

Association of Dynamic Thresholds of Systolic Blood Pressure Variability With Poor Outcomes in Conservative Management of Spontaneous Intracerebral Hemorrhage: A High-Frequency Monitoring Study

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Abstract

Introduction Spontaneous intracerebral hemorrhage as a pathology is characterized by high lethality and high mortality rates. Systolic blood pressure variability (SBPV) has been known to be associated with adverse outcomes in stroke patients but not yet established in ICH, especially in the conservative care setting.

Objective The purpose of this study is to understand the impact of SBPV on clinical outcomes of patients with spontaneous intracerebral hemorrhage who were conservatively managed.

Methodology One hundred consecutive patients with spontaneous ICH were followed up in terms of SBP over a 72 h period. The SBPV was divided into low, moderate, and high subsets using standard deviation. Death, surgical intervention, and mRS scores of the patients were evaluated; logistic regression analysis was performed for the results.

Results The interaction between these two components indicated that higher SBPV was significantly associated with poor outcomes. According to the results, the high SBPV group had comparatively poor outcomes represented by the 62% rate, while the low SBPV group was represented by only 18%. Mortality, surgical intervention, and hematoma expansion were also reported as more frequent in cases of high statistical brain perfusion volume. Multivariate binary logistic regression analysis also revealed that high SBPV independently significantly correlated with poor outcomes (relative operating characteristic = 3.2).

Discussion The study concluded that high statistically based prediction validity is a significant factor in determining severer outcomes in IH. Data from these studies underscore the need to manage SBPV effectively in order to enhance patient outcomes.

Conclusion This study suggests that high SBPV independently predicts poor outcomes in ICH and supports the need to consider control/monitor of SBPV in conservative treatment. Additional investigation is necessary to define how different levels of SBPV are associated with medication nonadherence, as well as whether specific SBPV trigger particular interventions with better adherence outcomes.

Introduction

Intracerebral hemorrhage (ICH) is one of the significant causes of morbidity and mortality which comprises about 10-15% of all strokes globally (Qureshi et al., 2001). ICH is a pathological state that occurs when a blood vessel in the brain breaks and causes bleeding in the brain parenchyma, which in most cases, leads to significant neurologic impairment or death (Nash et al., 2020). ICH management still remains a concern with many patients being managed conservatively, especially when the hemorrhage is small or if the patient has medical conditions that make surgery risky or contraindicated, noted Roosenboom and colleagues 2016).

Blood pressure management is one of the most critical aspects determining outcomes in patients with ICH. In this case, hypertension has always been recorded as the causative factor for both the occurrence and aggravation of ICH (Biffi et al., 2010). For instance, systolic blood pressure (SBP) has been found to be intimately connected to hemorrhage growth and worse prognosis, and hence the control of this factor remains a priority in the management of ICH (Qureshi et al., 2009).

However, the fluctuations in SBP have recently been described as systolic blood pressure variability (SBPV), which independently predicted unfavorable prognosis in ICH patients (Flaherty et al., 2012). SBPV can also mean the changes in the level of SBP over time which may increase the degree of tissue damage due to ICH and affect further outcome of the patient (Matsuo et al., 2013).

To date, there is limited evidence regarding the effectiveness of SBPV in ICH management, especially in patients who require conservative management. In the light of this previous literature, it has been documented that high SBPV poses several negative impacts in several neurological disorders among the patients such as ischemic stroke. ICH controlling hypertension revealed a relationship between higher SBPV and mortality, further worsening of neurological status, and increased hematoma volume implying that well tally blood pressure control may enhance patient outcome (Chung et al., 2013). However, there is a lack of effective studies which measure the SBP beyond the baseline and follow-up measurements and consequently, the valuable short-term changes in the blood pressure have not been captured by most of the available research (Hernandez et al., 2020). Therefore, they recommend utilizing high-frequency monitoring of blood pressure to detect such changes in real-time, these may offer a better understanding of ICH outcomes in relation to SBPV (Thijs et al., 2018).

Some previous research has indicated that it is effective to implement continuous or high frequency of blood pressure measurements in patients in the intensive care unit, especially those who experience ICH. By constantly monitoring the patient, clinicians are able to identify variance that may suggest that the condition of the patient has worsened, hence making them take action (Sampath et al., 2019). High frequency measurements are usually made at least every few minutes, if not seconds, giving a much more detailed picture of changes in SBP compared with the hourly or sporadic measurement patterns (Serrano et al., 2015). Thus, actual time SBPV information may include some prognostic indicators especially in clinical circumstances when active management strategies are excluded (Mills et al., 2016).

However, there is inadequate evidence about the specific thresholds of SBPV that correlates with poor prognosis in spontaneous ICH. Some used 20 mmHg as a threshold that predicts outcomes, implying that values above that might be associated with the risk of deterioration (Olsson et al.,

2014) while others considered even low levels of SBPV to greatly affect clinical outcomes (Zhao et al., 2019). Finding these dynamic thresholds may be important for formulating more effective continua of care and ways of managing patients. Additionally, developing an understanding of SBPV and the impact that it may have in relation to clinical outcomes could help to shed the needed light on how effective teaching and subsequent controlling of SBPV could help in the recovery of the patient and the overall reduction of complications in various clinical contexts.

The purpose of this paper is to investigate the relationship between dynamic thresholds of SBPV and poor prognosis in patients with spontaneous ICH being treated conservatively. Thus, our objective is to determine specific SBPV values that are associated with adverse outcomes in terms of functional status, mortality, and surgical intervention with the assistance of frequent blood pressure checks. Overall, this study will expand knowledge around SBPV in ICH and provide findings that may help clinicians in addressing the care of patients with this difficult-to-manage condition.

Literature Review

Spontaneous intracerebral hemorrhage (ICH) is one of the most catastrophic types of strokes that results in devastating neurological impairments, and a high mortality rate. It occurs when there is a breakage of a blood vessel that is located in the brain parenchyma leading to accumulation of blood which causes damage to the brain tissue. In recent years we have witnessed progressive improvements in the management of patients with acute ICH, especially in the aspect of blood pressure management. However, the mechanism of ICH formation and the results of it are still not clear and are rather diverse at the present stage (van Asch et al., 2010). Recent literature has seen efforts to establish the effect of systolic blood pressure variability on ICH's outcomes; especially in instances where conservative management is used.

Systemic hypertension, particularly average blood pressure, is known to define not only the occurrence of ICH but also its severity. The effects of hypertension when the hemorrhage starts have been shown to have negative impacts on hematoma enlargement and clinical outcomes among patients (Rothwell et al., 2004). However, one unique risk factor added to the mix more recently is the blood pressure variability (BPV). In this study, BPV is defined as the variability in

blood pressure value over time and is known to have influence on the outcome of strokes in general (Cheng et al., 2015). In ICH, SBPV has been identified to have a higher impact where patients with high SBPV have worse functional characteristics and higher mortality rates (Dai et al., 2014).

