Blood pressure variability and clinical outcome in patients with acute intracerebral hemorrhage

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Abstract

Objective: The aim of this study was to evaluate whether fluctuations of BP levels occurring in the acute stage of spontaneous intra-cerebral hemorrhage (ICH) affect the 3-month clinical outcome.

Methods: We retrospectively identified consecutive patients hospitalized for acute spontaneous ICH. BP measurements over the first 72 hours from onset of symptoms were recorded, and SD, coefficient of variation (CV) and maximum-minimum difference (Max-Min) were determined to characterize both systolic and diastolic BP variability (BPV). The measure of outcome was the 3-month functional status assessed by the modified Rankin Scale following a baseline severity-adjusted analysis.

Results: Among the 138 enrolled patients with ICH, 67 (48.6%) were classified as having a poor 3-month functional recovery. A dose response-relationship with poor outcome was found for each measure of systolic BPV (adjusted ORs for the highest thirds of SD 7.95 [95% CI 2.88-21.90], CV 7.74 [95% CI 2.88-20-80] and Max-Min 8.36 [95% CI 2.72-25.62]; $p<0.001$). The strength of association with diastolic BPV turned out to be weaker and significant only for the higher values (adjusted ORs for the highest thirds of SD 6.74 [95% CI 2.52-18.04], CV 4.57 [95% CI 1.77-11.81] and Max-Min 4.34 [95% CI 1.72-10.93]).

Conclusions: In patients with acute ICH, BPV was a strong predictor of the 3-month clinical outcome and may represent a still neglected potential therapeutic target.

Introduction

Intracerebral hemorrhage (ICH) represents approximately 10 to 30% of all strokes and affects over one million people worldwide every year. It is associated to consistent medical and socio-economic costs with high rates of early mortality and long-term disability among survivors (1,2). Despite the wide spread of this disease, there are no specific medical or surgical strategies currently approved to improve prognosis and only supportive treatments are usually provided. High blood pressure (BP) is recognized as one of the most important risk factors for ICH (3), and BP levels have also been related to early neurological deterioration, hematoma enlargement, unfavorable clinical outcome and risk of recurrence (4-7). Despite the high prevalence of post-stroke hypertension and its prognostic significance, however, the management of BP during the acute stage still remains controversial and a matter of ongoing debate (8). The Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial 2 (INTERACT-2) showed that early intensive control of BP with a target systolic level of < 140 mmHg improved functional outcome but did not result in a significant reduction in the rate of the primary outcome of death or major disability (9). Additionally, there is increasing evidence that not only absolute BP values but also their variations over time may represent a strong vascular risk factor and contribute to the prediction of either the occurrence, recurrence and prognosis of cerebrovascular events (10-14).

The aim of this study is to evaluate whether variability of BP during the first 72 hours from spontaneous cerebral hemorrhage was associated with the 3-month clinical outcome.

Materials and methods

Participants and study outcome. We retrospectively identified consecutive patients hospitalized at the Stroke Unit of Università Politecnica delle Marche from January 2007 to December 2013 for stroke syndrome due to acute spontaneous intracerebral hemorrhage within 6 hours from onset of symptoms and confirmed by CT scan. Baseline demographics, past medical history, current

medications at stroke occurrence, vascular risk factors, stroke severity at admission measured by the Glasgow Coma Scale (15) and National Institutes of Health Stroke Scale (NIHSS) (16) were collected from medical records. Exclusion criteria were onset of symptoms > 6 hours from admission or unknown onset time, comatose state at admission (defined as a score ≤ 8 on the Glasgow Coma Scale), isolated intraventricular hemorrhage, structural cerebral cause for the intracerebral hemorrhage as tumor, ruptured arteriovenous malformation or aneurysm, and use of anticoagulants. Potential study subjects were also excluded if they were not prospectively assessed for functional status at 3 months after stroke onset. The BP readings obtained at admission and subsequently at a time interval of four (±1) hours during the acute phase of stroke were extracted from medical records and considered to characterize the BP status of each patient through the mean, maximum and minimum values for both systolic and diastolic BP. BP variability (BPV) was thus determined as the SD, the coefficient of variation (CV) (SD x 100/mean) and the maximum-minimum difference. We defined the acute stage as the first 72 hours from stroke symptoms onset. In all patients, supine BP was obtained by non-invasive measurements with an automated cuff consistently on the same, non-paralyzed arm.

