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ORIGINAL RESEARCH

Physical and Cognitive Impairments at ICU Discharge are Associated with High Long-Term Mortality in ICU Survivors with Solid Malignancies: A Retrospective Cohort Study

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Background: Many ICU survivors experience post-ICU physical, cognitive, or mental impairments. In ICU survivors with solid malignancies, post-ICU impairments can impede further cancer treatments and negatively impact their outcomes. This study aimed to investigate post-ICU mortalities and their risk factors at ICU discharge in ICU survivors with solid malignancies.

Methods: In this retrospective cohort study, adult patients with solid malignancies who were unexpectedly admitted to the medical ICU of a tertiary hospital between 2016 and 2022 and survived to ICU discharge were included. Data at ICU discharge were collected from electronic medical records. In-hospital and 1-year mortality and their risk factors were analyzed.

Results: Of the 708 ICU survivors, 25.1% died in the hospital, and 61% died within one year. At ICU discharge, 20.9% had delirium, 3.8% had coma, and 80.6% had impaired mobility. Respiratory support, including bilevel positive airway pressure (BiPAP), high-flow nasal cannula (HFNC), or other oxygen therapies was used in 88.7% of patients. Delirium (adjusted OR 1.73; 95% CI 1.04–2.87; $p = 0.035$), coma (adjusted OR 5.63; 95% CI 2.09–16.17; $p < 0.001$), limited mobility (adjusted OR 2.41; 95% CI 1.22–5.14; $p = 0.015$), and use of BiPAP (adjusted OR 21.63; 95% CI 5.36–99.57; $p < 0.001$) or HFNC (adjusted OR 7.08; 95% CI 2.45–23.99; $p < 0.001$) were independently associated with in-hospital mortality. One-year survival was significantly lower in patients with delirium (35%, $p < 0.001$), coma (26%, $p < 0.001$), limited mobility (37%, $p = 0.003$), or those receiving respiratory support at ICU discharge (35%, $p < 0.001$).

Conclusion: A considerable portion of ICU survivors with solid malignancies died in the hospital or within one year after ICU discharge in our study. Cognitive, mobility, and pulmonary impairments at ICU discharge were significant risk factors for both in-hospital and long-term mortality.

Keywords: solid cancer, solid malignant tumor, ICU survivors, in-hospital mortality

Background

Patients with solid malignancies account for 10% to 15% of all admissions to the intensive care unit (ICU) admissions.[1] ICU mortality rates have decreased due to significant advances in critical care management.[2,3] However, ICU mortality is not the only outcome of interest.[4] The long-term impact of critical illness has become an increasingly important concern beyond ICU discharge.[5,6] Despite recent advances, long-term outcomes in patients with cancer treated in the ICU are worse than those in patients without cancer.[7,8] While 5% to 27% of ICU survivors die in the hospital after ICU discharge,[9] those with solid malignancies have a higher risk of in-hospital death.[10]

ICU survivors may experience a period of impaired quality of life.[11,12] Up to 80% of ICU survivors experience new or worsening post-ICU physical, cognitive, and/or mental impairments, specifically referred to as post-intensive care syndrome (PICS).[6] Particularly for advanced cancer patients, post-ICU impairments can serve as barriers to receiving additional cancer treatment, as decisions regarding the resumption of treatment are based on a patient's overall functional status and general condition.[13–15] In individuals with limited life expectancy, treatment delays caused by post-ICU

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impairments may lead to poor outcomes, including disease progression or reduced survival.[16,17] To date, there has been a lack of studies on short- and long-term outcomes and their risk factors in patients with solid malignancies who survive in the ICU.

The aim of this study was to identify risk factors at the time of ICU discharge associated with in-hospital mortality and to investigate long-term outcomes in ICU survivors with solid malignancies.

Methods

Study Design and Patients

This is a retrospective cohort study conducted at a single tertiary hospital in South Korea. Among adult patients with solid malignancies actively treated by oncologists and admitted to the medical ICU between 2016 and 2022, those who survived in the ICU and were transferred to the general ward were included. This study included patients who met the following criteria: (1) patients aged over 18 years and (2) patients treated for more than 1 day in the ICU and transferred to the general ward. Exclusion criteria were as follows: (1) patients who died in the ICU, (2) patients who were transferred from the ICU to another hospital, and (3) patients admitted to the ICU for 1 day for monitoring or post-operative care. Only the first ICU admission per patient was included. ICU discharge decisions were made by board-certified intensivists based on institutional protocols and the patient's clinical condition (Appendix 1).

