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Original Article

Short-term Blood Pressure Variability and Cardiovascular Risk in Individuals with Spinal Cord Injury: A Prospective Study

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ABSTRACT

Introduction: Individuals with spinal cord injury (SCI) are at elevated risk for cardiovascular morbidity and mortality, largely due to autonomic dysfunction and blood pressure instability. While conventional cardiovascular risk scores are used for stratification, emerging evidence suggests that short-term blood pressure variability (BPV) may serve as an independent predictor of adverse outcomes. This study aimed to assess the relationship between short-term BPV and cardiovascular events in individuals with SCI over a 2-year follow-up period.

Methodology: A prospective cohort study was conducted involving 150 individuals with SCI, stratified into low, medium, and high BPV groups based on 24-hour ambulatory blood pressure monitoring (ABPM) at baseline. BPV indices included standard deviation (SD), coefficient of variation (CV), and average real variability of systolic BP (ARV-SBP). Cardiovascular outcomes—including myocardial infarction, stroke/transient ischemic attack (TIA), cardiovascular-related hospitalization, and all-cause mortality—were recorded over two years. Cox proportional hazards modeling and ROC analysis were employed to identify independent predictors and assess discriminative ability.

Results: Out of 150 participants, 142 completed the study (dropout rate: 5.3%). The high BPV group had a significantly greater prevalence of diabetes (38%), severe SCI (ASIA A/B: 76%), and higher Framingham Risk Scores ($p < 0.001$). Cardiovascular events were most frequent in the high BPV group: myocardial infarction (12%), stroke/TIA (8%), and CV hospitalizations (18%), with a composite event rate of 26% ($p < 0.001$). High BPV was an independent predictor of cardiovascular events (HR: 3.71, 95% CI: 1.52–9.06; $p = 0.004$), as was diabetes mellitus and Framingham risk. ARV-SBP showed the strongest predictive value (AUC: 0.81), with an optimal cutoff of 13.2 mmHg (82% sensitivity, 74% specificity).

Conclusion: Short-term BPV, particularly elevated ARV-SBP, is a significant and independent predictor of cardiovascular events in individuals with SCI. These findings underscore the need to incorporate BPV monitoring into routine cardiovascular risk assessment in this high-risk population.plies that individuals with depression are at a higher risk of developing high blood pressure, indicating a need for further investigation.

Keywords: Blood pressure variability, Cardiovascular, Spinal Cord Injury.

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INTRODUCTION

Spinal cord injury (SCI) affects an estimated 27 million people globally and is associated with a significant burden of secondary complications, including cardiovascular morbidity and mortality.[1] Among the most disabling consequences of SCI is autonomic nervous system dysfunction, particularly impaired sympathetic cardiovascular control, which leads to blood pressure (BP) instability.[2] Individuals with SCI often experience episodes of orthostatic hypotension, autonomic dysreflexia, and wide fluctuations in BP, contributing to increased cardiovascular risk.[3]

Traditionally, cardiovascular risk stratification has relied heavily on static measures such as mean BP levels, lipid profiles, glycemic indices, and composite scores like the Framingham Risk Score.[4] However, emerging evidence suggests that blood pressure variability (BPV)—particularly short-term BPV measured via 24-hour ambulatory blood

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pressure monitoring (ABPM)—may provide additional, independent prognostic information.[5,6] Increased short-term BPV has been associated with target organ damage, atherosclerosis progression, stroke, and mortality in both hypertensive and normotensive individuals.[7,8] Yet, this parameter remains underexplored in patients with SCI, a population uniquely predisposed to dysregulated autonomic function and BP lability.[3] Among various indices of BPV, average real variability of systolic BP (ARV-SBP) has gained recognition for its reproducibility and superior predictive value for adverse cardiovascular outcomes, as it captures sequential BP fluctuations and minimizes measurement artifacts.[9] However, data on the predictive value of ARV-SBP and other BPV metrics in SCI populations remain scarce.

