Original Article

Role of 24-Hr Blood Pressure Variability as a Target Therapeutic Risk Factor for Poor Functional Outcome of Acute Ischemic Stroke

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Abstract

Background and Purpose: The present study aims to evaluate the role of blood pressure variability (BPV) as a target therapeutic risk factor for poor outcome of ischemic stroke by finding the association between the two and by finding the population attributable risk (PAR) of BPV compared to other baseline outcome predictors. **Methods:** A prospective observational study was carried out at GMCH, Nagpur, India from January to June 2019 in 75 patients diagnosed with acute ischemic stroke. BP was recorded hourly for the first 24 hours of admission and base line factors were collected along with measurement of stroke severity. BPV was measured by index of average real-time variability (ARV) while discharge outcome was measured by Barthel Index. **Results:** 36.5% of patients had poor outcome at discharge. A significant association was found between 24-hr ARV of systolic BP and poor outcome ($P = 0.002$, 95% CI = 2.22-23.5). Five factors were found to be independent outcome predictors on multiple logistic regression (OR, 95% CI): age (1.07, 1.03–1.10), NIHSS score (1.12, 1.04–1.27), on admission SBP (5.12, 4.01–16.23), on admission RBS (2.23, 1.92–6.49) and 24 Hr ARV-SBP (9.65, 3.02–20.1). The PAR of 24 hr ARV-SBP was 23.6%, second only to NIHSS score (26.4%). **Conclusions:** Reduction in BP variability might have a beneficial impact on the outcome of patients with acute ischemic stroke. There is further scope to explore optimum therapeutic strategies to minimize BPV in the management of acute ischemic stroke.

Keywords: Blood pressure variability, ischemic stroke, outcome predictors, population attributable risk

Introduction

Although significant achievements have been made in the field of early treatment, management, and secondary prevention of ischemic stroke, a remarkable proportion of patients still experience morbidity and mortality.[1,2] Large number of studies have aimed at identifying the predictors of outcomes in ischemic stroke patients of in order to formulate and improve treatment decisions.[3-5] Since blood pressure (BP) generally undergoes abrupt changes in the acute phase (first 24 hours of onset) of ischemic stroke, BP level at admission has been established as an important independent predictor of stroke outcome.[6-8] Hence, present treatment guidelines were made to target elevated BP.

Data from randomized controlled trials (RCTs) suggest that though BP can be safely reduced after the acute stroke period, there seems to be no indication that doing so is beneficial.[9-11] The Cochrane meta-analysis and guidelines state that optimal BP management in the context of initial stroke treatment remains uncertain.[12]

BP variability (BPV) might serve as an alternative explanation for the lack of evidence and uncertainty of treating elevated BP levels in acute stroke.[13] Current hypertension guidelines predominantly focus on mean casual BP measurements, dismissing BPV as random and merely an obstacle in the estimation of usual BP. Nevertheless, the importance of BPV has been emphasized recently and focus has shifted to "increased BPV" as a risk factor for cardiovascular morbidity and mortality.[14-16] A transient alteration in the autonomic nervous system occurs during the acute phase of ischemic stroke resulting in sympathetic hyperactivity, which is thought to be responsible for this increased BPV.[17,18] Due to impaired cerebrovascular autoregulation after ischemic stroke, BP fluctuation, that is, increased BPV directly affects the brain tissue, leading to the growth of the ischemic lesion resulting in poor functional outcomes.[14,19]

Although several studies have proved that increased BPV results in poor functional outcomes, the potential of BPV as a target therapeutic risk factor has not been studied extensively. Before embarking on RCTs for controlling BPV, its prevalence in the population and its impact on patient outcome have to be studied. Researchers use population attributable risk (PAR) as a tool to prioritize the risk factors that should be modified

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so that effective treatment strategies can be planned.[3-5] With this background, the current study aims to (i) confirm the association between 24 Hr BPV in acute phase of ischemic stroke and poor functional outcome at the time of discharge and (ii) find the PAR of BPV compared to other known outcome predictors.