Data Collection

Data from patients' electronic medical records were gathered as follows: underlying cancer type, cancer stage, sex, age, weight, height, body mass index (BMI), and causes of ICU admission; dates of hospital admission and discharge, dates of ICU admission and discharge, date of last follow-up, date of death. During the ICU stay, information on the use of vasopressors, use of mechanical ventilation, initiation of renal replacement therapy and whether tracheostomy was performed were collected. At the time of ICU discharge, clinical status and treatment variables were collected based on the patient's condition at the time of transfer from the ICU to the general ward. These included body weight and BMI change; respiratory support devices such as bilevel positive airway pressure (BiPAP), high-flow nasal cannula (HFNC), or other oxygen therapies, and FiO_2; vasopressor use and dosages; whether hemodialysis was discontinued; Glasgow Coma Scale (GCS) score; results of the Confusion Assessment Method for the ICU (CAM-ICU); Richmond Agitation Sedation Scale (RASS); and laboratory data including arterial blood gas analysis. Whether patients had delirium at the time of ICU discharge was assessed using CAM-ICU in patients with a RASS score of ≥ -3.[18] If patients had a RASS score of −4 or −5, they were recorded as "unable to assess delirium due to coma status".

Patient's mobility was assessed using the Braden Scale, which was developed to predict the risk of pressure ulcers.[19,20] In the Braden scale, mobility is defined as the ability to change and control body position. There are 4 categories to assess mobility: no limitation (make major and frequent changes in position without assistance), slightly limited (make frequent though slight changes in body or extremity position independently), very limited (make occasional slight changes in body or extremity position but unable to make frequent or significant changes independently), completely immobile (does not make even slight changes in position without assistance). Based on the recorded scores, we classified patients into "no mobility limitation" or "limited mobility" (including slightly limited to completely immobile).

The primary outcome was the risk factor for in-hospital mortality, and the secondary outcomes were in-hospital mortality rates and 1-year mortality rate.

Statistical Analysis

The distribution of continuous variables was assessed using the Shapiro–Wilk test. Variables were summarized as mean ± standard deviation when normally distributed, or as median with interquartile range when not. The included patients were categorized as survivors and non-survivors according to in-hospital mortality. The characteristics at the time of ICU admission, discharge, and post-ICU outcomes were compared between the two groups. Continuous variables were compared using Student's *t*-test when the assumption of normality was met; otherwise, the Mann–Whitney *U*-test was used. Categorical variables were compared using the chi-squared test or Fisher's exact test. Multivariable logistic regression analysis was used to identify risk factors for in-hospital mortality. Variables with p-values < 0.1 in the univariable analysis were included in the multivariable model to ensure that potentially important predictors were not excluded prematurely. Backward elimination was applied for variable selection. Kaplan-Meier method and the Log rank test were used for survival analysis. All p-values were two-tailed, and the threshold for statistical significance was set at a p-value of less than 0.05. Missing data were not imputed. All statistical analyses were conducted using R software (version 4.2.1, R Core Team, Vienna, Austria).

Ethical Approval and Informed Consent

The study protocol was approved by the Institutional Review Board of Asan Medical Center (IRB number: 2023–0922) with a waiver of informed consent granted due to the observational design of the study. All research was performed in accordance with national guidelines and regulations. Patient data were anonymized prior to analysis, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Of the 955 patients with solid malignancies admitted between 2016 and 2022, 224 patients who died in the ICU and 23 patients who were transferred to another hospital during their ICU stay were excluded (Figure 1). Among the 708 patients who survived in the ICU and were transferred to the general ward, 178 patients (25.1%) died in the hospital. Lung cancer (30.4%) was the most common type of cancer among the study patients, and 77.7% had metastatic cancer at the time of ICU admission (Table 1).

Mechanical ventilation was used in 58.1% of patients, and the median length of ICU stay was 5 (interquartile range [IQR], 3–9) days. At the time of ICU discharge, 88.7% of patients were using oxygen devices, including BiPAP (4.9%)