All patients were managed according to the current national guidelines for stroke (17). Briefly, in addition to the baseline brain CT performed on admission (to confirm the diagnosis), patients underwent brain CT on follow-up as part of routine practice and CT angiography or conventional cerebral angiography to exclude the presence of structural parenchymal or vascular abnormalities. Size, location and intraventricular extension of ICH were considered. In order to estimate haematoma volume, the previously validated ABC/2 or ABC/3 methods were used for round and ellipsoid or irregularly and separately shaped haemorrhages, respectively (18,19). The threshold for the initiation of acute intravenous treatment (e.g., labetalol, urapidil, nitroprusside) was a systolic level greater than 180 mmHg or a diastolic level above 105 mmHg. Patients who had been taking antihypertensive therapy prior to hospitalization were allowed to continue their usual medication

when oral administration was possible, unless the agents were considered to be inappropriate by the physician in charge.

The measure of outcome was the 3-month functional status prospectively assessed by direct clinical evaluation and measured using the modified Ranking Scale (mRS) (20). According to the baseline severity-adjusted analysis (responder analysis) for dichotomization of outcome status, we considered as poor outcome a 3-month mRS score of 2 to 6 if the baseline NIHSS score was ≤7 points, mRS score of 3 to 6 if the NIHSS score was 8 to 14 points, and mRS score of 4 to 6 if the NIHSS score was ≥15 points (21,22).

Statistical analysis. Values are presented as mean ± SD or median (interquartile range [IQR]) for continuous variables and as the number (percent) of subjects for categorical variables. The Student t test, Mann-Whitney test or Chi-squared test, as appropriate, were used to test differences on each of the subjects' characteristics. In order to examine the relationship between acute BP fluctuations and clinical outcome, BPV parameters were categorized into tertiles and firstly analyzed by the Chi-squared test for linear trend. The risk of a poor outcome was then evaluated using a logistic regression model, after adjusting for the effect of the potential confounding variables. Odds ratios (ORs) and corresponding 95% CIs were calculated to quantify this effect. The variables with p values <0.02 from comparisons of baseline characteristics and associations with outcome that were biologically plausible were chosen as potential confounders for statistical adjustment in the multivariate analysis. Selected variables were: age, sex, baseline NIHSS score, initial ICH volume, location of the hematoma (deep vs. lobar), and intraventricular hemorrhage (presence vs. absence). As a sensitivity analysis, multiple logistic regression analyses for the BPV parameters were repeated using simple dichotomization of mRS score into 0–2 vs. 3–6, instead of the baseline severity-adjusted dichotomization. Separate models were constructed for each systolic and diastolic BPV index. Results were considered significant for p values < 0.05 (two sided). Data analysis was performed using STATA/IC 13.1 statistical package.

Standard protocol approvals, registrations, and patient consents. The study was approved by the local ethical committee and performed in accordance with the Declaration of Helsinki. The board allowed the study to be conducted without patients' consent because of the retrospective nature of the study.

Results

A total of 197 Caucasian patients admitted to our Stroke Unit for acute spontaneous ICH were initially considered, out of which 59 were excluded: 18 had the onset of symptoms more than 6 hours before admission, 15 were still using anticoagulants, 1 was diagnosed with an isolated intraventricular hemorrhage, 11 were detected with a structural cause for the intracerebral hemorrhage, and 14 had not been assessed for functional outcome at 3 months. As a result, a total of 138 patients were included in the analysis. Following the baseline severity-adjusted dichotomization of functional outcome, 67 patients (48.6%) were classified as having a poor 3-month outcome. Baseline characteristics and their comparisons according to the outcome are summarized in table 1. The median GCS at admission was 14 (IQR, 13-15) in both groups. The BP profile of the acute stage was derived from a median number of 18 (IQR, 17-18) BP readings for each subject, and is summarized in table 2. Maximum BP and all BPV parameters (SD, CV, maximum-minimum difference) for both systolic and diastolic BP were significantly higher in patients with poor outcome. Each parameter of BPV was only weakly correlated to both baseline NIHSS and initial ICH volume (Spearman's correlation coefficients ranging from 0.17 to 0.21 and from 0.08 to 0.18 for systolic and diastolic indices, respectively). After categorization into tertiles, a dose-response relationship with poor outcome was found for each systolic and diastolic BPV parameter as demonstrated by the Chi-squared test for linear trend (figure 1). In the multiple logistic regression analysis after adjustment for potential confounders, all systolic BPV parameters turned out to be significantly associated to poor outcome, while for diastolic BPV indices, the association resulted

significant only for their highest tertiles (table 3).The associations between BPV parameters and poor outcome remained significant when adjusting for mean and maximum BP values (supplemental tables e-1-2), and when substituting the simply dichotomized outcome for the baseline severity-adjusted outcome (supplemental tables e-3-5).

