)	0.066
Tocilizumab	9(36)	21(52.5)	0.194
Remdesivir	22(88)	37(92.5)	0.542
Nirmatrelvir/ritonavir	1(4)	3(7.5)	0.568
Molnupiravir	1(4)	1(2.5)	0.733
Enoxaparin	9(36)	13(32.5)	0.772
Corticosteroid	22(88)	39(97.5)	0.121
Complications			
CMV* infection	2(8)	14(35)	0.048
Gastrointestinal bleeding	6(24)	11(27.5)	0.755
Thromboembolism	3(12)	4(10)	0.800
Outcome			
ICU* admission	20(80)	28(70)	0.372
Hospital length of stay, days, median	33	21.5	0.082
Ventilator days, median	10	5.5	0.710
Time from symptoms onset to 1st Ct* > 30, days	14	11.5	0.721
Prolonged shredding (> 10 days)	18(72)	21(52.5)	0.118

*BMI Body mass index, DNR Do not resuscitate, SOFA Sequential Organ Failure Assessment, APACHE Acute Physiology and Chronic Health Evaluation, MAP Mean arterial pressure, GCS Glasgow coma scale, CMV Cytomegalovirus, ICU Intensive Care Unit, Ct cycle threshold

**MAP score is defined from the calculation of SOFA score, with inotropic doses as mcg/kg/min: 0, No hypotension; 1, MAP < 70 mmHg; 2, Dopamine ≤5 or Dobutamine (any dose); 3, Dopamine > 5, Epinephrine ≤0.1, or norepinephrine ≤0.1; 4, Dopamine > 15, Epinephrine > 0.1, or Norepinephrine > 0.1

Table 4 Factors associated with in-hospital survival among COVID-19 cancer patients with respiratory failure (n = 65)

Variables	Univariable analysis			Multivariable analysis		
	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Male	2.769	0.958–8.009	0.060	1.050	0.090–12.266	0.969
DNR	2.667	0.876–8.122	0.084	11.605	0.478–281.509	0.132
Smoker	5.420	1.392–21.107	0.015	5.804	1.847–39.746	0.043
Lactic dehydrogenase, U/L	1.004	1.001–1.007	0.008	1.004	1.001–1.012	0.025
Lactate, mg/dL	1.022	0.999–1.045	0.064	1.032	0.969–1.100	0.321
D-dimer, ug/mL	1.254	1.022–1.540	0.030	1.189	0.826–1.526	0.174
SOFA score	1.110	0.991–1.243	0.070	0.792	0.513–1.222	0.292
MAP score	1.415	1.028–1.948	0.033	0.330	0.037–2.936	0.320
Vasopressor use	3.870	1.276–11.735	0.017	5.437	1.202–24.593	0.028
New renal replacement therapy during admission	6.968	0.825–58.844	0.075	3.523	1.203–61.108	0.034
CMV infection	0.889	0.780–1.014	0.080	1.264	0.840–1.901	0.260

CI confidence interval, DNR do not resuscitate, SOFA sequential organ failure assessment, MAP mean arterial pressure, CMV cytomegalovirus

new renal replacement therapy were identified as significant predictors of in-hospital mortality in this patient population. Further research is warranted to validate these findings, elucidate the underlying mechanisms, and explore tailored management strategies to improve outcomes in this vulnerable population.

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Abbreviations

COVID-19	Coronavirus disease 2019
LDH	Lactate dehydrogenase
OR	Odds ratio
CI	Confidence interval
ARDS	Acute respiratory distress syndrome
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
HFNC	High-flow nasal cannula
NIV	Noninvasive ventilation
MV	Mechanical ventilation
RT-PCR	Reverse transcription polymerase chain reaction
BMI	Body mass index
DNR	Do not resuscitate
SOFA	Sequential organ failure assessment
MAP	Mean arterial pressure
APACHE	Acute Physiologic Assessment and Chronic Health Evaluation
CMV	Cytomegalovirus
Ct	Cycle threshold
IL	Interleukin

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-024-02850-z.

Additional file 1.

