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Blood Pressure Control and Variability Reduction with Clevidipine in Hypertensive Intracerebral Hemorrhage (CLEVER-ICH): A Prospective Observational Study

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Research Article

Keywords: Intracerebral hemorrhage, clevidipine, blood pressure variability, hypertension, hematoma expansion, neurocritical care

Posted Date: November 12th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11393044/v1

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Abstract

Background

Acute systolic hypertension after spontaneous intracerebral hemorrhage (ICH) is associated with hematoma expansion and worse outcomes. Although rapid blood pressure lowering is recommended, the physiologic effects of clevidipine on high-frequency systolic blood pressure variability (BPV) in acute ICH remain incompletely characterized.

Methods

We conducted a single-center, prospective, open-label observational study of adults with spontaneous supratentorial ICH presenting within 12 hours of last known well who required continuous intravenous antihypertensive therapy. Clevidipine was initiated at 1 mg/hour and titrated to a target systolic blood pressure (SBP) of 130–160 mmHg. Beat-to-beat arterial SBP was recorded at 300 Hz after neurointensive care unit admission. Primary outcomes were descriptive measures of BPV before and after clevidipine initiation, including standard deviation, average real variability (ARV), and coefficient of variation (CV). Secondary outcomes included time to target SBP, time to control with stability, hematoma expansion, neurologic deterioration, hypotension exposure, and in-hospital mortality.

Results

Twenty patients were enrolled between March 2022 and February 2025. Mean age was 57.8 ± 15.4 years, 60% were female, and 70% were Black/African American. Median peak pre-enrollment SBP was 193.5 mmHg. Median time to achieve SBP 130–160 mmHg was 5.9 minutes (IQR 0.6–10.2), and median time to control with stability was 6.3 minutes (IQR 1.7–14.2). Patients remained within target SBP for a median 73.7% of infusion time. Relative hypotension (SBP < 130 mmHg) occurred during 9.6% of infusion time, whereas absolute hypotension (SBP < 90 mmHg) was rare (0.05%). Mean SBP decreased from 169.5 mmHg before infusion to 151.9 mmHg in the first hour and remained controlled through 12 hours. Standard deviation and ARV did not significantly change after clevidipine initiation, while CV increased modestly (7.1% vs 9.9%, p = 0.037). Hematoma expansion occurred in 30% and in-hospital mortality was 20%.

Conclusions

In acute spontaneous ICH, clevidipine provided rapid, sustained SBP control with minimal clinically significant hypotension and no clear increase in absolute short-term BPV. These findings support its feasibility and safety for intensive hyperacute blood pressure management.

Introduction

Arterial hypertension in the acute setting following acute intracerebral hemorrhage (ICH) is common and associated with a higher risk of hematoma expansion (HE) and poor outcomes.[1–3] Rapid and systolic blood pressure (SBP) reduction, particularly when achieved within 60 minutes and maintained during the first 24 hours, has been associated with improved outcomes.[4,5] Consequently, prompt blood pressure reduction has become a central component of modern ICH management.

Recent evidence suggests that the effectiveness of blood pressure management extends beyond attainment of a predefined SBP target alone. Post-hoc analyses of INTERACT2 and other contemporary cohorts have demonstrated that rapid achievement of target SBP, intensive blood pressure reduction, and sustained maintenance of SBP control during the first 24 hours are associated with lower rates of hematoma expansion, reduced early neurologic deterioration, and improved long-term functional outcomes. [4–6] These findings have shifted attention from the magnitude of blood pressure reduction alone to the speed and stability with which blood pressure targets are achieved.

In parallel, increasing evidence suggests that blood pressure variability (BPV) may independently influence neurologic outcomes following ICH. Several studies have demonstrated consistent associations between greater short-term SBP variability during the acute phase of ICH and increased risks of hematoma expansion, mortality, and poor functional recovery, even after adjustment for mean SBP levels. [7–9] These observations raise the possibility that an ideal antihypertensive strategy in acute ICH should rapidly lower SBP while minimizing excessive fluctuations that could contribute to secondary brain injury. However, detailed physiologic characterization of BPV during continuous intravenous antihypertensive therapy remains limited, particularly when assessed using high-frequency arterial blood pressure recordings.

Although intravenous antihypertensive therapy is a cornerstone of acute ICH management, current guidelines generally emphasize timely achievement and maintenance of SBP targets rather than recommending one specific intravenous agent over another.[10] Accordingly, titratable continuous intravenous (IV) dihydropyridine (DHP) L-type calcium channel antagonists, such as nicardipine and clevidipine, are both used in contemporary practice, despite their unique pharmacokinetic profiles. This reflects ongoing clinical equipoise regarding whether one agent provides superior BP control, reduced BPV, or improved clinical outcomes in this setting. This uncertainty underscores the importance of better characterizing the physiologic effects of individual antihypertensive agents during the hyperacute period after ICH.

