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Epidemiology of continuous renal replacement therapy in Korea: Results from the National Health Insurance Service claims database from 2005 to 2016

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Background: Continuous renal replacement therapy (CRRT) is an important treatment modality for severe acute kidney injury. As such, the epidemiology of CRRT in Korea needs further investigation.
Methods: We conducted a nationwide, population-based study analyzing the claims data from National Health Insurance Service of Korea. All index intensive care unit admission cases of CRRT in government-designated tertiary referral hospitals in Korea from 2005 to 2016 were included. Patients with a history of renal replacement therapy or who were under 20 years old were not considered. In addition to baseline and treatment characteristics, patient outcomes, including all-cause mortality and renal survival rates, were investigated. We stratified the study patients according to 3-year time periods and major regions of the nation.
Results: We included 37,337 patients who received CRRT in Korea. The overall use of CRRT increased over time, and more than 80% of cases of acute renal replacement therapy were CRRT after 2014. Seoul was the region in which the majority of CRRT (45.0%) was performed. The clinical characteristics of CRRT patients were significantly different among time-intervals and regions. Both all-cause mortality and renal survival rates after CRRT were prominently improved in the recent time periods ($P < 0.001$).
Conclusion: CRRT is a widely used treatment strategy for severe acute kidney injury in Korea. The prognosis of CRRT patients has improved compared to the past. This epidemiological study of CRRT in Korea revealed notable trends with regard to time period and geographic region.

Keywords: Acute kidney injury, Continuous renal replacement therapy, Critical care, Dialysis, Intensive care units

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Introduction

Acute kidney injury (AKI) is one of the most important medical issues in modern medicine and is associated with patient outcomes [1,2]. The prognosis of AKI has improved over time, but a substantial portion of patients who experience AKI continue to suffer from a poor prognosis, including progression to chronic kidney disease and associated comorbidities [3]. Moreover, the risk of developing end-stage renal disease (ESRD), which is a critical condition for both survival and quality of life for patients, is increased in AKI patients, and this increased risk is more prominent after severe AKI events.

Acute renal replacement therapy (ARRT) is a major treatment strategy for severe AKI. Recent advances in continuous renal replacement therapy (CRRT), a crucial component of ARRT in the intensive care unit (ICU), has made dialysis possible for patients with hemodynamic instability. Due to this benefit, use of CRRT in many countries has been expanded, although the limited accessibility and higher costs were considered to be drawbacks of the modality. Recent epidemiological studies have investigated the time trends and regional differences of CRRT usage in their countries [3–6].

Herein, we performed the first nationwide, population-based study of CRRT in Korea. We accessed the database of National Health Insurance Service (NHIS) and collected information from all CRRT cases in government-designated tertiary referral hospitals. We investigated the differences in the use of CRRT according to time-periods and geographical regions. Moreover, we analyzed the prognosis of CRRT patients, including patient mortality and renal survival.

Methods

Ethical considerations

The institutional review boards (IRBs) of Seoul National University Hospital (IRB number: E-1711-04-897) and Konkuk University (IRB number: 7001355-201708-E-050) approved this study and waived the need for informed consent. This study was conducted in accordance with the principles of the Declaration of Helsinki. The approach to using the government database was approved by the according government, and anonymous patient data were studied.

Study design and population

This was a nationwide population-based study performed in Korea, using the claims database of the NHIS. Korea provides national health insurance service for all people with Korean nationality. All data on insured medical services, including diagnosis codes, medications, and other charged medical procedures, are accumulated in the NHIS [7]. After appropriate approval by the organization, we reviewed the database and collected the information of patients who underwent care in an ICU and received CRRT treatment in all government-designated tertiary referral hospitals from 2005 to 2016.

We included all index admission cases (the patient's first ICU stay) in our study. We excluded: 1) pediatric patients (aged under 20 years old), 2) those who had a previous history of any renal replacement therapy including transplantation or 3) those with a history of ICU care within three years of CRRT treatment. In addition, 4) those who underwent ICU care or CRRT treatment for less than a day were not considered.

Data collection

We collected the following demographic information: age, sex, income status, and date and region of ICU admission. Information regarding comorbidities were collected following the Charlson Comorbidity Index, which was identified following the system of International Classification of Diseases, 10th revision (ICD-10); and the index score was calculated [8]. The presence of baseline comorbidities was assessed for one year before the enrolled CRRT treatment event, and when the diagnostic codes or related medication history existed for more than a single time, patients were considered to have the underlying comorbidity. The principal diagnosis used during the admission period was also reviewed. Information regarding the usage of common ICU care modalities, including mechanical ventilation and inotropic agents, were collected. The operations and procedures performed during the ICU admission were included in our data.

Prognosis of patients who underwent CRRT

We included all-cause mortality and progression to ESRD as prognostic outcomes. Information regarding all-cause mortality was merged from the Korean Statistical Information Service (KOSIS) database, as the organization gathers the death dates of all people with Korean nationality. ESRD was defined as the condition in which the patient required renal replacement therapy for more than 90 days after discharge.

Statistical analysis

Collected data were stratified according to 3-year time periods: 2005 to 2007, 2008 to 2010, 2011 to 2013, and 2014 to 2016. Also, data according to the region in which government-designated tertiary referral hospitals were located, including seven metropolitan cities and seven states of Korea, were shown. Categorical variables were presented as frequencies (percentages) and analyzed by chi-squared tests. Continuous variables were shown as medians (interquartile ranges) and analyzed by the Mann-Whitney *U* test or Kruskal-Wallis test. The Cochran-Mantel-Haenszel test was used to calculate *P* values for trends, and time trends were investigated using this method. We used a Kaplan Meier survival curve to show the prognosis of CRRT patients, and the log-rank method to compare the prognostic outcomes between the time-intervals and regions. A multivariable Cox regression analysis was also performed to investigate the outcomes. However, regional differences were not assessed by this method, as the survival data according to region showed complex results and the assumption required for use of the Cox model were not met. Adjusted variables included age, sex, the Charlson Comorbidity Index, and geographical regions. All statistical analyses were performed using the SAS ver. 9.4 software (SAS Institute, Cary, NC, USA), and two-sided *P* values less than 0.05 were considered to indicate statistical significance.

Results

Study population

From January 2005 to December 2016, 1,129,824 patients who were admitted to the ICU were screened for having undergone CRRT (Fig. 1). Among them, the total number of patients who received CRRT was 42,822 (3.8%). The final study cohort consisted of 37,337 patients who underwent CRRT for more than 24 hours, and their mean follow-up duration was 12.4 months. In-hospital mortality was identified in 22,581 (60.5%) CRRT patients, and additional 6,566 (17.6%) patients died during the follow-up period.

