Impact of Downtime on Clinical Outcomes in Critically Ill Patients with Acute Kidney Injury Receiving Continuous Renal Replacement Therapy

Jungho Shin, Hyun Chul Song, Jin Ho Hwang, and Su Hyun Kim

Continuous renal replacement therapy (CRRT) downtime is considered a quality indicator; however, it remains uncertain whether downtime affects outcomes. This study retrospectively investigated the impact of downtime on clinical outcomes. Patients were classified as downtime <20% or ≥20% of potential operative time over 4 days from CRRT initiation. Patients with ≥20% downtime were matched to those with <20% downtime using 1:2 propensity score matching. There were 88 patients with <20% downtime and 44 patients with ≥20% downtime. The cumulative effluent volume was lower in patients with ≥20% downtime ($p < 0.001$). The difference in levels of urea and creatinine widened over time ($p = 0.004$ and <0.001). At days 2 and 3, daily fluid balance differed ($p = 0.046$ and 0.031), and the levels of total carbon dioxide were lower in those with ≥20% downtime ($p = 0.038$ and 0.020). Based on our results, ≥20% downtime was not associated with increased 28 day mortality; however, a subgroup analysis showed the interaction between downtime and daily fluid balance ($p = 0.004$). In conclusion, increased downtime could impair fluid and uremic control and acidosis management. Moreover, the adverse effect of downtime on fluid control may increase mortality rate. Further studies are needed to verify the value of downtime in critically ill patients requiring CRRT. *ASAIO Journal* 2022; 68;744–752

Key Words: downtime, continuous renal replacement therapy, fluid balance, outcome

Acute kidney injury (AKI) is common in critically ill patients admitted to the intensive care unit (ICU). In cases with severe injury, renal replacement therapy (RRT) is required to support failing kidneys. Acute RRT is performed in 8–10% of critically ill patients,[1,2] and its utilization is gradually increasing.[2–4] Continuous RRT (CRRT) is the most common modality of acute RRT used in the ICU setting for its advantages in critically ill patients. Continuous RRT was performed on 80% of patients with acute RRT after 2014 in Korea.[4] However, despite the extended application of CRRT, mortality rate in these patients is quite high, approximately 50–60%.[1,5] Various trials have explored practical issues such as the timing of initiation, modality of acute RRT, anticoagulation method, and dose of RRT to establish an evidence-based guidance for performing acute RRT.[6] Yet, there remain several controversies.[7,8] These unmet issues may enhance variations in CRRT delivery and impede the quality control for AKI management.

A high-quality CRRT care based on evidence should be guaranteed for severely ill patients with AKI. Several studies have reported that continuous coordination and communication between physicians of different specializations could optimize the delivery of CRRT.[9–11] However, a specialized team for CRRT is difficult to create with limited resources, thus making it a challenge for most centers to implement this ideal protocol. In this context, more studies are needed to identify quality indicators to measure and improve care for patients with AKI requiring CRRT. A recent systematic review identified potential quality indicators for CRRT and classified them into three categories: structure, process, and outcome.[12] Of these, downtime is considered a quality indicator related to the care process. Continuous RRT can be interrupted due to various reasons, such as filter clots or procedures performed out of the ICU, and an increase in downtime can adversely influence the efficacy and safety of CRRT.[13] On the other hand, current evidence suggest that intermittent RRT is not inferior to CRRT with regard to mortality,[6,14,15] and it has been demonstrated that lower dose-intensity CRRT is as effective as higher dose intensity.[16,17] Considering both conclusions, it is necessary to study the effect of downtime on hospital course and outcome in patients receiving CRRT.

Previously, our center had been limited to providing qualified process care for CRRT and downtime frequently occurred. Based on previous experiences, this study aimed to identify the impact of CRRT downtime on clinical outcomes using propensity score matching. We compared the control properties of CRRT—intensity, fluid balance, and uremic and electrolyte parameters—according to the downtime status. Furthermore, this study investigated whether downtime is independently associated with clinical outcomes such as mortality and renal recovery or whether it interacts with certain situations for outcomes.

Materials and Methods

Patients

We retrospectively reviewed the medical records of patients admitted to the ICU for medical illness between March 2015 and June 2017. All patients requiring ICU admission were referred to an attending intensivist and those were treated by specialists in this center. As part of a tertiary teaching hospital, physicians aimed to provide evidence-based management to ICU patients based on the current guidelines, including the Kidney Disease: Improving Global Outcomes Clinical Practice

From the Department of Internal Medicine, Chung-Ang University Hospital, Seoul, Korea.

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Correspondence: Su Hyun Kim, Division of Nephrology, Department of Internal Medicine, Chung-Ang University Hospital, 102, Heukseok-ro, Dongjak-gu, Seoul 06973, Korea. Email: sh76so@cau.ac.kr.

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Guideline for AKI.[6] Based on electronic medical records, a total of 357 adult (age >18 years) patients who had received CRRT during the study period were identified. Of them, we excluded 141 patients based on the following criteria: 20 received cardiopulmonary resuscitation before ICU admission, 58 died within 24 hours after admission, 20 received CRRT for less than 24 hours because of inadequate exposure time to assess the impact of downtime, 31 had preexisting end-stage renal disease requiring dialysis, four were transplant recipients, and eight had missing data related to CRRT. Finally, 216 patients were eligible for propensity matching.

This study was approved by the Institutional Review Board (IRB) of Chung-Ang University Hospital (IRB number: 2111-002-19349). Due to the retrospective nature of the study and because the patients were deidentified, the IRB waived the need for written consent from the patients.

