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Early Diastolic Blood Pressure Variability and Acute Kidney Injury after Acute Ischemic Stroke: A Single-center Retrospective Cohort Study

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Abstract

Background: Whether early in-hospital blood pressure variability (BPV) is associated with acute kidney injury (AKI) after acute ischemic stroke (AIS) is uncertain. In this study, we aimed to examine the association between early diastolic blood pressure (DBP) variability and AKI.

Methods: In a single-center retrospective cohort of 2,397 adults hospitalized with AIS (2008–2024), the 72-h coefficient of variation of DBP (DBP-CV) after emergency department arrival was analyzed continuously (per 0.10-unit increase) and by quartiles. AKI was defined via Kidney Disease: Improving Global Outcomes serum creatinine criteria. The primary outcome was any AKI (stages 1–3), and secondary outcomes were stages 2–3 and stage 3 AKI. Logistic regression was adjusted for age, sex, baseline kidney function, mean DBP, hypertension, diabetes mellitus, heart failure, and National Institutes of Health Stroke Scale category.

Results: Any AKI occurred in 90 patients (3.8%), stages 2–3 in 40 (1.7%), and stage 3 in 27 (1.1%). The incidence of any AKI rose from 1.2% in Q1 to 7.2% in Q4 (*p*for trend < 0.001). In the fully adjusted model, each 0.10-unit increase in the DBP-CV was associated with any AKI (adjusted odds ratio [aOR], 1.55; 95% confidence interval [CI], 1.06–2.28; *p*= 0.024); the Q4 versus Q1 DBP-CV conferred higher odds of any AKI (aOR, 3.75; 95% CI, 1.61–8.75; *p* = 0.002). Associations were attenuated after adjusting for the total number of blood pressure measurements and upon restriction of outcomes to events beyond the exposure window.

Conclusions: Greater early DBP variability during the first 72 h was independently associated with in-hospital AKI after AIS. The DBP-CV may serve as a clinically accessible marker for AKI risk stratification in this population.

Background

Acute ischemic stroke (AIS) is a common neurologic emergency, and elevated blood pressure (BP) is frequently observed at the initial presentation. In a nationally representative study of emergency departments (EDs) in the United States, a systolic BP (SBP) ≥ 140 mmHg was recorded for approximately 77% of patients with ischemic stroke [1], consistent with a contemporary review that indicated that an elevated BP is present in up to 75% of patients at the time of hospital admission [2]. Beyond its neurologic effects, AIS is also complicated by systemic events, among which acute kidney injury (AKI) is clinically important; pooled cohort evidence suggests that post-stroke AKI is associated with higher mortality and worse functional outcomes [3]. As acute-phase hemodynamics may contribute to the post-stroke AKI risk, the identification of early hemodynamic markers for risk stratification after AIS is clinically relevant.

Beyond absolute BP levels, BP variability (BPV) has emerged as a hemodynamic marker with prognostic relevance independent of the mean BP [4]. Short-term BP fluctuations may reflect autonomic instability, impaired vascular regulation, acute illness severity, treatment effects, or evolving systemic

complications. As diastolic BP (DBP) contributes to the mean arterial pressure, marked short-term DBP fluctuation may be relevant to kidney perfusion, particularly in acutely ill patients in whom kidney autoregulatory and autonomic buffering may be impaired. Consistent with this concept, short-term BPV has been associated with AKI in critically ill patients [5], surgical cohorts [6], and patients with traumatic intracranial hemorrhage (tICH) [7].

In AIS, however, evidence linking early BP patterns to AKI remains limited. In one single-center study, a higher DBP at admission was associated with AKI [8], whereas a larger pooled analysis of clinical trial data (N = 1,931) revealed no significant association between baseline SBP and AKI [9]. In both studies, however, a single admission BP value was evaluated, rather than BPV during the early hospital course. Studies of BPV in AIS have, in turn, been focused primarily on neurologic outcomes, including functional recovery [10] and cognitive impairment [11], and the association between early BPV and kidney-related outcomes has been insufficiently characterized.

Therefore, we aimed to investigate whether early DBP variability was associated with AKI in patients hospitalized with AIS. We hypothesized that greater DBP variability would be associated with a higher risk of AKI.

Methods

Study design and population

We conducted a retrospective cohort study at the Veterans Health Service Medical Center in Seoul, Republic of Korea. Consecutive adult patients admitted with AIS between April 1, 2008 and December 31, 2024, were identified from a prospectively maintained institutional stroke registry and the electronic medical records.

We excluded patients with hemorrhagic transformation of the index infarct, those who were readmitted within the study period, those on maintenance dialysis, those who underwent endovascular thrombectomy (EVT), those with meningitis, and those with community-acquired AKI (CA-AKI). Patients on maintenance dialysis were excluded because creatinine-based AKI staging is unreliable in this population; those treated with EVT were excluded to avoid confounding due to peri-procedural hemodynamic management and iodinated contrast exposure; and patients with CA-AKI, defined as AKI judged upon chart review to be present upon arrival at the ED, were excluded to ensure that all analyzed events represented AKI developing after admission.

The study was approved by the Institutional Review Board of the Veterans Health Service Medical Center (approval no. BOHUN 2025-05-011), which waived the requirement for informed consent because of the retrospective study design.

