



# Hospital mortality and prognostic factors in critically ill patients with acute kidney injury and cancer undergoing continuous renal replacement therapy

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**Background:** Whether continuous renal replacement therapy (CRRT) should be applied to critically ill patients with both acute kidney injury (AKI) and cancer remains controversial because of poor expected outcomes. The present study determined prognostic factors for all-cause in-hospital mortality in patients with AKI and cancer undergoing CRRT.

**Methods:** We included 471 patients with AKI and cancer who underwent CRRT at the intensive care unit of a Korean tertiary hospital from 2013 to 2020, and classified them by malignancy type. The primary outcomes were 28-day all-cause mortality rate and prognostic factors for in-hospital mortality. The secondary outcome was renal replacement therapy (RRT) dependency at hospital discharge.

**Results:** The 28-day mortality rates were 58.8% and 82% in the solid and hematologic malignancy groups, respectively. Body mass index (BMI), presence of oliguria, Sequential Organ Failure Assessment (SOFA) score, and albumin level were common predictors of 28-day mortality in the solid and hematologic malignancy groups. A high heart rate and the presence of severe acidosis were prognostic factors only in the solid malignancy group. Among the survivors, the proportion with RRT dependency was 25.0% and 33.3% in the solid and hematologic malignancy groups, respectively.

**Conclusion:** The 28-day mortality rate of cancer patients with AKI undergoing CRRT was high in both the solid and hematologic malignancy groups. BMI, presence of oliguria, SOFA score, and albumin level were common predictors of 28-day mortality in the solid and hematologic malignancy groups, but a high heart rate and severe acidosis were prognostic factors only in the solid malignancy group.

**Keywords:** Acute kidney injury, Continuous renal replacement therapy, Malignancy

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## Introduction

Because of remarkable advances in the diagnosis and treatment of cancer, an increasing number of cancer patients are admitted to intensive care units (ICUs) [1]. A retrospective cohort study using validation of Simplified Acute Physiology Score (SAPS) 3 data from Korean ICUs reported that patients with cancer accounted for 34.8% of the total number of patients admitted [2]. Acute kidney injury (AKI) is a common and severe complication in this population. AKI has various etiologies, including cancer itself (multiple myeloma, neoplastic urinary tract obstruction, and renal malignant infiltration), cancer treatment (nephrotoxic chemotherapy and tumor lysis syndrome), sepsis, antibiotics, and iodine contrast [3]. In recent studies, up to 54% of cancer patients who are admitted to an ICU have AKI, and some of them require renal replacement therapy (RRT) [4,5].

However, whether continuous RRT (CRRT) can be applied to critically ill patients with both AKI and cancer remains controversial because of the poor expected outcomes of the dual diagnosis. In-hospital mortality rates in cancer patients who require dialysis are reported to be between 51% and 90% [6–8]. Because of geographic variations in the diagnosis of different types of cancer, domestic epidemiologic data are essential to guide the management of patients with both AKI and cancer, but few studies have reported the clinical characteristics, prognoses, and prognostic factors of such Korean patients. Therefore, the present study investigated 28-day all-cause mortality, prognostic factors of mortality, and RRT dependency at hospital discharge among patients with AKI and a solid or hematologic malignancy who received CRRT.

## Methods

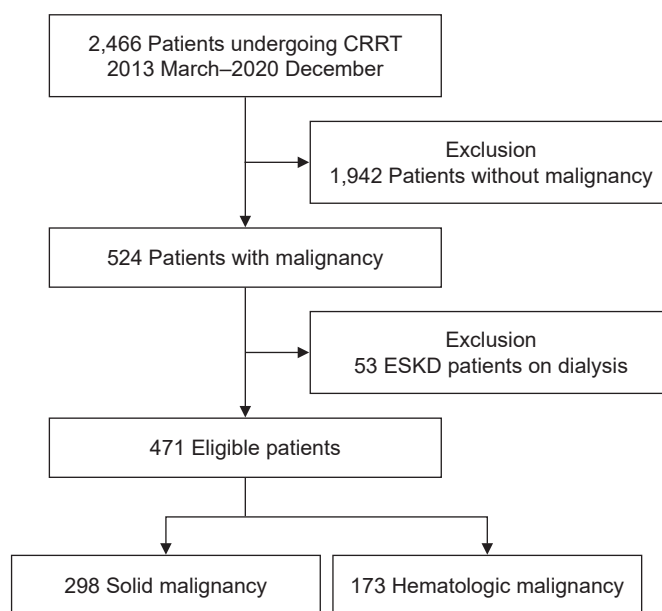
This study was approved by the Institutional Review Board of Pusan National University Hospital (No. 2102-022-100), which waived the requirement for informed patient consent because of the retrospective design of the study. All clinical investigations were conducted in accordance with the principles of the Declaration of Helsinki.

## Study design and subjects

This was a retrospective, single-center study. Data collected from the medical records of 2,466 patients who underwent CRRT from March 2013 to December 2020 in the ICU of a single-center university-affiliated hospital were reviewed (Fig. 1). All patients were aged >18 years. After excluding patients without malignancy and with end-stage kidney disease on dialysis, 471 were eligible for inclusion in this study. Patients were grouped according to type of malignancy as solid malignancy group (n = 298) and hematologic malignancy group (n = 173).