Clevidipine is an ultra-short-acting IV DHP calcium channel antagonist characterized by a rapid onset of action, predictable dose-response relationship, and an elimination half-life of approximately one minute. [11] These pharmacokinetic properties allow for rapid titration and precise blood pressure control, making clevidipine an attractive therapeutic option for acute ICH. In the ACCELERATE trial, clevidipine monotherapy was safe and effective at reducing elevated SBP in a cohort of ICH patients.[12] We

hypothesized that, due to its pharmacokinetic properties (i.e., quick onset and short duration of action), clevidipine infusion would rapidly achieve and maintain a narrow target SBP range and minimize BPV during the acute ICH period.

The main objective of this study was to leverage high-frequency time series physiologic monitoring to describe systolic BPV in critically ill ICH patients treated with clevidipine for SBP reduction. Furthermore, we aimed to determine rates of HE, neurologic deterioration, in-hospital mortality, and overall safety. Lastly, as a new large, multicenter study of SBP control with stability comparing nicardipine and clevidipine in ICH has opened for enrollment (NCT06402968), we wanted to explore the feasibility and the time to achieve the novel proposed SBP endpoint.[13]

Methods

This was a single-center, single-arm, open-label, prospective observational study that enrolled hypertensive ICH patients and was conducted at the Cleveland Clinic Main Campus from March 1, 2022, to February 28, 2025.

Inclusion and Exclusion Criteria

Adult hypertensive patients aged 18 years and older with acute spontaneous ICH confirmed on computed tomography imaging (CT scan) and presenting within 12 hours of last known well were screened for eligibility. Patients were considered for inclusion if, in the judgment of the clinical team, continuous IV antihypertensive therapy was required to achieve and maintain a target SBP of 130 to 160 mmHg.

Exclusion criteria included prior treatment with another continuous IV antihypertensive infusion; ICH secondary to anticoagulation, vascular malformation, trauma, or underlying neoplasm; infratentorial hemorrhage; or planned surgical hematoma evacuation. Additional exclusions include a history of defective lipid metabolism (i.e. pathologic hyperlipidemia), allergy to soybeans or eggs, severe aortic stenosis, heart failure, known or suspected aortic dissection, or pheochromocytoma.

Patients who met all inclusion criteria, had no exclusion criteria, and for whom the treating team elected to initiate continuous clevidipine infusion for BP management were included in the study. Given the acute need for rapid SBP reduction, the clinical equipoise between clevidipine and nicardipine, and the FDA-approved use of clevidipine for this indication, the local Institutional Review Board approved a waiver of consent for this observational study. Instead, patients or their legally authorized representative (LAR) were given an information sheet describing the study and the data being collected and were given the opportunity to decline participation or withdraw from the study at any time.

Clinical Care

Patients were admitted to the Neurointensive Care Unit (NICU) of a comprehensive Stroke Center and managed by a multidisciplinary team consisting of neurointensivists, vascular neurologists, neurosurgeons, and clinical pharmacists. Given the perceived equipoise between clevidipine and nicardipine, the choice of continuous intravenous antihypertensive agent was left to the discretion of the treating team. During the study period, institutional guidelines recommended a targeted SBP goal of 130–160 mmHg following acute spontaneous ICH. Otherwise, clinical care followed published AHA/ASA guidelines for the management of acute, non-traumatic spontaneous ICH.[10]

Admission blood pressure was defined as the first blood pressure recorded since last known well. All SBP values prior to admission to the NICU were recorded as per standard of care. Upon NICU admission, an arterial catheter was placed for continuous blood pressure monitoring. Beat-to-beat SBP data were acquired at a sampling frequency of 300Hz using Intensive Care Monitoring (ICM +) software platform (Cambridge Enterprise, Cambridge, United Kingdom).

Clevidipine was initiated at a rate of 1mg/hr and titrated by doubling the infusion rate every 90 seconds until the target SBP range was achieved or a maximum dose of 21mg/hour was reached. Once the target SBP target was attained, the infusion rate was maintained without further adjustment and continued for up to 12 hours or until continuous intravenous antihypertensive therapy was no longer clinically indicated. Rescue intravenous injection therapies (e.g., labetalol, hydralazine) were permitted before and during clevidipine administration per standard of care. If additional continuous intravenous antihypertensive therapy were required, patients were transitioned to nicardipine according to institutional practice. Blood pressure measurements obtained after initiation of a second continuous antihypertensive infusions were excluded from analyses to the primary endpoint. Oral antihypertensive medications were initiated within the first 24 hours as clinically appropriate.

Demographics data as well as admission Glasgow coma scale (GCS) score, National Institutes of Health Stroke Scale (NIHSS) score, ICH score, and pre-morbid as well as discharge modified Rankin scale (mRS) score were collected. Follow up NIHSS and GCS scores were recorded at the 12-hour mark following initiation of continuous clevidipine intravenous infusion.