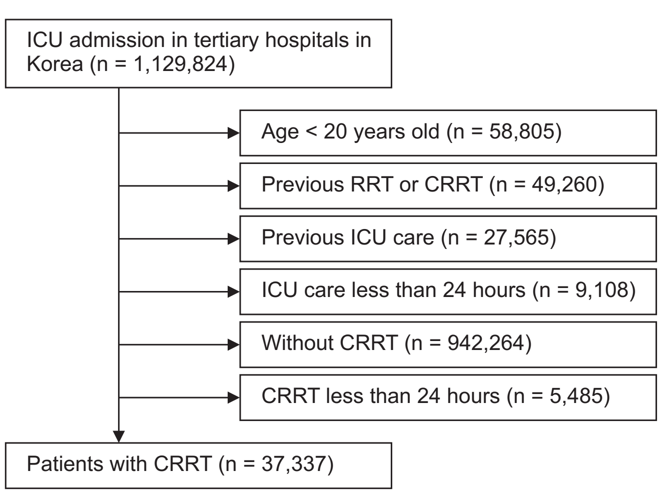

Figure 1. Study population.
CRRT, continuous renal replacement therapy; ICU, intensive care unit; RRT, renal replacement therapy.

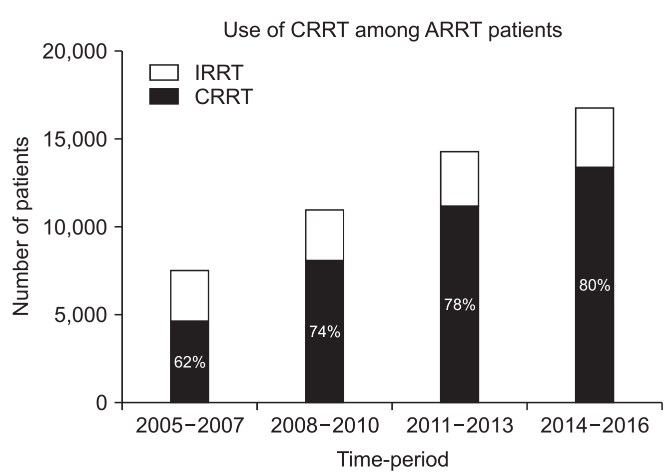

Figure 2. Use of the continuous renal replacement therapy (CRRT) and the acute renal replacement therapy (ARRT) from 2005 to 2016 in Korea.
IRRT, intermittent renal replacement therapy, including hemodialysis and peritoneal dialysis.

Time trends of patients who underwent CRRT

Use of CRRT was identified in 4,667, 8,090, 11,166, and 13,414 patients in 2005 to 2007, 2008 to 2010, 2011 to 2013, and 2014 to 2016, respectively. The proportion of CRRT patients among all ARRT patients continuously increased from 62% in the 2005 to 2007 period to 80% in 2014 to 2016 (Fig. 2). With regards to the baseline characteristics of CRRT patients (Table 1), the most common underlying comorbidity was hypertension (62.1%), followed by diabetes mellitus (36.4%), pulmonary disease (27.3%), peptic ulcers (26.1%), and cancer (22.7%). Of several time trends seen in patients with underlying comorbidities, it was noteworthy that the portion of patients with cerebrovascular accidents ($P < 0.001$), peripheral vascular disease ($P < 0.001$) and dementia ($P < 0.001$) increased over

Table 1. Baseline characteristics of continuous renal replacement therapy patients and their time-trends

Characteristic	Total (n = 37,337)	2005–2007 (n = 4,667)	2008–2010 (n = 8,090)	2011–2013 (n = 11,166)	2014–2016 (n = 13,414)	*P*	*P* for trend†
Age (yr)	62 (50–71)	62 (50–71)	64 (52–73)	66 (54–75)	67 (55–76)	< 0.001	< 0.001
< 60	13,863 (37.13)	2,007 (43.00)	3,207 (39.64)	4,024 (36.04)	4,625 (34.48)		
≥ 60	23,474 (62.87)	2,660 (57.00)	4,883 (60.36)	7,142 (63.96)	8,789 (65.52)		
Male sex	23,328 (62.48)	3,009 (64.47)	5,081 (62.81)	6,917 (61.95)	8,321 (62.03)	0.013	0.005
Income status						< 0.001	< 0.001
Receiving free medical benefits	2,930 (7.85)	415 (8.89)	500 (6.18)	777 (6.96)	1,238 (9.23)		
1st quartile (low)	5,979 (16.01)	717 (15.36)	1,309 (16.18)	1,794 (16.07)	2,159 (16.10)		
2nd quartile	6,316 (16.92)	817 (17.51)	1,410 (17.43)	1,855 (16.61)	2,234 (16.65)		
3rd quartile	8,108 (21.72)	1,029 (22.05)	1,821 (22.51)	2,479 (22.20)	2,779 (20.72)		
4th quartile (high)	14,004 (37.51)	1,689 (36.19)	3,050 (37.70)	4,261 (38.16)	5,004 (37.30)		
Charlson Comorbidity Index	2 (1–4)	2 (0–4)	2 (0–4)	2 (1–4)	2 (1–4)	< 0.001	< 0.001
0–3	25,090 (67.20)	3,359 (71.97)	5,487 (67.82)	7,516 (67.31)	8,728 (65.07)		
≥ 4	12,247 (32.8)	1,308 (28.03)	2,603 (32.18)	3,650 (32.69)	4,686 (34.93)		
Baseline comorbidities							
Cerebrovascular accident	4,847 (12.98)	451 (9.66)	1,012 (12.51)	1,506 (13.49)	1,878 (14.00)	< 0.001	< 0.001
Acute myocardial infarction	839 (2.25)	143 (3.06)	178 (2.20)	248 (2.22)	270 (2.01)	< 0.001	< 0.001
CVD other than MI	6,397 (17.13)	788 (16.88)	1,436 (17.75)	1,862 (16.68)	2,311 (17.23)	0.551	0.853
Hypertension	23,188 (62.10)	2,886 (61.84)	5,189 (64.14)	7,338 (65.72)	7,775 (57.96)	< 0.001	< 0.001
Secondary hypertension	231 (0.62)	30 (0.64)	54 (0.67)	63 (0.56)	84 (0.63)	0.729	0.740
Diabetes	13,576 (36.36)	1,389 (29.76)	2,955 (36.53)	4,348 (38.94)	4,884 (36.41)	< 0.001	< 0.001
Diabetic complication	4,335 (11.61)	530 (11.36)	996 (12.31)	1,328 (11.89)	1,481 (11.04)	0.009	0.087
Connective tissue disease	1,493 (4.00)	192 (4.11)	279 (3.45)	500 (4.48)	522 (3.89)	0.001	0.620
Congestive heart failure	3,079 (8.25)	359 (7.69)	600 (7.42)	961 (8.61)	1,159 (8.64)	0.001	0.002
Peripheral vascular disease	2,800 (7.50)	211 (4.52)	599 (7.40)	900 (8.06)	1,090 (8.13)	< 0.001	< 0.001
Dementia	1,655 (4.43)	65 (1.39)	224 (2.77)	537 (4.81)	829 (6.18)	< 0.001	< 0.001
Pulmonary disease	10,196 (27.31)	1,141 (24.45)	2,243 (27.73)	3,322 (29.75)	3,490 (26.02)	< 0.001	0.499
Peptic ulcer disease	9,743 (26.09)	1,326 (28.41)	2,364 (29.22)	3,211 (28.76)	2,842 (21.19)	< 0.001	< 0.001
Liver disease	2,316 (6.20)	309 (6.62)	526 (6.50)	763 (6.83)	718 (5.35)	< 0.001	< 0.001
Severe liver disease	1,378 (3.69)	265 (5.68)	377 (4.66)	376 (3.37)	360 (2.68)	< 0.001	0.034
Paraplegia	504 (1.35)	63 (1.35)	133 (1.64)	152 (1.36)	156 (1.16)	0.015	0.012
Renal disease	3,776 (10.11)	423 (9.06)	780 (9.64)	1,201 (10.76)	1,372 (10.23)	0.006	< 0.001
Cancer	8,478 (22.71)	980 (21.00)	1,981 (24.49)	2,776 (24.86)	2,741 (20.43)	< 0.001	< 0.001
Metastatic cancer	1,625 (4.35)	201 (4.31)	421 (5.20)	539 (4.83)	464 (3.46)	< 0.001	< 0.001
HIV	38 (0.10)	2 (0.04)	10 (0.12)	10 (0.09)	16 (0.12)	0.239	< 0.001