## Clinical data collection and laboratory measurements

The following demographic and clinical data including age, sex, body mass index (BMI), cause of AKI, and comorbidities at the time of CRRT initiation were reviewed. The following clinical data were collected from the patients' medical records: presence, type (solid or hematologic malignancy), site (breast, lung, digestive tract, prostate/bladder/kidney, and others), extent (localized to the primary tumor site or distant metastasis to other sites), status (diagnosis, induction, remission [complete or partial], stabiliza-



**Figure 1.** Flowchart of the patient selection process.

CRRT, continuous renal replacement therapy; ESKD, end-stage kidney disease.

tion, or progression) [9], and treatment history (adjuvant or palliative chemotherapy, radiotherapy, concurrent chemoradiation therapy, and steroids) of malignancy, as well as AKI etiology (sepsis, ischemia/ shock, drugs, tumor lysis syndrome, urinary tract obstruction, and others, which included multiple myeloma, postoperation, and hepatorenal syndrome). Laboratory test results of complete blood counts and albumin, potassium, bicarbonate, serum blood urea nitrogen, creatinine, and phosphorus levels were collected. The Sequential Organ Failure Assessment (SOFA) score was calculated to assess disease severity [10].

### Continuous renal replacement therapy protocol

Among critically ill patients with AKI, those with sustained oliguria (urine output of  $<0.3$  mL/kg/hr for  $\geq 24$  hours), uncontrolled volume overload (as evidenced by edema or pleural effusion despite maximal medical care), intractable hyperkalemia (serum potassium of  $>6.0$  mmol/L despite maximal medical care), severe acidosis (arterial pH of  $<7.2$  despite maximal medical care), or other conditions such as uremic encephalopathy received CRRT at the discretion of their physicians. All CRRT patients received continuous venovenous hemodiafiltration through the internal jugular or femoral vein. A Prismaflex (Gambro Lundia AB, Lund, Sweden) CRRT machine and AN 69 ST 100 filter set (1.0 m<sup>2</sup>; Gambro Lundia AB) were used. The initial effluent flow rates were between 35 and 40 mL/kg/hr, and additional adjustments were made according to the patient's catabolic state or the presence of hyperkalemia and acidosis. The actual delivered dose was calculated as the mean effluent volume divided by the weight of the patient during the entire CRRT period. The downtime was calculated by adding all the times (hours) of CRRT interruption during the treatment. Patients' body weights were measured continuously during the CRRT period. The blood flow rate was started at 150 mL/min and adjusted according to patients' metabolic demands and hemodynamic instabilities. Heparin-free, heparin, and nafamostat mesylate were used to maintain the patency of the extracorporeal circuit while minimizing patient complications according to individual bleeding risk.

### Outcomes

Patients were observed until the time of hospital discharge.

The primary outcomes of the present study were 28-day all-cause mortality during the follow-up period and the prognostic factors for in-hospital mortality. The secondary outcome was RRT dependency at the time of hospital discharge. Outcomes were investigated separately in the solid and hematologic malignancy groups.

### Statistical analysis

Continuous variables are expressed as mean  $\pm$  standard deviation or median (interquartile range [IQR]), and categorical variables are expressed as number (percentage). Comparisons between the two groups were performed using Student t test or Mann-Whitney U test for continuous variables and the chi-square test for categorical variables. Cox proportional hazards models and logistic regression models were used in univariable and multivariable analyses to determine the hazard ratios (HRs) of variables related to in-hospital mortality and RRT dependency. Variables were selected for multivariate analysis according to study aim and were adjusted. The results are reported as HR and 95% confidence interval (CI). We conducted a receiver operating characteristic (ROC) analysis to confirm the predictive accuracy of the prognostic factors for all-cause in-hospital mortality and calculated the area under the curve (AUC). All probabilities were two-tailed, and the level of statistical significance was defined as  $p < 0.05$ . All statistical analyses were performed using IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA).

## Results

### Baseline clinical characteristics of patients

The baseline clinical characteristics of the patients are presented in [Table 1](#) according to type of malignancy. Of the 471 patients, 298 (63.3%) had a solid malignancy, and 173 (36.7%) had a hematologic malignancy. In patients with a solid malignancy, the median age was 70 years (IQR, 62–77 years) and 212 (71.1%) were male. The extent of cancer was mostly localized (79.2%), and the digestive tract was the most common site of cancer (57.0%). About half of the patients were in remission (53.4%), and 52 (17.4%) patients had a history of chemotherapy before ICU admission, and the purpose of most of that chemotherapy was palliative