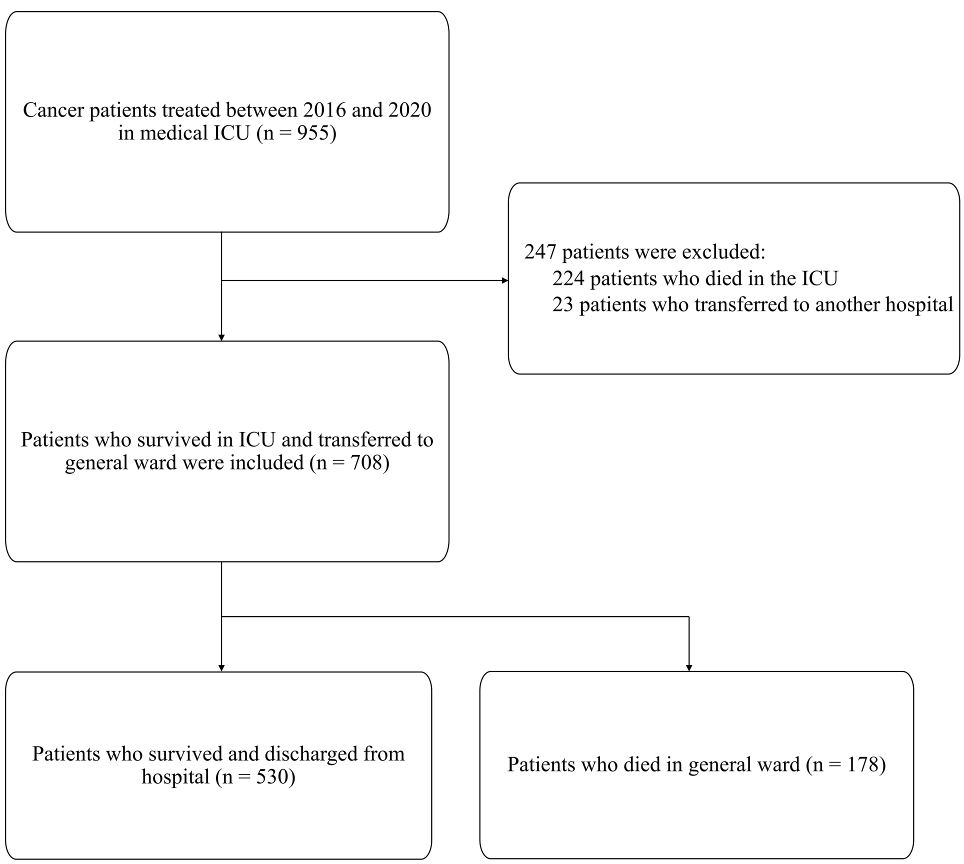

Figure 1 Patient inclusion flow diagram.

Table 1 Characteristics of the Patients at ICU Admission and ICU Treatment According to in-Hospital Mortality

	Hospital Survivor (n = 530)	**Hospital Non-Survivor (n = 178)**	**Total (n = 708)**	**p-value**
Age, median [IQR]	64.0 [57.0; 71.0]	65.0 [56.0; 71.0]	64.0 [57.0; 71.0]	0.928
Male sex, n (%)	363 (68.5)	117 (65.7)	480 (67.8)	0.556
BMI, n (%)	22.3 ± 3.4	22.0 ± 3.4	22.2 ± 3.4	0.260
Malignancy site, n (%)				0.014
Lung	147 (27.7)	68 (38.2)	215 (30.4)	
Pancreas-Biliary	144 (27.2)	30 (16.9)	174 (24.6)	
Gastrointestinal	79 (14.9)	29 (16.3)	108 (15.3)	
Urogenital	50 (9.4)	11 (6.2)	61 (8.6)	
Others*	110 (20.8)	40 (22.5)	150 (21.2)	
Stage, n (%)				0.262
Localized	27 (5.1)	6 (3.4)	33 (4.7)	
Locally advanced	99 (18.7)	26 (14.6)	125 (17.7)	
Metastatic	404 (76.2)	146 (82.0)	550 (77.7)	
Diagnosis to ICU admission, month, median [IQR]	12.4 [4.4; 33.8]	12.0 [4.4; 39.7]	12.2 [4.4; 35.6]	0.910
Recent chemotherapy[†], n (%)	83.4 (442)	147 (82.6)	589 (83.2)	0.893
Recent radiation therapy[†], n (%)	80 (15.1)	44 (24.7)	124 (17.5)	0.005
ECOG performance status, n (%)				0.273
0-1	402 (75.8)	127 (71.3)	529 (74.7)	
2-4	128 (24.2)	51 (28.7)	179 (25.3)	
Causes of ICU admission, n (%)				< 0.001
Respiratory failure	198 (37.4)	97 (54.5)	295 (41.7)	
Shock	205 (38.7)	37 (20.8)	242 (34.2)	
Cardiac arrest	15 (2.8)	7 (3.9)	22 (3.1)	
Altered mental status	22 (4.2)	12 (6.7)	34 (4.8)	
Metabolic acidosis	13 (2.5)	5 (2.8)	18 (2.5)	
Post-operative/procedure	36 (6.8)	12 (6.7)	48 (6.8)	
Others	41 (7.7)	8 (4.5)	49 (6.9)	
SOFA score at ICU admission	9.0 [6.0; 12.0]	11.0 [8.0; 14.0]	10.0 [6.5; 13.0]	< 0.001
ICU treatment				
Mechanical ventilation, n (%)	282 (53.2)	129 (72.5)	411 (58.1)	< 0.001
Duration of mechanical ventilation days, median [IQR]	5.0 [2.0; 9.0]	7.0 [3.0; 14.0]	5.0 [2.0; 10.0]	0.001
Tracheostomy, n (%)	68 (12.8)	35 (19.7)	103 (14.5)	0.035

(*Continued*)

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Table 1 (Continued).

	Hospital Survivor (n = 530)	Hospital Non-Survivor (n = 178)	Total (n = 708)	p-value
Vasopressor received, n (%)	353 (66.6)	127 (71.3)	480 (67.8)	0.28
Initiation renal replacement therapy, n (%)	79 (14.9)	42 (23.6)	121 (17.1)	0.011
ICU length of stay, days, median [IQR]	4.0 [2.0; 8.0]	7.0 [4.0; 14.0]	5.0 [3.0; 9.0]	< 0.001

Notes: *Others include head and neck cancers, bone and soft tissue sarcomas, brain tumors, liver cancer, breast cancer, thyroid cancer, skin cancer, and miscellaneous cancers. †Recent refers to chemotherapy or radiation therapy administered within 6 months prior to ICU admission.
Abbreviations: IQR, interquartile range; BMI, body mass index; ECOG, Eastern cooperative oncology group; SOFA, Sequential Organ Failure Assessment.