Continuous Renal Replacement Therapy Protocol

The initiation, maintenance, and termination of CRRT were determined by nephrologists. Continuous RRT was initiated if patients had refractory pulmonary edema, intractable hyperkalemia or metabolic acidosis, uremic symptoms including pericarditis and encephalopathy, or oliguria with progressive azotemia and could not tolerate intermittent hemodialysis due to hemodynamic instability. A central venous catheter was inserted into the internal jugular or femoral vein. Continuous venovenous hemodiafiltration was performed using Prismaflex (Baxter, Deerfield, IL) machines with a high flux hemofilter (ST100, Baxter), and dialysate and replacement fluids (Hemosol-B0 or Phoxilium, Baxter). Replacement fluids were administered using combined pre- and postdilution methods at a proportion of 3:1 or 3:2. Considering the difference between prescribed and delivered CRRT doses, the minimum effluent flow rate was established at 40 ml/kg/hr,[18] which could be adjusted by the physician depending on the patient's condition. Anticoagulation was conducted using nafamostat mesilate (SK Chemicals, Seoul, Korea).

Serum levels of electrolytes were checked regularly during delivery of CRRT. Depending on the blood potassium and bicarbonate levels or clinical requirements, appropriate amounts of potassium chloride and sodium bicarbonate were added to the dialysate or replacement fluid. Nurses monitored and reported the CRRT acting time, effluent volume, patient fluid removal, and kit status, which were derived from the software built in the CRRT device on a flowsheet. The software and machine have been appropriately tested and are regularly validated by the manufacturer. The CRRT circuit was exchanged by a CRRT nurse on a working day or by duty residents at night or on holidays, while the fluid bags of dialysate, replacement, and effluent were exchanged by a bed-side nurse. Continuous RRT termination was considered when the amount of urine increased, whereas transition to intermittent RRT was attempted if the blood pressure was maintained without the assistance of vasopressors.

Data Collection

Baseline demographic and clinical data collected at the time of CRRT initiation included age, sex, comorbidities, and reasons for AKI. Body weight was measured using a bed scale before conducting the CRRT. Comorbidity burden was assessed using the Charlson comorbidity index.[19] The baseline disease severity was assessed using the Sequential Organ Failure Assessment (SOFA) score. To calculate the SOFA score, related parameters were obtained at the time of CRRT initiation.[20] Blood lactate levels were also collected.

We collected data on the acting time and effluent volume over 4 days, after the start of CRRT. The delivered cumulative volume and daily flow rate of the effluent were assessed and the median flow rate was calculated. Acting time was calculated as the sum of actual machine running time, and downtime (hr) was defined as the period during which CRRT was not running from the beginning to the end of the prescription—downtime (hr) was extracted by the potential operative time (hr) minus acting time (hr).[21] The reasons for the downtime were reviewed. The percentage of downtime to potential operative time was estimated over 4 days from initiation of CRRT, and patients were then divided into two groups using a cut-off of 20% based on a previous study:[21] patients whose downtime was <20% or those whose downtime was ≥20%. All available intake and output data during the first 4 days of CRRT implementation were collected. Intake was composed of oral and parenteral fluids administered, and the output included urine, gastrointestinal losses, and drains. Cumulative and daily fluid balances were computed using the total intake and output data.

Outcomes

First, CRRT acting time, delivered cumulative effluent volume, and daily and median effluent flow rates were compared according to the downtime groups. The fluid balance, uremic control, and electrolyte control were estimated between subjects with <20% and ≥20% downtime. The parameters for assessing uremic and electrolyte control were the levels of urea, creatinine, potassium, phosphorus, total carbon dioxide, and uric acid. Thereafter, the impact of downtime on 28 day mortality and renal recovery was evaluated. To determine whether downtime had an impact on mortality in specific clinical scenarios, we explored the interaction between downtime and variables using subgroup analyses. Subgroups ware based on age, sex, comorbidity index, SOFA score, sepsis, ventilator and vasopressor use, lactate level, oliguria, and daily fluid balance. For the assessment of renal outcomes, dialysis dependence and serum creatinine levels at discharge were analyzed. Dialysis dependence was defined as the requirement for RRT after hospital discharge among survivors.

Statistical Analysis

Of the eligible 216 patients, 54 had a downtime of ≥20% over 4 days of CRRT and 162 had downtime of <20%. In the multivariate logistic regression model, the propensity score for ≥20% downtime was generated with adjustments for age, sex, Charlson comorbidity score, and organ failure score as assessed by SOFA. We then matched patients with ≥20% downtime to the remainder having <20% downtime with similar propensity scores at a 1:2 ratio using the nearest neighbor method, no replacement, and a 0.25 caliper width. Ultimately, the study included 44 patients with ≥20% downtime and 88 patients with <20% downtime.

Continuous variables were expressed as mean ± standard deviation or median (interquartile range [IQR]). The data

were compared using the independent *t* test or Wilcoxon rank sum test. Categorical variables, expressed as numbers (percentages), were analyzed using the χ^2 test. The cumulative incidence of 28 day mortality was estimated using the Kaplan-Meier method and compared using the log-rank test. Univariate and multivariate Cox proportional hazard models were used to determine the hazard ratio and 95% confidence interval (CI) for 28 day mortality. All statistical analyses were performed using SPSS software (version 18.0; IBM Corp., Armonk, NY). A two-sided *p* value of <0.05 was considered significant.