**Table 1.** Baseline clinical characteristics of study patients according to type of malignancy

Characteristic	Solid malignancy	Hematologic malignancy
No. of patients	298	173
Age (yr)	70 (62–77)	65 (52–73)
Male sex	212 (71.1)	99 (57.2)
Solid tumor, localized/distant	236/62	
Breast	16 (5.4)	-
Lung	35 (11.7)	-
Digestive tract	170 (57.0)	-
Prostate/bladder/kidney	35 (11.7)	-
Others	42 (14.1)	-
Hematologic malignancy		
Leukemia	-	84 (48.6)
Lymphoma	-	58 (33.5)
Multiple myeloma	-	23 (13.3)
Myelodysplastic syndrome	-	7 (4.0)
Cancer status		-
Diagnosis	37 (12.4)	15 (8.7)
Induction	0 (0)	49 (28.3)
Remission	159 (53.4)	53 (30.6)
Stabilization	33 (11.1)	25 (14.5)
Progression	63 (21.1)	31 (17.9)
Underlying disease, overlapped		
Hypertension	131 (44.0)	53 (30.6)
Diabetes mellitus	127 (42.6)	45 (26.0)
Cardiovascular disease	81 (27.2)	33 (19.1)
Chronic pulmonary disease	19 (6.4)	3 (1.7)
Liver disease	50 (16.8)	7 (4.0)
Chronic kidney disease	63 (21.1)	14 (8.1)
Treatment history before ICU admission		
Chemotherapy	52 (17.4)	145 (83.8)
Adjuvant	18 (34.6)	
Palliative	34 (65.4)	
Radiotherapy	9 (3.0)	1 (0.6)
Concurrent chemoradiation therapy	27 (9.0)	0 (0)
Steroid	0 (0)	5 (2.9)
Bone marrow transplantation	-	33 (19.1)
Admission (day)	15 (5–32)	26 (14–45)
ICU admission (day)	6 (3–14)	6 (3–12)
ICU admission to CRRT start (day)	0 (0–1)	1 (0–3)
Body mass index (kg/m <sup>2</sup> )	22.6 (19.8–25.3)	23.2 (20.9–26.1)
Mean arterial pressure (mmHg)	75 (67–89)	77 (68–85)
Heart rate (beat/min)	104 ± 24	115 ± 25
ICU risk factor		
Ventilator use	180 (60.4)	112 (64.7)
Vasopressor use	212 (71.1)	123 (71.1)
SOFA score	11 (8–13)	13 (10–16)
6-Hr urine output before CRRT (mL)	95 (20–255)	160 (50–380)

(Continued to the next page)

**Table 1. Continued**

Characteristic	Solid malignancy	Hematologic malignancy
Sepsis	110 (36.9)	100 (57.8)
Trauma	6 (2.0)	0 (0)
Surgery	71 (23.8)	3 (1.7)
Cause of ICU admission		
Acute kidney injury	117 (39.3)	54 (31.2)
Respiratory failure	56 (18.8)	48 (27.7)
Shock	125 (41.9)	71 (41.0)
Acute kidney injury etiology		
Sepsis	146 (49.0)	123 (71.1)
Ischemia/shock	84 (28.2)	11 (6.4)
Drugs	21 (7.0)	3 (1.7)
Tumor lysis syndrome	2 (0.7)	22 (12.7)
Urinary tract obstruction	13 (4.4)	0 (0)
Others	32 (10.7)	14 (8.1)
CRRT indication, overlapped		
Sustained oliguria	163 (54.7)	83 (48.0)
Uncontrolled volume overload	154 (51.7)	102 (59.0)
Intractable hyperkalemia	25 (8.4)	9 (5.2)
Severe acidosis	94 (31.5)	49 (28.3)
Others	122 (40.9)	81 (46.8)
CRRT duration (hr)	37 (14–74)	47 (15–107)
Downtime (hr)	1 (0–5)	1 (0–4)
CRRT prescription		
Prescribed dose (mL/kg/hr)	38.1 (35.3–41.1)	38.5 (35.1–42.9)
Delivered CRRT dose (mL/kg/hr)	33.2 (30.1–36.6)	34.7 (31.6–38.7)
Laboratory finding		
White blood cell ( $\times 10^3/\mu\text{L}$ )	12.8 (8.0–19.4)	3.9 (0.4–13.9)
Hemoglobin (g/dL)	9.9 (8.5–11.5)	8.8 (7.9–10.0)
RDW-CV (%)	15.5 (14.2–17.0)	16.3 (15.2–17.9)
Platelet ( $\times 10^3/\mu\text{L}$ )	139 (80–209)	38 (20–61)
Albumin (g/dL)	2.9 (2.5–3.2)	2.7 (2.3–3.2)
Potassium (mmol/L)	5.1 (3.8–7.2)	4.3 (3.8–4.9)
Arterial pH	7.29 (7.19–7.38)	7.30 (7.19–7.39)
Bicarbonate (mEq/L)	15.8 (11.4–20.7)	18.1 (14.4–22.5)
BUN (mg/dL)	52.2 (26.8–73.5)	58.6 (38.4–84.4)
Creatinine (mg/dL)	2.53 (1.65–4.02)	2.40 (1.76–3.49)
Uric acid (mg/dL)	7.5 (5.5–10.3)	6.9 (4.9–9.5)
Corrected calcium (mg/dL) <sup>a</sup>	8.8 (8.4–9.4)	8.8 (8.0–9.4)
Phosphorus (mg/dL)	5.1 (3.8–7.2)	4.8 (3.3–7.1)
Lactic acid (mmol/L)	4.4 (1.9–9.0)	3.7 (2.1–8.4)
BNP (pg/mL)	287 (195–717)	737 (279–1,796)
Pro-BNP (pg/mL)	2,411 (655–8,680)	4,906 (1,155–17,139)

Data are expressed as number only, number (%), median (interquartile range), or mean  $\pm$  standard deviation.

BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CRRT, continuous renal replacement therapy; ICU, intensive care unit; RDW-CV, red cell distribution width-coefficient of variation; SOFA, Sequential Organ Failure Assessment.

<sup>a</sup>Corrected calcium (mg/dL) = measured total Ca (mg/dL) + 0.8  $\times$  [4–measured serum albumin (g/dL)].

(65.4%). The median SOFA score was 11 (IQR, 8–13), and the median 6-hour urine output before the start of CRRT was 95 mL (IQR, 20–255 mL). The most common reason for ICU admission was shock (41.9%), and the most common cause of AKI was sepsis (49.0%). Sustained oliguria was a major indication for CRRT (54.7%). In terms of initial laboratory findings at ICU admission, the median albumin level was 2.9 g/dL (IQR, 2.5–3.2 g/dL), and the median creatinine level was 2.53 mg/dL (IQR, 1.65–4.02 mg/dL).

In patients with hematologic malignancy, the median age was 65 years (IQR, 52–73 years) and 99 (57.2%) were male. Leukemia was the most common subtype (48.6%), and about one-third of patients were in remission (30.6%). Most of the patients had a history of chemotherapy before ICU admission (83.8%). The median SOFA score was 13 (IQR, 10–16), and the median 6-hour urine output before the start of CRRT was 160 mL (IQR, 50–380 mL). The most common reason for ICU admission was shock (41.0%), and the most common cause of AKI was sepsis (71.1%). Uncontrolled volume overload was a major indication for CRRT (59.0%). In terms of initial laboratory findings at ICU admission, the median albumin level was 2.7 g/dL (IQR, 2.3–3.2 g/dL), and the median creatinine level was 2.40 mg/dL (IQR, 1.76–3.49 mg/dL).

### Primary outcome

**Table 2** shows the all-cause mortality of the study patients according to type of malignancy. The median follow-up duration was 15 days (IQR, 5–32 days) in the solid malignancy group and 26 days (IQR, 14–45 days) in the hematologic malignancy group. In the solid malignancy group, 175 patients (58.7%) died during the 28-day hospitalization, as did 142 of the patients (82.1%) in the hematologic malignancy group. The baseline clinical characteristics of non-survivors and survivors are presented in **Supplemen-**

**tary Table 1** and **2** (available online) for patients in the solid and hematologic malignancy groups, respectively.

The results of the Cox regression univariable and multivariable analyses for 28-day all-cause mortality according to the baseline clinical parameters in the solid and hematologic malignancy groups are presented in **Table 3** and **4**, respectively. In the solid malignancy group, BMI (HR, 0.96 [95% CI, 0.93–0.98];  $p = 0.001$ ), presence of oliguria (HR, 1.82 [95% CI, 1.24–2.66];  $p = 0.002$ ), severe acidosis (HR, 1.71 [95% CI, 1.18–2.45];  $p = 0.004$ ), heart rate (HR, 1.01 [95% CI, 1.01–1.02];  $p = 0.02$ ), SOFA score (HR, 1.09 [95% CI, 1.04–1.15];  $p = 0.001$ ), and albumin level (HR, 0.74 [95% CI, 0.55–0.99];  $p = 0.04$ ) were associated with 28-day all-cause mortality. In the hematologic malignancy group, BMI (HR, 0.96 [95% CI, 0.92–0.99];  $p = 0.03$ ), presence of oliguria (HR, 1.49 [95% CI, 1.03–2.16];  $p = 0.04$ ), SOFA score (HR, 1.11 [95% CI, 1.05–1.17];  $p < 0.001$ ), and albumin level (HR, 0.69 [95% CI, 0.49–0.96];  $p = 0.03$ ) were associated with 28-day all-cause mortality. A high heart rate and presence of severe acidosis were specific prognostic factors for 28-day mortality only in patients with solid malignancy.

The ROC curves constructed using the prognostic factors predicting 28-day all-cause mortality are plotted in **Fig. 2**. The AUC of the variables in the solid malignancy group (BMI, oliguria, severe acidosis, heart rate, SOFA score, and albumin level) was 0.831 ( $p < 0.001$ ), with a positive predictive value of 78.16% and a negative predictive value of 74.87%. The AUC of the variables in the hematologic malignancy group (BMI, oliguria, SOFA score, and albumin level) was 0.802 ( $p < 0.001$ ), with a positive predictive value of 84.71% and a negative predictive value of 62.73%.

### Secondary outcome

**Table 2** shows the RRT dependency of the survivors according to type of malignancy. At the time of hospital discharge,

**Table 2.** All-cause mortality and RRT dependency in patients with cancer according to type of malignancy

Outcome	Solid malignancy (n = 298)	Hematologic malignancy (n = 173)
Death	190 (63.8)	146 (84.4)
Intensive care unit death	183 (61.4)	146 (84.4)
28-Day death	175 (58.7)	142 (82.1)
RRT dependency among survivors	27/108 (25.0)	9/27 (33.3)

Data are expressed as number (%).  
RRT, renal replacement therapy.