and HFNC (15.5%; Table 2). The proportion of patients receiving vasopressors at the time of ICU discharge was 17.4%, and they were administered 0.01 ± 0.04 mcg/kg/min of norepinephrine. Delirium was observed in 20.9% of patients, and 3.8% of patients were in a comatose state. The proportion of patients with limited mobility was 80.6%. Among ICU survivors, those who died later during hospitalization had a longer ICU length of stay compared to hospital survivors (7.0 [4.0–14.0] vs 4.0 [2.0–8.0], $p < 0.001$). The proportion of patients receiving hemodialysis (18.5% vs 8.7%, $p < 0.001$), oxygen therapy (96.6% vs 86%, $p < 0.001$), and vasopressors (28.7% vs 13.6%, $p < 0.001$) was higher in hospital non-survivors than in hospital survivors. In addition, patients who died in the hospital had a lower mean GCS score (13.3 ± 3.2 vs 14.5 ± 1.3, $p < 0.001$) and a higher proportion of delirium (34.3% vs 16.4%, $p < 0.001$) and coma (10.7% vs 1.5%, $p < 0.001$). Patients who died in the hospital were more likely to have limited mobility (93.3% vs 76.4%, $p < 0.001$).

The 1-year mortality rate of the study patients was 61% (Table 3). Patients in the hospital non-survivor group died after a median of 10 (3–22) days from ICU discharge. For patients who survived and were discharged from the hospital,

Table 2 Characteristics of the Patients at the Time of ICU Discharge According to in-Hospital Mortality

	Hospital Survivor (n = 530)	Hospital Non-Survivor (n = 178)	Total (n = 708)	p-value
BMI, kg/m^2, mean ± SD	21.8 ± 3.4	21.8 ± 3.5	21.8 ± 3.4	0.972
Body weight change at discharge, %, mean ± SD	98.1 ± 7.0	99.7 ± 9.8	98.5 ± 7.8	0.047
Hemodialysis, n (%)	46 (8.7)	33 (18.5)	79 (11.2)	< 0.001
FiO_2, mean ± SD	0.38 ± 0.10	0.41 ± 0.09	0.38 ± 0.10	< 0.001
Oxygen device, n (%)				< 0.001
No oxygen treatment	74 (14.0)	6 (3.4)	80 (11.3)	
BiPAP	12 (2.3)	23 (12.9)	35 (4.9)	
HFNC	62 (11.7)	48 (27.0)	110 (15.5)	
Others*	382 (72.1)	101 (56.7)	483 (68.2)	
Vasopressor received, n (%)	72 (13.6)	51 (28.7)	123 (17.4)	< 0.001
Equivalent norepinephrine dose, ug/kg/min, mean ± SD	0.01 ± 0.03	0.03 ± 0.06	0.01 ± 0.04	0.001
GCS, mean ± SD	14.5 ± 1.3	13.3 ± 3.2	14.2 ± 2.1	< 0.001
GCS ≥ 13, n (%)	510 (96.2)	146 (82.0)	656 (92.7)	< 0.001
GCS < 13, n (%)	20 (3.8)	32 (18.0)	52 (7.3)	

(*Continued*)

Table 2 (Continued).

	Hospital Survivor (n = 530)	Hospital Non-Survivor (n = 178)	Total (n = 708)	p-value
Delirium, n (%)				< 0.001
Negative	435 (82.1)	98 (55.1)	533 (75.3)	
Positive	87 (16.4)	61 (34.3)	148 (20.9)	
Unable to assess (coma)	8 (1.5)	19 (10.7)	27 (3.8)	
Mobility, n (%)				< 0.001
No limitation	125 (23.6)	12 (6.7)	137 (19.4)	
Limitation	405 (76.4)	166 (93.3)	571 (80.6)	
Laboratory findings				
Hemoglobin, g/dL	9.3 ± 1.6	9.0 ± 1.6	9.2 ± 1.6	0.054
White blood cell, x10^3/uL	10.5 ± 7.3	14.4 ± 11.7	11.5 ± 8.8	< 0.001
Absolute neutrophil count, /uL	8348 ± 6371	11,756 ± 9133	9205 ± 7310	< 0.001
Platelet, x10^3/uL	169 ± 132	154 ± 124	165 ± 130	0.157
BUN, mg/dL	24.6 ± 16.7	34.2 ± 22.5	27.0 ± 18.8	< 0.001
Creatinine, mg/dL	0.95 ± 0.91	1.02 ± 0.95	0.97 ± 0.92	0.371
Total bilirubin, mg/dL	1.7 ± 2.8	3.3 ± 6.4	2.1 ± 4.1	0.001
Prothrombin time, INR	1.2 ± 0.2	1.3 ± 0.2	1.2 ± 0.2	0.015
Albumin, g/dL	2.5 ± 0.4	2.3 ± 0.4	2.4 ± 0.4	< 0.001
CRP, mg/dL	8.8 ± 7.3	8.9 ± 6.9	8.8 ± 7.2	0.917
Lactic acid, mmol/dL	1.3 ± 0.8	1.7 ± 09	1.4 ± 0.8	< 0.001
Neutropenia, n (%)	25 (4.7)	7 (3.9)	32 (4.5)	0.82

Notes: *Includes conventional oxygen devices such as nasal cannulas, venturi masks, reservoir masks, and T-pieces.
Abbreviations: IQR, interquartile range; BMI, body mass index; FiO_2, Fraction of inspired oxygen; BiPAP, Bilevel positive airway pressure; HFNC, high-flow nasal cannula; GCS, Glasgow coma scale; BUN, blood urea nitrogen; CRP, C-reactive protein.

the 1-year mortality rate was 47.9%. Among patients with metastatic cancer (n = 550), 44.5% of patients received further chemotherapy after ICU discharge (Supplementary Table 1).