Continuous variables are shown as medians (interquartile ranges) and categorical variables as numbers (percentages).
CVD, cardiovascular disease; HIV, human immunodeficiency virus; MI, myocardial infarction.
†*P* for trends were calculated with regards to time trends.

time. Other comorbidities and their trends with regard to time are shown in Table 1.

The principal diagnoses and treatment modalities implemented during the index admission are shown in Table 2. The common principal diagnosis categories were neoplasms/hematological diseases (23.1%), circulatory diseases (22.8%), digestive diseases (10.7%), and genitourinary diseases (10.5%). Several time trends with regards to the proportion of principal diseases were observed. The portion of CRRT patients who received mechanical ventilation ($P < 0.001$) or cardiac operations ($P < 0.001$) became less frequent in recent time periods while, by contrast, percutaneous cardiovascular procedures were more widely used with time ($P < 0.001$).

Table 2. Characteristics of intensive care unit (ICU) care according to time periods

Characteristic	Total (n = 37,337)	2005-2007 (n = 4,667)	2008-2010 (n = 8,090)	2011-2013 (n = 11,166)	2014-2016 (n = 13,414)	*P*	*P* for trend[†]
Principal diagnosis						< 0.001	< 0.001
Certain infectious and parasitic diseases	3,617 (9.69)	623 (13.35)	982 (12.14)	1,019 (9.13)	993 (7.40)		
Neoplasms or hematological diseases	8,630 (23.11)	1,033 (22.13)	2,055 (25.40)	2,667 (23.89)	2,875 (21.43)		
Endocrine, nutritional, and metabolic diseases	651 (1.74)	57 (1.22)	120 (1.48)	184 (1.65)	290 (2.16)		
Mental and behavioral diseases	69 (0.18)	9 (0.19)	16 (0.20)	21 (0.19)	23 (0.17)		
Diseases of the nervous system	377 (1.01)	42 (0.90)	69 (0.85)	134 (1.20)	132 (0.98)		
Diseases of the ear and mastoid process	7 (0.02)	1 (0.02)	1 (0.01)	1 (0.01)	4 (0.03)		
Diseases of the circulatory system	8,499 (22.76)	1,035 (22.18)	1,746 (21.58)	2,581 (23.11)	3,137 (23.39)		
Diseases of the respiratory system	3,366 (9.02)	344 (7.37)	662 (8.18)	1,028 (9.21)	1,332 (9.93)		
Diseases of the digestive system	3,987 (10.68)	577 (12.36)	909 (11.24)	1,108 (9.92)	1,393 (10.38)		
Diseases of the skin and subcutaneous tissue	84 (0.22)	9 (0.19)	18 (0.22)	33 (0.30)	24 (0.18)		
Diseases of the muscle and connective tissue	801 (2.15)	99 (2.12)	172 (2.13)	252 (2.26)	278 (2.07)		
Diseases of the genitourinary system	3,916 (10.49)	569 (12.19)	816 (10.09)	1,128 (10.10)	1,403 (10.46)		
Pregnancy-related status	91 (0.24)	13 (0.28)	25 (0.31)	28 (0.25)	25 (0.19)		
Congenital diseases	85 (0.23)	10 (0.21)	22 (0.27)	22 (0.20)	31 (0.23)		
Abnormal clinical and laboratory findings not elsewhere classified	824 (2.21)	17 (0.36)	58 (0.72)	246 (2.20)	503 (3.75)		
Injury poisoning and other consequences of external causes	1,840 (4.93)	221 (4.74)	357 (4.41)	562 (5.03)	700 (5.22)		
Factors influencing health status and contact with health services	489 (1.31)	8 (0.17)	62 (0.77)	149 (1.33)	270 (2.01)		
Treatment during ICU stay							
Ventilator care	31,610 (84.66)	4,174 (89.44)	7,117 (87.97)	9,451 (84.64)	10,868 (81.02)	< 0.001	< 0.001
Use of intravenous inotropic agents	34,598 (92.66)	4,326 (92.69)	7,489 (92.57)	10,380 (92.96)	12,403 (92.46)	0.503	0.670
Cardiac operations	1,967 (5.27)	313 (6.71)	516 (6.38)	537 (4.81)	601 (4.48)	< 0.001	< 0.001
Cardiovascular procedures	2,052 (5.50)	195 (4.18)	405 (5.01)	663 (5.94)	789 (5.88)	< 0.001	< 0.001
In-hospital mortality	22,581 (60.48)	2,959 (63.40)	5,061 (62.56)	6,879 (61.61)	7,682 (57.27)	< 0.001	< 0.001

Categorical variables are shown as numbers (percentages).
[†]*P* for trends were calculated with regards to time trends.

Table 3. Number of continuous renal replacement therapy patients according to time period and region

Region	2005–2007 (n = 4,667)	2008–2010 (n = 8,090)	2011–2013 (n = 11,166)	2014–2016 (n = 13,414)
Seoul (n = 16,805)	2,716 (58.20)	4,136 (51.12)	5,095 (45.63)	4,858 (36.22)
Busan (n = 4,149)	500 (10.71)	869 (10.74)	1,232 (11.03)	1,548 (11.54)
Daegu (n = 1,869)	229 (4.91)	394 (4.87)	510 (4.57)	736 (5.49)
Incheon (n = 1,059)	110 (2.36)	154 (1.90)	246 (2.20)	549 (4.09)
Gwangju (n = 2,431)	161 (3.45)	335 (4.14)	863 (7.73)	1,072 (7.99)
Daejeon (n = 766)	73 (1.56)	151 (1.87)	227 (2.03)	315 (2.35)
Ulsan (n = 317)	None	None	None	317 (2.36)
Gyeonggi (n = 4,461)	227 (4.86)	966 (11.94)	1,424 (12.75)	1,844 (13.75)
Gangwon (n = 1,191)	246 (5.27)	338 (4.18)	335 (3.00)	272 (2.03)
Chungbuk (n = 586)	94 (2.01)	113 (1.40)	147 (1.32)	232 (1.73)
Chungnam (n = 1,273)	163 (3.49)	271 (3.35)	369 (3.30)	470 (3.50)
Jeonbuk (n = 1,180)	64 (1.37)	202 (2.50)	444 (3.98)	470 (3.50)
Jeonnam (n = 270)	None	None	93 (0.83)	177 (1.32)
Gyeongnam (n = 980)	84 (1.80)	161 (1.99)	181 (1.62)	554 (4.13)

Categorical variables are shown as numbers (percentages).