Discussion

The key finding of our study was that the variability of systolic BP (SBP) during the first 72 hours from the ICH onset represented a strong predictor of the 3-month functional outcome and, furthermore, the greater was the variability, the stronger was the association. Also wider fluctuations in diastolic BP (DBP) were associated to a greater risk of poor functional recovery, although the strength of the association turned out to be weaker with respect to the systolic counterpart and was only evident for the highest values of variability.

BP variability has been clearly recognized as a risk factor for first-ever and recurrent stroke, and its role even as prognostic indicator is growing. In this respect, the current evidence is still scarce, conflicting and mostly related to ischemic rather than hemorrhagic stroke subtype. Although many researches involving patients with acute ischemic stroke have linked the increased fluctuations of BP to the likelihood of worse clinical outcome, early neurological deterioration or cerebral hemorrhage after intravenous thrombolysis (23-25), similar correlations have not been found in other clinical investigations enrolling patients with cerebral infarcts whether of ischaemic or haemorrhagic type (26). Conversely, our findings are consistent with post-hoc analysis of the INTERACT-2 and the Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI)- ICH study which found the variability of SBP to be predictor of unfavorable outcome (27,28), and a small-scale observational investigation which showed systolic BPV to be associated to early neurological deterioration (29). The most striking and relevant difference towards these trials lied in the BP levels of the included patients: all patients enrolled in

the interventional investigations should in fact present high initial systolic BP, while the absence of this restriction among the inclusion criteria of the present study allowed our findings to reach greater generalizability to population affected by ICH and for a wider range of BP levels.

Different mechanisms may be hypothesized to explain the relationship between BPV and outcome in patients with ICH. High BPV during the acute stage might favor continuous bleeding, resulting in larger initial hemorrhage, or increase the likelihood of early rebleeding, leading to hematoma expansion. Although the real pathogenesis of primary ICH still remains unknown, the fibrinoid necrosis of small-vessels has been advocated as possible etiology, and it is reasonable to hypothesize that damaged vessels may be particularly vulnerable to the effects of BP variations (30,31). Furthermore, blood pressure fluctuations might enhance the formation or promote the enlargement of the edema around cerebral hematoma (32,33). Finally, when cerebral autoregulatory capacities are impaired, as frequently occurs during the acute and subacute stages of hemorrhagic stroke (34), high BPV might negatively affect blood flow and brain perfusion enhancing the injury of the perihematoma tissue, hypoperfused and thus particularly susceptible to BP changes, and in turn amplifying the secondary brain damage (35-37).

Our study has some limitations that should be taken into consideration when interpreting the results. The small number of patients involved does not allow for definitive conclusions. Moreover, the observational design and retrospective nature of the study may be only considered reliable for the development of preliminary insights, and for suggesting working hypotheses. Our findings do not necessarily imply a direct causal involvement of BPV in determining the poor outcome. BPV might represent a consequence of stroke and a marker of the severity of ICH rather than a predictor of subsequent recovery. However, the independence of BPV values from either the baseline NIHSS score or ICH volume and the adjustment of the outcome for baseline severity, strongly suggests a causative role for the BPV. Our analysis did not differentiate between medical treatments and antihypertensive agents, but their potential influence on BPV could be expected to reflect on the BP

status. Furthermore, the study sought to assess the impact of BP fluctuations rather than the effects of specific antihypertensive agents, ensuring the results maximal generalizability to routine clinical practice. Finally, our study did not provide the assessment of cerebral hemodynamics and a follow-up neuroimaging; in this perspective, future studies including appropriate and serially performed evaluations of cerebral perfusion state and infarct size are desirable to clarify the pathological mechanisms underlying the relationship between BP variability and ICH outcome. The strengths of the study include the enrollment of patients despite their initial BP values and ICH location, either lobar or deep, and the outcome dichotomization through a severity-adjusted analysis based on different cutoffs for the 3-month mRS score for different baseline NIHSS scores. This method has been indicated as particularly useful to measure the real strength of associations (21,22). The number of BP readings is in accordance with the evidence that the reproducibility of measures of variability increases with the availability of BP monitoring values, independently of the mean BP (38). Furthermore, the automatized system of BP measurement reduced the potential variability and observer bias related to manually performed assessments.