**Table 3. Prognostic factors for 28-day all-cause mortality in solid malignancy patients**

Variable	Model 1		Model 2		Model 3	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.01 (0.99–1.02)	0.36				
Male sex	1.03 (0.74–1.43)	0.86				
BMI	0.96 (0.94–0.99)	0.00	0.97 (0.95–0.99)	0.01	0.96 (0.93–0.98)	0.001
Cancer status		0.22				
Diagnosis	1.23 (0.78–1.95)	0.38				
Remission	Reference					
Stabilization	1.14 (0.70–1.86)	0.59				
Progression	1.49 (1.03–2.15)	0.03				
Sepsis	1.64 (1.22–2.21)	0.001	1.37 (0.98–1.90)	0.06	1.19 (0.84–1.68)	0.33
Oliguria	2.36 (1.72–3.25)	<0.001	2.45 (1.75–3.45)	<0.001	1.82 (1.24–2.66)	0.002
Severe acidosis	2.23 (1.56–2.89)	<0.001	1.78 (1.28–2.46)	0.001	1.71 (1.18–2.45)	0.004
Admission cause				0.01		0.44
Acute kidney injury	Reference					
Respiratory failure	1.93 (1.26–2.95)	0.003	1.84 (1.18–2.88)	0.007	1.29 (0.78–2.12)	0.32
Shock	2.46 (1.72–3.51)	<0.001	1.01 (1.01–1.02)	0.006	1.29 (0.86–1.94)	0.22
Heart rate	1.01 (1.01–1.02)	<0.001	1.01 (1.01–1.02)	0.006	1.01 (1.01–1.02)	0.02
SOFA	1.18 (1.13–1.23)	<0.001			1.09 (1.04–1.15)	0.001
White blood cell	1.01 (0.99–1.02)	0.22				
Albumin	0.51 (0.39–0.65)	<0.001			0.74 (0.55–0.99)	0.04
Uric acid	0.96 (0.92–0.99)	0.04			0.99 (0.94–1.04)	0.62
Corrected calcium <sup>a</sup>	1.14 (1.02–1.27)	0.03			1.04 (0.91–1.20)	0.56
PT INR	1.38 (1.21–1.58)	<0.001			0.99 (0.81–1.22)	0.96

Model 1: unadjusted (n = 298). Model 2: BMI, sepsis, oliguria, severe acidosis, admission cause, heart rate (n = 292). Model 3: BMI, sepsis, oliguria, severe acidosis, admission cause, heart rate, SOFA, albumin, uric acid, corrected calcium, PT INR (n = 262).

BMI, body mass index; CI, confidence interval; HR, hazard ratio; PT INR, prothrombin time international normalized ratio; SOFA, Sequential Organ Failure Assessment.

<sup>a</sup>Corrected calcium (mg/dL) = measured total Ca (mg/dL) + 0.8 × [4 – measured serum albumin (g/dL)].

25.0% of the patients in the solid malignancy group and 33.3% of the patients in the hematologic malignancy group were RRT dependent. The results of multivariate logistic regression analysis of prognostic factors for RRT dependency are shown in [Supplementary Table 3](#) (available online). In the solid malignancy group, only underlying chronic kidney disease was related to RRT dependency (HR, 3.95 [95% CI, 1.69–9.24]; p = 0.001). In the hematologic malignancy group, the presence of oliguria as a CRRT indication (HR, 60.38 [95% CI, 1.02–3,576.82]; p = 0.049) and serum creatinine level at CRRT initiation (HR, 8.29 [95% CI, 1.07–64.23]; p = 0.04) were related to RRT dependency.

## Discussion

This retrospective study investigated in-hospital mortality

and prognostic factors for in-hospital mortality among critically ill Korean patients with both AKI and cancer who received CRRT. As expected, the 28-day all-cause mortality rates were high, 58.8% in the solid malignancy group and 82.0% in the hematologic malignancy group. Low BMI, presence of oliguria, high SOFA score, and low serum albumin level were common prognostic factors for 28-day mortality in patients with solid and hematologic malignancies, whereas a high heart rate and presence of severe acidosis were predictive only for patients with a solid malignancy. The proportion of patients who survived to hospital discharge with RRT dependency was 25.0% in the solid malignancy group and 33.3% in the hematologic malignancy group.

CRRT is an indispensable treatment modality for AKI in critically ill patients, and its overall use among patients un-