Results

Characteristics of the Patients with Acute Kidney Injury Receiving Continuous Renal Replacement Therapy

After the propensity score matching, the included patients numbered 88 in the <20% downtime group and 44 in the ≥20% downtime group. Over 4 days from the start of CRRT, the median and cumulative downtimes were 1.8 (IQR, 1.2–2.7) hr/day and 7.1 (IQR, 4.5–10.2) hr in patients with <20% downtime and 4.9 (IQR, 4.2–7.0) hr/day and 19.0 (15.0–25.7) hr in those with ≥20% downtime ($p < 0.001$ in both groups). **Table 1** shows the baseline characteristics of the two groups, which did not differ significantly.

A total of 391 instances of documented interruption occurred during the CRRT care, mostly when a resident on duty was responsible for circuit exchange (n = 258, 66.0%). The median downtime was 110 (IQR, 60–239) minutes when a duty resident was in charge, and 50 (IQR, 40–80) minutes when a CRRT nurse was in charge. The main reason for interruption was filter clotting (76.0%), followed by procedures performed outside the ICU (11.3%), problems with the catheter (6.9%), inexperienced operation (2.3%), and time spent in the operation room (1.5%). Other reasons involved extremely low blood pressure (0.8%), plasma exchange (0.8%), and transfer to different types of ICUs (0.5%).

Table 1. Characteristics of Patients with AKI Receiving CRRT, Subdivided into Groups

	Downtime <20% (n = 88)	Downtime ≥20% (n = 44)	*p*
Age, years, mean ± SD	69 ± 15	69 ± 14	0.872
Male, n (%)	52 (59.1)	27 (61.4)	0.802
Comorbidities, n (%)			
Hypertension	42 (47.7)	23 (52.3)	0.622
Diabetes	40 (45.5)	17 (38.6)	0.456
Chronic kidney disease	10 (11.4)	5 (11.4)	1.000
Coronary artery disease	16 (18.2)	6 (13.6)	0.509
Heart failure	22 (25.0)	8 (18.2)	0.378
Cerebrovascular accident	21 (23.9)	8 (18.2)	0.457
Liver disease	14 (15.9)	3 (6.8)	0.175
Chronic lung disease	8 (9.1)	4 (9.1)	1.000
Charlson comorbidity index, median (IQR)	3 (1–4)	2 (1–5)	0.362
AKI reason, n (%)			0.932
Sepsis	48 (54.5)	24 (54.2)	
Ischemic	13 (14.8)	8 (18.2)	
Cardiorenal	11 (12.5)	4 (9.1)	
Hepatorenal	8 (9.1)	3 (6.8)	
Others	8 (9.1)	5 (11.4)	
SOFA, median (IQR)	12 (9–14)	12 (9–14)	0.843
Respiratory	2 (1–3)	2 (1–3)	0.577
Nervous	2 (1–4)	2 (1–4)	0.978
Cardiovascular	3 (0–4)	3 (0–4)	0.799
Liver	0 (0–1)	0 (0–1)	0.759
Coagulation	1 (0–2)	1 (0–2)	0.809
Kidney	4 (3–4)	4 (3–4)	0.464
Vasopressor use, n (%)	48 (54.5)	25 (56.8)	0.804
Ventilator use, n (%)	44 (50.0)	22 (50.0)	1.000
Blood lactate, mmol/L, median (IQR)	1.8 (1.2–3.9)	2.0 (1.1–4.8)	0.885
Urine output, ml/day, median (IQR)	335 (100–680)	428 (131–846)	0.602
Oliguria, n (%)	48 (54.5)	20 (45.5)	0.325
Access, n (%)			0.389
Internal jugular vein	41 (46.6)	16 (36.4)	
Femoral vein	46 (52.3)	28 (63.6)	
Extracorporeal membrane oxygenation	1 (1.1)	0 (0)	
CRRT duration, day, median (IQR)	5 (3–10)	4 (2–9)	0.352
ICU day, day, median (IQR)	10 (5–21)	9 (5–13)	0.420
In-hospital death, n (%)	52 (59.1)	26 (59.1)	1.000
Downtime			
Median, hr/day, median (IQR)	1.8 (1.2–2.7)	4.9 (4.2–7.0)	<0.001
Cumulative, hr, median (IQR)	7.1 (4.5–10.2)	19.0 (15.0–25.7)	<0.001
Documented interruption*, n (%)	2 (1, 3)	4 (2, 5)	<0.001
Downtime/prescribed time, %, median (IQR)	9.5 (6.6–14.4)	25.6 (22.0–32.0)	<0.001

Continuous variables are expressed as mean ± SD or median (IQR), and categorical variables are expressed as number (percentage).
*Documented interruption is defined as an instance of the device stopping as reported in the electronic medical records.
AKI, acute kidney injury; CRRT, continuous renal replacement therapy; ICU, intensive care unit; IQR, interquartile range; SD, standard deviation; SOFA, sequential organ failure assessment.

Delivery of Continuous Renal Replacement Therapy According to the Downtime Groups

The median acting time was 90.5% (IQR, 85.6–93.4) in the <20% downtime group and 74.4% (IQR, 68.0–78.0) in the ≥20% downtime group ($p < 0.001$). The delivered daily flow rate and cumulative volume of effluent were compared (**Figure 1**). The median delivered effluent flow rate was 43.6 (IQR, 39.2–49.4) ml/kg/hr in patients with <20% downtime and 41.7 (IQR, 37.0–44.7) ml/kg/hr in patients with ≥20% downtime ($p = 0.062$). In addition, the delivered cumulative effluent volume in the ≥20% downtime group was lower than in the <20% downtime group after day 2, and this difference increased over time ($p < 0.001$).

Fluid, Uremic, and Electrolyte Control According to Downtime

Daily and cumulative fluid balances were compared between the two groups (**Figure 2**). On days 2 and 3, daily fluid balance significantly differed ($p = 0.046$ and 0.031, respectively), while the cumulative fluid balance did not differ although there was a trend. The mean daily fluid balance was comparable between the groups ($p = 0.253$).