The relationship between BP and the clinical outcome of cerebral infarct has been widely investigated, but little is known about the effects of BPV. Our study adds to the currently available knowledge that wide BP fluctuations over the first days of ICH are independently associated with the risk of poor functional outcome or death despite the mean BP levels. These findings strengthen the importance of close BP monitoring in the acute phase of a stroke and suggest that stability of BP values may favorably influence recovery and represent a potential therapeutic target beside early BP lowering. This perspective stimulates the ongoing debate about the best appropriate ICH policy management and may have relevant clinical implications in the selection criteria of the antihypertensive drug and approach to be used in routine medical practices in view of the different effects exerted on BPV by each class of BP lowering agents (39-41). Although the currently available stroke guidelines insist on a reduction of BP per se, BPV could reasonably provide to

clinicians useful complementary prognostic information and even influence the strategies of care. Further investigations are needed to explore whether and how antihypertensive treatments influence BPV during the acute stage of ICH and to evaluate whether the early reduction of overall BP variability might reduce patient morbidity and mortality risk.

Conflict of interests

The authors declare that they have no conflict of interest.

References

1. Qureshi AI, Tuhrim S, Broderick JP, et al. Spontaneous Intracerebral hemorrhage. N Engl J Med 2001;344:1450-1460.
2. Feigin VL, Lawes CM, Bennett DA, et al. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. Lancet Neurology 2003;2:43-53.
3. Ariesen MJ, Claus SP, Rinkel GJ, et al. Risk factors for intracerebral hemorrhage in the general population: a systematic review. Stroke 2003;34:2060-2065.
4. Leira R, Dávalos A, Silva Y, et al. Early neurologic deterioration in intracerebral hemorrhage: predictors and associated factors. Neurology 2004;63:461-467.
5. Ohwaki K, Yano E, Nagashima H, et al. Blood pressure management in acute intracerebral hemorrhage: relationship between elevated blood pressure and hematoma enlargement. Stroke 2004;35:1364–1367.
6. Dandapani BK, Suzuki S, Kelley RE, et al. Relation between blood pressure and outcome in intracerebral hemorrhage. Stroke 1995;26:21-24.
7. Arakawa S, Saku Y, Ibayashi S, et al. Blood pressure control and recurrence of hypertensive brain hemorrhage. Stroke 1998;29:1806-1809.

8. Spengos K, Tsivgoulis G, Zakopoulos N. Blood pressure management in acute stroke: a long-standing debate. Eur Neurol 2006;55:123-135.
9. Anderson CS, Heeley E, Huang Y, et al. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. N Engl J Med 2013;368:2355-2365.
10. Rothwell PM, Howard SC, Dolan E, et al. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension Lancet 2010;375:895-905.
11. Rothwell PM. Limitations of the usual blood-pressure hypothesis and importance of variability, instability, and episodic hypertension. Lancet 2010;375:938-948.
12. Kang J, Ko Y, Park JH, et al. Effect of blood pressure on 3-month functional outcome in the subacute stage of ischemic stroke. Neurology 2012;79:2018-2024.
13. Buratti L, Cagnetti C, Balucani C, et al. Blood pressure variability and stroke outcome in patients with internal carotid artery occlusion. J Neurol Sci 2014;339:164-168.
14. Igase M, Igase K, Kohara K, et al. Visit-to-visit variability in systolic blood pressure is a novel risk factor for the growth of intracranial aneurysms. Cerebrovasc Dis 2013;36:401-406.
15. Teasdale G, Jannett B. Assessment of coma and impaired consciousness: a practical scale. Lancet 1974;2:81-84.
16. Wityk RJ, Pessin MS, Kaplan RF, et al. Serial assessment of acute stroke using the NIH stroke scale. Stroke 1994;25:362-365.
17. Stroke Prevention and Educational Awareness Diffusion (SPREAD). The Italian Stroke Guidelines. Catel Hyperphar Group Spa, 2007, Milan.
18. Kothari RU, Brott T, Broderick JP, et al. The ABCs of measuring intracerebral hemorrhage volumes. Stroke 1996;27:1304-1305.