Neuroimaging Analysis

Non-contrasted head CT was performed at baseline and approximately six hours after presentation in accordance with institutional ICH protocols. Additional neuroimaging, including CT angiography, magnetic resonance imaging, and digital subtraction angiography, was obtained at the discretion of the treating team to evaluate secondary causes of hemorrhage. All imaging studies were reviewed by a board-certified neuroradiologist.

Hematoma volume was quantified on baseline and follow-up non-contrast CT scans using semi-automated volumetric segmentation performed with Siemens Syngo.via software (Siemens Healthineers, Erlangen, Germany). Regions of ICH were manually reviewed and edited as necessary by

trained study personnel blinded to clinical outcomes. Hematoma expansion was defined as a relative increase in hematoma volume ≥ 33% between baseline and follow-up CT imaging.

Statistical Analysis

Patient demographics and clinical characteristics were summarized by mean with standard deviation or median with interquartile range for continuous variables and frequency with percentage for categorical variables. The primary outcome was to describe measures of BPV in hypertensive ICH patients treated with continuous clevidipine infusion for BP control. Additional outcomes included time to goal BP, rates of hematoma expansion, and neurologic deterioration during the time of clevidipine infusion.

Time from clevidipine infusion to SBP within 130-160mmHg and time from clevidipine infusion to maintaining SBP ≤ 160 mmHg for ≥ 5 minutes were identified. Percent of time out of total infusion time where SBP within 130–160 mmHg, SBP < 130 mmHg and SBP < 90 mmHg were calculated.

Blood pressure variability was examined by mean, standard deviation, average real variability and coefficient of variation prior to clevidipine infusion, and within 1, 6, and 12 hours since infusion. Those measures were calculated for each patient and then summarized across patients. Average real variability was calculated as the average of absolute difference between successive blood pressure values. Coefficient of variation was calculated as standard deviation divided by mean.

Control with stability was achieved if SBP was within 130-160mmHg and maintained within 130-160mmHg at subsequent 15-min and 30-min time point. The median SBP within 13-17min was used as the SBP value for 15-min time point, and the median SBP within 28-32min was used as the SBP value for 30-min time point. Time from clevidipine infusion to control with stability was identified. Blood pressure variability between baseline and first hour after clevidipine infusion was compared using paired t-tests.

All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, NC).

Results

Study Population

Twenty patients with acute spontaneous ICH were enrolled between March 2022 and February 2025. The mean age was 57.8 ± 15.4 years, 60.0% were female, and 70.0% identified as Black/African American. Median admission ICH volume was 9.7 mL (IQR 5.8–18.1), increasing to 10.0 mL (IQR 6.6–22.9) on the 6-hour follow-up CT scan. Half of patients (50.0%) had intraventricular hemorrhage, and the majority of hemorrhages were located in deep brain structures (85.0%). Median admission Glasgow Coma Scale (GCS) score was 14.0 (IQR 11.5–15.0) and median NIHSS score was 13.5 (IQR 6.0–20.5). Prior to enrollment, the highest recorded mean systolic blood pressure (SBP) was 193.5 mmHg (IQR 180.0–212.0).

Blood Pressure Control Following Clevidipine Initiation

Clevidipine achieved rapid blood pressure reduction following infusion initiation. The median time to achieve the target SBP range of 130–160 mmHg was 5.9 minutes (IQR 0.6–10.2). Nearly half of patients (45%) reached target SBP within 5 minutes, while 75% achieved target within 10 minutes. The median time to achieve and maintain an SBP ≤ 160 mmHg for at least 5 minutes was 16.2 minutes (IQR 11.5–27.3). Median clevidipine infusion duration was 719 minutes (IQR 619.0–723.8), and the median maximum infusion dose reached 21 mg/hr (IQR 15.0–21.0).

Patients remained within the target SBP range for a median of 73.7% (IQR 62.5–87.7) of the total clevidipine infusion duration. Relative hypotension (SBP < 130 mmHg) occurred during a median of 9.6% (IQR 3.3–12.8) of infusion time, whereas absolute hypotension (SBP < 90 mmHg) was rare, occurring during only 0.05% (IQR 0.03–0.07) of infusion time.

Control with stability, defined as achieving the target SBP and maintaining it at subsequent 15- and 30-minute assessments, was achieved after a median of 6.3 minutes (IQR 1.7–14.2). Following achievement of control with stability, patients remained within the target range for a median of 70.6% and 78.3% of the subsequent 15- and 30-minute intervals, respectively.

Blood Pressure Variability

The median patient-level mean SBP decreased from 169.5 mmHg (IQR 159.2–184.0) prior to clevidipine initiation to 151.9 mmHg (IQR 147.7–160.3) during the first hour, with sustained reductions observed at 6 hours (148.2 mmHg, IQR 146.1–149.8) and 12 hours (147.7 mmHg, IQR 145.2–150.7).