Figure 3 shows the comparisons of uremic and electrolyte parameters according to the downtime status. The gaps in blood urea and creatinine levels became apparent over time ($p = 0.004$ and <0.001 at day 4). The differences in the levels of total carbon dioxide and uric acid were observed on a certain day of CRRT.

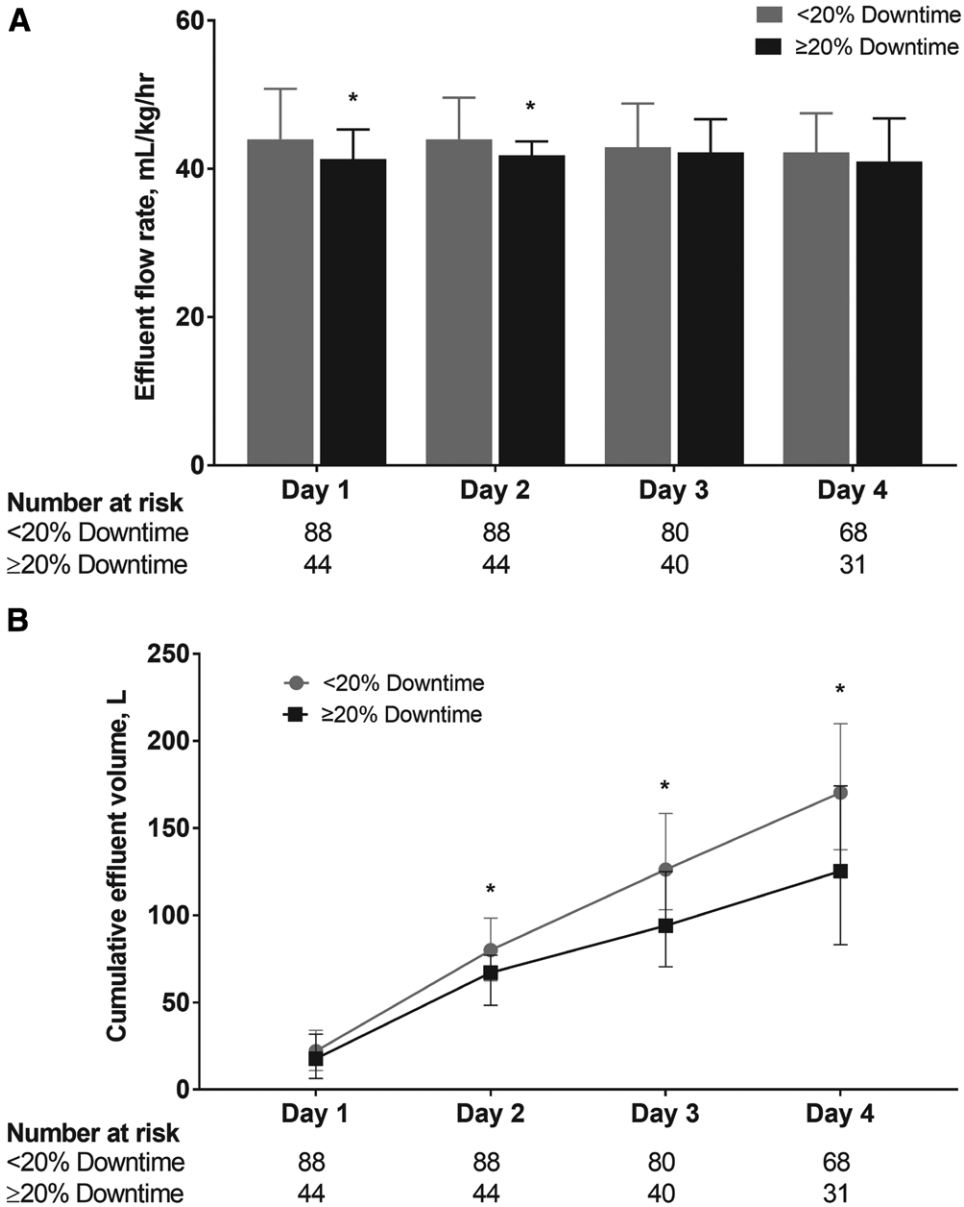

Figure 1. Delivered effluent volume and flow rate in the two groups. **A:** Delivered daily flow rate of effluent is lower in the ≥20% downtime group at days 1 and 2, compared to the <20% downtime group (41.3 [IQR, 36.5–45.3] *vs.* 44.0 [IQR, 39.0–50.8] ml/kg/hr at day 1 and 41.8 [IQR, 36.5–43.7] *vs.* 44.0 [IQR, 39.6–48.7] ml/kg/hr at day 2; $p = 0.048$ and 0.013). Those at days 3 and 4 are comparable between the groups ($p = 0.582$ and 0.361). **B:** Delivered cumulative effluent volume differs from day 2 and the deviation becomes larger over time, according to the downtime status. Delivered cumulative effluent volume is 170.4 (IQR, 137.7–209.9) L in patients with <20% downtime, while it is 125.4 (IQR, 83.2–174.3) L in those with ≥20% downtime ($p < 0.001$). Data are expressed as medians (IQRs). IQR, interquartile range. *p <0.05.