BP measurements and variability

All BP values recorded during routine clinical care in the ED, stroke unit, general ward, and intensive care unit within the first 72 h after ED arrival were extracted from the electronic medical records. The total number of BP measurements per patient during this window was recorded for descriptive and sensitivity analyses.

For each patient, the mean SBP, mean DBP, within-patient DBP standard deviation (SD), and DBP coefficient of variation (CV; the DBP SD divided by the mean DBP) were calculated. The primary exposure was 72-h DBP-CV, analyzed both as a continuous variable (per 0.10-unit increase) and as quartiles: Q1, < 0.0972; Q2, 0.0972 to < 0.1247; Q3, 0.1247 to < 0.1584; and Q4, ≥ 0.1584. The SBP-CV was calculated in the same way for sensitivity analysis. The DBP-CV was also calculated over 24- and 48-h windows for temporal sensitivity analyses.

Kidney function and definition of AKI

The baseline serum creatinine concentration was determined using a prespecified hierarchy designed to prioritize documented preadmission kidney function over surrogate or admission-based estimates, as such methods can result in bidirectional misclassification of AKI [12–14]. The most recent outpatient non-ED serum creatinine concentration measured 7–365 days before admission was used as the primary baseline value [13, 15, 16]. When no outpatient baseline measurement was available, the first ED serum creatinine concentration value was used as baseline only if a chart review revealed no evidence of AKI at presentation. Patients judged to have AKI at ED arrival were excluded because the use of the admission creatinine concentration as baseline can underestimate AKI when kidney injury is already present at hospital arrival [13, 15, 16].

The estimated glomerular filtration rate (eGFR) was calculated from the baseline serum creatinine concentration by using the 2021 Chronic Kidney Disease Epidemiology Collaboration creatinine equation (without the race coefficient) [17]. AKI was defined and staged according to the serum creatinine component of the Kidney Disease: Improving Global Outcomes (KDIGO) criteria [18]. Urine-output criteria were not applied because hourly urine output was not reliably documented outside the intensive care unit. The highest AKI stage during hospitalization was used for analysis, and the AKI onset was defined as the time at which the creatinine concentration first met the KDIGO criteria. Baseline kidney function was categorized according to the eGFR as G1–G2 (≥ 60 mL/min/1.73 m^2), G3a–G3b (30–59 mL/min/1.73 m^2), or G4–G5 (< 30 mL/min/1.73 m^2). The primary outcome was any AKI (KDIGO stages 1–3). Secondary outcomes were moderate-to-severe AKI (stages 2–3) and severe AKI (stage 3).

Covariates

Covariates were selected a priori based on clinical relevance, prior studies on AKI after stroke [3, 19], and BPV literature and methodology [4, 20, 21]. The mean DBP during the first 72 h was included to distinguish variability from the underlying BP level, consistent with methodological guidelines

emphasizing the need to account for mean BP when BP variability indices are evaluated [21]. The prespecified adjustment set comprised age; sex; baseline kidney function category; mean DBP during the first 72 h; presence of hypertension, diabetes mellitus, or heart failure; and stroke severity at admission, assessed using the National Institutes of Health Stroke Scale (NIHSS) category (0–4, 5–15, or ≥ 16).

Statistical analysis

Baseline characteristics are presented across DBP-CV quartiles as means ± SDs, medians with Q1–Q3, or counts with percentages, as appropriate. Between-quartile differences were tested using one-way analysis of variance for continuous variables and the chi-square or Fisher's exact test for categorical variables. Percentages were calculated using non-missing observations. Multivariable models were fitted using complete cases for the included covariates. Trends in the AKI incidence across quartiles were assessed using the Cochran–Armitage trend test.

Multivariable logistic regression was used to evaluate the association between the 72-h DBP-CV and AKI. The DBP-CV was entered as a continuous variable (per 0.10-unit increase) and as quartiles (with Q1 as the reference). Four progressively adjusted models were prespecified: model 1, unadjusted; model 2, adjusted for age, sex, baseline kidney function category, and mean DBP; model 3, additionally adjusted for the presence of heart failure, diabetes mellitus, and hypertension; and model 4, additionally adjusted for the NIHSS category. Model 4 was the primary, fully adjusted model.

Prespecified subgroup analyses for the primary outcome and for moderate-to-severe AKI were performed according to age (< 75 vs. ≥ 75 years), baseline eGFR (< 60 vs. ≥ 60 mL/min/1.73 m^2), sex, NIHSS category (0–4 vs. ≥ 5), and presence of hypertension, diabetes mellitus, and heart failure. The fully adjusted covariate structure was preserved within each stratum, the stratifying variable being removed. In eGFR-stratified analyses, the baseline kidney function category was replaced with the continuous eGFR. Effect modification was tested using multiplicative interaction terms.

Three prespecified sensitivity analyses were performed. First, to assess whether the association was specific to DBP variability, the 72-h SBP-CV was used instead of the DBP-CV, with the mean SBP replacing the mean DBP. Second, to account for monitoring intensity, the fully adjusted model was additionally adjusted for the total number of BP measurements obtained during the first 72 h. This analysis was interpreted with caution, as the total number of BP measurements may reflect clinical instability and could act as a collider, potentially introducing rather than removing bias. Third, to address potential reverse causality, analyses using the 24-, 48-, and 72-h DBP-CV were repeated after outcomes were restricted to AKI events occurring after the corresponding exposure window.

