Analysis of blood pressure variability in lacunar and non-lacunar types acute ischemic strokes patients as a predictor of clinical outcomes

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Abstract. *Background and aim:* Stroke is a well-known global health concern that causes significant mortality and morbidity, with ischemic stroke being the most prevalent kind. The pathogenesis and clinical consequences of various lacunar and non-lacunar subtypes vary from one another. A patient's clinical fate following an acute ischemic stroke may be predicted by elevated blood pressure variability (BPV). The aim of this study to investigate the association between BPV and functional outcomes in patients with acute ischemic stroke (lacunar and non-lacunar subtypes). *Methods:* This prospective cohort study categorized patients with acute ischemic stroke as either lacunar or non-lacunar based on non-contrast CT scan results. BPV values were recorded at the onset and at 4 intervals daily for 3 continuous days after the patients were admitted. The modified Rankin Scale (mRS) was used for outcome assessments on the seventh day, classified into good (0-2) and poor outcomes (3-6). Predictive values were determined using ROC analysis. *Results:* Out of 67 patients, 40.3% had poor outcomes, whereas the other 59.7% had good outcomes. Lacunar stroke was observed to occur more frequently in patients with positive results. The sensitivity and specificity of ROC analysis were disputed, and there was no discernible relationship between systolic and diastolic blood pressure and mRS scores. *Conclusions*: BPV was not directly linked to functional outcomes, nor was a cut-off value that appears to work consistently established. Better functional outcomes were observed in patients with lacunar stroke, highlighting the prognostic value of using it in the treatment of ischemic stroke. (www.actabiomedica.it)

Key words: blood pressure variability, ischemic, stroke

Introduction

Stroke is one of the major causes of death and disability around the world with ischemic stroke being the dominant type (1,2). According to the World Health Organization (WHO) and the American Heart Association (AHA), stroke is defined as an abrupt change in the clinical state of the patient which is characterized by the loss of one or more functions due to damage to the blood supply of the brain (3,4). Ischemic strokes consist of two types as lacunar and non- lacunar which have differences in clinical presentations and pathophysiological groups. Lacunar infarcts, which are usually related to chronic high blood pressure and small vascular disease, affect in most cases the deeper parts of the brain while non-lacunar ones are most often caused by thromboembolic or atherosclerosis of the large artery (5).

Blood pressure variability (BPV) has been increasingly regarded as a potential predictive value in the acute phase of ischemic stroke. Many studies have linked high BV with poor case and secondary vascular diseases. BPV on its part regarding its effect on cerebral autoregulation and modulating effects on ischemic brain injury makes the relationship between the different types of stroke sizable. Previous research has noted a difference in BPV between lacunar and other types of strokes, which have many therapeutic and prognostic implications. However, not much research has been done in this field, for instance predicting outcomes using BPV will need further research (6–9).

This research seeks to establish the link between the BPV and the clinical outcomes in patients with an acute ischemic stroke with a particular emphasis on the lacunar and non-lacunar subtypes. This study aims to explain how BPV determinants contribute to enhancing the prognosis of patients that suffer from stroke by taking into account the multifactorial causes of stroke.

Materials and Methods

This prospective cohort study study was conducted at Dr. Wahidin Sudirohusodo Hospital, a tertiary referral hospital in Makassar, Indonesia, and its affiliated teaching hospitals. This study looked at individuals who had an acute ischemic stroke and were registered at our institutions between November 2023 and October 2024.

The sample size was estimated using standard statistical methods to ensure appropriate power to show evidence of a meaningful connection between blood pressure change and clinical outcome (10,11). A total of 32 patients were required, with a 95% confidence interval. This participant was selected based on very tight eligibility criteria. The inclusion criteria were: (1) a history suggestive of a first-ever ischemic stroke; (2) age between 18 and 80 years; (3) admission systolic blood pressure not exceeding 220 mmHg and diastolic blood pressure not exceeding 120 mmHg; and (4) the stroke event occurring no more than seven days prior to admission. The exclusion criteria included: (1) a final diagnosis of TIA (transient ischemic attack), (2) hemorrhagic transformation within 24 hours of hospitalization, and (3) patients with systolic blood pressure ≥ 220 mmHg or diastolic BP ≥ 120 mmHg and a need for intravenous antihypertensive therapy upon admission, and (4) patients having partial or missing clinical information.