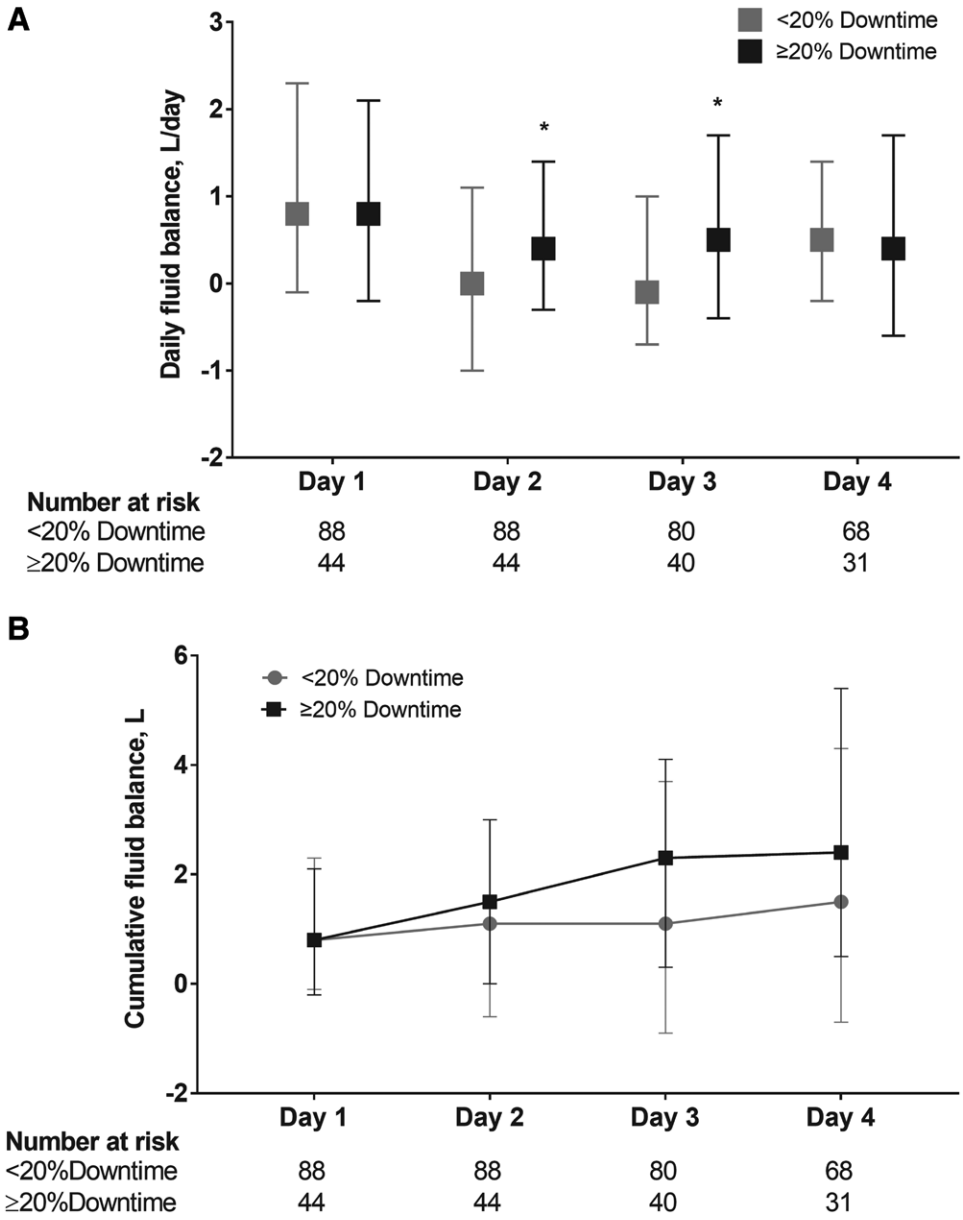

Figure 2. Fluid balance in the two groups. **A:** Daily fluid balance is compared between patients with <20% and ≥20% downtimes. Daily fluid balance is higher in the ≥20% downtime group than in the <20% group downtime at days 2 and 3 ($p = 0.046$ and 0.031). **B:** Although there is a trend, cumulative fluid balance did not differ between the groups over 4 days of CRRT care (1.5 [IQR, –0.7 to 4.3] L in the <20% downtime group and 2.4 [IQR, 0.5–5.4] L in the ≥20% downtime group; $p = 0.213$). Data are expressed as medians (IQRs). CRRT, continuous renal replacement therapy; IQR, interquartile range. *p <0.05.

Patient and Renal Outcomes According to Downtime

Of the patients, 68 died within 28 days (53.4%). However, this study revealed that ≥20% downtime was not related to 28 day mortality ($p = 0.757$). In the multivariate analysis, age, comorbidity index, SOFA score, and daily fluid balance had independent impact on 28 day mortality, unlike the ≥20% downtime ($p = 0.944$; **Table 2**).

Subgroup analysis reveals no association between downtime and variable status such as age, sex, comorbidity index, SOFA score, sepsis, use of ventilator and vasopressor, lactate level, and presence of oliguria (**Figure 4**) except for daily fluid balance ($p = 0.004$), although it was not significant in the subgroup of daily fluid balance <1 or ≥1 L/day.

In addition, renal outcomes were evaluated among the 54 survivors who were discharged—36 patients with <20% downtime and 18 with ≥20% downtime. Six patients (16.7%) with <20% downtime and three (16.7%) with ≥20% downtime required maintenance RRT even after discharge ($p = 0.754$). Serum creatinine levels were compared in the patients, excluding the nine who depended on dialysis. In this study, median creatinine levels at discharge were comparable between the two groups: 1.4 (IQR, 0.7–1.9) mg/dl in the <20% downtime group and 1.2 (IQR, 0.7–1.7) mg/dl in the ≥20% downtime group ($p = 0.754$).