Methodology

Study setup

A prospective observational study was undertaken from January 2019 to June 2019. Ethical clearance was obtained from the institutional ethics committee. Sample size was calculated with the following formula:

Equation I = $Z_{1-\alpha/2}^2 P (1-p)$

d^2

where $Z_{1-\alpha/2}^2$ is standard normal variate which is 1.96 at 5% type 1 error ($P < 0.05$), P = expected proportion in population based on previous studies, and d = absolute error which is 5%. A total of 75 patients who were diagnosed with ischemic stroke and admitted to Govt. Medical College and Hospital, Nagpur, India were included in the study. Patients admitted to GMCH within 6 hours of onset of ischemic stroke and confirmed by CT/MRI were included in the study but patients with secondary hemorrhagic transformation were excluded from the study. Written informed consent was obtained from all the patients.

Data collection

Data was collected by interview technique with a pre-tested and pre-designed questionnaire which included the sociodemographic variables and the predictor factors that are already known to have an impact on the outcome of ischemic stroke. The factors are described in detail below.

Assessment of stroke severity

Stroke severity was assessed by employing the widely used National Institute of Health Stroke Scale (NIHSS), performed by an experienced physician. The NIHSS is composed of 11 items and for each item, a score of 0 typically indicates normal function in that specific ability, while a higher score is indicative of some level of impairment. The individual scores from each item are summed up in order to calculate a patient's total NIHSS score. The maximum possible score is 42, while the minimum score is 0.

24 Hour ambulatory blood pressure monitoring

24-hour blood pressure was recorded with a hand-held portable device, CONTEC-ABPM50 (Ambulatory Blood Pressure Monitor) which employs the principle of oscillographic theory. Measurements were obtained hourly for 24 hours during the acute phase of ischemic stroke. Cuff size was selected according to subject's arm circumference. Based on the results of 24-hr ABPM, systolic and diastolic BPV was calculated using the index of Average Real Variability (ARV) according to the following formula:

Equation II: $ARV = \frac{1}{N-1}\sum_{k=1}^{n-1} X|\, BPk+1 - BPk\,|$

where N denotes the number of valid BP measurements and k is the order of measurements that ranges from 1 to n-1.

ARV is defined as the average of the absolute differences between consecutive BP measurements. Studies have shown it to be a more reliable prognostic indicator compared to other indices like standard deviation (SD) and coefficient of variation (CV) which only reflect the dispersion of BP measurements around the mean.[19] ARV is more sensitive to the individual BP measurement sequence and less sensitive to low sampling frequency.[20]

Definitions of outcome predictors

Factors that are already known to have an impact on functional outcome of stroke were collected at baseline and analysed. They are (i) age; (ii) female sex;[3-5] (iii) history of hypertension; (iv) history of diabetes mellitus;[3] (v) hyperlipidemia: total cholesterol (TCH) ≥ 5.70 mmol/L and/or triglyceride (TG) ≥ 2.04 mmol/L, high-density lipoprotein cholesterol (HDL-C) <1.0 mmol/L, low-density lipoprotein cholesterol (LDLC) >3.2 mmol/L; (vi) active smoking (current smoking vs. never or former smoking); (vii) Regular alcohol consumption (200 ml of wine/champagne or 500 ml of beer or 20 ml of hard liquor at least once per week); (viii) Body mass index;[3] (ix) history of atrial fibrillation (AF); (x) history of coronary artery disease (CAD); (xi) On admission random blood glucose levels (RBS) ranging from 70–400 mg/dl. Higher on-admission blood sugar level is proven to be associated with poor outcome;[3,21] (xii) Severity of stroke: stroke severity assessed by NIHSS score at the time of admission and a score >4 is considered to be a poor outcome predictor;[3,5] (xiii) On-admission systolic BP (SBP): the higher the initial SBP on admission, the worse is the outcome of the patients;[6-8] (xiv) etiologic subtype of stroke based on Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification;[3,4] (xv) systolic and diastolic BPV calculated by the index of ARV. Higher ARV values are proven to be associated with poor functional outcomes.[19]

Poor outcome at discharge measured by Barthel index score

Poor outcome is defined as functional impairment and dependency on others for daily activities, as measured by Barthel Index (BI) score <60 at the time of discharge.[22-24] BI is a scale that indicates the ability to perform a selection of activities of daily living. It comprises 10 items (tasks like feeding, bathing, grooming, dressing, bowel and bladder control etc.) with total scores ranging from 0 (worst mobility in activities of daily living/dependent on others) to 100 (full mobility in activities of daily living/independent). The environmental conditions were same for all the patients during hospital stay with no effect on patients' score. BI scale was applied exclusively by one investigator for all the patients to minimize interrater bias.