Regional differences in patients who underwent CRRT

During the study period, some tertiary referral centers were newly designated or closed by the government, and the overall number of the government-designated tertiary referral hospitals was 42 to 44. The number of CRRT patients according to geographical region and time periods is shown in Table 3. Seoul, with 14 tertiary hospitals, represented the largest portion of CRRT cases in every time period we studied (45.0%), but this fraction persistently decreased over time. This downward trend in CRRT prevalence was similar in Gangwon. However, the proportion of CRRT cases continuously increased in Busan, Gwangju, Daejeon, and Gyeonggi.

The baseline characteristics of CRRT patients in major regions of Korea are shown in Table 4. There were some differences in patient characteristics; notably, Gwangju had the highest proportion of CRRT patients who were 60 years old or older. Patients who received CRRT in Seoul more frequently were in the highest quartile with regards to income status (41.7%) and had a relatively higher frequency of cancer history (29.8%). CRRT patients in Jeonnam, in which a cancer-specialized tertiary center was the only local government-designated tertiary referral hospital, had the highest incidence of cancer as a comorbidity (64.8%), which was more than twice that of other regions.

The principal diagnosis and use of ICU care modalities according to regions are shown in Table 5. Infectious diseases were relatively common in Gangwon (14.1%), and Jeonnam had the highest proportion of patients with malignancy or hematological diseases (84.8%). Daegu (29.4%) and Gwangju (26.0%) were the areas in which more than a quarter of CRRT patients had a circulatory disease as the principal diagnosis. Mechanical ventilation was relatively less frequently used for CRRT patients in Jeonnam ($P < 0.001$). The combined use of ventilator, inotropic agents, and CRRT during the ICU stay was identified in more 80% of CRRT patients in most regions.

Prognosis of CRRT patients

The patients' prognoses according to time periods are shown in Fig. 3. We identified that the overall patient mortality rate was better in the most recent time period compared to the earlier time periods ($P < 0.001$). A similar trend was also seen regarding renal survival, as CRRT patients in 2014 to 2016 had the lowest incidence of ESRD among the studied time periods ($P < 0.001$). This improvement in patient prognosis over time remained significant in our multivariable model (Table 6). CRRT patients in 2014 to 2016 had a significantly lower risk of mortality (adjusted hazard ratio [HR], 0.858; 95% confidence interval [CI], 0.825–0.891; $P < 0.001$) and ESRD (adjusted HR, 0.580; 95% CI, 0.507–0.664; $P < 0.001$) when compared to those in 2005 to 2007.

On the other hand, trends in prognosis according to geographical region showed complex results (Fig. 4).

Table 4. Baseline characteristics of continuous renal replacement therapy patients according to major regions in Korea