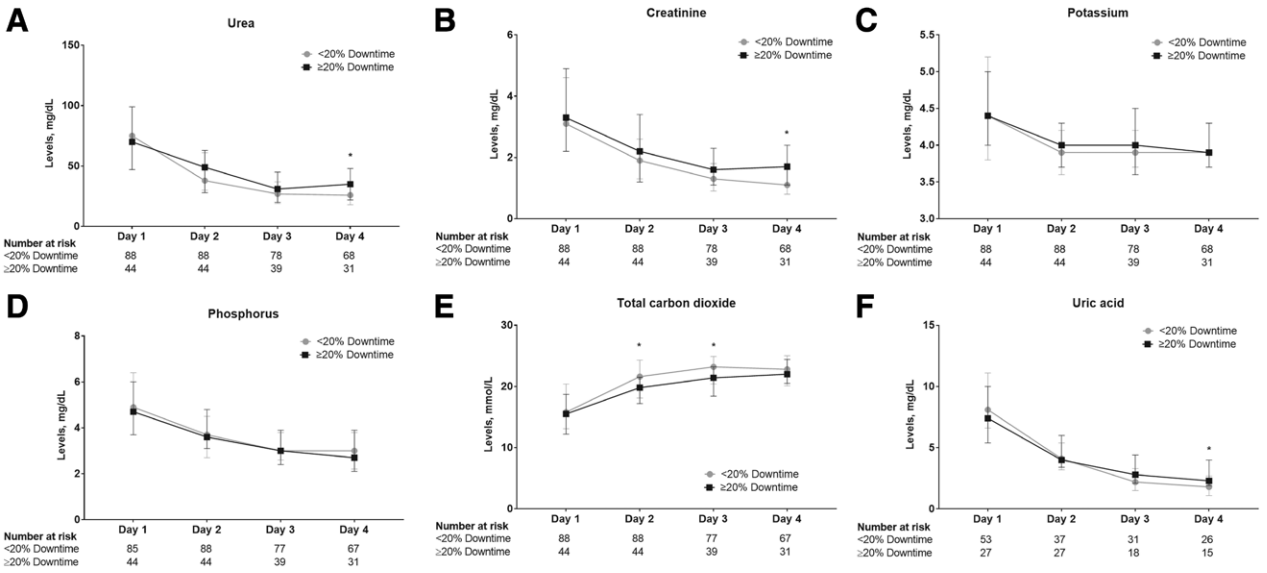

Figure 3. Comparisons of uremic and electrolyte parameters in the two groups. **A, B:** Blood urea and creatinine levels deviated over time. Levels of urea at day 4 are 26 (IQR, 18–33) mg/dl in the <20% downtime group and 35 (IQR, 22–48) mg/dl in the ≥20% downtime group ($p = 0.004$). In addition, levels of creatinine at day 4 are 1.1 (IQR, 0.8–1.6) and 1.7 (IQR, 1.1–2.4) mg/dl, respectively ($p < 0.001$). **C, D**: Levels of potassium and phosphorus are also examined; however, there are no differences between the groups. **E:** Total carbon dioxide levels are lower at days 2 and 3 in patients with ≥20% downtime than in those with <20% downtime (19.8 [IQR, 17.2–21.5] *vs.* 21.6 [IQR, 18.1–24.3] mmol/L at day 2 and 21.4 [IQR, 18.4–23.2] *vs*. 23.2 [IQR, 20.4–24.9] mmol/L at day 3; $p = 0.038$ and 0.020). **F:** Similar to urea and creatinine, levels of uric acid are higher in the ≥20% downtime group (2.3 [IQR, 1.9–4.0] *vs.* 1.8 [IQR, 1.1–2.7] mg/dl at day 4; $p = 0.039$). Data are expressed as medians (IQRs). IQR, interquartile range. *p <0.05.

Discussion

This retrospective study investigated the impact of downtime on clinical outcomes using a propensity score matching model. Patients with ≥20% downtime of potential operating time received a lower intensity of CRRT compared to those with <20% downtime. They also had trouble controlling fluid balance, although the mean daily and cumulative fluid balances did not differ. The uremic parameters, including levels of urea and creatinine, were higher in patients with ≥20% downtime, and the management of metabolic acidosis was also impeded in these patients. This study revealed that downtime *per se* might not independently affect 28 day mortality, but it can interact with fluid balance. In this study, we did not find any association between downtime and renal recovery.

Continuous RRT is now an essential tool in the management of AKI in critically ill patients, because it is the predominant modality of acute RRT in the ICU.[4,22] Despite the technological advances for the delivery of acute RRT, outcomes in these patients remain suboptimal with a high mortality rate.[1,5] Additionally, considerable variation in CRRT practice exists between physicians and between the centers. Such deviation seems to be caused not only by the quantitative debates of CRRT care but also by a paucity of research regarding the quality of CRRT care. A reliable, standardized care process is crucial to avoid low quality of care, which can be harmful to patients with increased vulnerability. The optimal delivery of CRRT requires a multidisciplinary approach with coordination by experts in different areas. An interprofessional and specialized team approach can provide high-quality critical care and improve patient-level outcomes.[23,24] In this context, retrospective observational studies in Korea reported that the implementation of the specialized CRRT team reduced mortality by improving the quality of care in CRRT delivery, based on comparisons before and after team implementation.[9,10,25] Nevertheless, not all centers dare to pursue a premium-quality CRRT in the ICU because it is difficult to implement with limited resources. The development of validated quality indicators is necessary, and they should be prioritized according to their importance. Our center had performed a limited quality of CRRT care with only one CRRT-specialized nurse. Based on our experiences, this study attempted to verify downtime as a quality indicator and evaluate its impact on clinical outcomes in critically ill patients with AKI undergoing CRRT.