All tests were two-sided, with $p < 0.05$ considered statistically significant. Secondary, subgroup, and sensitivity analyses were interpreted as exploratory. Analyses were performed using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria). Generative artificial intelligence tools (ChatGPT and Claude) were used solely to assist with language editing and to support consistency checks across

the text, tables, and figures; all artificial intelligence-assisted edits were reviewed, verified, and approved by the authors.

Results

Study population and baseline characteristics

Among 2,844 patients admitted with AIS during the study period, 447 were excluded as detailed in Fig. 1. The final analytic cohort comprised 2,397 patients, stratified into quartiles of 72-h DBP-CVs (Q1–Q4; n = 599, 599, 599, and 600, respectively; cutoffs in Table 1).

Table 1
Baseline characteristics of the study sample across quartiles of 72-h DBP-CV

Characteristic	Q1	Q2	Q3	Q4	*p* value
	(n = 599)	(n = 599)	(n = 599)	(n = 600)	
Age, y	73.8 ± 9.1	75.3 ± 9.1	76.5 ± 8.9	78.2 ± 8.5	< 0.001
Female sex	92 (15.4)	114 (19.0)	114 (19.0)	130 (21.7)	0.048
Mean SBP, mmHg	138.1 ± 14.9	138.5 ± 16.7	139.3 ± 16.2	140.3 ± 18.2	0.097
Mean DBP, mmHg	78.7 ± 7.9	77.6 ± 8.8	76.2 ± 8.7	74.9 ± 10.6	< 0.001
DBP SD, mmHg	6.0 ± 1.5	8.6 ± 1.1	10.7 ± 1.4	15.2 ± 3.9	< 0.001
DBP-CV	0.076 ± 0.017	0.111 ± 0.008	0.140 ± 0.010	0.204 ± 0.046	< 0.001
Total number of BP	10 (7–13)	12 (9–19)	13 (9–24)	20 (11–34)	< 0.001
NIHSS score at admission					< 0.001
0–4	463 (77.7)	455 (76.1)	435 (73.2)	398 (66.6)	
5–15	128 (21.5)	126 (21.1)	137 (23.1)	150 (25.1)	
≥ 16	5 (0.8)	17 (2.8)	22 (3.7)	50 (8.4)	
Baseline eGFR category					0.006
G1–G2	528 (88.1)	529 (88.3)	503 (84.0)	492 (82.0)	
G3a–G3b	61 (10.2)	66 (11.0)	82 (13.7)	91 (15.2)	
G4–G5	10 (1.7)	4 (0.7)	14 (2.3)	17 (2.8)	
Hypertension	369 (61.6)	377 (62.9)	392 (65.4)	407 (67.8)	0.113
Diabetes mellitus	228 (38.1)	184 (30.7)	219 (36.7)	213 (35.5)	0.046
Heart failure	54 (9.0)	56 (9.3)	66 (11.0)	74 (12.3)	0.204

Values are presented as the mean ± SD, median (Q1–Q3), or n (%). Percentages were calculated using non-missing observations. Variables with missing data are summarized in Additional file 1. DBP-CV quartiles were defined as follows: Q1, < 0.0972; Q2, 0.0972 to < 0.1247; Q3, 0.1247 to < 0.1584; and Q4, ≥ 0.1584. p values were calculated via one-way ANOVA for continuous variables and via the chi-square test or Fisher's exact test for categorical variables.

ANOVA, analysis of variance; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; DBP-CV, coefficient of variation of diastolic blood pressure; eGFR, estimated glomerular filtration rate; NIHSS, National Institutes of Health Stroke Scale; Q, quartile; RAS, renin–angiotensin system; SBP, systolic blood pressure; SD, standard deviation

Characteristic	Q1 (n = 599)	Q2 (n = 599)	Q3 (n = 599)	Q4 (n = 600)	*p* value
Angina	18 (3.0)	15 (2.5)	16 (2.7)	15 (2.5)	0.943
Atrial fibrillation	37 (6.2)	41 (6.8)	60 (10.0)	84 (14.0)	< 0.001
Cancer	44 (7.4)	61 (10.2)	32 (5.4)	62 (10.3)	0.004
Baseline RAS inhibitor	50 (9.5)	60 (10.9)	54 (9.7)	56 (9.8)	0.870
Baseline CCB	113 (21.6)	123 (22.4)	120 (21.6)	108 (19.0)	0.522
Baseline β-blockers	11 (2.1)	15 (2.7)	23 (4.1)	30 (5.3)	0.022
Baseline diuretics	13 (2.5)	17 (3.1)	11 (2.0)	18 (3.2)	0.572
Antiplatelet agents	167 (31.9)	174 (31.7)	180 (32.4)	161 (28.3)	0.433
Anticoagulants	14 (2.7)	11 (2.0)	16 (2.9)	22 (3.9)	0.31
Antiplatelet + anticoagulant	2 (0.4)	1 (0.2)	2 (0.4)	1 (0.2)	0.82
Hemoglobin, g/dL	13.5 ± 1.9	13.4 ± 1.9	13.2 ± 2.0	13.1 ± 1.9	< 0.001
Sodium, mmol/L	138.7 ± 3.1	138.9 ± 3.5	138.8 ± 3.4	138.4 ± 4.3	0.046
Potassium, mmol/L	4.2 ± 0.6	4.2 ± 0.5	4.2 ± 0.5	4.2 ± 0.5	0.619