Figure 1 demonstrates a rapid decline in mean SBP during the first 10–15 minutes after clevidipine initiation, followed by sustained maintenance within the target range throughout the remainder of the first hour. Average real variability (ARV) remained low throughout the observation period, with no evidence of marked oscillatory blood pressure behavior.

When baseline systolic blood pressure variability was compared with the first hour after clevidipine initiation, no significant differences were observed in standard deviation (11.9 ± 4.9 vs. 15.1 ± 6.9 mmHg; p = 0.10) or average real variability (4.8 ± 5.8 vs. 5.0 ± 6.3 mmHg; p = 0.75). However, variability relative to the mean SBP was slightly higher after clevidipine initiation, as reflected by an increase in the coefficient of variation from 7.1 ± 3.1% to 9.9 ± 4.3% (p = 0.037).

Clinical Outcomes

Despite presenting with severe hypertension (median peak SBP 193.5 mmHg) and moderate neurologic injury (median admission NIHSS 13.5, GCS 14), the cohort experienced relatively favorable early radiographic outcomes, with hematoma expansion occurring in 30% of patients. As seen in Fig. 2, most patients demonstrated stable hematoma volumes between baseline and the 6-hour follow-up CT scan,

with only a small subset exhibiting substantial interval expansion. Median ICU and hospital lengths of stay were 4.0 days (IQR 2.0–15.5) and 11.0 days (IQR 5.5–17.5), respectively. At discharge, the median modified Rankin Scale score was 4.0 (IQR 2.0–6.0), and in-hospital mortality was 20%. Among survivors, over half were discharged either home (20%) or to an acute inpatient rehabilitation facility (35%). Neurologic examination remained generally stable during the first 12 hours following clevidipine initiation, with only modest changes in median GCS (14 to 12) and NIHSS (13.5 to 14.0).

Discussion

In this prospective observational study of patients with acute spontaneous ICH, clevidipine achieved rapid and sustained systolic blood pressure (SBP) control with a low incidence of clinically significant hypotension. The median time to achieve the target SBP range of 130–160 mmHg was less than six minutes, and three-quarters of patients reached target within ten minutes of infusion initiation. In addition, patients remained within the desired SBP range for nearly three-quarters of the total infusion duration, supporting the ability of clevidipine to provide both rapid reduction and sustained control of blood pressure during the hyperacute phase of ICH.

Rapid blood pressure reduction has emerged as an important therapeutic target following spontaneous ICH. Post-hoc analyses of INTERACT2 and more recently Rodriguez-Luna and colleagues have demonstrated that early, intensive, and sustained SBP control is associated with reduced hematoma expansion and improved functional outcomes.[6,7,14,15] While prior investigations have largely focused on achievement of specific SBP thresholds, there has been increasing recognition that the quality and stability of blood pressure control may be equally important.[9,16] Our findings suggest that clevidipine's pharmacokinetic profile, characterized by an ultra-short half-life and rapid titratability, is particularly well suited to achieving this therapeutic goal. Notably, control with stability was achieved at a median of 6.3 minutes, a finding that aligns closely with the proposed endpoint of ongoing multicenter investigations evaluating rapid SBP control strategies in ICH.[12]

Blood pressure variability (BPV) has emerged as an independent predictor of poor neurologic outcome after ICH.[7, 9,16] Prior analyses from INTERACT2, ATACH-2, and other cohorts have demonstrated associations between increased BPV and hematoma expansion, early neurologic deterioration, mortality, and disability.[1,7–9] Given concerns that rapid antihypertensive titration may inadvertently increase short-term BPV, we specifically examined high-frequency arterial blood pressure recordings before and after clevidipine initiation.

Several measures of blood pressure variability were analyzed (Table 3). Standard deviation reflects the overall dispersion of SBP values around the mean, average real variability reflects the average absolute change between consecutive SBP measurements and may better capture short-term instability, and coefficient of variation reflects variability relative to the mean SBP. In our cohort, the coefficient of variation increased modestly during the first hour of treatment, whereas neither standard deviation nor average real variability changed significantly. Taken together, these findings suggest that absolute SBP

fluctuations did not meaningfully worsen after clevidipine initiation, and that the observed increase in coefficient of variation likely reflects variability in relation to a lower achieved mean SBP rather than a clear increase in clinically important hemodynamic instability. This interpretation is supported by Fig. 1, which demonstrates a rapid decline in mean SBP without evidence of excessive oscillation or rebound hypertension.