Characteristic	Seoul (n = 16,805)	Busan (n = 4,149)	Daegu (n = 1,869)	Incheon (n = 1,059)	Gwangju (n = 2,431)	Daejeon (n = 766)	Ulsan (n = 317)	Gyeonggi (n = 4,461)	Gangwon (n = 1,191)	Chungbuk (n = 586)	Chungnam (n = 1,273)	Jeonbuk (n = 1,180)	Jeonnam (n = 270)	Gyeongnam (n = 980)	P value
Age (yr)	64 (52–73)	66 (55–75)	66 (53–74)	64 (52–74)	69 (58–77)	66 (56–75)	64 (54–74)	66 (52–75)	65 (52–74)	69 (57–77)	67 (54–76)	68 (56–76)	68 (57–73)	66 (54–74)	< 0.001
< 60	6,674 (39.70)	1,387 (33.4)	681 (36.4)	443 (41.83)	677 (27.85)	257 (33.55)	117 (36.91)	1,695 (38.00)	473 (39.71)	181 (30.89)	455 (35.74)	372 (31.53)	84 (31.11)	367 (37.45)	
≥ 60	10,131 (60.29)	2,762 (65.57)	1,188 (63.56)	616 (58.17)	1,754 (72.15)	509 (66.45)	200 (63.09)	2,766 (62.00)	718 (60.29)	405 (69.11)	818 (64.26)	808 (68.47)	186 (68.89)	613 (62.55)	
Male sex	10,541 (62.73)	2,521 (60.76)	1,127 (60.3)	624 (58.92)	1,491 (61.33)	503 (65.67)	208 (65.62)	2,826 (63.35)	799 (67.09)	372 (63.48)	775 (60.88)	724 (61.36)	169 (62.59)	648 (66.12)	< 0.001
Charlson Comorbidity Index	2 (1–4)	2 (1–4)	2 (0–4)	2 (0–4)	2 (1–5)	2 (1–5)	3 (1–5)	2 (0–4)	2 (0–4)	2 (1–4)	2 (0–4)	3 (1–5)	3 (1–5)	2 (0–4)	< 0.001
0	11,226 (66.8)	2,795 (67.37)	1,302 (69.66)	757 (71.48)	1,530 (62.94)	481 (62.79)	181 (57.10)	3,160 (70.84)	868 (72.88)	382 (65.19)	922 (72.43)	676 (57.29)	165 (61.11)	645 (65.82)	
≥ 4	5,579 (33.20)	1,354 (32.63)	567 (30.34)	302 (28.52)	901 (37.06)	285 (37.21)	136 (42.90)	1,301 (29.16)	323 (27.12)	204 (34.81)	351 (27.57)	504 (42.71)	105 (38.89)	335 (34.18)	
Income status															< 0.001
Receiving free medical benefits	1,116 (6.64)	485 (11.69)	118 (6.31)	117 (11.05)	281 (11.56)	103 (13.45)	13 (4.10)	240 (5.38)	115 (9.66)	72 (12.29)	37 (2.91)	119 (10.08)	15 (5.56)	99 (10.10)	
1st quartile (low)	2,500 (14.88)	684 (16.49)	323 (17.28)	171 (16.15)	437 (17.98)	105 (13.71)	37 (11.67)	803 (18.00)	206 (17.3)	71 (12.12)	244 (19.17)	199 (16.86)	46 (17.04)	153 (15.61)	
2nd quartile	2,623 (15.61)	691 (16.65)	332 (17.76)	220 (20.77)	437 (17.98)	115 (15.01)	55 (17.35)	821 (18.4)	243 (20.4)	104 (17.75)	262 (20.58)	182 (15.42)	54 (20.00)	177 (18.06)	
3rd quartile	3,555 (21.15)	930 (22.42)	465 (24.88)	247 (23.32)	450 (18.51)	162 (21.15)	70 (22.08)	955 (21.41)	285 (23.93)	150 (25.60)	307 (24.12)	237 (20.08)	65 (24.07)	230 (23.47)	
4th quartile (high)	7,011 (41.72)	1,359 (32.75)	631 (33.76)	304 (28.71)	826 (33.98)	281 (36.68)	142 (44.79)	1,642 (36.81)	342 (28.72)	189 (32.25)	423 (33.23)	443 (37.54)	90 (33.33)	321 (32.76)	
Baseline comorbidities															
Cerebrovascular accident	1,927 (11.47)	550 (13.26)	277 (14.82)	110 (10.39)	414 (17.03)	123 (16.06)	38 (11.99)	569 (12.75)	128 (10.75)	121 (20.65)	171 (13.43)	246 (20.85)	25 (9.26)	148 (15.10)	< 0.001
Acute myocardial infarction	364 (2.17)	132 (3.18)	59 (3.16)	15 (1.42)	77 (3.17)	13 (1.70)	6 (1.89)	64 (1.43)	30 (2.52)	10 (1.71)	24 (1.89)	13 (1.10)	3 (1.11)	29 (2.96)	< 0.001
CVD other than MI	2,925 (17.41)	788 (18.99)	311 (16.64)	148 (13.98)	423 (17.4)	143 (18.67)	55 (17.35)	716 (16.05)	180 (15.11)	100 (17.06)	250 (19.64)	161 (13.64)	34 (12.59)	163 (16.63)	< 0.001
Hypertension	10,661 (63.44)	2,594 (62.52)	1,189 (63.62)	619 (58.45)	1,568 (64.50)	489 (63.84)	180 (56.78)	2,640 (59.18)	669 (56.17)	373 (63.65)	732 (57.50)	754 (63.9)	157 (58.15)	563 (57.45)	< 0.001
Secondary hypertension	126 (0.75)	20 (0.48)	17 (0.91)	2 (0.19)	9 (0.37)	16 (2.09)	0 (0)	21 (0.47)	3 (0.25)	2 (0.34)	2 (0.16)	7 (0.59)	4 (1.48)	2 (0.20)	< 0.001
Diabetes	5,878 (34.98)	1,605 (38.68)	642 (34.35)	406 (38.34)	976 (40.15)	291 (37.99)	113 (35.65)	1,573 (35.26)	430 (36.1)	254 (43.34)	466 (36.61)	441 (37.37)	91 (33.7)	410 (41.84)	< 0.001
Diabetic complication	1,775 (10.56)	445 (10.73)	274 (14.66)	115 (10.86)	350 (14.4)	121 (15.80)	25 (7.89)	496 (11.12)	156 (13.1)	95 (16.21)	157 (12.33)	182 (15.42)	24 (8.89)	120 (12.24)	< 0.001
Connective tissue disease	732 (4.36)	161 (3.88)	89 (4.76)	24 (2.27)	96 (3.95)	28 (3.66)	9 (2.84)	168 (3.77)	38 (3.19)	19 (3.24)	35 (2.75)	51 (4.32)	9 (3.33)	34 (3.47)	0.008
Congestive heart failure	1,260 (7.5)	406 (9.79)	203 (10.86)	75 (7.08)	245 (10.08)	75 (9.79)	34 (10.73)	360 (8.07)	100 (8.4)	68 (11.6)	90 (7.07)	60 (5.08)	12 (4.44)	91 (9.29)	< 0.001
Peripheral vascular disease	1,067 (6.35)	379 (9.13)	164 (8.77)	77 (7.27)	210 (8.64)	71 (9.27)	24 (7.57)	334 (7.49)	69 (5.79)	43 (7.34)	99 (7.78)	147 (12.46)	25 (9.26)	91 (9.29)	< 0.001
Dementia	546 (3.25)	204 (4.92)	87 (4.65)	59 (5.57)	202 (8.31)	55 (7.18)	15 (4.73)	215 (4.82)	36 (3.02)	37 (6.31)	65 (5.11)	84 (7.12)	3 (1.11)	47 (4.80)	< 0.001
Pulmonary disease	4,458 (26.53)	1,182 (28.49)	483 (25.84)	243 (22.95)	789 (32.46)	174 (22.72)	98 (30.91)	1,128 (25.29)	300 (25.19)	163 (27.82)	343 (26.94)	393 (33.31)	121 (44.81)	321 (32.76)	< 0.001
Peptic ulcer	4,489 (26.71)	1,060 (25.55)	473 (25.31)	226 (21.34)	719 (29.58)	206 (26.89)	82 (25.87)	939 (21.05)	305 (25.61)	136 (23.21)	273 (21.45)	455 (38.56)	88 (32.59)	292 (29.80)	< 0.001
Liver disease	1,471 (8.75)	208 (5.01)	58 (3.10)	37 (3.49)	43 (1.77)	32 (4.18)	22 (6.94)	203 (4.55)	26 (2.18)	25 (4.27)	51 (4.01)	47 (3.98)	24 (8.89)	69 (7.04)	< 0.001
Paraplegia	199 (1.18)	76 (1.83)	26 (1.39)	10 (0.94)	38 (1.56)	21 (2.74)	4 (1.26)	55 (1.23)	14 (1.18)	11 (1.88)	13 (1.02)	23 (1.95)	3 (1.11)	11 (1.12)	< 0.001
Renal Disease	1,667 (9.92)	485 (11.69)	198 (10.59)	90 (8.5)	264 (10.86)	93 (12.14)	20 (6.31)	438 (9.82)	121 (10.16)	79 (13.48)	98 (7.70)	113 (9.58)	17 (6.30)	93 (9.49)	< 0.001
Cancer	4,999 (29.75)	815 (19.64)	275 (14.71)	154 (14.54)	211 (8.68)	147 (19.19)	64 (20.19)	815 (18.27)	120 (10.08)	94 (16.04)	206 (16.18)	215 (18.22)	175 (64.81)	188 (19.18)	< 0.001
Metastatic cancer	951 (5.66)	179 (4.31)	44 (2.35)	34 (3.21)	15 (0.62)	27 (3.52)	4 (1.26)	140 (3.14)	20 (1.68)	29 (4.95)	60 (4.71)	54 (4.58)	25 (9.26)	43 (4.39)	< 0.001
Severe liver disease	878 (5.22)	91 (2.19)	52 (2.78)	30 (2.83)	49 (2.02)	18 (2.35)	9 (2.84)	106 (2.38)	18 (1.51)	5 (0.85)	19 (1.49)	43 (3.64)	4 (1.48)	56 (5.71)	< 0.001
HIV	16 (0.10)	10 (0.24)	0 (0)	3 (0.28)	1 (0.04)	2 (0.26)	0 (0)	3 (0.07)	0 (0)	1 (0.17)	1 (0.08)	0 (0)	0 (0)	1 (0.10)	NA

Continuous variables are shown as medians (interquartile ranges) and categorical variables as numbers (percentages).
CVD, cardiovascular disease; HIV, human immunodeficiency virus; MI, myocardial infarction; NA, not applicable.