Values are presented as the mean ± SD, median (Q1–Q3), or n (%). Percentages were calculated using non-missing observations. Variables with missing data are summarized in Additional file 1. DBP-CV quartiles were defined as follows: Q1, < 0.0972; Q2, 0.0972 to < 0.1247; Q3, 0.1247 to < 0.1584; and Q4, ≥ 0.1584. p values were calculated via one-way ANOVA for continuous variables and via the chi-square test or Fisher's exact test for categorical variables.

ANOVA, analysis of variance; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; DBP-CV, coefficient of variation of diastolic blood pressure; eGFR, estimated glomerular filtration rate; NIHSS, National Institutes of Health Stroke Scale; Q, quartile; RAS, renin–angiotensin system; SBP, systolic blood pressure; SD, standard deviation

[Insert Table 1 here]

Baseline characteristics across the DBP-CV quartiles are shown in Table 1. The upper DBP-CV quartiles included a larger proportion of older and female patients. The patients in these quartiles also demonstrated a lower mean DBP but substantially greater within-patient DBP SD. The total number of BP measurements obtained during the first 72 h increased across quartiles, from a median of 10 (Q1–Q3, 7–13) in Q1 to 20 (Q1–Q3, 11–34) in Q4, indicating more frequent monitoring among patients with higher observed variability. Stroke severity also increased across quartiles, as reflected by the NIHSS category at admission. The proportions of patients with a baseline eGFR < 60 mL/min/1.73 m^2 and atrial fibrillation were also higher in the upper quartiles.

Incidence of AKI across 72-h DBP-CV quartiles

During hospitalization, any AKI occurred in 90 patients (3.8%), moderate-to-severe AKI in 40 (1.7%), and severe AKI in 27 (1.1%; Fig. 2). The AKI incidence increased in a graded manner across the DBP-CV quartiles. The incidence of any AKI increased from 1.2% in Q1 to 7.2% in Q4 (p for trend < 0.001). Similar graded increases were observed for moderate-to-severe AKI (0.7% to 3.2%; p for trend < 0.001) and severe AKI (0.3% to 2.3%; p for trend = 0.002).

Association between 72-h DBP-CV and any AKI

The multivariable logistic regression results are summarized in Table 2. In the fully adjusted model, each 0.10-unit increase in the 72-h DBP-CV was associated with higher odds of any AKI (adjusted odds ratio [aOR], 1.55; 95% confidence interval [CI], 1.06–2.28; p = 0.024). In the quartile analyses, the adjusted odds of any AKI increased across the DBP-CV quartiles, compared with Q1, reaching statistical significance for Q3 (aOR, 2.70; 95% CI, 1.13–6.49; p = 0.026) and Q4 (aOR, 3.75; 95% CI, 1.61–8.75; p = 0.002).

Table 2
Association of 72-h DBP-CV with any AKI after acute ischemic stroke (primary outcome)

Exposure	**Model 1**	**Model 2**	**Model 3**	**Model 4**
	OR (95% CI), *p* value	**OR (95% CI), *p* value**	**OR (95% CI), *p* value**	**OR (95% CI), *p* value**
Continuous (per 0.10-unit increase)	2.11 (1.55–2.88), < 0.001	1.92 (1.38–2.67), < 0.001	1.90 (1.35–2.65), < 0.001	1.55 (1.06–2.28), 0.024
Quartile				
Q1 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Q2	2.17 (0.88–5.37), 0.093	2.30 (0.92–5.74), 0.074	2.26 (0.91–5.65), 0.080	2.05 (0.81–5.16), 0.129
Q3	3.68 (1.58–8.58), 0.003	3.38 (1.43–7.96), 0.005	3.30 (1.40–7.80), 0.006	2.70 (1.13–6.49), 0.026
Q4	6.53 (2.91–14.63), < 0.001	5.80 (2.55–13.22), < 0.001	5.64 (2.47–12.88), < 0.001	3.75 (1.61–8.75), 0.002

The ORs and 95% CIs were estimated using logistic regression. Model 1 was unadjusted. Model 2 was adjusted for age (continuous), sex, baseline eGFR category (G1–G2, G3a–G3b, or G4–G5), and mean DBP. Model 3 was further adjusted for the presence of heart failure, the presence of diabetes mellitus, and the presence of hypertension. Model 4 was additionally adjusted for stroke severity (NIHSS category: 0–4, 5–15, or ≥ 16). Continuous DBP-CV was scaled per 0.10-unit (10%) increase. Only complete cases were included for covariate adjustment.