Statistical analysis

Continuous variables are reported as means ± SD and categorical variables are reported as percentages. 24 Hr ARV index of both SBP and DBP was calculated with above mentioned formula and association between functional outcome and ARV indices was reported by univariate analysis. Before estimating the PAR of a risk factor, the strength of association between the outcome predictor and functional outcome was determined using odds ratios (ORs) and 95% confidence intervals (CIs) by using univariable logistic regression. For binary risk factors, the reference was selected as the category that describes absence of the risk factor. For categorical risk factors, the reference was selected as the category with the lowest risk of poor functional outcome. Parameters with univariable *P* values <0.05 were transferred to multiple binary logistic regression analysis with backward selection (α stay = 0.05) to select predictors for further analysis, in order to identify the strongest and mutually independent risk factors. PAR was estimated using average PAR. To apply PAR software, non-dichotomous independent variables needed dichotomization before estimation, which was conducted as follows: age <75 vs. ≥75,[3] NIHSS <4 vs. ≥4 (minor vs. moderate/major stroke),[3-5] On-admission SBP <140 vs. ≥140 mm Hg,[5] 24 Hr ARV-SBP and on-admission RBS by their median values (mentioned below). Analysis was carried out with R software, Version 3.5.1.

Results

The analysis included 75 patients diagnosed with acute ischemic stroke who presented within 6 hours of onset. Their ages ranged from 35–90 and 28.6% were females. At the time of discharge, 29 (38.6%) patients had poor outcome. The 24-hr ARV index of both systolic and diastolic BP was calculated and divided into four quartiles as shown in Figures 1 and 2 along with their BI scores. The BI scores tend to decrease with each successive quartile of both 24-hr ARV-SBP (Q1-83 to Q4-53) and 24-hr ARV-DBP (Q1-76 to Q4-65). Simple univariate analysis was performed between the functional outcome and 24-hr ARV-SBP and 24 Hr ARV-DBP by grouping them into high and low ARV groups by median. The results are tabulated in Table 1. Twenty three (60.5%) of the patients with high 24-hr ARV-SBP were found to have poor functional outcome (*P* = 0.002 and 95% CI = 2.66–23.5) showing significant association between high ARV-SBP and poor outcome. However, the association between 24-hr ARV-DBP and poor outcome was not significant. Comparisons of baseline outcome predictors between the two groups of outcome and their unadjusted odds ratios and 95% CI by univariable logistic regression analysis are tabulated in Table 2. Categorization of age and NIHSS was based on a study conducted by Kim KI, *et al*.[25] and BMI was based on a study conducted by Yong M, *et al*.[16] In unadjusted logistic regression, age, sex, hypertension, on-admission SBP, on-admission RBS, 24-hr ARV-SBP, and NIHSS score were associated with poor outcome (*P* < 0.05). Upon multiple regression analysis, the outcome predictors found to be independent (p = <0.05) were as follows: age, NIHSS score, on-admission SBP, and 24-hr ARV-SBP [Table 3]. The PAR estimations of independent outcome predictors and their respective rankings are given in Table 3. 86.5% of the risk is attributable to the top five independent predictors, the highest being NIHSS score (26.4%) followed in order by 24-hr ARV-SBP (23.6%), age (18.5%), on-admission RBS (9.8%), and on-admission SBP (8.2%).