Table 1
Demographics and clinical characteristics of the study sample

Age	**Statistics (N = 20)**
	57.8 ± 15.4
Gender	
Female	12 (60.0)
Male	8 (40.0)
Race	
White	6 (30.0)
Black/African American	14 (70.0)
BMI	33.2 ± 11.8
Intraventricular Hemorrhage	
No	10 (50.0)
Yes	10 (50.0)
Discharge disposition	
Acute rehab facility	7 (35.0)
Home w/ self-care	4 (20.0)
Long term acute care	3 (15.0)
Passed away	4 (20.0)
SNF	1 (5.0)
checked out AMA	1 (5.0)
Admission ICH	9.7 [5.8, 18.1]
ICH Location	
Deep	17 (85.0)
Lobar	3 (15.0)
ICH Volume at 6 hours	10.0 [6.6, 22.9]
Admission GCS	14.0 [11.5, 15.0]
GCS at 12 hours	12.0 [10.0, 15.0]
Admission NIHSS	13.5 [6.0, 20.5]
Statistics presented as Mean ± SD, Median [P25, P75], N (column %).	

Age	**Statistics (N = 20)**
	57.8 ± 15.4
NIHSS at 12 hours	14.0 [8.0, 18.5]
Baseline mRS	0.0 [0.0, 1.5]
Discharge mRS	4.0 [2.5, 5.5]
ICU Length of Stay (Days)	4.0 [2.0, 15.5]
Hospital length of stay (Days)	11.0 [5.5, 17.5]
Highest SBP prior to enrollment	193.5 [180.0, 212.0]
Hematoma Expansion (> 33%)	6 (30.0)
Statistics presented as Mean ± SD, Median [P25, P75], N (column %).	

Table 2
Summary of Clevidipine infusion and blood pressure variability

Time (minutes) to SBP 130-160mmHg from the initiation of Clevidipine infusion, median [Q1, Q3]	**Statistics (N = 20)**
	5.9 [0.60, 10.2]
Patients achieved SBP 130-160mmHg within 5 minutes of Clevidipine initiation, n (%)	9 (45.0)
Patients achieved SBP 130-160mmHg within 10 minutes of Clevidipine initiation, n (%)	15 (75.0)
Time (minutes) to achieve SBP ≤ 160mmHg for ≥ 5 minutes from the initiation of Clevidipine infusion, median [Q1, Q3]	16.2 [11.5, 27.3]
Percent of time (%) SBP 130-160mmHg out of total time while on Clevidipine infusion, median [Q1, Q3]	73.7 [62.5, 87.7]
Percent of time (%) SBP < 130mmHg (relative hypotension) out of total time while on Clevidipine infusion, median [Q1, Q3]	9.6 [3.3, 12.8]
Number (seconds) of relative hypotension events while on Clevidipine infusion, median [Q1, Q3]	1631.0 [359.0, 4720.0]
Percent of time (%) SBP < 90mmHg (absolute hypotension) out of total time while on Clevidipine infusion, median [Q1, Q3]	0.05 [0.03, 0.07]
Number (seconds) of absolute hypotension events while on Clevidipine infusion, median [Q1, Q3]	14.5 [5.0, 25.5]
Average SBP prior to Clevidipine initiation, median [Q1, Q3]	169.5 [159.2, 184.0]
Maximum SBP within 30 minutes before Clevidipine initiation, median [Q1, Q3]	197.5 [180.2, 206.7]
Minimum SBP within 30 minutes of Clevidipine initiation, median [Q1, Q3]	90.4 [74.2, 122.8]
Maximum Clevidipine dose (mg/hr), median [Q1, Q3]	21.0 [15.0, 21.0]
Duration of Clevidipine infusion (minutes), median [Q1, Q3]	719.0 [619.0, 723.8]
Blood Pressure Variability, median [Q1, Q3]	
Prior to Clevidipine initiation	
Mean	169.5 [159.2, 184.0]
Standard Deviation	11.3 [7.7, 14.0]
Average Real Variability	2.4 [2.0, 3.3]

Statistics presented as Mean ± SD, Median [P25, P75], N (column %). Average real variability = Average of absolute difference between successive blood pressure values. Coefficient of variation = Standard deviation/mean

Time (minutes) to SBP 130-160mmHg from the initiation of Clevidipine infusion, median [Q1, Q3]	**Statistics (N = 20)**
	5.9 [0.60, 10.2]
Coefficient of Variation (%)	6.8 [4.5, 8.4]
Within First hour after Clevidipine initiation	
Mean	151.9 [147.7, 160.3]
Standard Deviation	13.1 [10.1, 20.2]
Average Real Variability	2.4 [1.8, 4.6]
Coefficient of Variation (%)	8.8 [6.7, 13.0]
Within First 6 hours after Clevidipine initiation	
Mean	148.2 [146.1, 149.8]
Standard Deviation	13.2 [9.9, 17.9]
Average Real Variability	2.4 [1.9, 3.5]
Coefficient of Variation (%)	9.0 [6.8, 12.1]
Within First 12 hours after Clevidipine initiation	
Mean	147.7 [145.2, 150.7]
Standard Deviation	14.8 [10.1, 16.9]
Average Real Variability	2.6 [2.0, 3.4]
Coefficient of Variation (%)	10.2 [7.0, 11.1]
Time (minutes) to achieve control with stability from the initiation of Clevidipine infusion, median [Q1, Q3]	6.3 [1.7, 14.2]
Percent of time (%) SBP 130-160mmHg within 15 minutes of control with stability, median [Q1, Q3]	70.6 [50.0, 93.4]
Percent of time (%) SBP 130-160mmHg within 30 minutes of control with stability, median [Q1, Q3]	78.3 [67.9, 93.8]
Statistics presented as Mean ± SD, Median [P25, P75], N (column %). Average real variability = Average of absolute difference between successive blood pressure values. Coefficient of variation = Standard deviation/mean	