In the multivariable logistic regression analysis (Table 4), the administration of vasopressors (Odds Ratio [OR] 2.08; 95% Confidence Interval [CI] 1.20–3.61; p = 0.009), delirium (OR 1.73; 95% CI 1.04–2.87; p = 0.035), coma (OR 5.63; 95% CI 2.09–16.17; p < 0.001), limited mobility (OR 2.41; 95% CI 1.22–5.14; p = 0.015), and oxygen therapy with

Table 3 Post-ICU Outcomes

	Hospital Survivor (n = 530)	Hospital Non-Survivor (n = 178)	Total (n = 708)	p-value
Hospital length of stay, median [IQR]	14.0 [8.0; 24.0]	10.0 [3.0; 22.0]	13.0 [7.0; 24.0]	< 0.001
1-year mortality, n (%)	254 (47.9)	178 (100.0)	432 (61.0)	< 0.001
ICU readmission, n (%)	18 (3.4)	31 (17.4)	49 (6.9)	< 0.001

Abbreviation: IQR, interquartile range.

BiPAP (OR 21.63; 95% CI 5.36–99.57; p < 0.001), HFNC (OR 7.08; 95% CI 2.45–23.99; p < 0.001), and other oxygen devices (OR 3.16; 95% CI 1.20–9.92; p = 0.031) used at the time of ICU discharge were identified as independent risk factors for in-hospital mortality. Hyperbilirubinemia (OR 1.12; 95% CI 1.06–1.19; p < 0.001), and hyperlactatemia (OR

Table 4 Risk Factors Associated with in-Hospital Mortality in ICU Survivors (n = 704)

	Univariable			**Multivariable**		
	Beta	**95% CI**	**P-value**	**Beta**	**95% CI**	**P-value**
Malignancy site						
Others	1			1		
Lung cancer	1.28	0.81, 2.04	0.3	1.15	0.66, 2.01	0.628
Pancreas-Biliary cancer	0.59	0.34, 1.00	0.005	0.48	0.23, 0.99	0.048
Gastrointestinal	1.01	0.57, 1.76	> 0.9	0.52	0.20, 1.26	0.160
Urogenital cancer	0.61	0.28, 1.24	0.2	1.28	0.62, 2.62	0.494
Causes of ICU admission						
Respiratory failure	1			1		
Shock	0.37	0.24, 0.56	< 0.001	0.36	0.19, 0.67	0.001
Cardiac arrest	0.95	0.35, 2.34	> 0.9	1.18	0.35, 3.62	0.781
Altered mental status	1.22	0.56, 2.58	0.6	1.60	0.63, 3.91	0.315
Metabolic acidosis	0.85	0.26, 2.36	0.8	0.75	0.17, 2.79	0.676
Post-operative/procedure	0.68	0.33, 1.33	0.3	1.32	0.55, 3.04	0.522
Others	0.40	0.17, 0.84	0.023	0.56	0.20, 1.45	0.255
SOFA score at ICU admission	1.10	1.06, 1.15	< 0.001			
Mechanical ventilation during ICU	2.30	1.59, 3.35	< 0.001			
Tracheostomy done	1.68	1.06, 2.61	0.024	0.53	0.26, 1.04	0.075
ICU length of stay	1.04	1.02, 1.06	< 0.001			
At the time of ICU discharge						
Weight change %	1.03	1.00, 1.05	0.020	1.03	1.00, 1.06	0.034
Received hemodialysis	2.37	1.45, 3.84	< 0.001			
Received vasopressors	2.57	1.70, 3.87	< 0.001	2.08	1.20, 3.61	0.009
GCS						
GCS ≥ 13	1					
GCS < 13	5.85	3.25, 10.8	< 0.001			
Delirium						
Negative	1			1		
Positive	3.17	2.13, 4.71	< 0.001	1.73	1.04, 2.87	0.035
Unable to assess (coma)	10.5	4.61, 26.1	< 0.001	5.63	2.09, 16.17	< 0.001

(*Continued*)

Table 4 (Continued).