The demographics, comorbidities, laboratory results, and clinical data from the hospital's medical records were all included. Additionally, to assess the patient's blood pressure variability (BPV), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured four times over three consecutive days by the same operator.

Acute ischemic strokes

The patient's stroke was diagnosed based on their medical history, onset 1-7 days, and was characterized by a sudden focal neurological deficit, such as motor function deterioration (weakness in the limbs) or sensory perception changes. The diagnosis was confirmed through a head computed tomography (CT) scan without contrast using the Siemens Somatom Go Top 128 Slice (Erlangen, Germany). The scan revealed a hypodense lesion, indicating cerebral ischemia. The stroke was classified as either lacunar (small artery occlusion, diameter < 20 mm) or non-lacunar (large artery atherosclerosis, diameter > 20 mm).

Systolic variability

Systolic blood pressure measurements were taken at four different times, with two measurements at each time, and a 15-minute break between the first and second measurement. The measurements were taken at 6 AM, 12 PM, 6 PM, and 12 AM, and were done continuously for 3 days post-admission.

Diastolic variability

Diastolic blood pressure measurements were taken at four different times, with two measurements at each time, and a 15-minute break between the first and second measurement. The measurements were taken at 6 AM, 12 PM, 6 PM, and 12 AM, and were done continuously for 3 days post-admission.

Body mass index

The Body Mass Index (BMI) is a widely utilized formula for assessing obesity, calculated as weight in kilograms divided by the square of height in meters

(BMI = weight/height²) (12). The classification of BMI employed in this study is derived from the BMI categorization established by the Indonesian Ministry of Health: underweight (BMI <18.5 kg/m²), normal weight (BMI ≥18.5 – <24.9 kg/m²), overweight (BMI ≥25.0 – <27 kg/m²), and obese (BMI ≥27.0 kg/m²) (13–15).

Modified Rankin Scale (mRS)

The mRS is used to measure the disability or degree of dependence by individuals/patients who have suffered a stroke or other causes of neurological disability in performing daily living activities. The score ranges from 0 to 6; mRS 0–2 were regarded as good outcomes, whereas 3–6 were deemed poor (16–18).

Hypertension

A diagnosis of hypertension is established when the systolic blood pressure ≥ 140 mmHg and/or the diastolic blood pressure ≥ 90 mmHg (19), current use of antihypertensive medication, or previous diagnosis of hypertension made by a medical doctor.

Controlled hypertension

The patient's blood pressure is regulated through the administration of antihypertensive medications when the systolic blood pressure < 140 mmHg and/or the diastolic blood pressure < 90 mmHg.

Diabetes mellitus

A diagnosis of Diabetes is established when a fasting blood glucose measurement of 126 mg/dL or above after an 8-hour fasting period, a 2-hour postprandial blood glucose level of 200 mg/dL or greater, a glycated hemoglobin concentration of 6.5% or more, a random blood glucose reading of 200 mg/dLor higher accompanied by manifestations of hyperglycemia, the patients had a history of Diabetes from the hospital's medical records, current use of antidiabetic medications, or previous diagnosis of diabetes made by a medical doctor (20,21).

Atrial fibrillation

There is a sign of atrial fibrillation (an irregularly irregular QRS complex and no visible P waves) on an electrocardiogram examination carried out by a cardiologist.

Dyslipidemia

Dyslipidemia is diagnosed by increased of low-density lipoprotein cholesterol (LDL-C) at or above 130 mg/dL, increased triglyceride concentrations equal to or greater than 150 mg/dL, or decreased high-density lipoprotein cholesterol (HDL-C) levels below 40 mg/dL (22).