Table 3
Comparison of Blood Pressure Variability between baseline and first hour after Clevidipine infusion

Standard Deviation	Baseline (prior to Clevidipine)	Within First hour after Clevidipine initiation	p-value
	11.9 ± 4.9	**15.1 ± 6.9**	**0.10**
Average Real Variability	4.8 ± 5.8	5.0 ± 6.3	0.75
Coefficient of Variation (%)	7.1 ± 3.1	9.9 ± 4.3	**0.037**

Statistics presented as Mean ± SD. p-value: paired t-test. *One patient was excluded given only one record of SBP prior to Clevidipine infusion

Safety remains a critical consideration when implementing intensive blood pressure lowering strategies after ICH. Excessive blood pressure reduction may theoretically impair cerebral perfusion and contribute to secondary ischemic injury. In the present study, exposure to absolute hypotension (SBP < 90 mmHg) was exceedingly uncommon, accounting for only 0.05% of infusion time. Relative hypotension (SBP < 130 mmHg) occurred more frequently but still represented less than 10% of total treatment time. These findings are reassuring and support previous observations from the ACCELERATE trial demonstrating the safety of clevidipine in acute ICH populations.[12]

The observed hematoma expansion rate of 30% is generally consistent with rates reported in prior studies of spontaneous ICH despite enrollment of a cohort characterized by severe hypertension and moderate neurologic deficits (Fig. 2). Although this study was not designed or powered to evaluate clinical efficacy, the relatively low exposure to uncontrolled hypertension combined with rapid achievement of target SBP suggests that clevidipine may represent an attractive strategy for minimizing the period of highest hematoma expansion risk. Future comparative studies will be required to determine whether these physiologic advantages translate into improvements in radiographic or clinical outcomes.

Several limitations should be acknowledged. First, this was a single-center observational study with a relatively small sample size, limiting generalizability and precluding robust assessment of clinical outcomes. Second, there was no concurrent nicardipine control group, preventing direct comparison between antihypertensive agents. Third, treatment selection was determined by the clinical team, introducing the possibility of selection bias. Finally, while high-frequency physiologic monitoring allowed detailed characterization of BPV, the study was not powered to evaluate associations between BPV metrics and hematoma expansion, mortality, or functional outcomes. Despite these limitations, the present study provides one of the most detailed physiologic descriptions of clevidipine use in acute ICH using high-resolution arterial blood pressure monitoring.

Conclusion

Clevidipine achieved rapid blood pressure reduction, sustained target-range control, and minimal exposure to clinically significant hypotension in critically ill patients presenting with acute ICH. These findings support the feasibility and safety of clevidipine as a strategy for intensive blood pressure management following spontaneous ICH and provide important preliminary data for ongoing comparative effectiveness studies evaluating optimal antihypertensive therapy in this population.

Declarations

Authors Conflict of Interest:

Catherine E. Hassett DO, MS – No Conflicts of Interest

Christine Ahrens PharmD – No Conflicts of Interest

Grace Conroy PharmD – No Conflicts of Interest

Yadi Li MS – No Conflicts of Interest

Brittany Lapin PhD – No Conflicts of Interest

Sydney M. Moseley MD – No Conflicts of Interest

Justin Lindsay BS – No Conflicts of Interest

Anjan Nagesh Ballekere MS – No Conflicts of Interest

Joao A. Gomes MD – No Conflicts of Interest

Author Contributions: Catherine Hassett: Conceptualization, study design, data interpretation, manuscript drafting, and critical revision. Christine Ahrens: Conceptualization, study design, data interpretation, data collection, manuscript drafting. Grace Conroy: Conceptualization, study design, data interpretation, manuscript drafting, and critical revision. Yadi Li: Statistical analysis, data management, data interpretation, and critical revision. Brittany Lapin: Statistical analysis, data management, data interpretation, and critical revision. Yadi Li: Statistical analysis, data management, data interpretation, and critical revision. Justin Lindsay: Data collection. Syndey Moseley: Data collection. Anjan Ballekere: data collection, data management. Joao Gomes: Conceptualization Study design, data interpretation, manuscript drafting and editing, and critical revision. All authors reviewed and approved the final manuscript.