	Univariable			Multivariable		
	Beta	**95% CI**	**P-value**	**Beta**	**95% CI**	**P-value**
Mobility limitation	4.31	2.41, 8.42	< 0.001	2.41	1.22, 5.14	0.015
Oxygen therapy						
No oxygen	1			1		
Received BiPAP	25.8	9.12, 84.0	< 0.001	21.63	5.36, 99.57	< 0.001
Received HFNC	9.55	4.10, 26.2	< 0.001	7.08	2.45, 23.99	< 0.001
Others*	3.29	1.50, 8.66	0.007	3.16	1.20, 9.92	0.031
Laboratory findings						
Hemoglobin	0.89	0.79, 1.00	0.046			
White blood cell	1.06	1.03, 1.08	< 0.001	1.03	1.01, 1.06	0.018
BUN	1.03	1.02, 1.03	< 0.001	1.01	1.00, 1.06	0.022
Total bilirubin	1.09	1.05, 1.14	< 0.001	1.12	1.06, 1.19	< 0.001
Albumin	0.45	0.29, 0.68	< 0.001			
Lactic acid	2.06	1.64, 2.63	< 0.001	1.57	1.18, 2.09	0.002

Notes: *Includes conventional oxygen devices such as nasal cannulas, venturi masks, reservoir masks, and T-pieces.
Abbreviations: CI, confidence interval; GCS, Glasgow coma scale; BiPAP, Bilevel positive airway pressure; HFNC, high-flow nasal cannula; BUN, blood urea nitrogen; CRP, C-reactive protein.

1.57; 95% CI 1.18–2.09; p = 0.002) were also significant risk factors for hospital mortality. In our cohort, ICU survivors with pancreas-biliary cancer was associated with a lower risk of hospital mortality (OR 0.48; 95% CI 0.23–0.99; p = 0.048). ICU admission due to shock was associated with lower hospital mortality compared to admission due to respiratory failure (OR 0.36; 95% CI 0.19–0.67; p = 0.001). Figure 2 depicts 1-year survival curves of study patients according to their mental status (A), mobility status (B), and oxygen devices (C) at the time of ICU discharge. The one-year survival rates were significantly lower in patients with delirium (35%), coma (26%, p < 0.001), limited mobility (37%, p = 0.003), or on oxygen therapies (35%, p < 0.001).

Patients with mobility limitation had a significantly longer median duration of mechanical ventilation (5.0 [3.0–10.0] vs 2.0 [1.0–5.0] days, p < 0.001), and respiratory failure was more commonly identified as the cause of ICU admission among patients with mobility limitation (44.8% vs 28.5%, p < 0.001). (Supplementary Table 2). Missing data across the overall analysis are summarized in Appendix 2.

Discussion

This retrospective cohort study of ICU survivors with solid malignancies analyzed seven years of data from a single center in Korea. We previously published research on risk factors for ICU mortality at ICU admission among the entire cohort of ICU patients with solid malignancies.[21] This current study extends that research by focusing on a different patient population, namely ICU survivors at the time of ICU discharge, and emphasizes the role of post-ICU impairments in these patients, with a particular focus on patient characteristics at the time of ICU discharge. Patients who had delirium or coma, mobility limitations, or were receiving oxygen therapy at the time of ICU discharge had a significantly higher risk of both in-hospital and long-term mortalities. The in-hospital mortality rate for study patients was 25.1%, and they died a median of 10 days after ICU discharge. The 1-year mortality rate was as high as two-thirds. To our knowledge, this