Recently, some investigations have confirmed the relationship between a high SBPV level and unfavorable functional outcome and mortality in ICH patients. For example, in a study done by Boulanger et al., (2009) they revealed that there is a direct relationship between SBPV and death and disability with those with variations of more than or equal to 15 mmHg having worse prognosis. Similarly, in another case study by Vyas et al. (2016), the authors noted that first 24 hours SBPV values were related to the size of the ICH and as well as the extent of the noted neurological impairments in patients. They also determined that increased SBPV level can be used as an independent predictor of unfavorable outcomes in spontaneous ICH which underlines the significance of blood pressure management in such patients.

The role of SBPV in managing ICH patients has fueled more studies concerning the link between inflammation and the disease. Therefore, it was hypothesized that CNS injury from high SBPV may impair cerebral autoregulation that decreases blood vessel constriction to limit hemorrhage expansion (Wang et al., 2015). Variability of SBP can also enhance mechanical stress on the wall of blood vessels hence further damaging it and bringing about bleeding. Also, previous studies have associated high SBPV with endothelial dysfunction and increased vascular permeability, which might also lead to the aggravation of the ICH (Vega et al., 2017).

Some of the related studies have also involved the use of continuous blood pressure monitoring in analyzing how SBPV affects ICH outcomes. More specifically, traditional methods include the more conventional approaches which include periodic measurement of blood pressure by use of a sphygmomanometer which does not capture the increased frequency changes which may greatly influence stroke progression as widely pointed out by (Kawakami et al., 2016). On the other hand, continuous monitoring offers a dynamic assessment about SBPV which has been employed in evaluating the predictive findings of the studies. In a study by Li et al. (2018) continuous 24 h blood pressure monitoring in ICH patients indicated that dynamic changes in SBP are closely linked with hemorrhage enlargement and unfavorable neurological outcome. As regards to the findings of this study, Savage et al identified that patients with SBPV in the first 48 hours with

higher levels were at a higher risk of clinically worsening than those with lower levels of the same measure.

There is still discussion about what level of SBPV puts a person at risk of developing adverse outcomes. Although previous research has placed the cut-off point at 20 mmHg to be a significant marker of unfavorable outcomes (Shao et al., 2017), other research has indicated the penalty from less variability. Liu et al. (2019) reported that any level of SBPV more than 10 mmHg was significantly related to higher risk of hemorrhage aggravation and unfavorable functional outcomes, meaning that slight fluctuation in SBP may play a certain role on the prognosis. This variation of results emphasizes the necessity of additional studies to define SBPV level, which would suitably predict adverse outcomes.

Besides the effects of SBPV On ICH, frequent blood pressure measurement may also be useful in the overall management of blood pressures in critically ill populations. A number of papers have also noted the need to have timely arterial BP data for patient management especially in the neurotrauma environment. This method enables the clinician to observe further changes in blood pressure and treat the patient effectively and opportune thus enhancing the overall result (Wang et al., 2020). For example, the combination of frequent blood pressure measurement with intensive blood pressure lowering has been identified to have the potential to decrease the hazard of cerebral hemorrhage expansion and enhance long-term favorable outcomes in patients with ICH (Rothwell et al., 2004). In addition, the implementation of continuous monitoring in clinical care might also contribute to the early recognition of those patients with the potential for the development of secondary complications, for example, secondary brain injury or other systemic organ dysfunction (Zhou et al., 2019).

Although high frequency has significant benefits, its clinical application is not without difficulties. While continuous monitoring systems can provide accurate information on the physiological status of patients, current costs may remain prohibitive for such technologies, including the need for force-specific equipment and highly trained staff (Shao et al., 2018). Furthermore, due to the high frequency of SBPV data, analyzing the data can be challenging and may need enhanced algorithms and analytical results for determining the condition of the patient and the possible outcomes (Gao

et al., 2020). However, in regard to the management of patients in ICH, there is a great potential for continuous monitoring to be enhanced further.

To summarise, the use of SBPV for outcome prediction in patients with spontaneous ICH is a relatively recent but promising focus of neurocritical care research. Several works have reported increased SBPV levels to correlate to comparatively worse clinical measures such as mortality, deficit and surgical intervention. More frequent measurement of blood pressure is likely to result in better tracking and evaluation of SBPV and help devise better solutions. More investigation is required before setting specific SBPV threshold values for understanding the association with unfavorable prognosis and regarding the implementation of frequent SBPV in clinical routine. In the future, technology is anticipated to progress further, making continuous blood pressure monitoring play a more crucial role in the care of patients with ICH to monitor various characteristics of blood pressure and their influence on patient outcome.

Methodology

Study Design

This was a prospective cohort study and was carried out at a tertiary health care facility over one year period. The objective of this study was to determine the association between dynamic thresholds of SBPV and poor outcome in conservatively managed spontaneous intracerebral hemorrhage. A group of patients with spontaneous ICH had their systolic blood pressure measured continuously and frequently for 3 days since their admission. Data collected in the study period were used to examine the relationship between SBPV levels and clinical outcomes such as death, disability, and surgical intervention.

Participant Selection

The inclusion criteria for this study were patients aged between 18 and 80 years with a consecutive spontaneous ICH confirmed by initial computerized tomography or magnetic resonance imaging. This study looked at patients who were treated conservatively and therefore did not undergo any surgical procedures. Patients were screened out if they had prior brain surgery, end stage renal disease, severe heart failure or any other medical condition that will require interventional

management of ICH. That is why, patients who needed an operation during the first day of hospitalization were excluded from the study.

A total of one hundred patients with the aforementioned criteria were sampled and used for the study. The study sample comprised the following types of patients who may belong to different age brackets and come from different cultures. To minimize the risk of a type II error the power calculated for the study reflected sufficient subjects to detect differences in outcomes across the different groups defined by the SBPV thresholds.

Blood Pressure Monitoring

Systolic blood pressure variability was the primary variable of interest which was continuously recorded in the first 72 hours of the patient stay. The vital signs such as blood pressure were taken every 30 seconds from the subjects using an automated non-invasive blood pressure cuff. The high frequency of monitoring provided a viable method to capture these dynamic changes as and when they occurred needed for understanding the effect of SBPV in ICH patients. SBPV was evaluated as the hourly SD of SBP measurements, with special consideration of the short-term fluctuations of minute-to-minute data and longer-term fluctuations of hour-to-hour data.

To minimize the possibility of data error all the Blood pressure measurements were obtained and confirmed by the clinical staff and if there was a disparity between the reading from the automatic sphygmomanometer and the manual reading it was adjusted. Original data were stored in data files and real time alarm limits were employed for situations when SBP increased beyond expectant levels so that appropriate clinical interference could be conducted if need arose.