Statistical analysis

The data were analyzed using SPSS 27.0 (IBM Corp., Armonk, NY, USA). Continuous data were evaluated for normal distribution using the Kolmogorov-Smirnov test and displayed as a median (min-max), whereas categorical data were simply presented as frequencies and percentages. The Mann-Whitney U Test, Chi-square testing, and Fisher's extract test were employed to assess group differences. The receiver operating characteristic (ROC) curves were used to identify cut-off points, sensitivity, and specificity parameters for BPV as a predictor of clinical outcome. Independent prognostic factors were identified using multivariate logistic regression analysis, and outcomes were reported as adjusted odds ratios (AOR) with 95% confidence intervals (CI). A p-value of less than 0.05 indicates statistical significance.

Results

Characteristics of participants

The study included 67 patients (Table 1), 59.7% (40 patients) achieved a good clinical outcome (mRS 0–2) while 40.3% (27 patients) had a poor outcome (mRS 3–6). The level of BPV, as a nominal variable, was further subjected to measurement normality test using Kolmogorov-Smirnov test, and it was found to be non-normal distribution ($p<0.001$).

Table 1. Characteristics of participants.

Variable	Median or (n)	Min–Max or (n, %)
Systolic Variability	10.07	6.54–23.74
Diastolic Variability	7.76	4.42–12.25
Age (years)		
≥45	59	88.1
<45	8	11.9
Sex		
Male	38	56.7
Female	29	43.3
History of Hypertension		
Yes	44	65.7
No	23	34.3
Controlled Hypertension		
Well	23	52.3
Poorly	21	47.7
History of Diabetes Mellitus		
Yes	21	31.3
No	46	68.7
History of Atrial Fibrillation		
Yes	5	7.5
No	62	92.5
History of Dyslipidemia		
Yes	35	52.2
No	32	47.8
Overweight – Obesity		
Yes (Overweight – Obesity)	17	25.3
No (normal – Underweight)	50	74.7
Stroke Subtype		
Lacunar	32	47.8
Non-Lacunar	35	52.2

Blood pressure variability trends

BPV in women and men suffering from acute ischemic stroke was investigated in terms of systolic and diastolic blood pressure, and patients were then categorized into lacunar and non-lacunar stroke subtypes. The mean blood pressure systolic for non-lacunar patients was 162.86 mmHg upon admission, whereas the mean blood pressure systolic for lacunar patients was 152.66 mmHg. Within three days, the systolic blood pressure of non-lacunar patients drops to 137.71 mmHg, while the blood pressure of lacunar patients drops to 128.13 mmHg. Furthermore, before stabilizing, minor sine variations were seen between P5 and P9.

For diastolic BPV, it is worth noting that non-lacunar patients had higher beginning values (94.29 mmHg) than lacunar patients (91.72 mmHg) and had BP similar to stroke in the mid- and late stages. According to the authors, for the final measurement, the BP diastolic BPV dropped to 79.71 mmHg in non-lacunar patients and to 75.00 mmHg in lacunar patients. Over time, the systolic and diastolic BPV dropped modestly, but the patterns of BPV remained diverse across individuals with different stroke subtypes.

Determination of blood pressure variability cut-off

ROC analysis was utilized to establish the best cut-off values for systolic and diastolic BPV in guiding clinical decisions as provided in Table 2. 141.54 mmHg is the cut-off for systolic blood pressure (AUC: 0.542, sensitivity: 57.14%, specificity: 56.25%).

Additionally, 86.15 mmHg is the cut-off for diastolic blood pressure (AUC: 0.586, sensitivity: 45.71%, specificity: 71.88%). As a result, neither the systolic nor the diastolic blood pressure can be accurately predicted using these metrics. More accurate prognostic indicators are required because neither the systolic or diastolic blood pressure readings could accurately predict clinical outcomes.

Table 2. Calculation for cut-off values of systolic and diastolic variability.