Authorship Statement: All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship, have made substantial intellectual contributions to the work, approved the final version of the manuscript, and agree to be accountable for all aspects of the work. The authors confirm that this manuscript complies with all Instructions for Authors, including requirements for manuscript preparation, ethical conduct, authorship, conflict of interest disclosure, and reporting standards.

Prior Publication: The authors certify that this manuscript has not been previously published, except in abstract form if applicable, and is not under consideration for publication elsewhere.

Artificial Intelligence (AI) Disclosure: The authors confirm that no artificial intelligence (AI) tools, including generative AI or large language models, were used in the study design, data collection, statistical analysis, interpretation of results, manuscript preparation, or editing.

Ethical Approval: This study was conducted in accordance with the Declaration of Helsinki and applicable institutional regulations. The study was approved by the Cleveland Clinic Institutional Review Board (IRB 21-958). Given the need for rapid SBP reduction, clinical equipoise between clevidipine and nicardipine, and FDA approval of clevidipine, the Institutional Review Board approved a waiver of consent, with patients or their legally authorized representatives provided an information sheet and the opportunity to decline or withdraw participation at any time.

Funding: This investigator-initiated study was supported by Chiesi USA. Financial support totaling $100,000 was provided for research coordinator support and data analysis. In-kind drug support was also provided for use of the study.

Reporting Guidelines: The authors confirm adherence to the appropriate reporting guideline (STROBE Checklist) for this observational cohort study.

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Figures

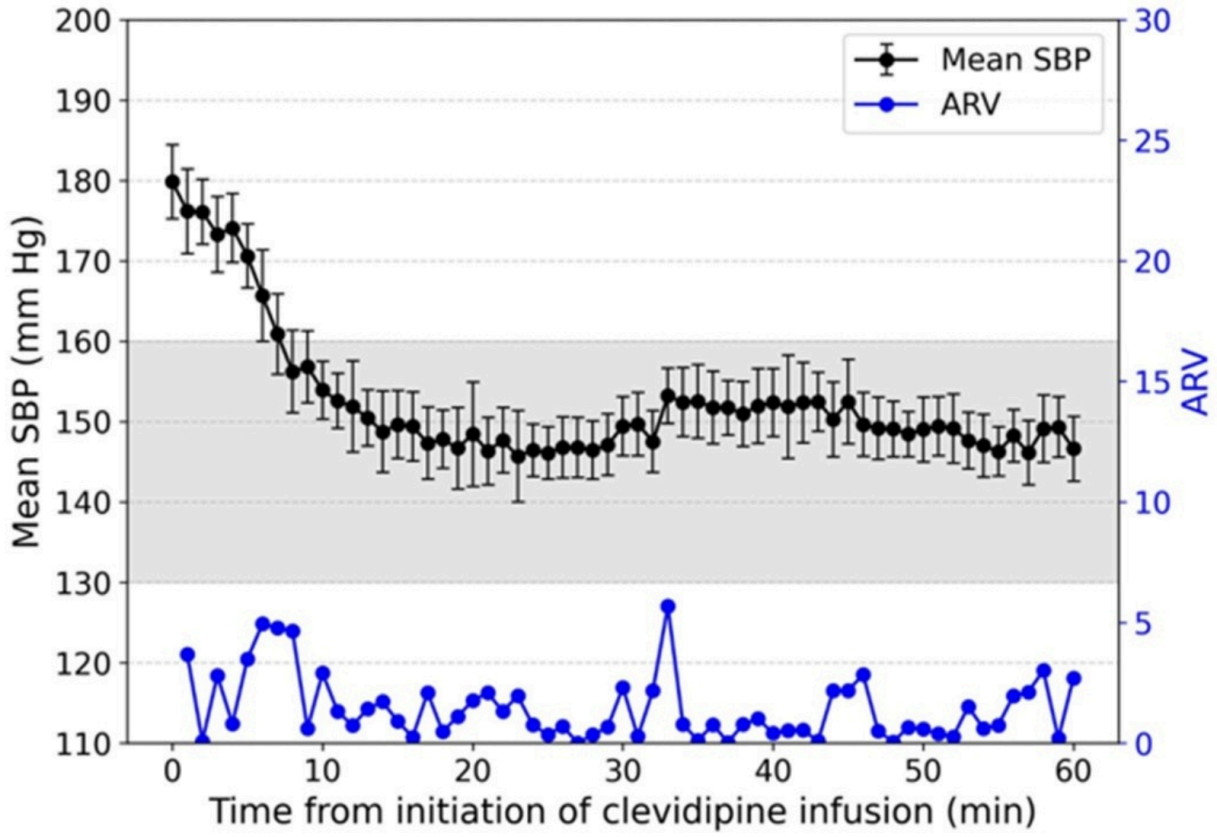


Figure 1

Rapid systolic blood pressure reduction and maintenance of low blood pressure variability during the first hour of clevidipine infusion. Mean systolic blood pressure (SBP, black circles) and average real variability (ARV, blue circles) during the first 60 minutes following initiation of continuous clevidipine infusion in patients with spontaneous intracerebral hemorrhage. Error bars represent standard error of the mean. The shaded gray region denotes the target SBP range (130–160 mmHg). Mean SBP declined rapidly into the target range within the first 10–15 minutes and remained stable thereafter, while ARV remained low throughout the observation period without evidence of excessive blood pressure oscillation.