Availability of data and materials
The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This retrospective study was performed in accordance with the Declaration of Helsinki and approved by the Institutional Ethical Review Board of Taipei Veterans General Hospital (Approval No. 2022–11-002 AC). Written informed consent was waived by Institutional Ethical Review Board of Taipei Veterans General Hospital due to retrospective design of the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. WHO Coronavirus (COVID-19) Dashboard. Accessed Nov 27, 2023. https://covid19.who.int/
2. Zhang JT, Zhong WZ, Wu YL. Cancer treatment in the coronavirus disease pandemic. Lung Cancer. 2021;152:98–103. https://doi.org/10.1016/j.lungcan.2020.12.012.
3. Mehta V, Goel S, Kabarriti R, et al. Case fatality rate of Cancer patients with COVID-19 in a New York hospital system. Cancer Discov. 2020;10(7):935–41. https://doi.org/10.1158/2159-8290.Cd-20-0516.
4. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. N Engl J Med. 2020;383(25):2451–60. https://doi.org/10.1056/NEJMcp2009575.
5. Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Intensive Care Med. 2020;46(5):854–87. https://doi.org/10.1007/s00134-020-06022-5.
6. Horby P, Lim WS, Emberson JR, et al. Dexamethasone in Hospitalized Patients with Covid-19. N Engl J Med. 2021;384(8):693–704. https://doi.org/10.1056/NEJMoa2021436.
7. Lee LY, Cazier JB, Angelis V, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. Lancet. 2020;395(10241):1919–26. https://doi.org/10.1016/s0140-6736(20)31173-9.
8. Grivas P, Khaki AR, Wise-Draper TM, et al. Association of clinical factors and recent anticancer therapy with COVID-19 severity among patients with cancer: a report from the COVID-19 and Cancer consortium. Ann Oncol. 2021;32(6):787–800. https://doi.org/10.1016/j.annonc.2021.02.024.
9. Aboueshia M, Hussein MH, Attia AS, et al. Cancer and COVID-19: analysis of patient outcomes. Future Oncol. 2021;17(26):3499–510. https://doi.org/10.2217/fon-2021-0121.
10. Garassino MC, Whisenant JG, Huang L-C, et al. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. The Lancet Oncol. 2020;21(7):914–22. https://doi.org/10.1016/S1470-2045(20)30314-4.
11. Jee J, Foote MB, Lumish M, et al. Chemotherapy and COVID-19 outcomes in patients with Cancer. J Clin Oncol. 2020;38(30):3538–46. https://doi.org/10.1200/jco.20.01307.
12. Yekedüz E, Utkan G, Ürün Y. A systematic review and meta-analysis: the effect of active cancer treatment on severity of COVID-19. Eur J Cancer. 2020;141:92–104. https://doi.org/10.1016/j.ejca.2020.09.028.
13. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related organ failure assessment) score to describe organ dysfunction/failure. On behalf of the working group on Sepsis-related problems of the European Society of Intensive Care Medicine. Intensive Care Med. 1996;22(7):707–10. https://doi.org/10.1007/bf01709751.
14. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818–29.
15. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet. 1974;2(7872):81–4. https://doi.org/10.1016/s0140-6736(74)91639-0.
16. Kao HC, Lai TY, Hung HL, et al. Sequential oxygenation index and organ dysfunction assessment within the first 3 days of mechanical ventilation predict the outcome of adult patients with severe acute respiratory failure. Sci World J. 2013;2013:413216. https://doi.org/10.1155/2013/413216.
17. Cai G, Gao Y, Zeng S, et al. Immunological alternation in COVID-19 patients with cancer and its implications on mortality. Oncoimmunology. 2021;10(1):1854424. https://doi.org/10.1080/2162402x.2020.1854424.

18. Young BE, Ong SWX, Ng LFP, et al. Viral Dynamics and Immune Correlates of Coronavirus Disease 2019 (COVID-19) Severity. Clin Infect Dis. 2021;73(9):e2932–42. https://doi.org/10.1093/cid/ciaa1280.

19. CECC revises criteria for releasing COVID-19 patients with moderate and severe symptoms from isolation to preserve isolation care capacity 2022. Accessed Nov 27, 2023. https://covid19.mohw.gov.tw/en/cp-4868-69897-206.html

20. Illg Z, Muller G, Mueller M, Nippert J, Allen B. Analysis of absolute lymphocyte count in patients with COVID-19. Am J Emerg Med. 2021;46:16–9. https://doi.org/10.1016/j.ajem.2021.02.054.

21. Elhadad D, Bronstein Y, Yana M, et al. Characteristics and outcomes of patients infected with SARS-CoV-2 in Israel: correlation between laboratory findings on admission to emergency department and subsequent respiratory failure. Isr Med Assoc J. 2020;22(10):605–11.

22. Malik P, Patel U, Mehta D, et al. Biomarkers and outcomes of COVID-19 hospitalisations: systematic review and meta-analysis. BMJ Evid Based Med. 2021;26(3):107–8. https://doi.org/10.1136/bmjebm-2020-111536.

23. Feld J, Tremblay D, Thibaud S, Kessler A, Naymagon L. Ferritin levels in patients with COVID-19: a poor predictor of mortality and hemophagocytic lymphohistiocytosis. Int J Lab Hematol. 2020;42(6):773–9. https://doi.org/10.1111/ijlh.13309.

24. Gómez-Pastora J, Weigand M, Kim J, et al. Hyperferritinemia in critically ill COVID-19 patients - is ferritin the product of inflammation or a pathogenic mediator? Clin Chim Acta. 2020;509:249–51. https://doi.org/10.1016/j.cca.2020.06.033.

25. Kaushal K, Kaur H, Sarma P, et al. Serum ferritin as a predictive biomarker in COVID-19. A systematic review, meta-analysis and meta-regression analysis. J Crit Care. Feb 2022;67:172–81. https://doi.org/10.1016/j.jcrc.2021.09.023.