Discussion

The findings of the present study place a greater importance on BPV as a target therapeutic risk factor and have important implications in the management of patients with acute ischemic stroke. 36.5% of the patients had poor outcome at discharge which is in accordance with prior

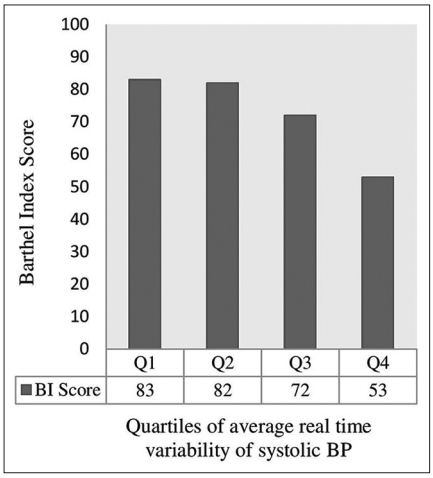

Figure 1: Correlation between 24-hr average real-time variability of systolic BP and Barthel index score. Barthel index score is taken on y-axis and the 4 quartiles of ARV index of systolic BP are taken on the x-axis. The average Barthel index score for each quartile is shown in the box

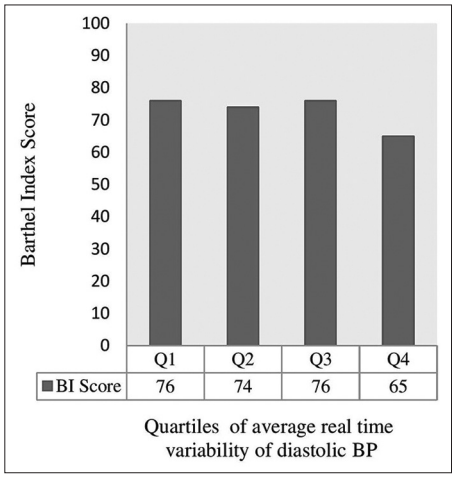

Figure 2: Correlation between 24-hr average real-time variability of diastolic BP and Barthel index score. Barthel index score is taken on y-axis and the 4 quartiles of ARV index of diastolic BP are taken on the x-axis. The average Barthel index score for each quartile is shown in the box

Table 1: Univariate analysis of patients with various high and low systolic and diastolic BP indices between good and poor outcomes groups

	Poor Outcome (*n*=29)	Good Outcome (*n*=46)	Total (*n*=75)	*p*	95% CI
24-hr SBP					
ARV- Low (Q1 and Q2) ≤ 10.6	6 (16.2%)	31 (83.8%)	37 (100%)	**0.002**	**(2.66-23.5)**
High (Q3 and Q4) >10.6	23 (60.5%)	15 (39.5%)	38 (100%)		
Mean -Low (Q1 and Q2) ≤ 134	11 (28.9%)	27 (71.1%)	38 (100%)	0.09	(0.16-1.11)
High (Q3 and Q4) >134	18 (48.6%)	19 (51.4%)	37 (100%)		
SD - Low (Q1 and Q2) ≤13.5	6 (15.7%)	32 (84.3%)	38 (100%)	**0.004**	(1.33-19.6)
High (Q3 and Q4) >13.5	23 (62.1%)	14 (37.9%)	37 (100%)		
CV- Low (Q1 and Q2) ≤11.2	7 (17.9%)	32 (82.1%)	39 (100%)	0.112	(5.88-11.36)
High (Q3 and Q4) >11.2	22 (61.1%)	14 (38.9%)	36 (100%)		
24 Hr DBP					
ARV - Low (Q1 and Q2) ≤ 7.47	16 (43.2%)	21 (56.8%)	37 (100%)	0.482	(0.57-3.72)
High (Q3 and Q4) > 7.47	13 (34.2%)	25 (65.8%)	38 (100%)		
Mean - Low (Q1 and Q2) ≤ 77.6	18 (45%)	22 (55%)	40 (100%)	0.246	(0.69-4.16)
High (Q3 and Q4) > 77.6	11 (31.4%)	24 (68.6%)	35 (100%)		
SD-Low (Q1 and Q2) ≤ 9.57	15 (34.8%)	28 (65.2%)	43 (100%)	0.471	(0.26-1.76)
High (Q3 and Q4) > 9.57	14 (43.7%)	18 (56.3%)	32 (100%)		
CV-Low (Q1 and Q2) ≤ 8.19	17 (36.1%)	30 (63.9%)	47 (100%)	1.297	(0.71-6.71)
High (Q3 and Q4) > 8.19	12 (42.8%)	16 (57.2%)	28 (100%)		