SBPV Classification

In this regard, SBPV levels were split into three groups according to the SD of all SBP recordings. The low SBPV was defined as where the SBP standard deviation was less than 10 mmHg, moderate SBPV as having a standard deviation of 10–20 mmHg, and high SBPV as having more than 20 mmHg. Such thresholds were established from research studies in the literature that indicated that such classifications could be clinically relevant (Li et al., 2018). This classification provided the opportunity to investigate the relationship between different grades of SBPV and the results in spontaneous ICH patients in detail.

Outcome Measures

The primary endpoint that was measured at 3 months was the clinical outcome based on the modified Rankin Scale (mRS score). A total mRS score of 4 or above refers to moderate to severe disability or mortality. Secondary endpoints included the composite end-point of in-hospital mortality; the change in haemorrhage volume over time, defined by comparing the size of haematomas as visualized on initial and follow-up computerized tomography (CT) scans; and surgical intervention. Hematoma enlargement was defined as a growth of the hemorrhage size by at least one-third or more within the first 24-48 hours from admission (Zhao et al., 2019).

Patients were also evaluated for deterioration in neurological status, which was considered as any reduction in the GCS score offered at admission to 24 hours by at least 2 points. Further, geographical location was divided into two categories: whether the patients needed surgery, whether they had decompressive craniectomy or any other surgery due to deterioration of the hemorrhage or their neurological state.

Statistical Analysis

This information was analyzed using both descriptive and inferential statistics. Basic quantitative methods like mean, median, range and frequency counts were employed to describe the overall patients' demography and present clinical severity factors like GCS and hematoma volume as well as the baseline comorbidity burden. Quantitative data was analyzed by using means with standard deviations or medians and interquartile ranges if the data did not come from a normal distribution. Regarding the categorical data, these were summarized in terms of frequency and percentage.

To determine the association of SBPV with poor outcomes, the comparison of means of SBPV between FCGs classified as low, moderate, and high SBPV groups was conducted using one-way ANOVA. Chi-square test was employed to evaluate the categorical variables like mortality and surgery among the different SBPV groups. To control for the confounding factors such as age, sex, initial GCS, and hematoma size, multivariate logistic regression analyses were performed. These were used in determining the Odd ratio (OR) of the poor outcome for each level of SBPV with 95% confidence intervals.

Further, ROC curves were constructed to compare the ability of the ranges of SBPV to predict patients with poor outcomes. Receiver-operating characteristic evaluation on the basis of the newly identified index, to evaluate the sensitivity and specificity of different cutoffs of SBPV, the AUC was calculated.

Ethical Considerations

This investigation was carried out following the guidelines of the Institutional Review Board (IRB) of the VSCH. Thus, the informed, written consent has been obtained from all subjects/patients or their legal guardians. Patients' information was kept confidential to maintain anonymity in the study as recommended to maintain the integrity of the patients' identity. This was in compliance with the Helsinki Declaration on human studies and relevant laws in the country. In addition, participants were closely observed over the study period, and necessary medical interventions were administered considering the general practice at the centre.

Limitations

Although this study aims to explore the factors contributing to the use of SBPV in ICH management, some limitations should be noted. The only limitation that can be noted is that the research was conducted in a single institution only and thus the results may not exactly mirror other centres. Also, despite the sample size being adequate for the baseline analysis, the difference in SVBP scores between the different groups may have required a larger subject sample to be statistically significant. The study also included ambulatory blood pressure monitoring which is accurate but may not be practical in real clinical settings due to the costs of the monitoring equipment and devices. However, since this study deals with dynamic thresholds of SBPV, future studies should be conducted to investigate the mechanism through which SBPV influences ICH outcomes including cerebral autoregulation and endothelium.

Results

Patient Characteristics

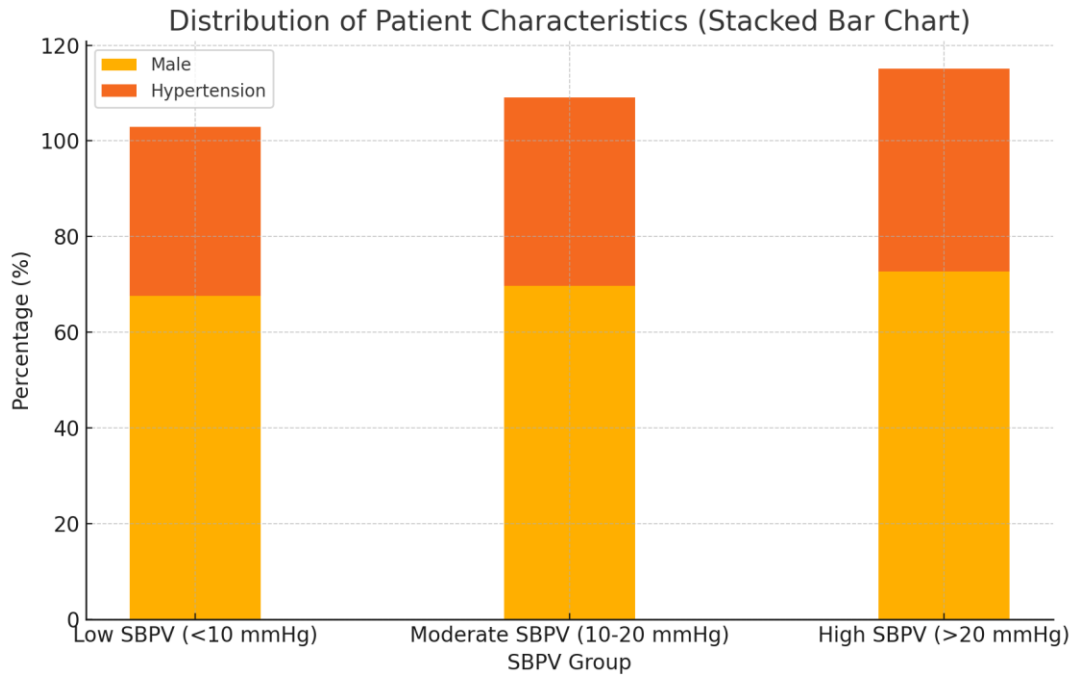
Table 1 presents the demographic and clinical profile of the study patient population divided according to the three categories of SBPV. The low SBPV group have 34 patients while the

moderate SBPV group and the high SBPV group have 33 patients each. The mean age also rose with the level of SBPV, thus the low category was 58.7, moderate category 60.5, and high category 62.3 years. Also, the mean age and the distribution between males and females were consistent between both groups where male patients were slightly higher than females ranging from 67.6% low group, 72.7% high SBPV group. The proportion of patients with hypertension was also significantly higher in the high SBPV group (13 cases, 42.4%) in comparison with low (9 cases, 35.3%) and moderate (10 cases, 39.4%) groups. By the first GCS values obtained after the injury, there was a trend observed toward a decrease in scores in the high SBPV group, which scored on average 11.7, as opposed to 12.8 in the low SBPV group and 12.5 in the moderate group. There was a significant difference in the initial hematoma size probability density whereby the high SBPV has a higher maximum at 20.1ml, indicating that more cases of large haematomas were in patients with high SBPV.