**Table 4.** Prognostic factors for 28-day all-cause mortality in hematologic malignancy patients

Variable	Model 1		Model 2		Model 3	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.01 (0.99–1.02)	0.25				
Male sex	0.96 (0.69–1.34)	0.81				
BMI	0.97 (0.95–1.01)	0.05	0.97 (0.93–1.01)	0.08	0.96 (0.92–0.99)	0.03
Cancer status		0.48				
Diagnosis	1.06 (0.56–1.99)	0.86				
Induction	1.26 (0.83–1.91)	0.29				
Remission	Reference					
Stabilization	0.77 (0.44–1.32)	0.77				
Progression	0.96 (0.59–1.58)	0.96				
Sepsis	1.32 (0.94–1.84)	0.11	1.03 (0.67–1.58)	0.89	0.94 (0.60–1.46)	0.77
Oliguria	1.85 (1.33–2.59)	<0.001	1.72 (1.21–2.45)	0.002	1.49 (1.03–2.16)	0.04
Severe acidosis	1.83 (1.28–2.62)	0.001	1.33 (0.91–1.94)	0.14	1.18 (0.80–1.75)	0.40
Admission cause				0.09		0.57
Acute kidney injury	Reference					
Respiratory failure	1.89 (1.21–2.96)	0.005	1.68 (1.05–2.69)	0.03	1.28 (0.76–2.17)	0.36
Shock	2.01 (1.33–3.06)	0.001	1.44 (0.86–2.39)	0.17	1.04 (0.59–1.84)	0.89
Heart rate	1.01 (1.00–1.02)	0.007	1.01 (0.99–1.01)	0.11	1.01 (0.99–1.01)	0.14
SOFA	1.13 (1.08–1.18)	<0.001			1.11 (1.05–1.17)	<0.001
White blood cell	0.99 (0.98–1.00)	0.04			0.99 (0.98–1.01)	0.76
Albumin	0.58 (0.43–0.78)	<0.001			0.69 (0.49–0.96)	0.03
Uric acid	0.96 (0.92–0.99)	0.03			0.99 (0.95–1.04)	0.87
Corrected calcium <sup>a</sup>	1.03 (0.92–1.16)	0.61				
PT INR	1.17 (0.96–1.42)	0.13				

Model 1: unadjusted (n = 173). Model 2: BMI, sepsis, oliguria, severe acidosis, admission cause, heart rate (n = 170). Model 3: BMI, sepsis, oliguria, severe acidosis, admission cause, heart rate, SOFA, WBC, albumin uric acid (n = 163).

BMI, body mass index; CI, confidence interval; HR, hazard ratio; PT INR, prothrombin time international normalized ratio; SOFA, Sequential Organ Failure Assessment.

<sup>a</sup>Corrected calcium (mg/dL) = measured total Ca (mg/dL) + 0.8 × [4 – measured serum albumin (g/dL)].

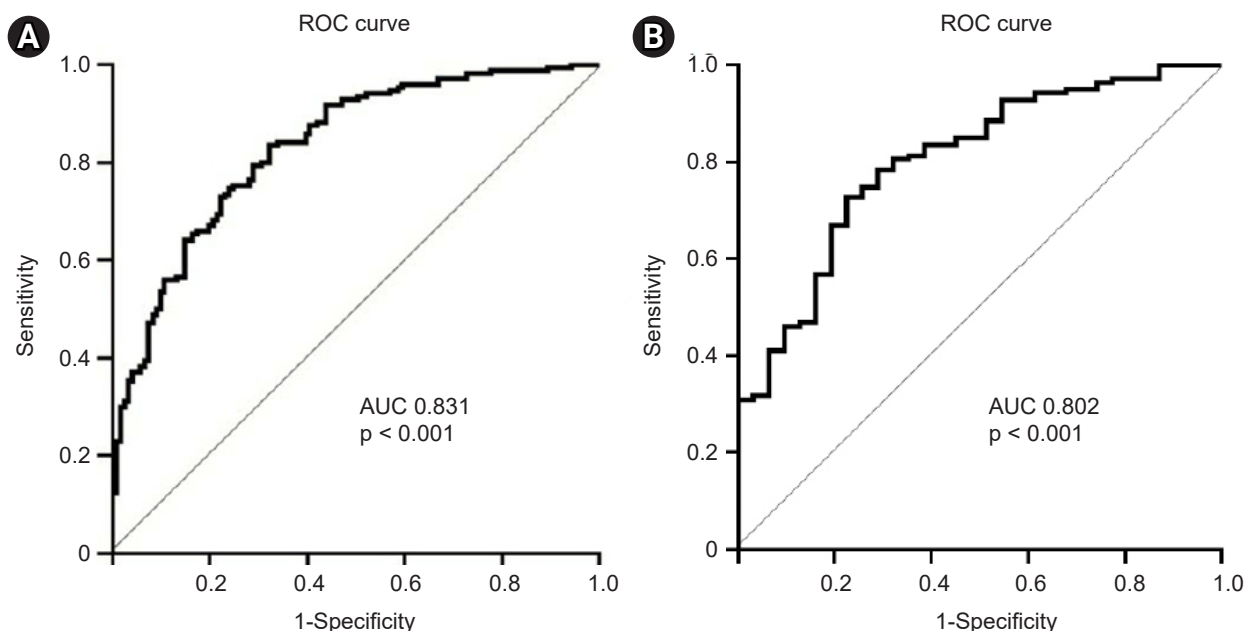
dergoing acute RRT is increasing [11,12]. In recent studies, CRRT greatly improved the rates of all-cause mortality and survival [11,12]. Because of remarkable advances in both cancer treatment and ICU treatment, patients with cancer now account for 13.5% to 34.8% of all patients admitted to ICUs [2,13–16]. Several studies have reported the outcomes of patients with both AKI and cancer who underwent RRT (Table 5) [7,16–26]. The differences in the proportions of solid and hematologic malignancies and indications for RRT among those studies make it difficult to directly compare their results. The in-hospital mortality rate ranged from 50% to 86% in patients with solid malignancy and from 72% to 86% in patients with hematologic malignancy. In this study, the prognoses for those patients were comparable to those from other studies.