Table 5. Characteristics of intensive care unit (ICU) care according to major regions of Korea

Characteristic	Seoul (n = 16,805)	Busan (n = 4,149)	Daegu (n = 1,869)	Incheon (n = 1,059)	Gwangu (n = 2,431)	Daejeon (n = 766)	Ulsan (n = 317)	Gyeonggi (n = 4,461)	Gangwon (n = 1,191)	Chungbuk (n = 586)	Chungnam (n = 1,273)	Jeonbuk (n = 1,180)	Jeonnam (n = 270)	Gyeongnam (n = 980)	*P* value
Principal diagnosis															< 0.001
Certain infectious and parasitic diseases	1,255 (7.47)	432 (10.41)	167 (8.94)	109 (10.29)	343 (14.11)	48 (6.27)	26 (8.20)	437 (9.80)	299 (25.10)	66 (11.26)	162 (12.73)	157 (13.31)	9 (3.33)	107 (10.92)	
Neoplasms or hematological diseases	5,288 (31.47)	770 (18.56)	305 (16.32)	196 (18.51)	141 (5.80)	131 (17.10)	55 (17.35)	850 (19.05)	122 (10.24)	77 (13.14)	163 (12.80)	175 (14.83)	229 (84.81)	128 (13.06)	
Endocrine, nutritional, and metabolic diseases	213 (1.27)	63 (1.52)	21 (1.12)	31 (2.93)	96 (3.95)	15 (1.96)	9 (2.84)	67 (1.50)	36 (3.02)	19 (3.24)	24 (1.89)	34 (2.88)	1 (0.37)	22 (2.24)	
Mental and behavioral diseases	41 (0.24)	4 (0.10)	1 (0.05)	2 (0.19)	2 (0.08)	0 (0)	0 (0)	15 (0.34)	2 (0.17)	1 (0.17)	0 (0)	1 (0.08)	0 (0)	0 (0)	
Diseases of the nervous system	164 (0.98)	57 (1.37)	13 (0.70)	11 (1.04)	21 (0.86)	7 (0.91)	0 (0)	51 (1.14)	12 (1.01)	3 (0.51)	9 (0.71)	14 (1.19)	1 (0.37)	14 (1.43)	
Diseases of the ear and mastoid process	2 (0.01)	1 (0.02)	0 (0)	1 (0.09)	1 (0.04)	0 (0)	0 (0)	2 (0.04)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Diseases of the circulatory system	3,822 (22.74)	971 (23.40)	549 (29.37)	215 (20.30)	631 (25.96)	166 (21.67)	76 (23.97)	1,051 (23.56)	223 (18.72)	136 (23.21)	277 (21.76)	182 (15.42)	3 (1.11)	197 (20.10)	
Diseases of the respiratory system	1,241 (7.38)	381 (9.18)	166 (8.88)	94 (8.88)	259 (10.65)	67 (8.75)	39 (12.30)	468 (10.49)	110 (9.24)	60 (10.24)	152 (11.94)	204 (17.29)	4 (1.48)	121 (12.35)	
Diseases of the digestive system	1,903 (11.32)	393 (9.47)	190 (10.17)	129 (12.18)	265 (10.9)	64 (8.36)	41 (12.93)	476 (10.67)	108 (9.07)	53 (9.04)	150 (11.78)	121 (10.25)	3 (1.11)	91 (9.29)	
Diseases of the skin and subcutaneous tissue	33 (0.20)	17 (0.41)	3 (0.16)	2 (0.19)	5 (0.21)	5 (0.65)	0 (0)	7 (0.16)	2 (0.17)	2 (0.34)	2 (0.16)	3 (0.25)	0 (0)	3 (0.31)	
Diseases of the muscle and connective tissue	380 (2.26)	133 (3.21)	47 (2.51)	18 (1.70)	45 (1.85)	20 (2.61)	4 (1.26)	70 (1.57)	8 (0.67)	11 (1.88)	13 (1.02)	29 (2.46)	1 (0.37)	22 (2.24)	
Diseases of the genitourinary system	1,263 (7.52)	599 (14.44)	247 (13.22)	117 (11.05)	355 (14.6)	154 (20.10)	30 (9.46)	438 (9.82)	124 (10.41)	124 (21.16)	156 (12.25)	168 (14.24)	15 (5.56)	126 (12.86)	
Pregnancy related status	39 (0.23)	8 (0.19)	13 (0.70)	9 (0.85)	3 (0.12)	0 (0)	0 (0)	9 (0.20)	0 (0)	3 (0.51)	3 (0.24)	3 (0.25)	0 (0)	1 (0.10)	
Congenital diseases	59 (0.35)	8 (0.19)	1 (0.05)	0 (0)	1 (0.04)	1 (0.13)	1 (0.32)	8 (0.18)	0 (0)	1 (0.17)	3 (0.24)	2 (0.17)	0 (0)	0 (0)	
Abnormal clinical and laboratory findings not elsewhere classified	301 (1.79)	33 (0.80)	18 (0.96)	40 (3.78)	74 (3.04)	59 (7.7)	1 (0.32)	107 (2.40)	57 (4.79)	5 (0.85)	15 (1.18)	36 (3.05)	2 (0.74)	76 (7.76)	
Injury poisoning and other consequences of external causes	490 (2.92)	265 (6.40)	93 (4.98)	55 (5.19)	182 (7.49)	28 (3.7)	34 (10.7.)	344 (7.70)	85 (7.14)	25 (4.27)	142 (11.15)	41 (3.5)	2 (0.74)	54 (5.5)	
Factors influencing health status and contact with health services	308 (1.83)	14 (0.34)	35 (1.87)	30 (2.83)	7 (0.29)	1 (0.13)	1 (0.32)	60 (1.34)	3 (0.25)	0 (0)	2 (0.16)	10 (0.85)	0 (0)	18 (1.84)	
Treatment during ICU stay															
Ventilator care	14,604 (86.90)	3,307 (79.71)	1,607 (85.98)	921 (86.97)	1,950 (80.21)	650 (84.86)	260 (82.02)	3,750 (84.06)	1,007 (84.55)	460 (78.5)	1,031 (80.99)	1,040 (88.14)	172 (63.70)	851 (86.84)	< 0.001
Use of intravenous inotropic agents	15,788 (93.95)	3,755 (90.50)	1,790 (95.77)	1,013 (95.66)	2,181 (89.72)	702 (91.64)	296 (93.38)	4,097 (91.84)	1,030 (86.48)	486 (82.94)	1,156 (90.81)	1,149 (97.37)	241 (89.26)	914 (93.27)	< 0.001
Cardiac operations	1,191 (7.09)	116 (2.80)	177 (9.47)	42 (3.97)	60 (2.47)	21 (2.74)	11 (3.47)	218 (4.89)	7 (0.59)	16 (2.73)	41 (3.22)	31 (2.63)	0 (0)	36 (3.67)	< 0.001
Cardiovascular procedures	783 (4.66)	192 (4.63)	146 (7.81)	43 (4.06)	205 (8.43)	48 (6.27)	17 (5.36)	271 (6.07)	95 (7.98)	57 (9.73)	102 (8.01)	38 (3.22)	1 (0.37)	54 (5.51)	< 0.001
In-hospital mortality	10,193 (60.65)	2,425 (58.45)	1,165 (62.33)	693 (65.44)	1,361 (55.99)	442 (57.70)	165 (52.05)	2,761 (61.89)	719 (60.37)	299 (51.02)	767 (60.25)	807 (68.39)	181 (67.04)	603 (61.53)	< 0.001

Categorical variables are shown as numbers (percentages).