The risk factors with *p* value <0.05 were written in bold and considered to be significant. ARV=Average real time variability, SBP, DBP=Systolic and diastolic blood pressure, Q=Quartile and CI=Confidence interval, SD=standard deviation and CV=coefficient of variation

studies—Konstantinos (39.5%)[24] and Tziomalos (35.5%).[24] Significant association was reported between high BPV of SBP and poor outcome (*P* = 0.002, 95% CI = 2.66–23.5). However, studies carried out till date do not show any association between BPV and outcome at discharge.[24] This might be due to the use of an inappropriate scale for measuring outcome. According to the World Health Organization's International Classification of Functioning, Disability and Health (WHO-ICF), the levels of pathology (in this context stroke) are described in terms of impairment → activity limitation → participation. The type of scale used must be based on the level of pathology of interest and the clinimetric property of the stroke scale.[22] Hence, it is more appropriate to use Barthel Index to measure the activity limitation at the time of discharge instead of modified Rankin scale (mRAS), which is more suitable for measuring the participation at 3 months and/or 1 year post stroke.[14,19] However, when compared to studies which have measured functional outcome at 3 months and 1 year post stroke, a similar association between high BPV and poor outcome was obtained with SD of SBP (OR = 5.54,95% CI = 1.72–17.9, *P* = 0.004) from a study conducted by Adam *et al*.,[14] CV of SBP (OR = 2.36,95% CI = 0.56–11.43) from the study conducted by Tomii *et al*.[15] and mean SBP (OR = 0.76,95% CI = 0.66–0.86) from the study conducted by Yong M, *et al*.[16] The usage of ARV is limited to a few studies, including one that was conducted by Zefeng Tan, *et al*. which gave a *P* value of 0.05. ARV measures the average of absolute differences between consecutive BP measurements and is considered to be the most reliable measure of BPV.[19,20] The routinely used SD and CV for measurement of BPV have a notorious shortcoming in that they reflect the dispersion of BP measurements around a single value only (the mean) and do not take into account the order in which the BP measurements were obtained. As a result, two subjects with different BP measurement sets may have the same SD or CV.[19,20] This is proven to be correct by reviewing the BP variability (*P* = 0.002,95% CI = 2.22-23.5) in the present study which is quite high compared to above-mentioned studies.[14,15,16] The mechanisms underlying this finding are still uncertain and might be due to the (i) transient alteration of the autonomic nervous system that occurs during the acute phase of stroke, resulting in sympathetic hyperactivity and thereby affecting blood pressure control.[17] (ii) superimposed effect of BPV on already impaired cerebral autoregulation, resulting in hypoperfusion of ischemic penumbra.[14,25] (iii) the good collaterals could expose the areas of lesion core to cellular mediators of inflammation which are elevated in patients with high BPV.[25,26] and (iv) finally, possible mechanisms such as cerebral edema formation or other organ system damage resulting from increased BPV could be responsible for this finding.[26]

Before taking BPV into consideration as a potential risk factor to be controlled to improve stroke outcomes, knowing the prevalence of this risk factor in the population and the proportion of poor outcome that is attributable to BPV must be given importance. Moreover, knowing the impact of BPV on outcome compared to all other well-known outcome predictors is also necessary to emphasize the importance of controlling BPV. PAR is a methodological tool to choose targets for modification according to their estimated contribution to reduce the outcome of interest, like poor functional outcome of stroke.[3-5] The average PAR value of 24-hr ARV-SBP was found to be 23.6% which is quite high and sufficient to highlight the importance of BPV. It has been ranked second only to

Table 2: Outcome predictors at baseline and unadjusted associations with functional outcome of patients at the time of discharge assessed by univariable logistic regression analysis