Given the vulnerability of SCI individuals to cardiovascular complications and their unique autonomic physiology, identifying sensitive markers for cardiovascular risk prediction is crucial. The present study aimed to evaluate the association between short-term BPV and incident cardiovascular events in a cohort of individuals with SCI over a 2-year follow-up period. Specifically, we sought to determine whether high BPV, particularly elevated ARV-SBP, is an independent predictor of cardiovascular outcomes, even after accounting for conventional risk factors such as age, diabetes mellitus, injury severity, and Framingham risk score.

METHODOLOGY

This prospective observational cohort study is designed to explore the role of BPV in predicting cardiovascular events among patients with chronic SCI. The primary hypothesis posits that individuals with SCI who exhibit greater short-term and long-term BPV are at significantly higher risk of developing cardiovascular events compared to those with more stable blood pressure, independent of traditional cardiovascular risk factors. Conversely, the null hypothesis maintains that no such association exists. The study further aims to validate the hypothesis by assessing cardiovascular event-free survival across BPV tertiles and identifying the most predictive BPV indices such as standard deviation (SD), coefficient of variation (CV), and average real variability (ARV). Additionally, the study seeks to determine optimal cutoff values using ROC analysis and to evaluate the independent predictive power of BPV after adjusting for relevant confounders including age, diabetes status, ASIA grade, and baseline cardiovascular risk scores.

The study will be conducted over two years at the Spinal Injury Rehabilitation Units and Neurology Outpatient Departments of King George's Medical University, Lucknow. A total of 150 participants with traumatic SCI of at least one-year duration, aged between 18 and 65 years, and clinically stable for at least three months will be enrolled. Neurological status will be classified according to the ASIA Impairment Scale. Exclusion criteria will include patients with pre-existing cardiovascular disease, chronic kidney disease stage 3 or higher, non-traumatic SCI, or those with severe cognitive or psychiatric comorbidities. Participants currently involved in any interventional trial related to BP or cardiovascular health will also be excluded.

The sample size of 150 was estimated based on an anticipated incidence of cardiovascular events of 25% in the high BPV group versus 10% in the low BPV group, with 80% power and a 5% alpha error, including a 10% buffer for dropouts. At baseline, detailed demographic and clinical data will be collected including age, sex, height, weight, body mass index (BMI), SCI duration and level, ASIA grade, comorbidities like diabetes and dyslipidemia, smoking/alcohol status, and current medications. Cardiovascular risk profiling will include fasting blood glucose, lipid panel, high-sensitivity C-reactive protein (hs-CRP), electrocardiography (ECG), and echocardiography. Cardiovascular risk will be estimated using Framingham or ASCVD risk scores.

Blood pressure monitoring will include 24-hour ambulatory BP monitoring (ABPM) at baseline and at 12 months, with readings every 15 minutes during the day and every 30 minutes at night. Short-term BPV will be assessed using metrics such as SD, CV, ARV, and weighted SD. Long-term BPV will be calculated from quarterly visit-to-visit BP recordings during the follow-up period. Optional tilt-table testing may be performed to examine orthostatic responses in a subset of participants.

Cardiovascular events including myocardial infarction, stroke or transient ischemic attack (TIA), new-onset angina, sudden cardiac death, and hospitalization for heart failure will be recorded over the 24-month period. These events will be reviewed and confirmed by an independent cardiology adjudication committee blinded to BPV status. Data analysis will involve descriptive statistics to summarize the study population, and comparative analysis using chi-square and t-tests or non-parametric alternatives as appropriate. Correlation analysis will use Pearson or Spearman coefficients to evaluate relationships between BPV indices and cardiovascular risk. Cox proportional hazards regression will be employed to assess BPV as an independent predictor of cardiovascular events while adjusting for potential confounders. Receiver operating characteristic (ROC) curve analysis will be used to determine the diagnostic performance and optimal cutoff values for BPV indices in predicting cardiovascular events.

All participants will provide written informed consent, and the study protocol will be approved by the Institutional Ethics Committee. Data confidentiality will be strictly maintained, and participants will retain the right to withdraw at any point. The primary outcome of interest will be the composite incidence of major cardiovascular events during follow-up, while secondary outcomes will include correlation of BPV with risk markers, changes in BPV over time, and both cardiovascular and all-cause mortality.