Table 2. HR of Variables, Including Downtime, on 28 Day Mortality

Variables	Univariate HR (95% CI)	*p*	Multivariate HR (95% CI)	*p*
Age	1.02 (1.00–1.03)	0.090	1.03 (1.01–1.05)	0.007
Male	1.03 (0.63–1.67)	0.908	0.92 (0.56–1.52)	0.744
Charlson comorbidity index	1.08 (0.98–1.20)	0.120	1.14 (1.03–1.26)	0.014
SOFA score	1.09 (1.02–1.17)	0.008	1.10 (1.03–1.18)	0.007
Daily fluid balance	1.40 (1.24–1.59)	<0.001	1.52 (1.31–1.76)	<0.001
Downtime ≥20%	0.92 (0.56–1.54)	0.761	0.98 (0.59–1.65)	0.944

CI, confidence interval; HR, hazard ratio; SOFA, sequential organ failure assessment.

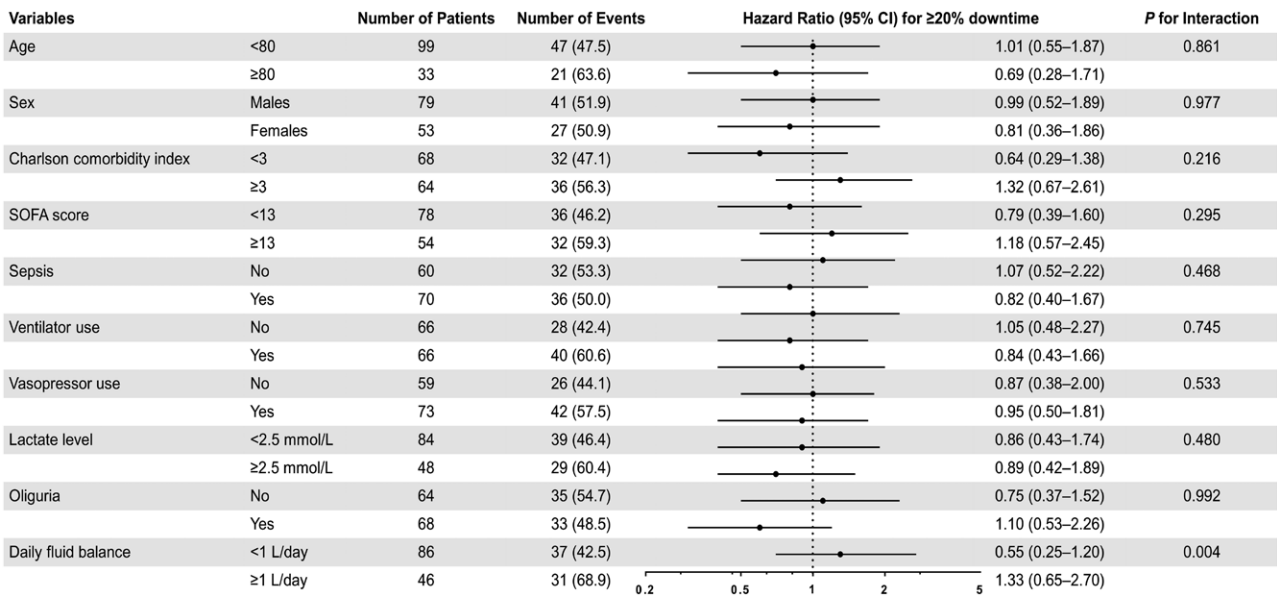

Figure 4. Impact of ≥20% downtime on 28 day mortality in each subgroup. Subgroups are divided in terms of age, sex, Charlson comorbidity index, SOFA score, sepsis, ventilator use, vasopressor use, lactate level, oliguria, and daily fluid balance. In each subgroup, there is no association between ≥20% downtime and increased mortality, excluding the subgroup of daily fluid balance. There is an interaction between downtime and daily fluid balance (p = 0.004); however, ≥20% downtime is associated with 28 day mortality neither in daily fluid balance <1 nor ≥1 L/day subgroups (hazard ratio 0.6 and 1.3, 95% CI, 0.3–1.2 and 0.7–2.7, respectively). CI, confidence interval; SOFA, sequential organ failure assessment.

Downtime is regarded as a quality indicator related with the process of CRRT care.[12] This study observed that downtime frequently occurred during the treatment, and median downtime was 2.6 (IQR, 1.5–4.2) hr/day. We had selected an effluent flow rate of 40 ml/kg/hr as the target level, which is a relatively high rate that might increase downtime because of frequent fluid bag changes. However, ICU bed-side nurses were responsible for bag exchanges, not CRRT nurses or residents, thus eliminating group-based differences. We found that the most common cause of circuit downtime was filter clotting, followed by a need for radiological procedures, similar to the results of previous studies.[13,21] In addition, an increase in downtime was related to the person responsible for filter exchange. Treatment interruption tended to increase because rotating residents were unfamiliar with filter exchange and could not focus only on CRRT care amid duty work. It is noteworthy that six cases of downtime of >1 hr occurred with a resident on duty. In contrast, Oh *et al.*[9] and Rhee *et al.*[10] reported that downtime decreased from 4.8 to 3.3 hr/day and from 1.78 to 1.38 hr/day, respectively, after the implementation of the specialized CRRT teams. Continuous RRT filter exchange is labor-intensive work; thus, it is necessary to assign specific personnel to be in charge of filter exchange, to reduce downtime and to operate CRRT smoothly. Although we used a downtime of 20% as the cut-off value to divide the groups, this value might not be an absolute measure to estimate the quality of CRRT delivery.