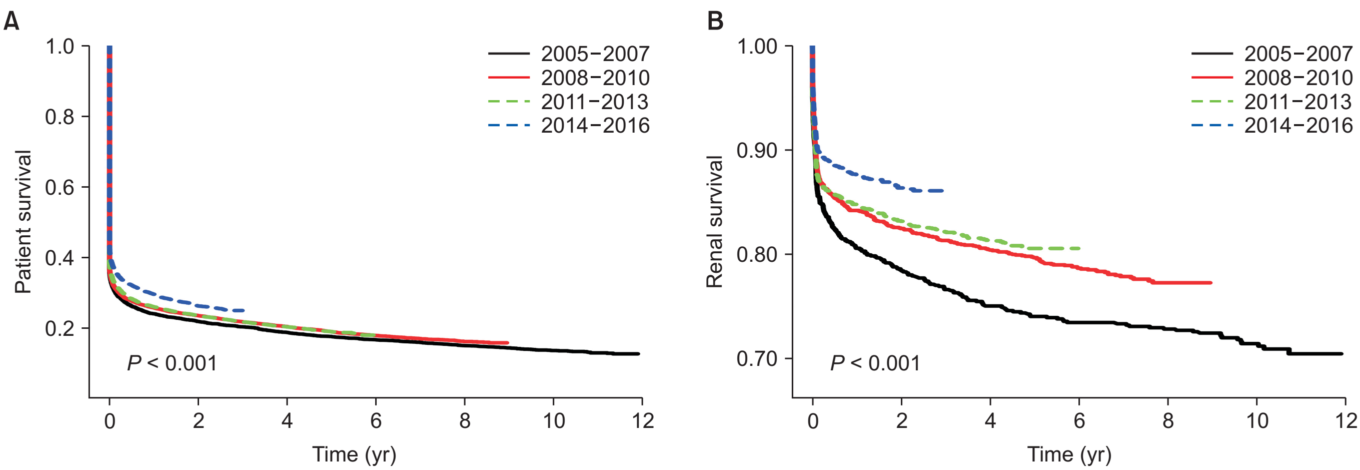

Figure 3. Patient prognosis according to 3-year time-periods. A Kaplan-Meier survival curve showing the all-cause mortality and renal survival rates according to time periods. The x-axes indicate years of index admission. The y-axis for all-cause mortality indicates cumulative patient survival (A) and cumulative renal survival (B).

Table 6. Prognosis of continuous renal replacement therapy patients according to time periods

	Adjusted HR (95% CI)†	*P* value
All-cause mortality		
2005–2007	1 (Reference)	1 (Reference)
2008–2010	0.956 (0.919–0.994)	< 0.001
2011–2013	0.927 (0.893–0.963)	< 0.001
2014–2016	0.858 (0.825–0.891)	< 0.001
Renal survival		
2005–2007	1 (Reference)	1 (Reference)
2008–2010	0.790 (0.691–0.903)	< 0.001
2011–2013	0.740 (0.650–0.843)	< 0.001
2014–2016	0.580 (0.507–0.664)	< 0.001

CI, confidence interval; HR, hazard ratio.
†Multivariable cox regression analysis performed after adjusting for age, sex, the Charlson Comorbidity Index, and geographical region.

CRRT patients in Jeonnam, which had the highest portion of patients with cancer as a comorbidity, related to included hospital's specialization, had relatively poor patient survival compared to other regions ($P < 0.001$). On the other hand, those who received CRRT in Ulsan had better overall survival than those in other regions ($P < 0.001$), yet the follow-up duration was the shortest in this region among the studied areas. Regional differences in renal outcome also showed diverse results. No prominent difference in renal survival was identified among the studied regions, except for that Jeonnam had a lower incidence of ESRD than other areas ($P < 0.001$)

Discussion

The results of our study show that, in Korea, the use of CRRT has been growing rapidly in recent years, and the proportion of CRRT cases of the total number of ARRT cases has increased. Moreover, the characteristics of CRRT patients changed over time, and regional differences were present. The general prognosis of CRRT patients has improved in recent year; however, differences in CRRT outcomes according to geographical area showed diverse results.

Recently, the use of CRRT has increased worldwide. The primary clinical benefit of CRRT is gradual dialysis or ultrafiltration, leading to hemodynamic stability, which is crucial in ICU patients [9,10]. Also, several other advantages, including the preservation of renal function and tolerance in patients with liver failure and increased intracranial pressure, have been proposed [11–13]. However, its limited availability and relatively higher expense were pointed out as major disadvantages of CRRT [14]. In Korea, we identified a rapid increase in the use of CRRT, and the proportion of CRRT patients among all ARRT patients, which reached 80% after 2014, was much higher than that of other nations [3,4]. One possible explanation for this phenomenon may be that we included only government-designated tertiary referral centers, not other ICUs. However, this widespread use of CRRT in Korea still merits attention.

The characteristics of patients who received CRRT changed over time. We showed that an increasing num-

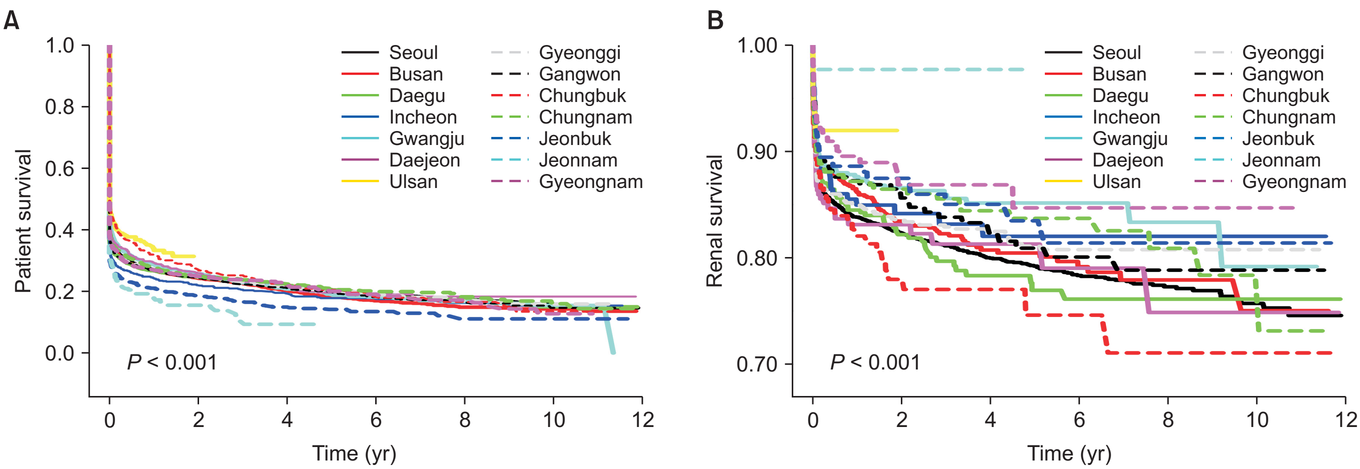

Figure 4. Patient prognosis according to studied regions. Kaplan-Meier survival curve showing the all-cause mortality and renal survival rates according to geographical region. The x-axes indicated years of index admission. The y-axis for all-cause mortality indicates cumulative patient survival (A) and cumulative renal survival (B).