AKI, acute kidney injury; CI, confidence interval; CV, coefficient of variation; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; Q, quartile

[Insert Table 2 here]

Secondary analyses: AKI stages 2–3 and AKI stage 3

Associations with more severe AKI phenotypes were directionally consistent with those in the primary analysis but imprecise after full adjustment because of limited event numbers (Additional file 1). For moderate-to-severe AKI, the aOR was 1.52 (95% CI, 0.86–2.68; $p = 0.153$) per 0.10-unit increase in the DBP-CV and 2.83 (95% CI, 0.89–9.00; $p = 0.077$) for Q4 versus Q1. For severe AKI, the corresponding estimates were 1.72 (95% CI, 0.89–3.35; $p = 0.109$) and 5.49 (95% CI, 1.16–25.90; $p = 0.032$); the wide CI for the latter indicates substantial uncertainty.

Subgroup analyses

Results of the prespecified subgroup analyses for any AKI are shown in Additional file 2 and those for moderate-to-severe AKI are shown in Additional file 3. For any AKI, the association was more pronounced among patients without hypertension (aOR per 0.10-unit increase, 2.85; 95% CI, 1.46–5.54; $p = 0.002$) than that among those with hypertension (aOR, 1.12; 95% CI, 0.68–1.84; $p = 0.664$; p for interaction = 0.024). For moderate-to-severe AKI, the association was more pronounced among patients aged < 75 years (aOR, 4.37; 95% CI, 1.63–11.72; $p = 0.003$) than that in those aged ≥ 75 years (aOR, 0.89; 95% CI, 0.42–1.89; $p = 0.766$; p for interaction = 0.003). No other prespecified interaction was significant. Given the small number of events and multiple comparisons, these findings should be interpreted as exploratory.

Sensitivity analyses

Results of the three sensitivity analyses are summarized in Additional file 1. First, when the 72-h SBP-CV was substituted for the DBP-CV, it was significantly associated with any AKI as a continuous exposure (aOR per 0.10-unit increase, 2.40; 95% CI, 1.47–3.92; $p < 0.001$); however, the Q4-versus-Q1 estimate was directionally consistent without reaching significance (aOR, 1.95; 95% CI, 0.94–4.04; $p = 0.074$; Additional file 1). Second, after additional adjustment for the total number of BP measurements during the first 72 h, the DBP-CV–AKI association was substantially attenuated, both as a continuous exposure (aOR per 0.10-unit increase, 1.10; 95% CI, 0.70–1.72; $p = 0.690$) and for Q4 versus Q1 (aOR, 2.05; 95% CI, 0.85–4.99; $p = 0.112$; Additional file 1). Third, after restricting outcomes to AKI events occurring after each exposure window, the 72-h DBP-CV–AKI association was attenuated (aOR per 0.10-unit increase, 1.35; 95% CI, 0.85–2.15; $p = 0.201$); the 48-h window showed a similar pattern (unrestricted aOR, 1.52; 95% CI, 1.04–2.22; $p = 0.029$; restricted aOR, 1.33; 95% CI, 0.87–2.05; $p = 0.189$), and the 24-h DBP-CV was not significantly associated with any AKI in either analysis (Additional file 1).

Overall, the direction of association between early DBP variability and in-hospital AKI was consistent across analyses, although the magnitude was attenuated after adjustment for the total number of BP measurements and after restricting outcomes to events occurring after the exposure window.

Discussion

In this retrospective cohort of 2,397 patients with AIS, greater DBP variability during the first 72 h of hospitalization was associated with a graded increase in the incidence of in-hospital AKI, rising from 1.2% in the lowest DBP-CV quartile to 7.2% in the highest (p for trend < 0.001). After adjustment for age, sex, baseline kidney function, mean DBP, presence of comorbidities, and stroke severity, patients in Q4 had approximately 3.75-fold higher adjusted odds of any AKI, compared with those in Q1. Associations with moderate-to-severe and severe AKI showed similar trends but wider CIs. The association was attenuated after adjustment for the BP measurement frequency and after restriction to AKI events occurring beyond the 72-h exposure window, indicating that a part of the observed relationship may reflect monitoring intensity and reverse causality. As the number of BP measurements plausibly lies on the causal pathway between clinical instability and AKI, however, adjusting for this variable might have caused overadjustment, and these attenuated estimates are therefore best regarded as conservative. The early DBP-CV should thus be interpreted primarily as a readily obtainable hemodynamic indicator of AKI vulnerability, rather than as evidence that BPV itself directly causes AKI.

Several mechanisms may link early DBP fluctuations to AKI. Kidney autoregulation, mediated chiefly by the afferent-arteriolar myogenic response and tubuloglomerular feedback, stabilizes the kidney blood flow and glomerular filtration across a defined range of kidney perfusion pressures and buffers transmission of systemic pressure to the glomerular capillaries [22]. Although DBP is not equivalent to the kidney perfusion pressure, it contributes substantially to the mean arterial pressure; large or abrupt DBP fluctuations can therefore translate into transient perturbations in the kidney perfusion pressure that outpace autoregulatory buffering. When fluctuations exceed the compensatory capacity, decreases in DBP may cause repeated tubular hypoperfusion, whereas increases may be transmitted to the glomerular microcirculation when preglomerular buffering is impaired [23, 24]. The mean DBP and DBP-CV thus convey complementary information: an acceptable mean DBP can coexist with repeated short-term fluctuations that mean alone cannot capture. In AIS, autonomic dysregulation and baroreflex impairment may contribute to acute BP instability [25], and increased early BPV has been independently associated with worse short-term functional outcomes after stroke [26].