Outcome Predictors	Poor Outcome at Discharge		Univariable Logistic Regression	
	Yes	No	OR (95%CL)	p
	29 (38.6%)		46 (61.3%)	
Age (in yrs) Mean±SD	62.2±11.9	58.4±14.2	1.05 (1.02-1.08)	**<0.001**
Age Groups				0.09
≤65	3 (10.3%)	9 (19.5%)	1	
66-75	16 (55.1%)	23 (50%)	2.26 (1.15-3.37)	
76-85	9 (31%)	13 (28.2%)	6.96 (3.20-10.66)	
>85	1 (3.4%)	1 (2.17%)	1.76 (1.16-2.75)	
Female Sex	13 (44.8%)	8 (17.3%)	1.95 (1.11-3.48)	**0.02**
Stroke risk factors, Pre stroke				
BMI in kg/m^2	28.2±6.2	27.4±5.4	1.04 (0.98-1.09)	0.12
BMI Groups			0.13	0.14
<25	8 (27.5%)	16 (34.7%)	1	
25-29.9	11 (37.9%)	19 (41.3%)	0.89 (0.45-1.47)	
≥30	10 (34.4%)	11 (23.9%)	1.49 (0.36-1.17)	
Hypertension	18 (62%)	28 (60.8%)	3.06 (1.16-8.05)	**0.03**
Type 2 Diabetes mellitus	11 (37.9%)	19 (41.3%)	0.86 (0.33-2.25)	0.96
Coronary artery disease	5 (17.2%)	10 (21.7%)	0.75 (0.22-2.46)	0.85
Current smoking	4 (13.7%)	11 (23.9%)	0.50 (0.14-1.78)	0.44
Regular alcohol consumption	11 (37.9%)	13 (28.2%)	1.55 (0.57-4.16)	0.53
Atrial fibrillation	11 (37.9%)	12 (26.1%)	1.73 (0.63-4.69)	0.40
Dyslipidemia	5 (17.2%)	7 (15.2%)	1.16 (0.33-4.07)	1
Clinical Characteristics				
On-admission SBP				
Mean±SD	159±27.2	140±23.4	7.18 (2.49-20.6)	**<0.001**
On-admission RBS				
Mean±SD	206±62.2	126±41.2	3.73 (1.36-10.1)	**<0.001**
24-hr ARV-SBP Mean±SD	15.2±3.05	8.36±2.4	10.1 (3.11-22.2)	**<0.001**
24-hr ARV-DBP Mean±SD	8.3±3.03	7.35±2.19	1.46 (0.57-3.72)	0.57
Etiologic subtype of ischemic stroke				0.08
Large artery atherosclerosis	7 (25%)	13 (28%)	1	
Cardiac embolism	11 (36.5%)	10 (20.8%)	1.95 (1.11-3.48)	
Small artery occlusion	4 (13.5%)	6 (15.1%)	1.01 (0.49-2.03)	
Stroke of another determined cause	1 (2.9%)	2 (4.34%)	0.97 (0.24-3.03)	
Stroke of undetermined cause	6 (22.1%)	15 (32.3%)	0.77 (0.42-1.42)	
NIHSS score, Mean±SD	19.2±7.2	7±2.98	1.16 (1.08-1.23)	**<0.001**
NIHSS Groups				**<0.001**
0-4	1 (62.5%)	6 (79.9%)	1	
5-15	11 (33.7%)	39 (19.6%)	2.20 (1.36-3.53)	
≥16	17 (3.8%)	1 (2.17%)	8.86 (1.92-51.71)	

The risk factors with *p* value <0.05 were written in bold and considered to be significant. SBP=systolic blood pressure, RBS=Random blood sugar, ARV=Average real time variability, NIHSS=National institute of health stroke scale, BMI=Body mass index, SD=Standard deviation, OR=Odds ration and CL=Confidence interval

NIHSS score (26.4%) which was found to have the highest PAR reported by majority of the studies.[3-5] Though PAR of age (18.5%), on-admission RBS (9.8%), and on-admission SBP (8.2%) were found to be independent outcome predictors in the studies conducted by Carolin *et al*.[3] and Davolin A, *et al*.[21] they are ranked below BPV with ranks third, fourth, and fifth, respectively.[3,21] This shows the relative importance of BPV compared to other predictors.