19. Huttner HB, Steiner T, Hartmann M, et al. Comparison of ABC/2 estimation technique to computer-assisted planimetric analysis in warfarin-related intracerebral parenchymal hemorrhage. Stroke 2006;37:404-408.
20. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. Stroke 2007;38:1091-1096.
21. Adams HP Jr, Leclerc JR, Bluhmki E, et al. Measuring outcomes as a function of baseline severity of ischemic stroke. Cerebrovasc Dis 2004;18:124-129.
22. Saver JL, Yafeh B. Confirmation of tPA treatment effect by baseline severity-adjusted end point reanalysis of the NINDS-tPA stroke trials. Stroke 2007;38:414-416.
23. Yong M, Kaste M. Association of characteristics of blood pressure profiles and stroke outcomes in the ECASS-II trial. Stroke 2008;39:366-372.
24. Stead LG, Gilmore RM, Vedula KC, et al. Impact of acute blood pressure variability on ischemic stroke outcome. Neurology 2006;66:1878-1881.
25. Endo K, Kario K, Koga M, et al. Impact of early blood pressure variability on stroke outcomes after thrombolysis: the SAMURAI rt-PA Registry. Stroke 2013;44:816-818.
26. Mistri A, Abdi Z, Potter JF, et al. Short-term blood pressure variability and early outcome following acute stroke. Cerebrovasc Dis 2011;31(suppl 2):48.
27. Manning L, Hirakawa Y, Arima H, et al. Blood pressure variability and outcome after acute intracerebral haemorrhage: a post-hoc analysis of INTERACT2, a randomised controlled trial. Lancet Neurol 2014;13:364-373.
28. Tanaka E, Koga M, Kobayashi J, et al. Blood Pressure Variability on Antihypertensive Therapy in Acute Intracerebral Hemorrhage: The Stroke Acute Management With Urgent Risk-Factor Assessment and Improvement-Intracerebral Hemorrhage Study. Stroke 2014; 45:2275-2279.

29. Rodriguez-Luna D, Piñeiro S, Rubiera M, et al. Impact of blood pressure changes and course on hematoma growth in acute intracerebral hemorrhage. Eur J Neurol 2013;20:1277-1283.
30. Lammie GA. Hypertensive cerebral small vessel disease and stroke. Brain Pathol 2002;12:358-370.
31. Lammie GA, Lindley R, Keir S, et al. Stress-related primary intracerebral hemorrhage: autopsy clues to underlying mechanism. Stroke 2000;31:1426-1428.
32. Xi G, Keep RF, Hoff JT. Pathophysiology of brain edema formation. Neurosurg Clin N Am 2002;13:371-383.
33. Vemmos KN, Tsivgoulis G, Spengos K, et al. Association between 24-h blood pressure monitoring variables and brain oedema in patients with hyperacute stroke. J Hypertens 2003;21:2167-2173.
34. Kuwata N, Kuroda K, Funayama M, et al. Dysautoregulation in patients with hypertensive intracerebral hemorrhage. A SPECT study. Neurosurg Rev 1995; 18:237-245.
35. Olivot JM, Mlynash M, Kleinman JT, et al. MRI profile of the perihematomal region in acute intracerebral hemorrhage. Stroke 2010;41:2681-2683.
36. Zazulia AR, Diringer MN, Videen TO, et al. Hypoperfusion without ischemia surrounding acute intracerebral hemorrhage. J Cereb Blood Flow Metab 2001;21:804-810.
37. Butcher KS, Baird T, MacGregor L, et al. Perihematomal edema in primary intracerebral hemorrhage is plasma derived. Stroke 2004;35:1879-1885.
38. Howard SC, Rothwell PM. Reproducibility of measures of visit-to-visit variability in blood pressure after transient ischaemic attack or minor stroke. Cerebrovasc Dis 2009;28:331-340.
39. Webb AJ, Rothwell PM. Effect of dose and combination of antihypertensives on interindividual blood pressure variability: a systematic review. Stroke 2011;42:2860-2865.

40. Webb AJ, Fischer U, Rothwell PM. Effects of β-blocker selectivity on blood pressure variability and stroke: a systematic review. Neurology 2011;77:731-737.
41. Webb AJ, Fischer U, Mehta Z, et al. Effects of antihypertensive-drug class on interindividual variation in blood pressure and risk of stroke: a systematic review and meta-analysis. Lancet 2010;375:906-915.