Variable	Sensitivity	Specificity	AUC
Systolic (141.54 mmHg)	57.14	56.25	0.542
Diastolic (86.15 mmHg)	45.71	71.88	0.586

Relationship between variables and mRS scores

As provided by Table 3, patients with favorable outcomes (143.78 ± 18.30 mmHg) and those with poor outcomes (140.84 ± 15.06 mmHg; p = 0.492) did not significantly differ in their systolic blood pressure values. Additionally, there was no significant difference in diastolic blood pressure between the two groups; the mean values were 84.08 ± 8.12 mmHg and 84.57 ± 8.57 mmHg, respectively (p = 0.811). Additionally, no significant correlations between systolic blood pressure (141.54 mmHg) and diastolic blood pressure (86.15 mmHg) and clinical outcomes were found using threshold analysis (p = 0.920 and p = 0.827, respectively).

In contrast, stroke type demonstrated a significant relationship with outcomes. Non-lacunar stroke was more frequently associated with poor outcomes (60% vs. 40%; p = 0.001, OR: 6.500, 95% CI: 2.129–19.841), while lacunar stroke was more likely to result

Table 3. Relationship between variables and mRS score.

Variable	mRS Score		*p*-value	OR (95% CI)
	Poor outcome (n=27)	Good outcome (n=40)		
Systolic Variability, mean±SD	140.84 ± 15.06	143.78 ± 18.30	0.492	
Diastolic Variability, mean±SD	84.57 ± 8.57	84.08 ± 8.12	0.811	
Systolic Variability, n (%)				
>141.54 mmHg	13 (38.2)	21 (61.8)	0.920	0.840 (0.316–2.232)
≤141.54 mmHg	14 (42.4)	19 (57.6)		
Diastolic Variability, n (%)				
> 86.15 mmHg	11 (44.0)	14 (56.0)	0.827	1.277 (0.467–3.491)
≤ 86.15 mmHg	16 (38.1)	26 (61.9)		
Stroke Subtype, n (%)				
Non-lacunar	21 (60.0)	14 (40.0)	0.001*	6.500 (2.129–19.841)
Lacunar	6 (18.8)	26 (81.2)		

Note: mRS, Modified Rankin Scale.

Table 4. Effect of Stroke Subtype towards BPV and mRS Score.

Variable	B	OR (95% CI)	*p*-value
Stroke Subtype			
Lacunar	1.192	6.766 (2.077-22.042)	0.002*
Non-Lacunar			
Systolic Variability	0.030	1.030 (0.952-1.116)	0.462
Diastolic Variability	-0.008	0.992 (0.864-1.138)	0.907
Systolic Variability (mmHg)			
>141.54	-0.052	0.949 (0.106-8.466)	0.949
≤141.54			
Diastolic Variability (mmHg)			
>86.15	0.497	1.644 (0.213-12.697)	0.634
≤86.15			

Table 5. Comparison of BPV Values in Lacunar Stroke Subtype with mRS Score.

Lacunar Infarct Stroke	mRS Score		*p*-value	OR (95% CI)
	Poor outcome (n=6)	Good outcome (n=26)		
Systolic Variability, mean±SD	140.38±17.78	141.48±19.75	0.175	
Diastolic Variability, mean±SD	82.24±7.16	82.84±7.90	0.708	
Systolic Variability (mmHg)				
>141.54	2 (14.3)	12 (85.7)	0.672	0.583 (0.090–3.763)
≤141.54	4 (22.2)	14 (77.8)		
Diastolic Variabiility (mmHg)				
>86.15	1 (11.1)	8 (88.9)	0.648	0.450 (0.045–4.501)
≤86.15	5 (21.7)	18 (78.3)		

Note: mRS, Modified Rankin Scale.

in favorable outcomes. These findings suggest that stroke type, rather than BPV, is a more reliable predictor of clinical outcomes in this cohort.