Given these findings, it is reasonable to hypothesize that reduction in BP variability during the acute phase of ischemic stroke might have a beneficial impact on the outcome of patients. However, there is a paucity of data directly comparing the predictive value of BPV, the timing and duration of BPV measurements, the practicality and acceptability of patients to the various BP measurement techniques, and how to best measure or define BPV. Further studies are needed on a large scale to determine the feasibility and efficacy of reducing BPV after stroke so that RCTs can be planned accordingly. The effects of antihypertensive agents on BP variability should be considered in ischemic stroke population and the classes of antihypertensives that exert

Table 3: Multiple binary logistic regression analysis with backward selection (odds ratios and respective confidence intervals) and their respective population attributable risks along with rankings

Outcome Predictor	Multiple Logistic Regression		Average PAR (%)	Rank
	OR	95% CL		
Age	1.07	1.03-1.10	18.5%	(3)
On-admission SBP	5.12	4.01-16.2	8.2%	(5)
On-admission RBS	2.23	1.92-6.49	9.8%	(4)
24-hr ARV-SBP	5.65	3.02-20.1	23.6%	(2)
NIHSS score	1.12	1.04-1.27	26.4%	(1)
Total Explained			86.5%	

SBP=systolic blood pressure, RBS=Random blood sugar, ARV=Average real time variability, NIHSS=National institute of health stroke scale, PAR=Population attributable risk, OR=Odds ration and CL=Confidence interval

greater reductions in BP variability might be more appropriate for management.

To our knowledge, this is the first study to report the PAR value of the 24-hr BPV which is increasingly gaining attention in the field of stroke. It is also one of the few studies which have used ARV index to measure BPV which is more reliable. However, some limitations of our study have to be considered. This is a small sample study conducted in a single center; so, our findings carry a risk of causality error. Due to issues of loss of follow up, our study is limited to measuring the functional outcomes at the time of discharge instead of the 3-month functional outcome that was supposed to be measured. As it is not appropriate to measure functional recovery with mRAS in such a short span, that is, at the time of discharge, we have used the BI score for finding the functional outcome in terms of activity limitation. Moreover, we did not consider the possible influence of antihypertensive medications or class of antihypertensive medications which may influence BP variability or outcome. Though all patients were kept on the same dual antihypertensives post stroke during their hospital stay, the antihyperstensives used by patients before the onset of stroke belong to a wide range of antihypertensive classes. Finally, we cannot fully exclude the possibility that BP variability may have been the result of stroke severity, rather than the cause of poor functional outcome because a deteriorating or fluctuating clinical course may lead to a variable BP profile. However, the adjustment of outcomes for baseline severity suggests that BP variability was causal.

Conclusions

Although robust conclusions cannot be drawn because of limitations in the quality of the present study, it provides important novel information that the increased variability in BP in acute phase of ischemic stroke is related to poor functional outcome. This underlines the importance of BP monitoring in the early phase of ischemic stroke to warrant reasonable target BP level and stability. Hence, large and multicenter prospective studies have to be undertaken in future to elucidate the causality between BP and the clinical outcomes after acute ischemic stroke.

Clearly, there is further scope to explore BPV, how best to measure or define BPV, the timing and duration of BPV measurements, feasibility and efficacy of reducing BPV, and the practicality and acceptability of patients to the various BP measurement techniques so as to determine its role as a target therapeutic risk factor in the management of acute ischemic stroke. In addition, our results have potential implications for clinical practice, whereby clinicians should aim for smooth and sustained control of BP in acute stroke and not solely focus on absolute or average BP values.

Trials to investigate the potential therapeutic targeting of BPV with specific classes of antihypertensive drugs and any potential benefit of doing so in acute stroke would be useful to address gaps in the current knowledge. Ongoing randomized trial on the effect of comparison of various classes of antihypertensives on controlling BPV after ischemic stroke may be of help in guiding the clinical recommendations for BPV management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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