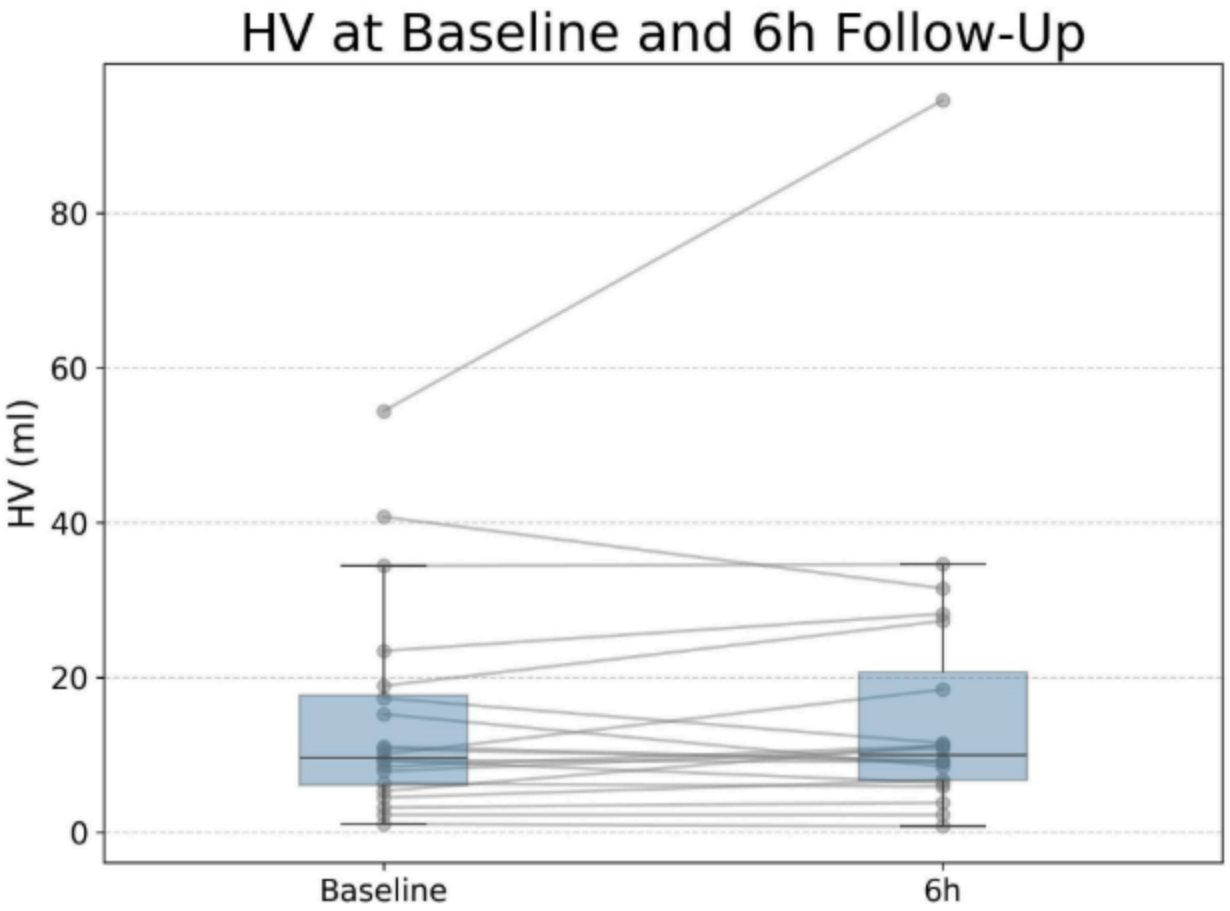


Figure 2

Individual changes in hematoma volume from baseline to the 6-hour follow-up CT scan. Paired hematoma volumes measured on baseline and 6-hour follow-up non-contrast CT scans. Gray lines connect individual patients, illustrating within-patient changes in hematoma volume over time. Boxplots display the median and interquartile range, with whiskers representing the distribution of observations. Most patients demonstrated stable hematoma volumes, whereas a minority experienced substantial interval hematoma expansion, consistent with the observed hematoma expansion rate of 30%.

Supplementary Files

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