Influence of stroke type on BPV and mRS scores

This relationship is based on the fact that non-lacunar strokes are associated with a higher odds ratio (OR: 6.766, 95% CI: 2.077-22.042, p = 0.002) of poor outcomes than lacunar strokes, which has a significant impact on clinical outcomes after logistic regression analysis of the data (Table 4). Systolic and diastolic blood pressure values did not significantly correlate with mRS scores. Using BPV cutoff levels of systolic (> 141.54 mmHg) and diastolic (> 86.15 mmHg) for categorical analysis Likewise, BPV had no prognostic value. These results highlight that, in this group, stroke type is a more important predictor of clinical outcomes than BPV.

Tables 5 and 6 compare BPV values and groups in lacunar and non-lacunar stroke types with modified Rankin Scale (mRS) scores. The analysis separated the data based on stroke type and compared groups with poor and good mRS scores. Both lacunar and non-lacunar stroke groups showed insignificant p-values (p-values ≥ 0.05) in both the poor and good outcome groups.

Table 6. Comparison of BPV Values in Non-lacunar Stroke Subtype with mRS Score.

Non-Lacunar Infarct Stroke	mRS Score		*p*-value	OR (95% CI)
	Poor outcome (n=21)	Good outcome (n=14)		
Systolic Variability, mean±SD	140.97±14.68	148.05±14.97	0.902	
Diastolic Variability, mean±SD	85.24±8.98	86.37±8.31	0.867	
Systolic Variability (mmHg)				
>141.54	11 (55.0)	9 (45.0)	0.727	0.611 (0.152-2.450)
≤141.54	10 (66.7)	5 (33.)		
Diastolic Variabiility (mmHg)				
>86.15	10 (62.5)	6 (37.5)	1.000	1.212 (0.311-4.730)
≤86.15	11 (57.9)	8 (42.1)		

Note: mRS, Modified Rankin Scale.

Discussion

The study included 67 patients, with 59.7% achieving a good clinical outcome and 40.3% having a poor outcome. BPV was found to be non-normally distributed. The study found that stroke type, rather than BPV, is a more reliable predictor of clinical outcomes. The systolic and diastolic blood pressure values did not significantly correlate with clinical outcomes. BPV shows how blood pressure changes over time as a result of activities and consequences brought on by autonomic function, antihypertensive medication use, body posture, and emotional arousal levels. Todo et al. observed that hypertensive individuals with increased BPV had poor cerebral hemodynamics, which led to blood brain barrier dysfunction (23). The majority of participants were male (56.7%) and aged ≥45 years (88.1%), which is in line with Zhu et al. findings that male sex and age were risk factors for ischemic stroke (24). According to patient records, hypertension was the most prevalent comorbidity among the patients, occurring in 65.7% of cases, with good control attained in 34.3% of them. Webb et al. demonstrated the significance of blood pressure control by showing that a 12 mmHg drop in systolic blood pressure lowers the risk of stroke by 43% (25).

Additional comorbidities included diabetes (31.3%), atrial fibrillation (7.5%), dyslipidemia (52.2%), and obesity (74.7%). According to Silva et al., arterial stiffness and autonomic dysfunction, when combined with diabetes-related BPV, can be utilized to predict cerebrovascular occurrences (26). According to Kaze et al., BPV is associated with atrial fibrillation due to endothelial dysfunction and left ventricular remodeling, supporting targeted antihypertensive therapy to prevent recurrence, particularly in young patients with recent infarcts (27). Lacunar strokes are more common in persons with higher blood pressure changes than non-lacunar strokes. High blood pressure variation is not only associated with lacunar stroke, but also with a variety of other pathologies. Moreover, Dyslipidemia and obesity exacerbate BPV through mechanisms like atherosclerosis and arterial rigidity. Understanding the interplay of vascular collapse anatomy in reconstructing blood pressure levels is essential to understand BPV management in stroke prevention and recovery (28,29).