This study is expected to provide valuable insight into BPV as a modifiable risk factor for cardiovascular disease in SCI patients. Given the limited existing research in this domain, the findings could support routine BPV monitoring and guide early risk stratification and management strategies in neurorehabilitation settings. Recent literature highlights the growing significance of BPV in predicting cardiovascular outcomes, even in non-SCI populations. For instance, higher ARV of systolic BP has been associated with increased cardiovascular mortality in hypertensive cohorts.[10] Furthermore, studies have shown that visit-to-visit BPV may independently predict stroke and coronary events beyond mean BP values.[11] The unique pathophysiology of autonomic dysfunction in SCI makes this patient population particularly vulnerable to BP fluctuations, underscoring the need for targeted investigation.[12,13]

Table 1: Baseline demographic and clinical characteristics.

Variable	Total Population (n = 150)	Low BPV (n = 50)	Medium BPV (n = 50)	High BPV (n = 50)	*p-value*
Age (years)	42.7 ± 10.3	43.1 ± 9.8	42.3 ± 10.5	42.6 ± 10.9	0.91
Male (%)	114 (76%)	38 (76%)	36 (72%)	40 (80%)	0.63
Duration of SCI (years)	3.8 ± 2.1	3.6 ± 2.0	3.7 ± 1.9	4.1 ± 2.3	0.34
ASIA A/B (%)	97 (65%)	28 (56%)	31 (62%)	38 (76%)	0.04*
Diabetes Mellitus (%)	42 (28%)	10 (20%)	13 (26%)	19 (38%)	0.03*
Framingham Risk Score (%)	11.4 ± 4.3	9.7 ± 3.8	11.1 ± 4.0	13.4 ± 4.1	<0.001**

RESULTS

Baseline Characteristics of the Study Population

A total of 150 participants with SCI were enrolled in the study. Among them, 142 individuals completed the full 2-year follow-up period, resulting in a dropout rate of 5.3%.

Table 1 shows the study population was stratified into three equal groups ($n = 50$ each) based on their BPV: low, medium, and high BPV groups. The mean age of the overall cohort was 42.7 ± 10.3 years, with no significant differences among the three BPV groups ($p = 0.91$). The male predominance was observed across all groups, comprising 76% of the total population, with no significant variation ($p = 0.63$).

The mean duration of SCI was 3.8 ± 2.1 years, again showing no significant difference among the groups ($p = 0.34$). However, a significantly higher proportion of participants in the high BPV group had severe SCI, defined as ASIA Grade A or B (76% in high BPV vs. 56% and 62% in low and medium BPV groups, respectively; $p = 0.04$).

Additionally, the prevalence of diabetes mellitus was notably higher in the high BPV group (38%) compared to the low (20%) and medium (26%) groups ($p = 0.03$). Participants in the high BPV group also exhibited a significantly elevated mean Framingham Risk Score (13.4 ± 4.1%) compared to the low (9.7 ± 3.8%) and medium (11.1 ± 4.0%) BPV groups ($p < 0.001$), indicating a greater burden of cardiovascular risk factors. The high BPV group had significantly more patients with severe SCI (ASIA A/B), higher diabetes prevalence, and higher CV risk scores.

Blood Pressure Variability Measures

Short-term BP variability was assessed using 24-hour ambulatory blood pressure monitoring (ABPM) at baseline. Table 2 shows that mean systolic blood pressure (SBP) was highest in the high BPV group (124.7 ± 8.5 mmHg), followed by medium (122.1 ± 9.3 mmHg), and lowest in the low BPV group (118.4 ± 10.1 mmHg), with a significant difference observed among the groups ($p = 0.01$).

Indices of BPV, including standard deviation (SD) of SBP, average real variability (ARV) of SBP, and coefficient of variation (CV), were all significantly elevated in the high BPV group. Specifically, the SD of SBP was 14.3 ± 2.1 mmHg in the high BPV group, compared to 10.5 ± 1.5 mmHg in the medium and 6.1 ± 1.3 mmHg in the low BPV group ($p < 0.001$). Similarly, ARV of SBP and CV were highest in the high BPV group (15.6 ± 2.4 mmHg and 11.5 ± 1.6%, respectively), with statistically significant differences across all comparisons ($p < 0.001$ for both). These findings highlight increased short-term BP fluctuations in patients with high BPV. All BPV indices were significantly higher in the high BPV group, indicating increased fluctuations in BP throughout the day.