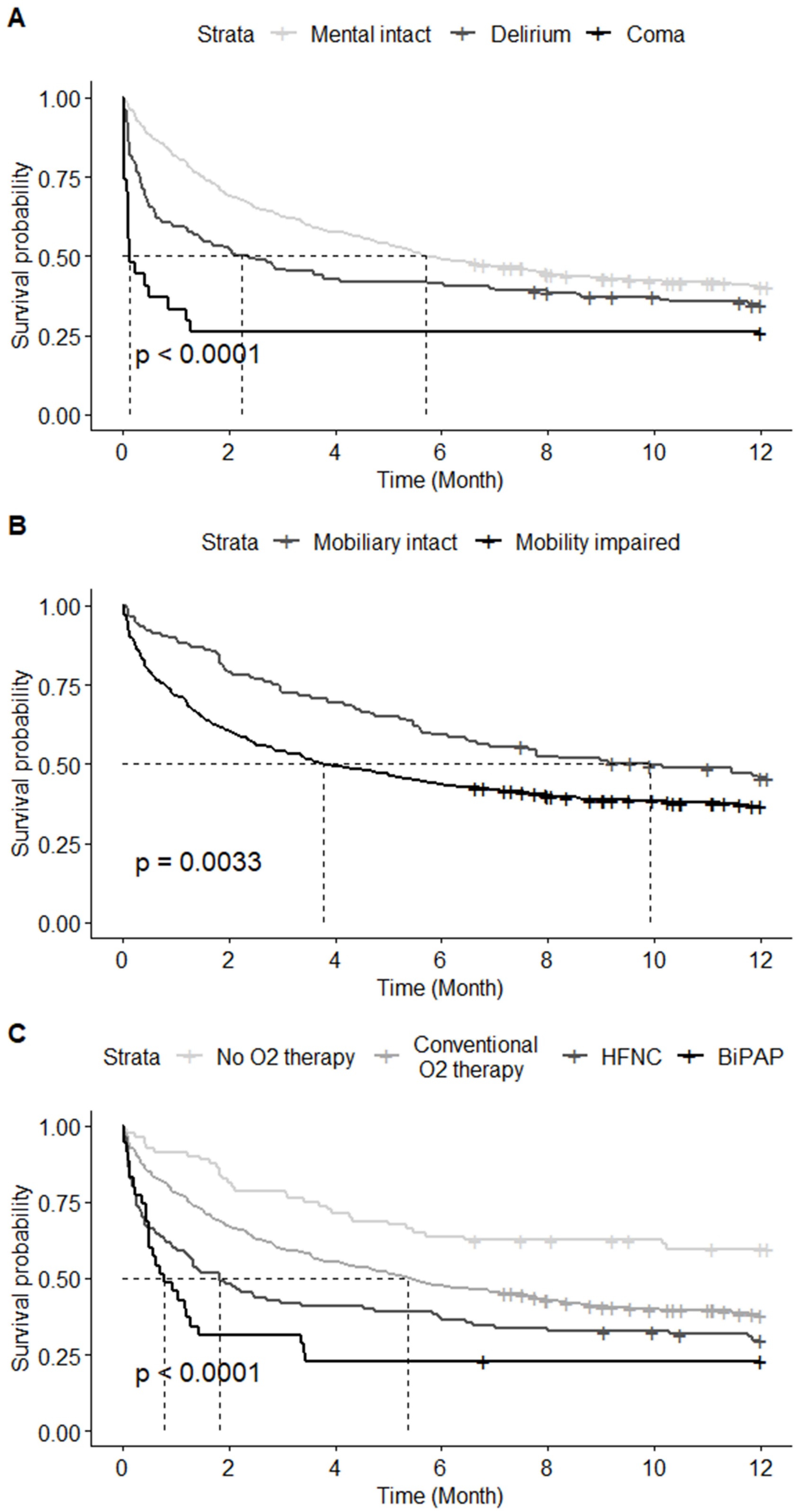

Figure 2 One-year survival curve (**A**) according to delirium and coma status (**B**) according to mobility status (**C**) according to oxygen device at the time of ICU discharge. Delirium was assessed using CAM-ICU assessment tools. Mobility was assessed using the Braden scale.

Abbreviations: BiPAP, Bilevel positive airway pressure; HFNC, high-flow nasal cannula.

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is the first study to report risk factors at the time of ICU discharge for short- and long-term mortality in ICU survivors with solid malignancies.

Our study examined the influence of cognitive and physical impairments present at the time of ICU discharge on post-ICU hospital mortality and 1-year mortality in patients with solid malignancies. After discharge from acute critical illness, patients may still suffer from persistent hypoxia, ICU-acquired weakness (ICU-AW), reduced physical function, and psychiatric and cognitive problems.[4] In our cohort, a quarter of the patients had altered mental status, including delirium or coma, at the time of ICU discharge. Previous studies have shown that delirium in critically ill adults is strongly associated with cognitive impairment 3 to 12 months after ICU discharge and longer hospital stays, while no consistent association with mortality has been reported.[22,23] Our findings showed that delirium at ICU discharge was associated with increased in-hospital mortality in patients with solid malignancies. As many as 80% of patients at the time of ICU discharge reported new physical impairments, including ICU-AW and pulmonary dysfunction.[24] ICU-AW specifically manifests as poor mobility, weakness, and reduced exercise tolerance. According to a previous report, this condition commonly occurs in patients with sepsis or in those receiving mechanical ventilation for more than 4 days.[25] Consistent with this, ICU survivors with mobility limitation in our cohort had a median of 5 days of mechanical ventilation, compared to 2 days in those without mobility limitation. In our cohort, 80% of patients had mobility limitations, and 89% of patients received oxygen therapy due to persistent pulmonary dysfunction at the time of ICU discharge. Our findings indicate that physical impairments in solid malignancies impact both hospital mortality and 1-year mortality. As ICU-acquired weakness and pulmonary dysfunction can persist for years,[4] and a previous study reported that more than half of patients experienced PICS at 1 year after hospital discharge,[26] these post-ICU impairments may substantially limit functional performance. In patients with cancer, especially those with limited life expectancy, impaired physical function may delay or prevent the resumption of cancer treatment, which in turn can contribute to disease progression or reduced survival.[27] Decline in performance caused by physical impairment could act as barriers to chemotherapy and other oncologic treatments. Although cognitive impairment alone may not necessarily preclude further treatment, significant changes in cognitive function could influence oncologists' decisions regarding chemotherapy. In our cohort, 96.5% of patients had physical or cognitive impairments at the time of ICU discharge, which is a higher proportion than the reported prevalence of PICS in the general population.[6] Due to the existing burden of chronic illness from underlying solid malignancies,[28] patients may be vulnerable to developing post-ICU impairments. Further research is needed on the impact of PICS on the quality of life in patients with solid malignancies, especially because quality of life is a major treatment consideration in patients with limited life expectancy.[29]