The DBP-CV–AKI association was more pronounced in patients without hypertension (p for interaction = 0.024) and, for moderate-to-severe AKI, in those aged < 75 years (p for interaction = 0.003). Pre-existing hypertension and its treatment may attenuate the kidney hemodynamic impact of acute DBP fluctuation, whereas multiple coexisting determinants of AKI in older patients may dilute its relative contribution. Stratum-specific residual confounding cannot be excluded. Because of the limited number of events and the multiple interactions tested, these subgroup associations are exploratory and warrant confirmation in larger cohorts.

Our findings extend the association between short-term BPV and AKI, previously reported in critically ill [5], perioperative [6], and tICH cohorts [7], to the context of AIS. Direct quantitative comparisons across these settings should be made with caution, given differences in pathophysiology and exposure windows. In tICH, SBP variability, rather than DBP variability, was the dominant predictor in fully adjusted models in one study [7], whereas the DBP-CV showed a robust quartile-based association in our cohort.

This divergence may reflect different dominant hemodynamic mechanisms—catecholamine-driven systolic surges after traumatic brain injury versus kidney perfusion dependent on systemic pressure in AIS. A post hoc analysis of the Systolic Blood Pressure Intervention Trial similarly found that long-term visit-to-visit DBP variability, but not SBP variability, independently predicted cardiovascular events and AKI [27]. By focusing on the short-term, in-hospital DBP-CV in the acute post-stroke period, our study reveals an early-phase candidate marker derived from routinely obtained BP measurements.

A further consideration is that the 72-h SBP-CV, when modeled as a continuous exposure, was also independently associated with any AKI (aOR per 0.10-unit increase, 2.40; 95% CI, 1.47–3.92), although the Q4-versus-Q1 comparison did not reach statistical significance. This concurrent SBP-CV association, together with the attenuation observed after adjustment for BP measurement frequency and after restriction to events occurring beyond the exposure window, suggests that the early DBP-CV likely reflects a composite signal of hemodynamic stress and broader clinical instability rather than a uniquely diastolic pathophysiologic signal. Nevertheless, the stronger and more consistent quartile-based association observed for the DBP-CV supports its potential utility as a practical, easily computed risk-stratification metric in this population.

This study has several strengths. To our knowledge, it is the first in which early in-hospital BPV was evaluated in relation to AKI in AIS, extending prior evidence based on a single admission BP value [8, 9]. The cohort was assembled from a prospectively maintained stroke registry over a 16-year period with consecutive enrollment, and the BP measurements, drawn from routine acute-phase care, reflect real-world hemodynamics. AKI was ascertained using a prespecified KDIGO criterion with a baseline creatinine hierarchy prioritizing preadmission values, and conditions likely to confound a creatinine-based AKI definition were excluded. The mean DBP was included as a covariate to separate the effect of variability from that of the absolute BP level, and prespecified sensitivity analyses were conducted to address alternative exposures, monitoring intensity, and reverse causality.

Some limitations should also be acknowledged. First, the single-center retrospective design at a Veterans Health Service hospital yielded a cohort that was older and predominantly male, which may limit the generalizability of our findings. Second, BP measurements were obtained during routine clinical care, rather than via a standardized protocol, and the measurement frequency increased across DBP-CV quartiles; we addressed monitoring-intensity bias in a prespecified sensitivity analysis, although residual bias cannot be excluded. Third, despite adjustment for prespecified covariates, including the mean DBP, residual confounding might have occurred owing to time-varying in-hospital exposures, such as nephrotoxic medications, iodinated contrast, sepsis, vasopressors, antihypertensives, and fluid management. Furthermore, because the mean DBP is less strongly related to outcomes than to the mean SBP, adjusting diastolic variability for the mean DBP alone may not fully capture the SBP level, particularly among older patients. Reassuringly, a sensitivity analysis in which we used the SBP-CV with adjustment for the mean SBP yielded directionally concordant associations. Fourth, AKI was defined using only the serum creatinine concentration criterion because hourly urine output was not reliably documented outside the intensive care unit; thus, the AKI incidence might have been underestimated.

Finally, the small numbers of stage 2–3 and stage 3 events yielded wide CIs and limited the power of severity-stratified analyses; although outcome-restricted sensitivity analyses addressed reverse causality, residual reverse causality cannot be fully excluded.

Conclusions

A greater DBP-CV during the first 72 h of hospitalization for AIS was independently associated with higher odds of in-hospital AKI after adjustment for the mean DBP, baseline kidney function, presence of comorbidities, and stroke severity. Associations with more severe AKI categories were directionally consistent but limited by event numbers, and sensitivity analyses indicate that a part of the observed relationship reflects clinical instability and monitoring intensity. As the DBP-CV can be derived from routine acute-phase BP measurements, it may serve as a clinically accessible marker of the in-hospital AKI risk. Prospective studies with standardized BP measurements, time-updated exposure assessments, and prespecified kidney outcomes are needed to determine whether early BPV provides an incremental prognostic value beyond established clinical risk factors.