ber of elderly people received CRRT, and they had more comorbidities than before. The specific distributions of baseline comorbidities also changed with time, which could be related to changes in the overall incidence rates of these diseases in Korea. Clinicians should pay attention to the alternating trend of underlying diseases or a principal diagnosis of CRRT patients, as this could show that certain disease categories may become more important for CRRT patients in the future.

Interestingly, despite an increase in the portion of elderly CRRT patients, the overall mortality and renal survival rates improved with time. This phenomenon was similarly shown in other cohorts, and AKI patients have also shown better clinical outcomes recently [3,4]. Advances in ICU care for sepsis and respiratory failure, which can coexist in CRRT patients, have been pointed out as a potential major reason for the improvements in AKI prognosis [15,16]. In addition, increasing implementation of CRRT in the ICU implies that expansion of treatment indications may have also contributed to the better prognosis of CRRT patients of late. Considering the recent trends, an increase in the number of survivors of severe AKI could be anticipated. Clinicians should be reminded that about 10% to 25% of CRRT patients progress to ESRD, most frequently shortly after their stay in the ICU, but also sometimes after a longer time has passed. Therefore, future studies regarding the long-term prognosis of AKI survivors after an ICU stay are warranted, and clinicians should closely monitor for possible deterioration in renal function and the development of related comorbidities in CRRT patients.

Regional differences in CRRT patients were diverse. The majority of CRRT (45%) was performed in Seoul, the capital of Korea, which has 14 government-designated tertiary referral hospitals. Considering that three urban regions, Seoul, Busan, and Gyeonggi, represented 68.1% of all CRRT cases we studied, the use of CRRT was concentrated in cities, in which many government-designated tertiary referral hospitals were located, rather than suburban area. The patients' prognoses also varied according to the geographical region. However, regional superiority could hardly be assessed, as significant differences in patient characteristics according to geographical region also existed. The clinical outcomes of CRRT according to geographical region should be investigated in a further study which includes more socioeconomic variables.

There are several limitations to the current study. First, being a nationwide study in a single country, the epidemiology of CRRT may be different in other nations. Notably, the high accessibility of CRRT in Korea, which may not be similar in other countries, should be considered when interpreting our study results. Second, due to the limitations of the data from the NHIS, we could not include information on the timing of CRRT initiation or discontinuation. Further studies which include a clear investigation into the timing of the diagnosis during admission and CRRT usage may provide valuable information. Third, as we analyzed information from the national health claims database, laboratory findings were not included in our dataset. Also, clinical parameters during the ICU stay were not included. Therefore, neither laboratory variables nor information regarding the clinical course used during the index admission, both of which might have a large impact on patient prognosis, were not studied. Lastly, past medical history was identified in a relatively limited time period, due to the availability of the data.

In conclusion, CRRT has been a widely used as an ARRT modality in Korea. Prognosis after CRRT has improved over time. Clinicians should understand the time trends and regional differences of CRRT patients, and appropriate distribution of medical resources and clinical attention should be considered.

Conflicts of interest

All authors have no conflicts of interest to declare.

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References

[1] Perico N, Remuzzi G. Acute kidney injury: more awareness needed, globally. *Lancet* 386:1425-1427, 2015

[2] Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol* 16:3365-3370, 2005

[3] Wald R, McArthur E, Adhikari NK, et al. Changing incidence and outcomes following dialysis-requiring acute kidney injury among critically ill adults: a population-based cohort study. *Am J Kidney Dis* 65:870-877, 2015

[4] Carlson N, Hommel K, Olesen JB, et al. Dialysis-requiring acute kidney injury in Denmark 2000-2012: time trends of incidence and prevalence of risk factors-a nationwide study. *PLoS One* 11:e0148809, 2016

[5] Iwagami M, Yasunaga H, Noiri E, et al. Choice of renal replacement therapy modality in intensive care units: data from a Japanese Nationwide Administrative Claim Database. *J Crit Care* 30:381-385, 2015

[6] Kolhe NV, Fluck RJ, Muirhead AW, Taal MW. Regional variation in acute kidney injury requiring dialysis in the English National Health Service from 2000 to 2015 - a national epidemiological study. *PLoS One* 11:e0162856, 2016

[7] Seong SC, Kim YY, Khang YH, et al. Data resource profile: the National Health Information Database of the National Health Insurance Service in South Korea. *Int J Epidemiol* 46:799-800, 2017

[8] Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 43:1130-1139, 2005

[9] Augustine JJ, Sandy D, Seifert TH, Paganini EP. A randomized controlled trial comparing intermittent with continuous dialysis in patients with ARF. *Am J Kidney Dis* 44:1000-1007, 2004

[10] Bagshaw SM, Berthiaume LR, Delaney A, Bellomo R. Continuous versus intermittent renal replacement therapy for critically ill patients with acute kidney injury: a meta-analysis. *Crit Care Med* 36:610-617, 2008

[11] Davenport A, Will EJ, Davidson AM. Improved cardiovascular stability during continuous modes of renal replacement therapy in critically ill patients with acute hepatic and renal failure. *Crit Care Med* 21:328-338, 1993

[12] Davenport A. Renal replacement therapy in the patient with acute brain injury. *Am J Kidney Dis* 37:457-466, 2001

[13] Vanholder R, Van Biesen W, Hoste E, Lameire N. Pro/con debate: continuous versus intermittent dialysis for acute kidney injury: a never-ending story yet approaching the finish? *Crit Care* 15:204, 2011

[14] Manns B, Doig CJ, Lee H, et al. Cost of acute renal failure requiring dialysis in the intensive care unit: clinical and resource implications of renal recovery. *Crit Care Med* 31:449-455, 2003

[15] Stevenson EK, Rubenstein AR, Radin GT, Wiener RS, Walkey AJ. Two decades of mortality trends among patients with severe sepsis: a comparative meta-analysis. *Crit Care Med* 42:625-631, 2014

[16] Liu KD, Matthay MA, Chertow GM. Evolving practices in critical care and potential implications for management of acute kidney injury. *Clin J Am Soc Nephrol* 1:869-873, 2006