The present study showed a higher in-hospital mortality rate (24% vs 12%) compared to the previous study by Lee et al,[10] which involved all medical ICU survivors in a single Korean center. In Lee's study, a solid malignancy was identified as a risk factor for in-hospital mortality, with an odds ratio of 4.1. In our ICU survivors with solid malignancies, the stage of the underlying solid malignancy was not related to in-hospital mortality after ICU discharge. However, the presence of remaining organ dysfunction at the time of ICU discharge, including hepatic, cardiovascular, pulmonary, and central nervous system dysfunction, was independently associated with in-hospital mortality. Among the different types of cancer, pancreatic-biliary cancer was associated with lower hospital mortality in our cohort of ICU survivors. This may be partly explained by previous reports suggesting that biliary septic shock, a potentially reversible condition when treated with prompt intervention, is a common cause of ICU admission in this population.[30] In our prior study, pancreatic-biliary cancer was also associated with lower ICU mortality compared to other cancer types, showing a similar pattern to what was observed in this study.[21] Rapid shock reversal through biliary interventions in these cases could lead to minimal residual organ dysfunction and improved short-term outcomes, including lower ICU or hospital mortality.

In those without cancer, the 1-year mortality rate of ICU survivors has been reported to be 10% to 20%.[31,32] However, in our study, 61% of ICU survivors with solid malignancies died within 1 year, and even among patients discharged alive from the hospital, 48% of them died within 1 year. Our significantly higher 1-year mortality rate compared to that of the general ICU population highlights that, despite the decreased ICU mortality in cancer patients due to improved critical care, their long-term outcomes still remain poor. This may be due to the nature of the advanced cancer itself or the discontinuation of oncologic treatment caused by the patient's post-ICU impairment. According to the study by

Borcoman et al,[8] the inability to receive oncologic treatment after ICU discharge was a significant risk factor for 1-year mortality after ICU discharge, with a hazard ratio of 5.34.

Our findings show that the prognosis of patients with solid malignancies who survived from the ICU is particularly poor. Therefore, considering the shortage of ICU beds and the poor prognosis of these patients, it is crucial that initial decisions regarding life-sustaining treatment be informed by an understanding of the anticipated long-term prognosis after ICU care and through a well-informed discussion involving the patient, family, and attending oncologist. In our cohort, 83% of the hospital non-survivor group made an informed decision not to receive further life-sustaining treatment after being discharged alive from the ICU. These results suggest that there was a discrepancy between the recovery expected by patients, their families, and oncologists, and the actual state of recovery after the initial ICU treatment in many patients. Because mechanical ventilation for more than 4 days and sepsis have been reported as risk factors for the development of ICU-acquired weakness, many patients who are treated in the ICU may continue to suffer from weakness after discharge from the ICU.[25] The patients and their families need to be aware of the possibility that patients may have remaining organ dysfunctions or mental or physical impairments, which can prevent them from undergoing further cancer treatment after discharge from the ICU.

This study has several limitations. First, due to its single-center design, the generalizability of our findings may be limited. Nevertheless, our study includes a substantial cohort of patients from one of the largest referral hospitals in Korea over a 7-year period. Second, most of the patients in this study were in the locally advanced or metastatic stage, and therefore, they are not representative of patients with all types of solid malignancies. This reflects the real-world composition of patients with solid malignancies who were unexpectedly admitted to the ICU in a tertiary hospital in Korea. Patients in locally advanced or metastatic stages may be more susceptible to life-threatening conditions, such as sepsis or acute respiratory failure, than patients in early stages because cancer treatments can weaken the immune system.[33] Third, our study lacks detailed information on responses to chemotherapy, which may influence long-term mortality. Fourth, our assessment of physical impairment was limited by the retrospective nature of the study. In the context of PICS, physical impairments encompass a broad spectrum of conditions including ICU-acquired weakness, impaired pulmonary function, cachexia, and fatigue.[6,34] These can be evaluated using structured questionnaires, pulmonary function tests, the 6-minute walk test, or objective assessments such as the Medical Research Council muscle strength score, nerve conduction studies, or electromyography.[35,36] However, such evaluations could not be performed in our study. Instead, we used the Braden mobility subscale to assess reduced physical function, and interpreted the persistent need for respiratory support at ICU discharge as indicative of pulmonary dysfunction. While these measures do not fully capture the diagnostic criteria of physical impairments in PICS, they represent clinically meaningful proxies for physical limitations in this patient population.[37] Lastly, since our study did not include a comparison group of patients with solid malignancies who were not admitted to the ICU, it limits our ability to compare post-discharge outcomes that are specific to ICU survivors.

Conclusions

In our study, a considerable portion of ICU survivors with solid malignancies died in the hospital and within one year after ICU discharge. Cognitive impairment, mobility impairment, and persistent pulmonary dysfunction at ICU discharge were significant risk factors for both in-hospital and long-term mortality.

Abbreviations

BiPAP, bilevel positive airway pressure; BMI, body mass index; CAM-ICU, Confusion Assessment Method for the ICU; GCS, Glasgow Coma Scale; HFNC, high-flow nasal cannula; ICU, intensive care unit; ICU-AW, ICU-acquired weakness; IQR, interquartile range; OR, Odds Ratio; PICS, post-intensive care syndrome; RASS, Richmond Agitation Sedation Scale.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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