Abbreviations

AIS
acute ischemic stroke
AKI
acute kidney injury
aOR
adjusted odds ratio
BP
blood pressure
BPV
blood pressure variability
CA-AKI
community-acquired acute kidney injury
CI
confidence interval
CV
coefficient of variation
DBP
diastolic blood pressure
DBP-CV
coefficient of variation of diastolic blood pressure
ED
emergency department
eGFR

estimated glomerular filtration rate
EVT
endovascular thrombectomy
KDIGO
Kidney Disease:Improving Global Outcomes
NIHSS
National Institutes of Health Stroke Scale
Q
quartile
SBP
systolic blood pressure
SBP-CV
coefficient of variation of systolic blood pressure
SD
standard deviation
tICH
traumatic intracranial hemorrhage

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The study protocol was reviewed and approved by the Institutional Review Board of Veterans Health Service Medical Center, Seoul, Republic of Korea (approval no. BOHUN 2025-05-011). The requirement for written informed consent was waived by the Institutional Review Board of Veterans Health Service Medical Center because of the retrospective study design and the use of de-identified data.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available because they contain information that could compromise the privacy of research participants but are available from the corresponding author on reasonable request and with permission from the Institutional Review Board of Veterans Health Service Medical Center, Seoul, Republic of Korea.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

WHC was a major contributor in data analysis and writing and editing of the manuscript. YL contributed to data analysis and writing of the manuscript. KK conceptualized the study. KHM, DL, HJK, and JSJ performed the investigation and reviewed the manuscript. All authors read and approved the final manuscript.

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Figures

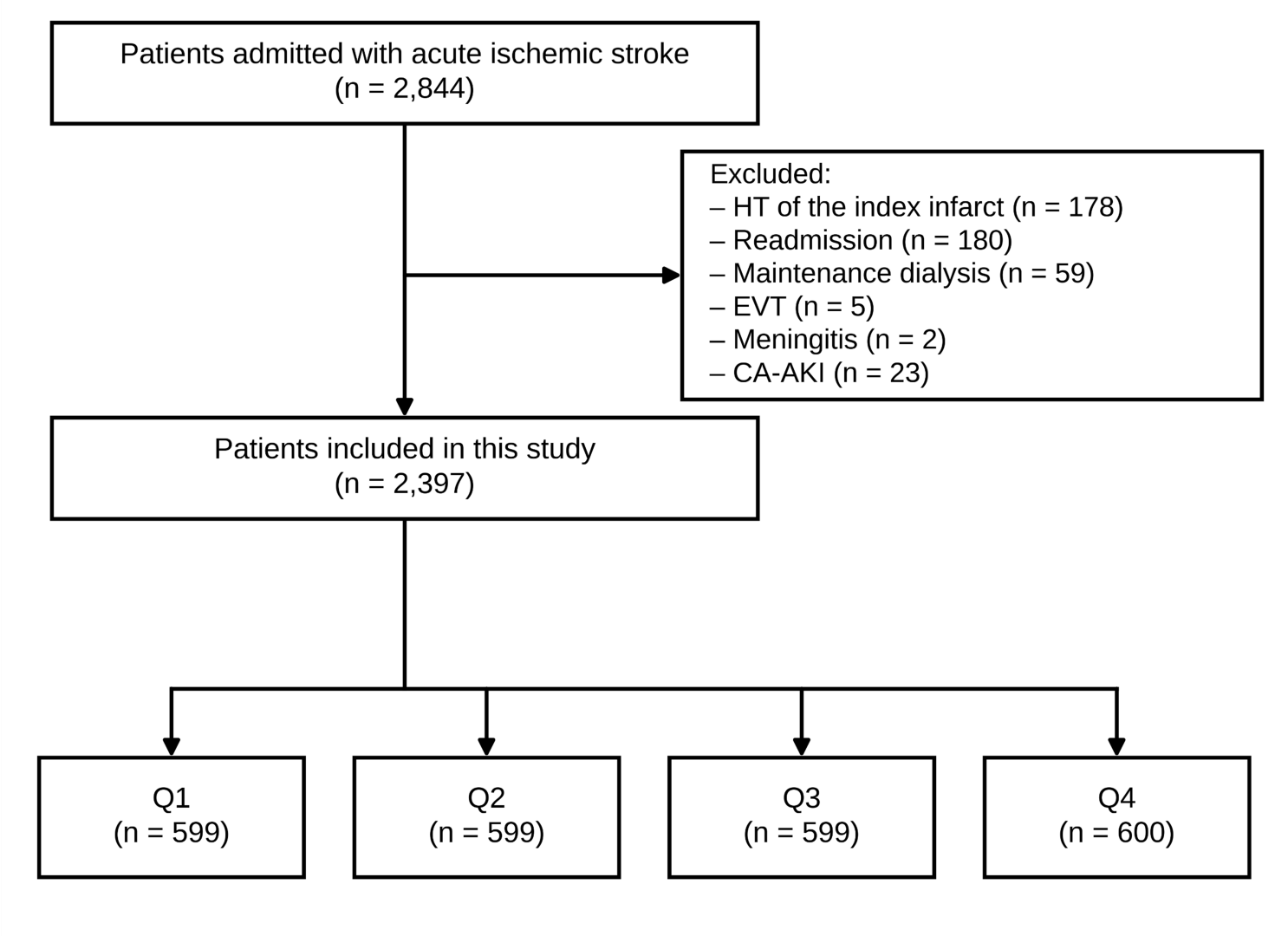


Figure 1

Flow diagram of the study population

The final analytic cohort of 2,397 patients was stratified into quartiles (Q1–Q4) according to the 72-h coefficient of variation of the diastolic blood pressure. AKI, acute kidney injury; CA-AKI, community-acquired acute kidney injury; EVT, endovascular thrombectomy; HT, hemorrhagic transformation; Q, quartile