The reported prognostic factors for in-hospital mor-

tality vary among studies and include number of organ failures, SOFA score or SAPS, and serum albumin level [5,16,18,19,21,23]. BMI reflects nutrition status, and both undernutrition (BMI of <18.5 kg/m<sup>2</sup>) and overweight/obesity (BMI of ≥25 kg/m<sup>2</sup>) carry a negative prognosis in cancer [27,28]. Because hypoalbuminemia is associated with several pathologic conditions, such as nutritional deficiency and chronic inflammation [29], a low BMI might reflect poor nutritional status and contribute as a prognostic factor for all-cause mortality in both malignancy groups.

In a systematic review of studies evaluating prognostic indices including SOFA, SAPS [30], and acute physiology and chronic health evaluations [31], all of the indices effectively predicted the outcomes of general medical or surgical ICU patients [32]. Among cancer patients, several studies, including this one, have confirmed that the indices that





**Figure 2. Receiver operating characteristic (ROC) curve for 28-day mortality according to type of malignancy.** (A) For solid malignancy patients, the ROC curve analysis considered body mass index (BMI), oliguria, severe acidosis, heart rate, Sequential Organ Failure Assessment (SOFA) score, and albumin level. The area under the curve (AUC) for 28-day mortality was 0.831 ( $p < 0.001$ ). The positive predictive value was 78.16%, and the negative predictive value was 74.87%. (B) An ROC curve was constructed for hematologic malignancy patients using BMI, oliguria, SOFA score, and albumin level. The AUC for 28-day mortality was 0.802 ( $p < 0.001$ ). The positive predictive value was 84.71%, and the negative predictive value was 62.73%.

reflect a patient's acute physiological status predict their prognosis. Consistent with the results of previous studies, cancer characteristics (cancer status, site of solid malignancy or subtype of hematologic malignancy, and treatment history) were not predictors of in-hospital mortality in the present study [9,20]. Although it was not investigated in this study, previous studies found that cancer variables influenced survival after hospital discharge, whereas acute physiologic changes were associated with in-hospital mortality [9,13,33]. The presence of oliguria was previously reported to be a prognostic variable in AKI patients admitted to the ICU [34], and our results are similar.

Patients with AKI commonly have metabolic acidosis, which is an independent predictor of unfavorable outcomes [35–37]. However, in the results of this study, the presence of severe and intractable acidosis (arterial pH of  $<7.2$  despite maximal medical care) was a prognostic factor for all-cause in-hospital mortality only in patients with a solid malignancy. Because of the retrospective design of the study, the maximal medical care used to correct acidosis was not unified among the patients. A high heart rate

was also a prognostic factor of 28-day all-cause mortality only in the solid malignancy group. It is well known that the heart rate fluctuates during the day, and the presence of combined arrhythmia was not investigated. The mortality rate in patients with hematologic malignancy was extremely high, which might explain why heart rate and severe acidosis were not meaningful as prognostic factors, unlike solid malignancy. Those results from this study need to be validated in a randomized controlled study.

In our study, the proportion of patients discharged alive from the hospital with RRT dependency was 25.0% in the solid malignancy group and 33.3% in the hematologic malignancy group. That was slightly higher than the results from other studies, which reported a range between 14% and 24% [7,23,25], and did not differ from the rates in general ICU populations [38,39]. In general ICU populations treated with RRT for AKI, age, diabetes, chronic kidney disease, and oliguria at the time of RRT initiation are associated with RRT dependency [39]. Our study showed similar results, though they differed according to type of malignancy.