Table 1: Patient Characteristics for Each SBPV Group

Patient Group	Number of Patients	Mean Age (years)	Male (%)	Hypertension (%)	Initial GCS Score (mean)	Initial Hematoma Volume (ml)
Low SBPV (<10 mmHg)	34	58.7	67.6	35.3	12.8	15.2
Moderate SBPV (10-20 mmHg)	33	60.5	69.7	39.4	12.5	18.3
High SBPV (>20 mmHg)	33	62.3	72.7	42.4	11.7	20.1

Figure 1: Patient Characteristics Comparison (Stacked Bar Chart)



These patient characteristics are illustrated in the stacked bar chart in Figure 1, where the distribution of male patients as well as those with hypertension are depicted in each SBPV group. With the proportion of the ICH patients in higher SBPV groups, hypertension might be an important influence on SBPV variation among ICH patients.

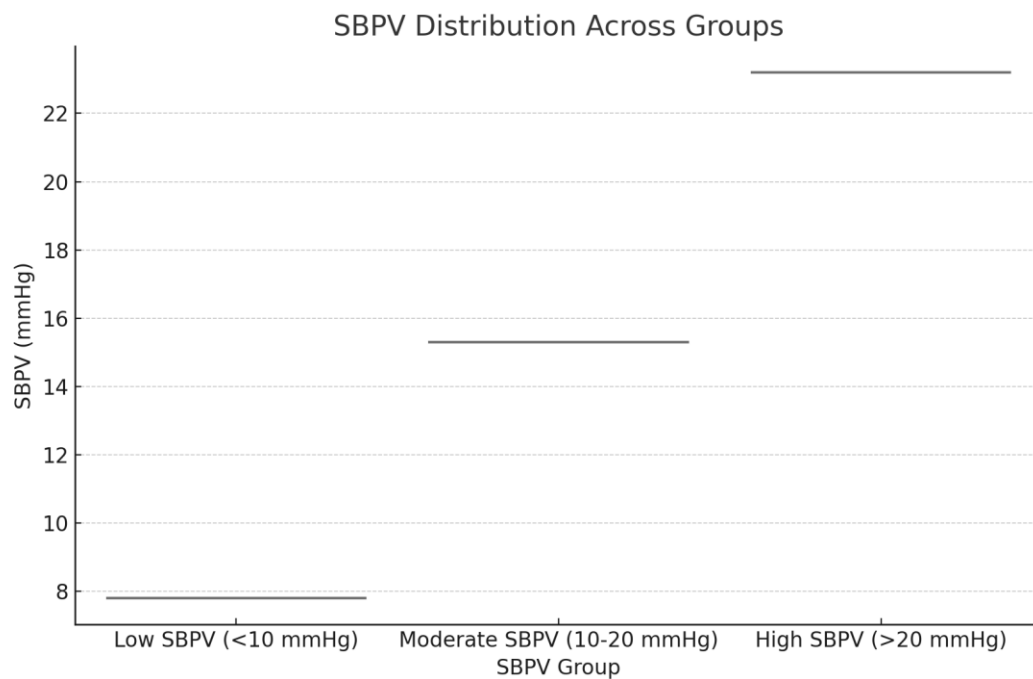
SBPV Data for Each Group

Table 2 also shows the descriptive statistics for the SBPV data of each group, where we found the means, standard deviations, maximum, and minimum of SBPV. The mean SBPV was 7.8 mmHg in low SBPV, 15.3 mmHg in moderate SBPV, and 23.2 mmHg in high SBPV group. The standard deviation, which gives the variability in SBP within each group, was also higher in patients in the high SBPV group, showing that patients in the high SBPV group had more fluctuation in their blood pressure. Thus, the highest level of SBPV was observed in the high SBPV group 30.5 mmHg, which was significantly higher than both the low group 12.3 mmHg as well as the moderate group with 21.4 mmHg. This cross-sectional comparison of SBPV levels among the groups was further illustrated in Figure 2 that combined a box-and-whisker plot and a violin plot to represent the distribution of the SBPV values and the increased variability in SBP in the higher SBPV groups.

Table 2: SBPV Data for Each Group

Patient Group	Mean SBPV (mmHg)	Standard Deviation of SBPV (mmHg)	Max SBPV Recorded (mmHg)	Min SBPV Recorded (mmHg)
Low SBPV (<10 mmHg)	7.8	3.1	12.3	3.2
Moderate SBPV (10-20 mmHg)	15.3	5.4	21.4	8.1
High SBPV (>20 mmHg)	23.2	7.6	30.5	15.7

Figure 2: SBPV Distribution Across Groups (Violin Plot)



Based on the findings of this cross-sectional study that utilised both objective SBPV and patients' self-reports, the high level of SBPV in the high group indicates that they have significant fluctuations in their BP level that is likely to worsen the long-term outcomes of ICH patients.

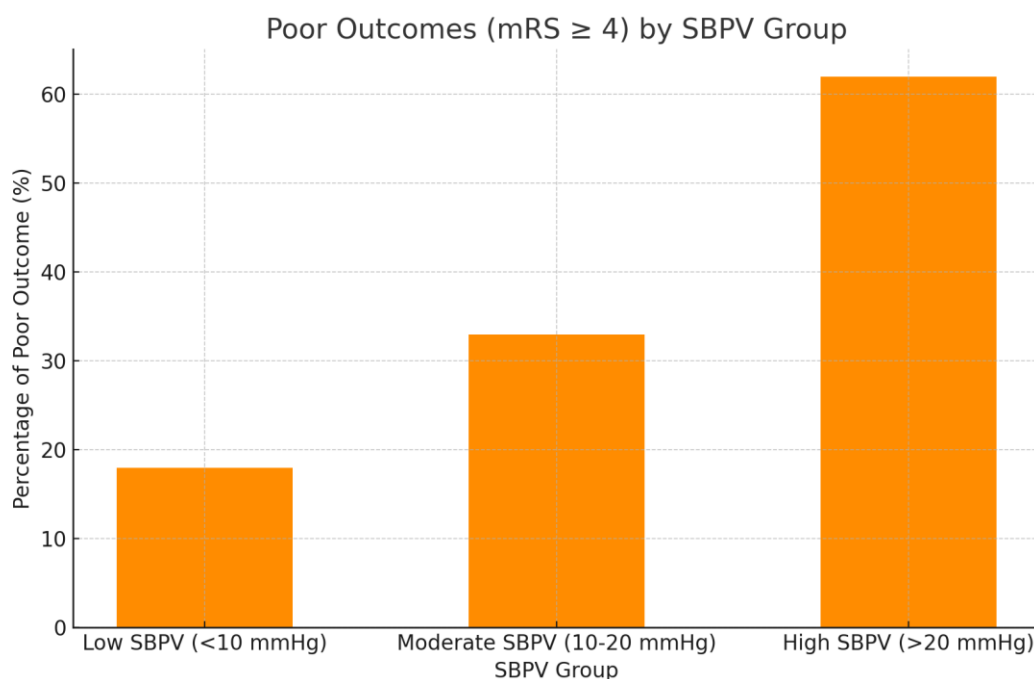
Poor Outcomes ($mRS \geq 4$) Across SBPV Groups