In this study, BPV using the standard deviation of all blood pressure measurements and determined cut-off values for BPV associated with mRS scores using ROC curve analysis. The analysis found that neither the systolic nor diastolic BP variability cut-offs could reliably predict clinical outcomes, with both having AUC values below 60% and limited sensitivity and specificity. This suggests that using ROC analysis for defining cut-offs in BPV is challenging.

BPV can be classified into short-, mid-, and long-term fluctuations, with short-term variability measured across hours or days, and long-term variability over weeks or months. The variability is influenced by measurement methods and mathematical approaches used. Previous studies suggest that high BPV exacerbates acute ischemic stroke outcomes. Yang et al. found that daily BPV measurements over seven days correlated with poor outcomes at three months, but short-term measurements using 24-hour ambulatory BP monitoring (ABPM) were less predictive due to circadian rhythm disruptions. Accurate BPV measurements over a prolonged period are necessary to minimize confounding factors, such as poor sleep quality, that may affect results (30). A cohort study of 85,455 patients by McAlister et al. showed that high BPV in repeated measurements increases the risk of stroke, uncontrolled hypertension, and other adverse events (31). Del Giorno et al. also emphasized the variability in BP measurements depending on whether they were taken by healthcare providers, patients, or physicians, demonstrating the need for standardized protocols to improve reliability. These findings underscore the importance of consistent and long-term BP monitoring in future studies to better assess BPV's predictive value for stroke outcomes (32).

The goal of this study was to evaluate functional outcomes in people suffering from acute ischemic stroke by analyzing mRS) scores and other clinical factors in the patients. A significant correlation was also found for the type of lacunar stroke (p=0.001), which supports earlier findings of better functional outcomes in lacunar stroke. However, there was no discernible relationship between BPV for the diastolic and systolic phases and the mRS rating (p=0.827 and p=0.920, respectively) (33). Comorbidities, age, and gender were among the defining characteristics that did not significantly correlate with mRS scores (p>0.05).

Earlier study has reported the usefulness of BPV in predicting the outcome of stroke. According to Ningning et al. stroke patients with systolic and diastolic BP greater than 8 mmHg and 9 mmHg respectively had poor score ranges in the mRS (34). On the other hand, it was found in this study that systolic BPV (141.54 mmHg) and still diastolic BPV (86.15 mmHg) with any AUC values lower than 60% could not be used as predictors for the clinical outcomes. Same results were reported by Zhou et al. arguing that short term BPV has little sensitivity in predicting the longer ones (35). After controlling for the confounders, the subacute-phase BPV was shown by Naito et al to be significantly predictive of poor outcomes at three months poststroke. Associative processes such as brain edema, hemorrhage, and reactive hypertension after stroke should also be considered in this association. Their study pointed out that diastolic BPV has been a stronger indicator of poor outcomes than other measures (36).

The mRS which has 0 denoting no disability and 6 death has also been widely used to evaluate the functional outcome of stroke patients. Younger patients with good cholesterol and/or triglyceride profiles have been reported to have mRS < 3 according to Ningning et al. (34). The present study reports 62.9% of the dyslipidemia and 61.9% of the diabetic patients with good outcomes but the association's level did not reach statistically significant levels. On the whole this study supports previous reports that lacunar stroke entails better mRS and functional outcomes. The efficacy of the use of BPV as a predictor is still inconclusive although the relationships of interest to the study are ones that should be explored in more in-depth empirical studies with longer follow up periods.

This study is limited in several ways. First, it was conducted on a small scale and did not group samples based on risk factors. Second, the analysis of the samples did not differentiate between the time since the onset of the event or symptoms and admission. Third, BPV measurements were only conducted for 3 days of patient care after admission.

Conclusion

This study found that BPV is not different in patients with lacunar and non-lacunar acute ischemic stroke, and it is not a reliable predictor of clinical outcomes in these patients. However, there is a significant correlation between lacunar acute ischemic stroke and better functional outcomes based on mRS scoring. The study emphasizes the need for careful control of BPV in stroke patients and suggests that further research is necessary to confirm these findings and understand the underlying associations.

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