Table 1. Baseline characteristics according to 3-month outcome

	Full cohort (n=138)	**Good outcome (n=71)**	**Poor outcome (n=67)**	**p value**
Age (mean (SD)) (years)	65.91 (12.83)	63.78 (12.09)	68.16 (13.30)	0.044[a]
Sex, females (no. (%))	53 (38.4)	25 (47.2)	28 (52.8)	0.427[b]
NIHSS score at admission (median (IQR))	10 (7-15)	9 (7-13)	12 (8-15)	0.009[c]
History of hypertension (no. (%))	86 (62.3)	41 (57.7)	45 (67.2)	0.254[b]
History of diabetes (no. (%))	31 (22.5)	15 (21.1)	16 (23.9)	0.698[b]
Intracerebral haemorrhage parameters				
Volume (mL) (median (IQR))	9.4 (4.8-18.0)	8.0 (4.2-13.6)	12.1 (6.4-18.1)	0.014[c]
[*]Deep location (no. (%))	94 (68.1)	46 (64.8)	48 (71.6)	0.388[b]
Intraventricular extension (no. (%))	34 (24.6)	14 (19.7)	20 (29.9)	0.167[b]

[a] Two-sample t test. [b] Chi-squared test.[c] Mann-Whitney test.

[*] Deep location refers to basal ganglia or thalamus.

Table 2. Systolic and diastolic blood pressure parameters according to 3-month outcome

BP parameter	Full cohort (n=138)	Good outcome (n=71)	Poor outcome (n=67)	p value[a]
SBP mean	142.40 (17.60)	139.51 (17.25)	145.47 (17.58)	0.046
SBP maximum	166.97 (24.60)	160.87 (23.63)	173.43 (24.12)	0.002
SBP minimum	116.80 (13.73)	117.45 (13.99)	116.10 (13.54)	0.567
SBP SD	15.37 (5.93)	13.04 (5.32)	17.85 (5.56)	<0.001
SBP CV	10.70 (3.70)	9.28 (3.53)	12.21 (3.27)	<0.001
SBP Max-Min	50.17 (19.53)	43.42 (18.34)	57.33 (18.28)	<0.001
DBP mean	78.21 (7.11)	77.43 (7.13)	79.05 (7.05)	0.180
DBP maximum	93.30 (9.54)	91.30 (8.43)	95.42 (10.24)	0.010
DBP minimum	63.21 (8.66)	63.72 (8.99)	62.67 (8.32)	0.480
DBP SD	8.97 (2.40)	8.21 (2.07)	9.77 (2.48)	<0.001
DBP CV	11.53 (3.15)	10.73 (3.02)	12.38 (3.10)	0.002
DBP Max-Min	30.09 (8.49)	27.58 (6.92)	32.75 (9.21)	<0.001

BP=blood pressure, CV=coefficient of variation, DBP=diastolic blood pressure, Max-Min=maximum-minimum difference, SBP=systolic blood pressure, SD=standard deviation.

Values are mean ± SD. [a] Two-sample t test.

Table 3. Associations between tertiles of blood pressure variability and poor 3-month outcome

Parameter	Systolic BP		Diastolic BP	
	OR (95% CI)	p value	OR (95% CI)	p value
SD				
1T	-	-	-	-
2T	3.58 (1.33-9.65)	0.012	1.42 (0.57-3.50)	0.449
3T	7.85 (2.85-21.63)	<0.001	7.43 (2.72- 20.32)	<0.001
CV				
1T	-	-	-	-
2T	3.52 (1.36-9.11)	0.009	1.80 (0.73- 4.40)	0.201
3T	7.75 (2.87-20.91)	<0.001	5.08 (1.92-13.44)	0.001
Max-Min				
1T	-	-	-	-
2T	5.76 (1.97-16.84)	0.001	1.29 (0.52- 3.22)	0.582
3T	8.08 (2.63-24.77)	<0.001	4.69 (1.83-12.01)	0.001

T for tertile categorization. ORs and their CIs are obtained with logistic regression analysis adjusted for age, sex, baseline NIHSS score, initial ICH volume, deep location of hematoma, presence of intraventricular hemorrhage. The lowest tertile is reference.

BP=blood pressure, CV=coefficient of variation, Max-Min=maximum-minimum difference, OR=odds ratio, SD=standard deviation.

FIGURE LEGEND

Figure 1. Associations of blood pressure variability and death or major disability at 3 months.

Proportions of poor outcome by tertiles of SD, CV and Max-Min for systolic (top row) and diastolic (bottom row) blood pressure are reported (p values are for Chi-squared test for linear trend with the lowest tertile as reference).

CV=coefficient of variation, DBP=diastolic blood pressure, Max-Min=maximum-minimum difference, SBP=systolic blood pressure, SD=standard deviation.