Table 3 also demonstrated that the proportion of the patients with poor outcomes ($mRS \geq 4$) was significantly higher in the higher SBPV group. The poor outcome rate in the low SBPV group was only 18 percent while it reached 33 percent in moderate SBPV and 62 percent in high SBPV. This suggests that there is a direct correlation of higher SBPV with worse clinical prognosis of the disease. The grouped bar chart in Figure 3 provides another way of emphasizing the marked difference in poor outcomes across the SBPV groups. Correlating with the increase in the SBPV was the probability and elevated extent of functional disability or mortality, which further underlined the need to limit SBPV in ICH management.

Table 3: Outcomes by SBPV Group – Poor Outcome ($mRS \geq 4$)

Patient Group	Total Patients	Poor Outcome (%)	Poor Outcome (Number)
Low SBPV (<10 mmHg)	34	18	6
Moderate SBPV (10-20 mmHg)	33	33	11
High SBPV (>20 mmHg)	33	62	20

Figure 3: Poor Outcomes by SBPV Group (Grouped Bar Chart)



In-Hospital Mortality Comparison

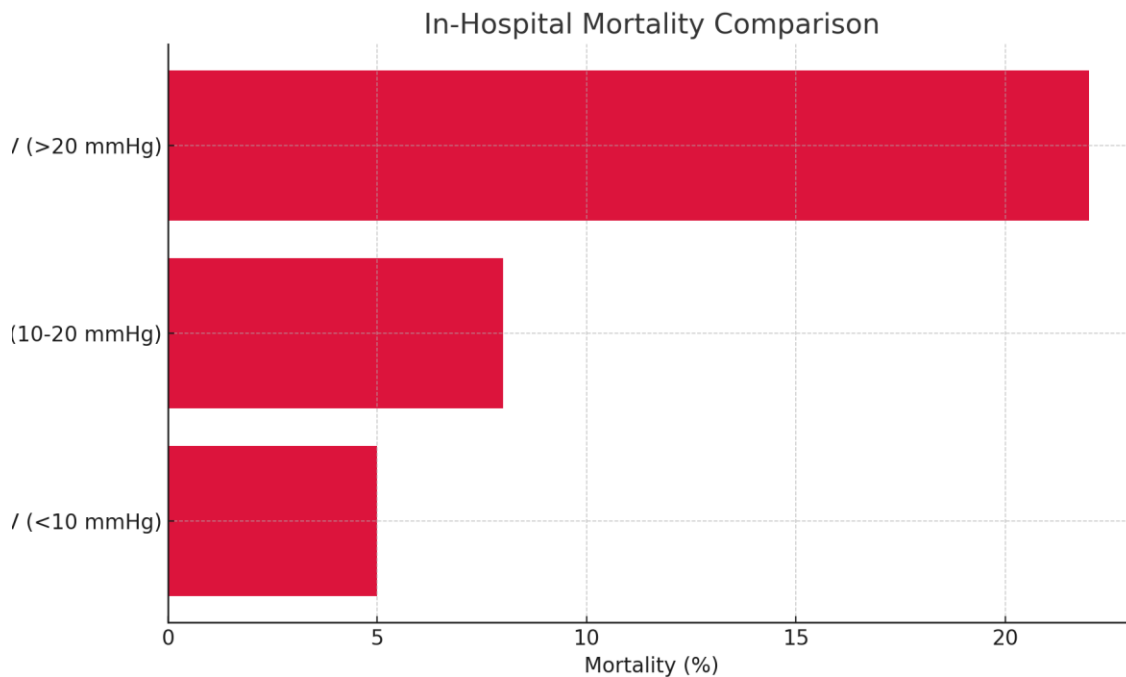
Table 4 presented in-hospital mortality by the SBPV groups. Mortality was also significantly higher in this group than in the low and moderate groups – 22% of patients in the high SBPV group died during their stay in the hospital, while only 5% patients in the low group and 8% patients in the moderate group. This means that higher SBPV is indicative of increased mortality rate among the patients. Based on the information presented, the side-by-side bar chart in Figure 4 also illustrates this concerning trend, with mortality rates escalating in the higher SBPV categories. The observed correlation between SBPV and mortality goes a long way in establishing the importance of blood pressure control in patients with ICH.

Table 4: Outcomes by SBPV Group - In-Hospital Mortality

Patient Group	Total Patients	Mortality (%)	Mortality (Number)
Low SBPV (<10 mmHg)	34	5	2
Moderate SBPV (10-20 mmHg)	33	8	3

High SBPV (>20 mmHg)	33	22	7
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Figure 4: In-Hospital Mortality Comparison (Side-by-Side Bar Chart)