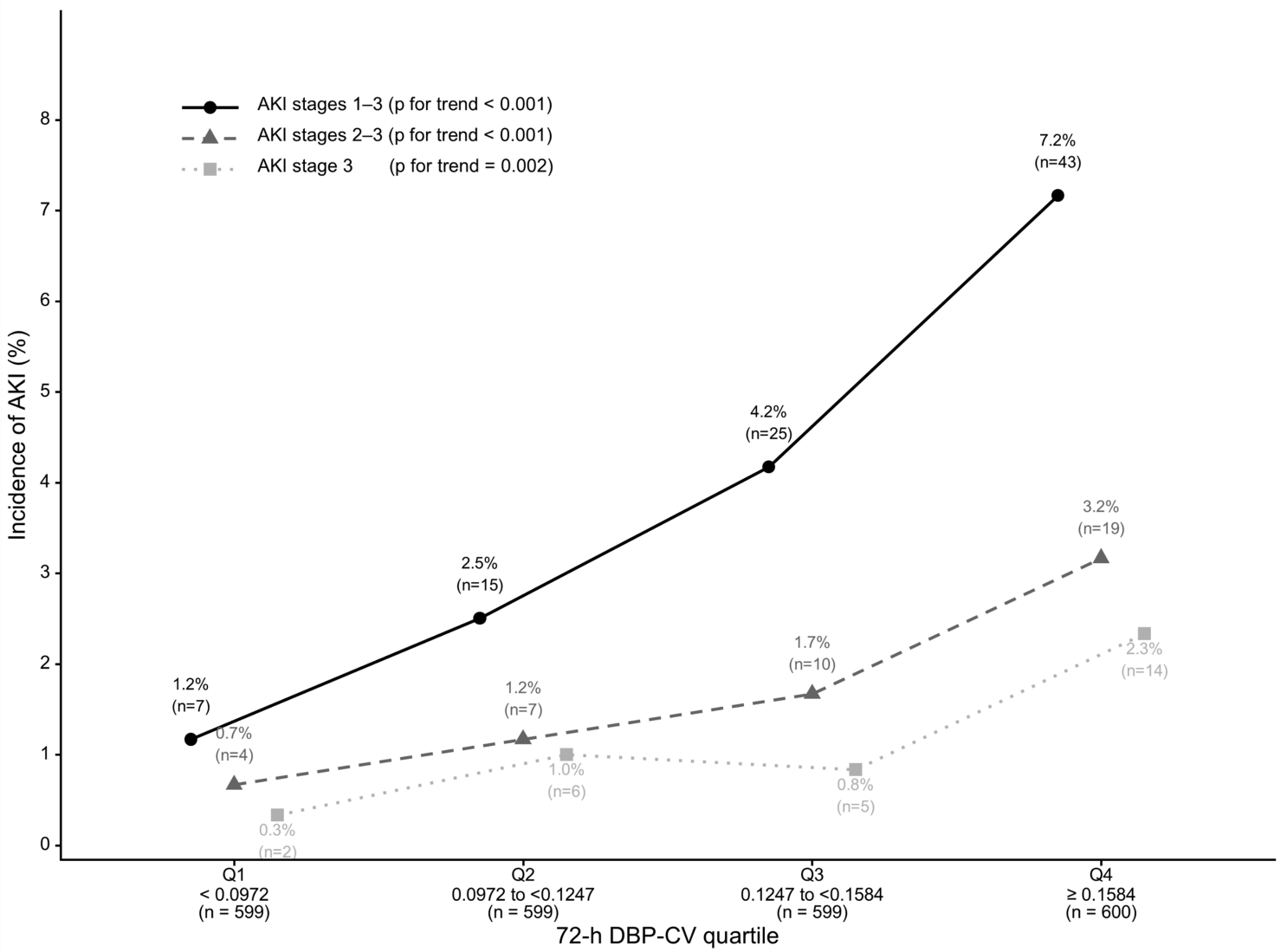


Figure 2

Incidence of AKI across quartiles of the 72-h DBP-CV

Each line shows the proportion of patients who developed any AKI (KDIGO stages 1–3), moderate-to-severe AKI (stages 2–3), and severe AKI (stage 3) within each 72-h DBP-CV quartile (Q1, < 0.0972; Q2, 0.0972 to < 0.1247; Q3, 0.1247 to < 0.1584; Q4, ≥ 0.1584; n = 599, 599, 599, and 600, respectively). DBP-CV is dimensionless (within-patient standard deviation of DBP divided by the mean DBP over the 72-h exposure window). The *p* for trend was calculated using the Cochran–Armitage trend test. AKI, acute kidney injury; CV, coefficient of variation; DBP, diastolic blood pressure; KDIGO, Kidney Disease: Improving Global Outcomes; Q, quartile

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