This study has several strengths. Unlike previous studies,

**Table 5. Summary of publications on RRT in critically ill patients with AKI and cancer**

Study	Year	Country and date of study	Study design	Proportions of cancer subtypes	No. of patients	RRT	Disease severity	Mortality	Prognostic factors for hospital mortality
Lanore et al. [21]	1991	France May 1983–November 1989	Retrospective single center	Hemato: 100% BMT: 11%	43	-	SAPS II Survivors: 13.25 ± 4.86 Non-survivors: 17.16 ± 4.37 (p < 0.02)	ICU: 72%	AKI secondary to sepsis, SAPS score, mechanical ventilation support
Létourneau et al. [22]	2002	Canada January 1994–December 1998	Retrospective single center	Hemato: 100% BMT: 100%	14	IRRT CWHDF	APACHE II BMT + ARF: 30 ± 8 BMT – ARF: 25 ± 7 (p = 0.03)	-	-
Berghmans et al. [19]	2004	Belgium January 1997–December 2002	Retrospective single center	Solid: 50% Hemato: 50% BMT: 28%	32	CWHDF	APACHE II Survivors: 25 Non-survivors: 34 (p = 0.006)	ICU: 50% Hospital: 53%	No. of organ failures
Benoit et al. [18]	2005	Belgium January 1997–June 2002	Retrospective single center	Hemato: 100% BMT: 22.4%	50	IRRT CRRT	APACHE II 30 (23–36)	ICU: 79.6% Hospital: 83.7% 6 Mo: 86% Hospital: 64%–86%	-
Soares et al. [25]	2006	Brazil May 2000–December 2004	Prospective single center	Solid: 75% Hemato: 25%	98	IRRT conventional IRRT extended CRRT	APACHE II 22.3 (IQR: 7) SAPS II 56.9 (IQR: 18.2) SOFA 9.6 (IQR: 4.1)	-	-
Darmon et al. [7]	2007	France January 2002–June 2005	Prospective single center	Solid: 7% Hemato: 78% Others: 15%	94	IRRT CRRT	SAPS II 53 (40–75)	ICU: 43.6% Hospital: 51.1% 6 Mo: 65.4%	LOD score, late RRT (>24 hr after ICU admission)
Maccariello et al. [23]	2011	Brazil December 2004–July 2008	Prospective three centers	Solid: 73% Hemato: 27%	118	IRRT daily conventional IRRT daily extended CRRT	SAPS II 49.3 ± 12.7 SOFA 9 (7–11)	ICU: 70% Hospital: 78%	No. of organ failures
Park et al. [24]	2011	Korea January 2004–December 2007	Retrospective single center	Hemato: 100% BMT: 22%	94	CWHDF CWH	SAPS II 81 (63–95) SOFA 16 (13–18) Modified SOFA 15 (11–17)	ICU: 77%	Modified SOFA score
Salahudeen et al. [26]	2009	USA January 2006–June 2007	Retrospective single center	Solid: 38% Hemato: 62% BMT: 18%	199	C-SLED	SOFA 13.0 ± 4.0	Day 30: 65%	SOFA score, pH, mean blood pressure

(Continued to the next page)

Table 5. Continued

Study	Year	Country and date of study	Study design	Proportions of cancer sub-types	No. of patients	RRT	Disease severity	Mortality	Prognostic factors for hospital mortality
Kim and Shin [16]	2015	Korea January 2010–December 2011	Retrospective single center	Solid: 78.6% Hemato: 19% Others: 2.4%	42	CWHDF	APACHE II Data not shown	Hospital: 69%	Female, number of organ failures
Fischer et al. [20]	2016	Belgium January 2003–December 2012	Retrospective single center	Solid: 66% Hemato: 34% BMT: 17%	103	CWHDF	SAPS II 56 (28–99)	Hospital: 63%	More than one organ failure, albumin level
Abudayeh et al. [17]	2020	United States 2005–2014	Retrospective single center	Solid (stage IV): 100%	176		SOFA (max) 16.21 ± 4.48	Hospital: 73.8%	-
This study		Korea March 2013–December 2020	Retrospective single center	Solid: 63% Hemato: 37%	471	CWHDF	SOFA Solid: 11 (8–13) Hemato: 13 (10–16)	Hospital (solid): 64% Hospital (Hemato): 84%	Solid: BMI, presence of oliguria or severe acidosis, heart rate, SOFA score, albumin level Hemato: BMI, presence of oliguria, SOFA score, albumin level

AKI, acute kidney injury; APACHE, Acute Physiology and Chronic Health Evaluation; ARF, acute renal failure; BMI, body mass index; BMT, bone marrow transplantation; C-SLED, sustained low-efficiency dialysis in continuous mode; CRRT, continuous renal replacement therapy; CVVH, continuous venovenous hemofiltration; CVVHDF, continuous venovenous hemodiafiltration; Hemato, hematologic; ICU, intensive care unit; IRR, intermittent RRT; LOD, logistic organ dysfunction; RRT, renal replacement therapy; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment.

this study analyzed in-hospital mortality and prognostic factors by dividing cancer patients into solid and hematologic malignancy groups. Our finding of different prognostic factors between the malignancy groups indicates that patient prognosis should be predicted without merging those groups under a cancer diagnosis. Moreover, the ability of the combined prognostic factors to predict in-hospital mortality, as shown by the high AUCs, is notable and worth validating in future studies. This study included critically ill cancer patients with AKI undergoing CRRT from 2013 to 2020, so our data are more recent than the data used in previous studies. The results of this study thus reflect the effects of rapidly developing treatments for cancer and ICU patients, but the mortality and RRT dependency were similar to those in previous studies. This study also has several limitations. Although the analyses were performed with appropriate adjustments, the possibility of residual confounders cannot be excluded because of the retrospective nature of the study. Most of the patients were Korean, which limits the generalizability of the findings to other races. Additionally, data evaluation and comparison of medium- and long-term survival rates and renal function were not performed.

In conclusion, the 28-day mortality rate was high in patients with AKI undergoing CRRT, reaching 58.8% in the solid malignancy group and 82.0% in the hematologic malignancy group. BMI, presence of oliguria, SOFA score, and serum albumin level were common predictors of in-hospital mortality in patients with all malignancies. These results could be helpful in establishing a therapeutic plan for CRRT in critically ill patients with cancer and AKI because the mortality rates and prognostic factors differed according to type of malignancy.

### Conflicts of interest

All authors have no conflicts of interest to declare.

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## Authors' contributions

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