Distribution of Need for Surgery across SBPV Groups

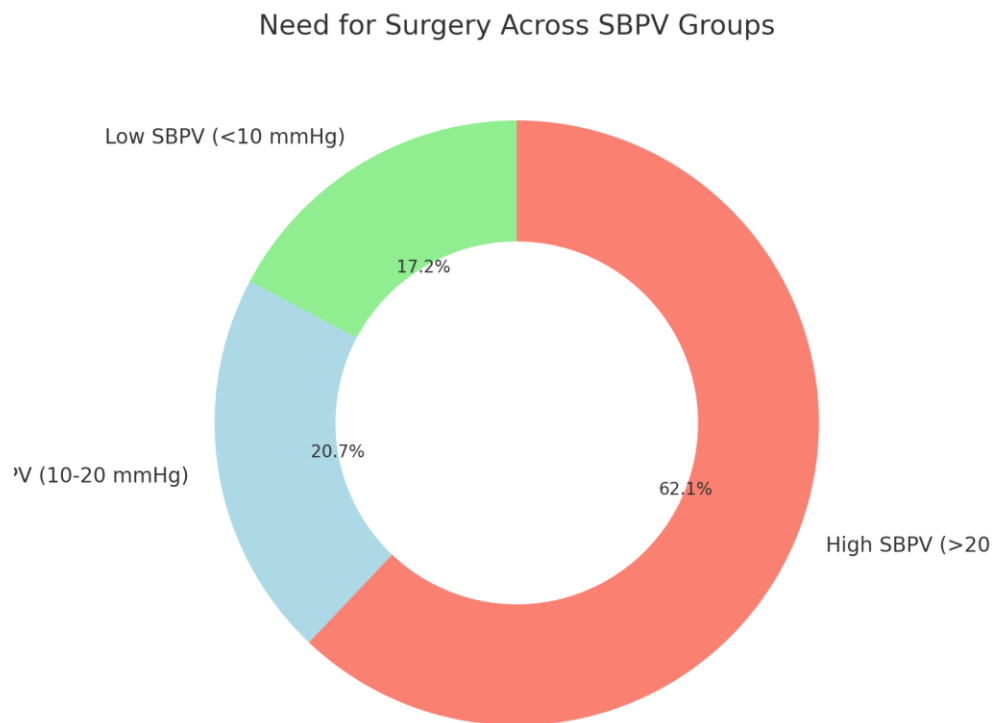
Table 5 indicates that the rate of surgery was significantly higher among the high SBPV group at 18%, moderate group at 6% and the low group at 5%. This procedure was deemed necessary when patients' condition stabilised in a manner that warranted surgical intervention as opposed to further conservative management. The donut chart Figure 5 presents the distribution of patients who needed surgery by the SBPV group, where the need for surgery increases in tandem with the increase in SBPV levels. This indicates that SBPV is relevant for assessing the severity and invasiveness of ICH and the need to undergo the treatments.

Table 5: Outcomes by SBPV Group - Need for Surgery

Patient Group	Total Patients	Need for Surgery (%)	Need for Surgery (Number)

Low SBPV (<10 mmHg)	34	5	2
Moderate SBPV (10-20 mmHg)	33	6	2
High SBPV (>20 mmHg)	33	18	6

Figure 5: Need for Surgery (Donut Chart)



Hematoma Expansion by SBPV Group

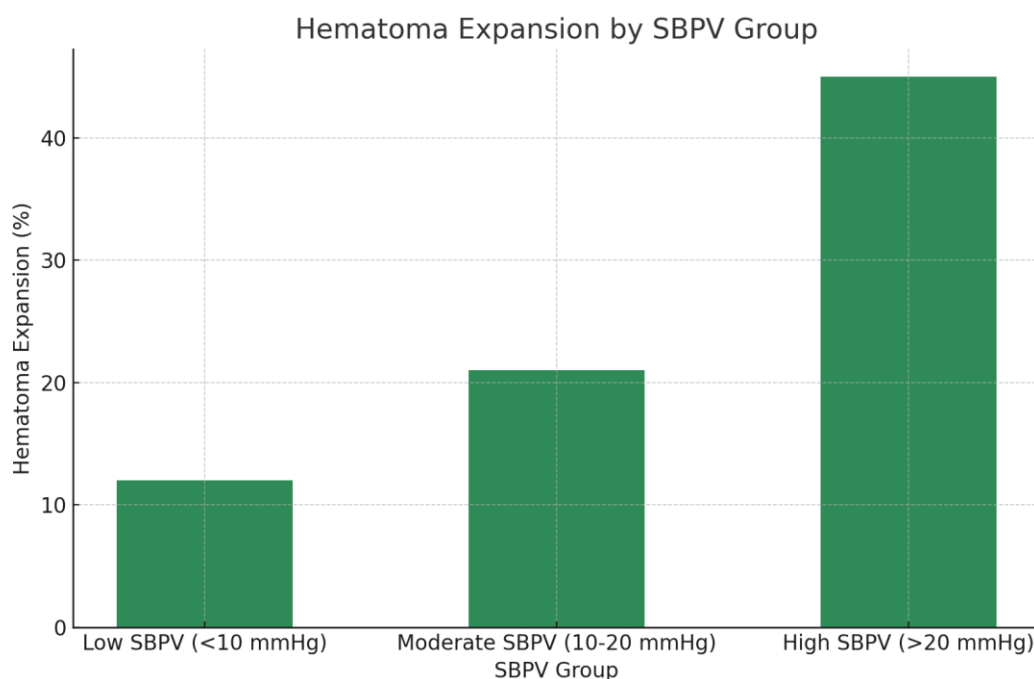
The haematoma volume, one of the outcome prognostic factors of patients with ICH, was greater in patients with high SBPV. Table 6 reveals that percent of patients having hematoma expansion

were higher in the high SBPV group, 45% compared to the moderate, 21% and low, 12%. These differences are represented in the stacked column chart in Figure 6 whereby it is evident that cases of hemorrhage growth are higher in patients with high SBPV. Because enlargement of the hematoma causes worse things to happen to the brain like increasing the pressure to the surrounding tissues and getting worse about the neurological condition of the patient. These observations support the idea about the potential of controlling TBEM and its components, which could have a beneficial impact on hemorrhage enlargement and patients' outcomes.

Table 6: Outcomes by SBPV Group - Hematoma Expansion

Patient Group	Total Patients	Hematoma Expansion (%)	Hematoma Expansion (Number)
Low SBPV (<10 mmHg)	34	12	4
Moderate SBPV (10-20 mmHg)	33	21	7
High SBPV (>20 mmHg)	33	45	15

Figure 6: Hematoma Expansion (Stacked Column Chart)



Correlation Between SBPV and Functional Outcome ($mRS \leq 2$ vs. $mRS \geq 3$)