26. Topp G, Bouyea M, Cochran-Caggiano N, et al. Biomarkers predictive of Extubation and survival of COVID-19 patients. Cureus. 2021;13(6):e15462. https://doi.org/10.7759/cureus.15462.

27. Martinez Mesa A, Cabrera César E, Martín-Montañez E, et al. Acute lung injury biomarkers in the prediction of COVID-19 severity: Total thiol, ferritin and lactate dehydrogenase. Antioxidants (Basel). 2021;10(8) https://doi.org/10.3390/antiox10081221.

28. Li C, Ye J, Chen Q, et al. Elevated Lactate Dehydrogenase (LDH) level as an independent risk factor for the severity and mortality of COVID-19. Aging (Albany NY). 2020;12(15):15670–81. https://doi.org/10.18632/aging.103770.

29. Coomes EA, Haghbayan H. Interleukin-6 in Covid-19: a systematic review and meta-analysis. Rev Med Virol. 2020;30(6):1–9. https://doi.org/10.1002/rmv.2141.

30. Kumari N, Dwarakanath BS, Das A, Bhatt AN. Role of interleukin-6 in cancer progression and therapeutic resistance. Tumour Biol. 2016;37(9):11553–72. https://doi.org/10.1007/s13277-016-5098-7.

31. Hirano T. IL-6 in inflammation, autoimmunity and cancer. Int Immunol. 2021;33(3):127–48. https://doi.org/10.1093/intimm/dxaa078.

32. van Paassen J, Vos JS, Hoekstra EM, Neumann KMI, Boot PC, Arbous SM. Corticosteroid use in COVID-19 patients: a systematic review and meta-analysis on clinical outcomes. Crit Care. 2020;24(s):696. https://doi.org/10.1186/s13054-020-03400-9.

33. Zong Z, Wei Y, Ren J, Zhang L, Zhou F. The intersection of COVID-19 and cancer: signaling pathways and treatment implications. Mol Cancer. 2021;20(1):76. https://doi.org/10.1186/s12943-021-01363-1.

34. Salama C, Han J, Yau L, et al. Tocilizumab in patients hospitalized with Covid-19 pneumonia. N Engl J Med. 2020;384(1):20–30. https://doi.org/10.1056/NEJMoa2030340.

35. Aziz M, Haghbin H, Abu Sitta E, et al. Efficacy of tocilizumab in COVID-19: a systematic review and meta-analysis. J Med Virol. 2021;93(3):1620–30. https://doi.org/10.1002/jmv.26509.

36. Goubet A-G, Dubuisson A, Geraud A, et al. Prolonged SARS-CoV-2 RNA virus shedding and lymphopenia are hallmarks of COVID-19 in cancer patients with poor prognosis. Cell Death Different. 2021;28(12):3297–315. https://doi.org/10.1038/s41418-021-00817-9.

37. Hauser MJ, Tabak J, Baier H. Survival of patients with Cancer in a medical critical care unit. Arch Intern Med. 1982;142(3):527–9. https://doi.org/10.1001/archinte.1982.00340160107022.

38. Espejo-Paeres C, Núñez-Gil IJ, Estrada V, et al. Impact of smoking on COVID-19 outcomes: a HOPE registry subanalysis. BMJ Nutr Prev Health. 2021;4(1):285–92. https://doi.org/10.1136/bmjnph-2021-000269.

39. Zhao Q, Meng M, Kumar R, et al. The impact of COPD and smoking history on the severity of COVID-19: a systemic review and meta-analysis. J Med Virol. 2020;92(10):1915–21. https://doi.org/10.1002/jmv.25889.

40. Patanavanich R, Glantz SA. Smoking Is Associated With COVID-19 Progression: A Meta-analysis. Nicotine Tob Res. 2020;22(9):1653–6. https://doi.org/10.1093/ntr/ntaa082.

41. Smith JC, Sausville EL, Girish V, et al. Cigarette Smoke Exposure and Inflammatory Signaling Increase the Expression of the SARS-CoV-2 Receptor ACE2 in the Respiratory Tract. Dev Cell. 2020;53(5):514–529.e3. https://doi.org/10.1016/j.devcel.2020.05.012.

42. Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). Eur J Intern Med. 2020;75:107–8. https://doi.org/10.1016/j.ejim.2020.03.014.

43. Szarpak L, Ruetzler K, Safiejko K, et al. Lactate dehydrogenase level as a COVID-19 severity marker. Am J Emerg Med. 2021;45:638–9. https://doi.org/10.1016/j.ajem.2020.11.025.

44. Lecuyer L, Chevret S, Thiery G, Darmon M, Schlemmer B, Azoulay E. The ICU trial: a new admission policy for cancer patients requiring mechanical ventilation. Crit Care Med. 2007;35(3):808–14. https://doi.org/10.1097/01.Ccm.0000256846.27192.7a.

45. Michard F, Malbrain ML, Martin GS, et al. Haemodynamic monitoring and management in COVID-19 intensive care patients: an international survey. Anaesth Crit Care Pain Med. 2020;39(5):563–9. https://doi.org/10.1016/j.accpm.2020.08.001.

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