Continuous RRT is intended to be applied for 24 hr/day, maintaining slower rates of fluid and solute exchange compared to intermittent hemodialysis. Therefore, an increase in downtime can lower the efficacy of CRRT, disturb fluid control and exacerbate uremic and electrolyte imbalance in critically ill patients with AKI. Previous studies investigating downtime have shown a strong correlation between downtime and solute control during CRRT delivery and suggested that the percentage of downtime is a useful marker of operative quality.[13,21] In this study, we found a significant deviation in the delivered cumulative effluent volume between the groups divided according to the percentage of downtime. However, it could not reflect the actual delivered dose because the effluent volume overestimates the delivered dose of small solutes in CRRT.[26,27] In addition, we did not show differences between the prescribed and delivered effluent flow rate because we could not obtain the prescribed flow rate. Although this study did not estimate the actual delivered dose and the deviation between prescribed and delivered dose of CRRT, an increase in downtime was found associated with low-quality CRRT, as represented by higher levels of urea and creatinine and lower levels of total carbon dioxide. Providing an adequate intensity of CRRT is important, and efforts to ensure efficacy should be continued. A recent study of a quality improvement initiative reported an increased rate of appropriate CRRT dosing and a reduction in dosing variability by making changes to the electronic medical record and documentation templates and by educating the CRRT providers about dosing.[28]

Fluid overload is commonly encountered in patients in the ICU, and it is associated with adverse outcomes.[29–31] Utilization of RRT is responsible for fluid control, especially in patients with severe AKI who have oliguria or anuria. Thus, fluid removal using ultrafiltration is critical to avoid volume overload and its complications.[32] Accordingly, an increase in downtime can impair fluid control in patients with AKI receiving CRRT. Continuous RRT has the advantage of fluid management as steady reduction of accumulated fluid, compared to intermittent RRT.[29] However, a longer duration of downtime could eliminate the advantage and more fluid removal would be needed during the acting time. Although this study showed that daily fluid balance was higher in patients with ≥20% downtime than in those with <20% downtime, we could not conclude that fluid balance is caused by increased downtime. On the other hand, Mottes *et al.*[33] reported that process-based

quality improvement using a CRRT dashboard enhanced the achievement of daily fluid removal goals.

As the impact of downtime on mortality remains unclear to date, we investigated the relationship between downtime and 28 day mortality rate, but we found that ≥20% downtime was not independently associated with mortality in critically ill patients with AKI undergoing CRRT. This result may correspond to the knowledge regarding modality and dose for acute RRT.[6,14–17] Intermittent RRT allows downtime during treatment and is a reasonable choice for acute RRT with noninferiority to CRRT, excluding the specific cases with concerns of increased intracranial pressure.[6] Further, an excessive dose of RRT is not necessary if it exceeds the minimum target value. Similar to our results, Goonasekera *et al*.[34] found that downtime did not influence mortality in 31 children with acute liver failure requiring CRRT. Downtime itself may not be a key factor in outcomes. Nevertheless, this study found that the impact of downtime on mortality was possible due to its interaction with fluid balance; thus, downtime should be monitored because increased interruption can impede fluid control in critically ill patients with AKI requiring CRRT. To confirm these results, more studies with a larger sample size are required to identify the relationship between downtime, fluid balance, and mortality in these patients.

This study did not identify an association between downtime and renal outcomes, including dialysis dependence and renal function at discharge. Moreover, we could not draw a conclusion because of the absence of data regarding baseline renal function. A previous study comparing renal recovery before and after the implementation of a specialized CRRT team also observed that there were no significant differences according to the quality of CRRT care.[9] Renal recovery is an important outcome indicator in patients with acute RRT. Therefore, efforts to improve the quality of care should be accompanied by an investigation of the renal outcomes of patients with severe AKI who are likely to lead to end-stage renal disease.

This study had several limitations that need to be mentioned. First, this study had a small sample size and was conducted in a single center, which limits the power of the results and may ignore some differences. In the subgroup analysis, we only found that there was an interaction between downtime and fluid balance on 28 day mortality, but we could not perform multivariate analysis because of the small sample size. In addition, the findings of this single-center study cannot be generalized; thus, further multicenter studies are needed. Second, this study was observational in nature. To minimize selection bias, this study used the propensity score matching model by adjusting for age, sex, Charlson comorbidity index, and SOFA score. Nevertheless, some confounders may have been overlooked despite our efforts. Third, this study was unable to analyze the latest data. No more information regarding the acting time and effluent volume was derived after the study period because of the software update built in the CRRT machine. Acting time derived from a machine was significantly unmatched to that calculated using medical records because there could be frequent pauses during the operation. We thought that the acting time derived from a machine was more accurate, and this study discarded the data after the software update. In addition, this method could allow the analysis of the cumulative and flow rates of effluent. Finally, this study was conducted in a resource-limited setting given the lack of trained staff to perform CRRT, which might have influenced the results. Nevertheless, excluding this issue, the staff at the center is trying to provide qualified care for severely ill patients. This hospital has been one of senior general hospitals since 2012, is accredited by the Ministry of Health and Welfare, and guarantees that severely ill patients can receive high-level medical services.

In conclusion, this study investigated the impact of downtime on various clinical outcomes using a propensity score matching model. An increase in downtime can impair uremic control and acidosis management by lowering the intensity of CRRT care. Moreover, it may influence patient mortality by making fluid control difficult, although downtime *per se* does not have an independent impact. Therefore, efforts should be made to reduce downtime as part of improving the quality of CRRT care. Further studies with a larger sample size are needed to confirm the impact of downtime on various clinical outcomes.

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