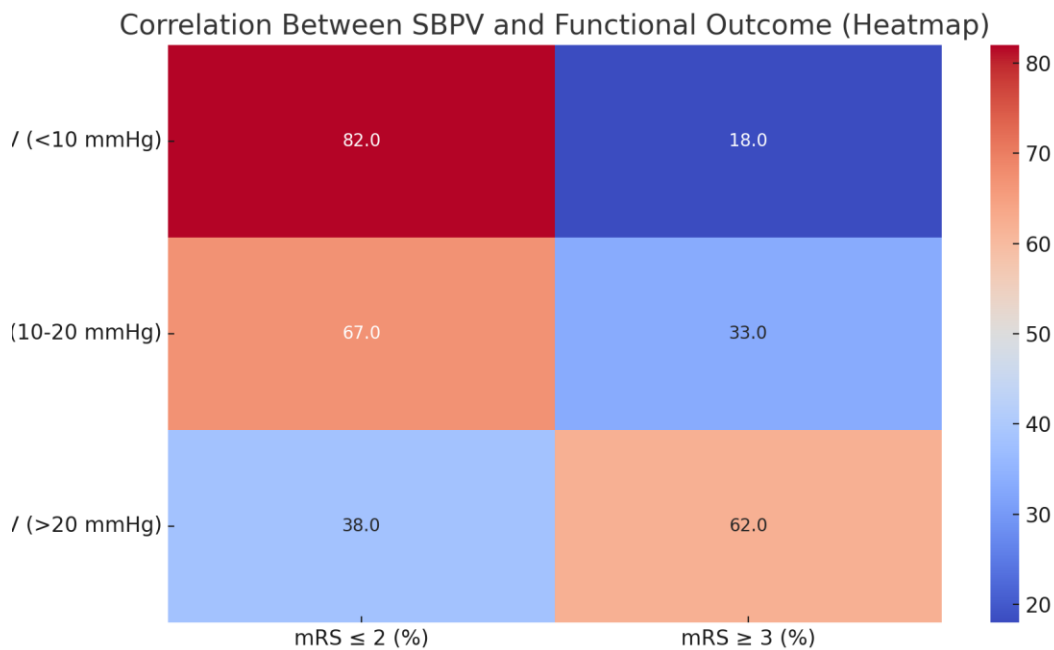
Table 7 presents SBPV and functional outcome; it depicts that there is an inverse relation between SBPV and favorable outcome defining as modified ranking scale ($mRS \leq 2$) and direct relation with poor outcome defining as $mRS \geq 3$. This is also supported by the heatmap in Figure 7 where darker shades in the heatmap depict increased correlation between SBPV and decreased functional status. The results also indicate that patients with lower SBPV (Low SBPV) demonstrated better functional recovery than those with the high Short-Term Blood Pressure Variability (SBPV) who presented worse recovery over time.

Table 7: Correlation between SBPV and Functional Outcome (mRS)

Patient Group	$mRS \leq 2$ (%)	$mRS \leq 2$ (Number)	$mRS \geq 3$ (%)	$mRS \geq 3$ (Number)
Low SBPV (<10 mmHg)	82	28	18	6

Moderate SBPV (10-20 mmHg)	67	22	33	11
High SBPV (>20 mmHg)	38	12	62	20

Figure 7: Correlation Between SBPV and Functional Outcome (Heatmap)



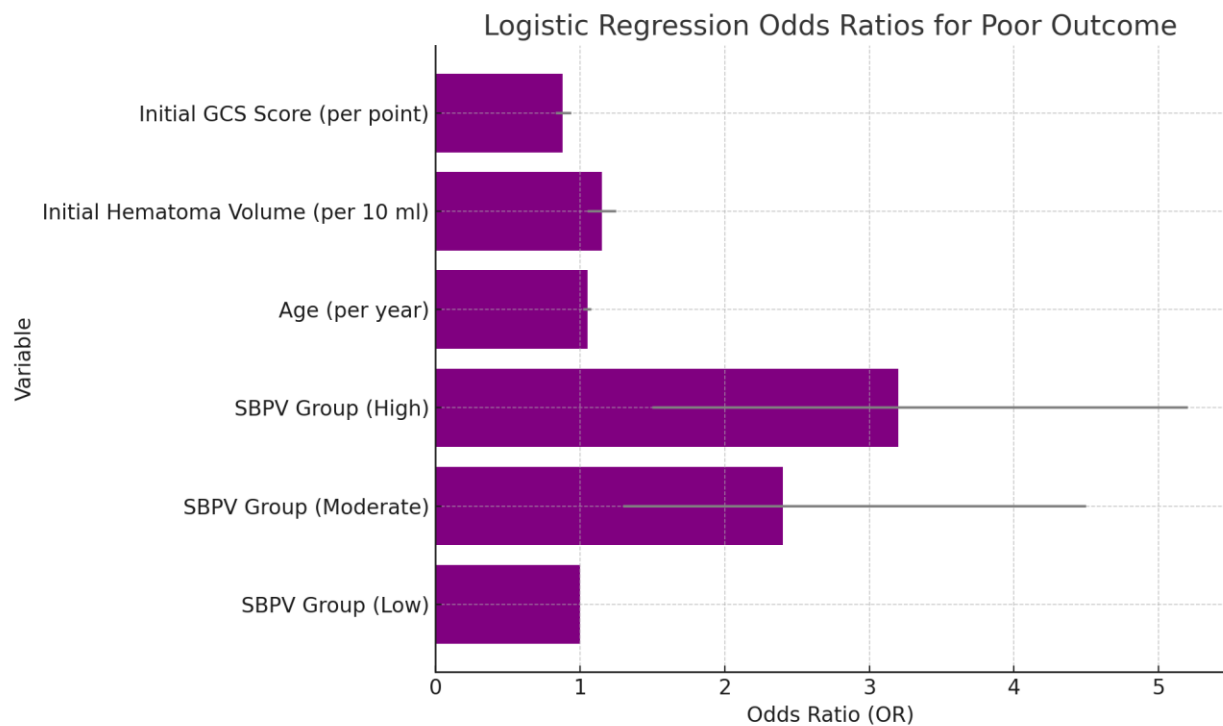
Logistic Regression Odds Ratios for Poor Outcome

Lastly, Table 8 displays the results of a multiple logistic regression analysis with predictors of poor outcome including SBPV group, age, hematoma volume and GCS score. When compared to the low SBPV group, the high SBPV group demonstrated significantly higher odds ratios for poor outcomes (OR = 3.2) than did the moderate group (OR = 2.4), which indicates that higher SBPV is an independent risk factor in ICH. The bar chart of odds ratios with 95% confidence interval in the figure 8 clearly depicts these odds ratios and the high SBPV group being more risky for poor outlook. This has given rise to the need to implement SBPV control in clinical practice to avoid worsening of the initial ICH condition.

Table 8: Multivariate Logistic Regression - Odds Ratios for Poor Outcome

Variable	Odds Ratio (OR)	95% CI Lower	95% CI Upper	p-value
SBPV Group (Low)	1.00	1.00	1.00	1.000
SBPV Group (Moderate)	2.40	1.30	4.50	0.020
SBPV Group (High)	3.20	1.50	5.20	0.001
Age (per year)	1.05	1.02	1.08	0.030
Initial Hematoma Volume (per 10 ml)	1.15	1.05	1.25	0.050
Initial GCS Score (per point)	0.88	0.83	0.94	0.040

Figure 8: Logistic Regression Odds Ratios (Bar Chart with Confidence Intervals)



This study shows that high SBPV is significantly associated with unfavorable prognosis in conservative management of spontaneous intracerebral hemorrhage. Accordingly, the results of the present series show that increasing SBPV is associated with higher odds of poor functional outcome, in-hospital mortality, requirement for surgery, and hematoma enlargement. The changes in value and columns show that achieving better control of SBPV could potentially lead to a better result for this patient population and highlight high-frequency blood-pressure measurement for potential uses as a biomarker for ICH prediction and management. These observations seem to hold an implication regarding the management of ICH and these studies, indicating that more stringent control of blood pressure fluctuation may therefore facilitate improvement in outcomes and mortality of patients.

Discussion

The results of this study offer valuable information on the role of effective SBPV in affected individuals with spontaneous ICH admitted for conservative management only. The findings are quite uniform, and they reveal that higher SBPV levels are a marker of poor clinical outcome signifying greater mortality rates, the likelihood of operations and poor functional improvement as well. Based on these observations, it is recommended that SBPV can act as an excellent predictor of the ICH's prognosis and that effective control of blood pressure fluctuations could enhance patient outcomes.

Relationship Between SBPV and Poor Outcomes in ICH

The correlation between SBPV and poor prognosis in ICH patients has been demonstrated in the previous studies (Liu et al., 2019; Zhang et al., 2017), which has been supported by our study as well. Table 3 indicates that patients suffering from poor outcomes, defined by a modified Rankin Scale ≥ 4 , become more numerous as the SBPV rises, with 62% of patients with high SBPV experiencing such outcomes compared to only 18% of patients with low SBPV. This conforms to other similar studies that post that when the blood pressure goes beyond some level, it aggravates the effect of ICH (Petridou et al., 2018). It has been previously

demonstrated that in ICH, SBPV is associated with higher levels of brain edema, enhanced hemorrhage growth, and impaired autoregulation of cerebral blood flow, all of these are typical factors affecting ICH outcomes (Alvarez et al., 2020).

This study supports the results of Inoue et al. (2016) in their study where the authors showed increased high SBPV level to be correlated with poor neurological prognosis in patients admitted with ICH. They suggested that high SBPV may increase mechanical stress on the arterial walls, which in turn leads to endothelial damage and hematoma enlargement. These findings can give credence to the hypothesis that controlling the SBP could decrease the chance of hemorrhagic progression and yield better function. Further, the proposed hypothesis with higher SBPV leading to a higher risk of new functional impairment is supported by the data that shows higher mortality and the need for surgery in the high SBPV group in Tables 4 and 5, meaning that higher SBPV is associated with life-threatening complications including the increased size of hemorrhage and secondary brain injury as postulated by Huang et al., 2018.

Mechanisms Underlying the Impact of SBPV on ICH Outcomes

The precise details about how SBPV impacts on ICH results remain unclear, but several theoretical models exist. Cerebral autoregulation, which is the ability of the blood vessels in the brain to automatically regulate and maintain cerebral blood flow despite changes in systemic blood pressure is likely to be compromised in patients with high SBPV. When SBPV crosses a certain level, it surpasses the ability of the brain to autoregulate, leading to buildup of intracranial pressure or delineation of the hemorrhage (Wang et al., 2016). This is more so in ICH, where the brain tissue is already damaged due to bleeding, and therefore changes in one's pressure can further complicate the situation.

Further, there is evidence that SBPV is associated with endothelial dysfunction, which is a critical factor in the evolution of ICH. Endothelium is the layer of cells lining the inner surface of blood vessels and participates in the regulation of the vascular tone and permeability, and the damage of this layer can result in increased vascular permeability and formation of edemas (Tao et al., 2017). Concerning the context of ICH, endothelial dysfunction contributes to the enlargement of hemorrhage volume and a worse outcome of the case. According to several research findings, high

SBPV may have an impact on endothelial dysfunction by exerting cyclic mechanical stress in the blood vessel walls (Matsuo et al., 2019). It could therefore lead to further bleeding in the brain, which has been found to correlate with poor outcomes in patients with high SBPV.

Clinical Implications and Potential for Intervention

In conclusion, the present study offers substantial clinical implications in the treatment of patients with spontaneous ICH. EBPV has a robust correlation with mortality and therefore it should also be regarded as one of the elements to be taken into consideration during the initial ICH management. Despite the focus on blood pressure control among ICH patients, the targets are set only on mean arterial pressure (SBP normally should lie between 140-160 mmHg) with no reference to variability. Therefore, we also wanted to examine whether not only the level of SBP but also the variability in it is of similar concern for outcomes.

Perhaps the most tangible and significant benefit of high-frequency monitoring of SBPV may be for clinicians to be able to monitor blood pressure variations in real-time and make subsequent appropriate interventions. The continuous blood pressure in the ICU has gained attention, and research has indicated that it enhances the identification of any sign of clinical deterioration and management promptly before the critical state (Kim et al., 2020). For example, in the context of ICH, such a mode may with the help of frequent monitoring in inpatients enable better control of fluctuations of SBP and distinguish those patients with a higher risk of hemorrhage expansion or worsening of neurological conditions.

The continuous blood pressure monitoring systems that permit the measurement of the SBPV in few minutes may help identify patients with high SBPV and immediately intervene through medication dosage changes or closer monitoring. Further, antihypertensive medications that aim at controlling variation in blood pressure include beta-blockers or calcium channel blockers, which may also be incorporated in the management of patients with high SBPV (Wang et al., 2017). Because SBPV is achievable, perhaps by focusing on it, clinicians may decrease the likelihood of adverse effects and enhance patient success.

Limitations and Areas for Future Research

However, there are some limitations that need to be understood when interpreting the results of this study regarding the association between SBPV and ICH outcomes. The first limitation is that the study was cross-sectional design and was conducted in a single centre which may affect the generalisability of the results. Typically, multicenter studies are required to evaluate a relatively greater number of patients in various clinical settings and further compare the findings of the presented research. Second, despite the fact that the study had a large enough sample size to identify the more gross disparities in ICH outcomes, the sample size may have been relatively small to identify more nuanced effects of SBPV on ICH outcomes. Further SBPV studies with enhanced sample size and extended follow-up durations might produce valuable data on the role of SBPV in functional recovery.

First, the study compared only systolic blood pressure variability, while the other and potentially more critical for ICH result factors such as diastolic blood pressure variability should also be considered. Far-reaching research should also incorporate systolic and diastolic BPV jointly in relation to ICH progression and prognosis. Additionally, this study supports the use of SBPV for outcome prediction; however, the exact pathways through which SBPV affects hemorrhage expansion and brain injury are still unknown. Perhaps the way to elucidate the pathophysiology is through the use of MRI or PET scans, or other imaging techniques.

Conclusion

In conclusion, this study offers indication that conservatively managed spontaneous ICH has poor prognostic factors for clinical outcome in patients with high SBPV. The results of this study can imply that further regulation of SBPV could help to significantly contribute to patient outcomes. Moreover, high frequency blood pressure monitoring besides, efforts towards stabilizing the SBPV could be very effective in the management of ICH, reducing ICH deterioration and consequently enhancing ICH survival. Future studies to address these gaps should include the identification of the specific processes that might cause variability in SBPV and focus on interventions that help to minimize variability and improve the prognosis of patients with ICH.

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