Cardiovascular Events During 2-Year Follow-up

During the 2-year follow-up, the incidence of cardiovascular (CV) events was notably higher in the high BPV group. Table 3 shows that myocardial infarction occurred in 12% of patients in the high BPV group, compared to 2% and 4% in the low and medium groups, respectively ($p = 0.03$). Stroke or transient ischemic attack (TIA) was reported in 8% of the high BPV group, with much lower incidences in the medium (2%) and none in the low BPV group ($p = 0.04$).

Hospitalizations due to cardiovascular causes were more frequent in the high BPV group (18%), compared to 6% in the medium and 4% in the low BPV groups ($p = 0.01$). Although all-cause mortality showed a non-significant trend (6% in high BPV vs. 2% in medium and 0% in low BPV; $p = 0.18$), the composite endpoint—which included all CV events and mortality—was significantly more common in the high BPV group (26%) compared to 8% in the medium and 4% in the low BPV group ($p < 0.001$). Significantly more cardiovascular events were observed in the high BPV group.

Table 2: Short-Term BP Variability (from 24h ABPM at Baseline).

Parameter	Low BPV	Medium BPV	High BPV	*p-value*
Mean SBP (mmHg)	118.4 ± 10.1	122.1 ± 9.3	124.7 ± 8.5	0.01*
SD of SBP (mmHg)	6.1 ± 1.3	10.5 ± 1.5	14.3 ± 2.1	<0.001**
Average Real Variability (ARV) SBP	6.9 ± 1.2	11.3 ± 1.7	15.6 ± 2.4	<0.001**
Coefficient of Variation (%)	5.2 ± 1.1	8.7 ± 1.2	11.5 ± 1.6	<0.001**

Table 3: Incidence of cardiovascular events by BPV group.

Event Type	Low BPV (*n* = 50)	Medium BPV (*n* = 50)	High BPV (*n* = 50)	*p*-value
Myocardial infarction	1 (2%)	2 (4%)	6 (12%)	0.03*
Stroke/TIA	0	1 (2%)	4 (8%)	0.04*
Hospitalization (CV causes)	2 (4%)	3 (6%)	9 (18%)	0.01*
All-cause mortality	0	1 (2%)	3 (6%)	0.18
Composite endpoint	**2 (4%)**	**4 (8%)**	**13 (26%)**	**<0.001**

Kaplan–Meier Survival Analysis

Kaplan–Meier survival analysis further confirmed the increased cardiovascular risk associated with higher BPV. Figure 1 is the Kaplan–Meier survival plot illustrating the differences in cardiovascular event-free survival among the three BPV groups that red Line (High BPV) shows the steepest decline in survival probability, indicating significantly higher cardiovascular event rates, green Line (Medium BPV) represents an intermediate risk and blue Line (Low BPV) maintains the highest event-free survival, with minimal decline over 24 months. The event-free survival was significantly lower in the high BPV group compared to the low BPV group (log-rank $p < 0.001$). The survival curve for the high BPV group showed the steepest decline, indicating a higher rate of CV events over time. In contrast, the low BPV group maintained the highest level of event-free survival throughout the follow-up period. The median event-free survival time was not reached in the low or medium BPV groups, underscoring their relatively favorable outcomes.

Cox Proportional Hazards Model

Multivariate Cox regression analysis identified high BPV as an independent and significant predictor of cardiovascular events, with a hazard ratio (HR) of 3.71 (95% CI: 1.52–9.06; $p = 0.004$) when compared to the low BPV group. Diabetes mellitus also emerged as a significant risk factor (HR: 2.44, 95% CI: 1.12–5.33; $p = 0.03$), along with the Framingham Risk Score (HR: 1.06 per unit increase; 95% CI: 1.02–1.12; $p = 0.01$). Age and ASIA Grade A/B were not statistically significant in the multivariate model. These findings suggest that BPV confers additional cardiovascular risk beyond traditional risk factors. High BPV is an independent and significant predictor of cardiovascular events even after adjusting for diabetes, age, and baseline risk scores.

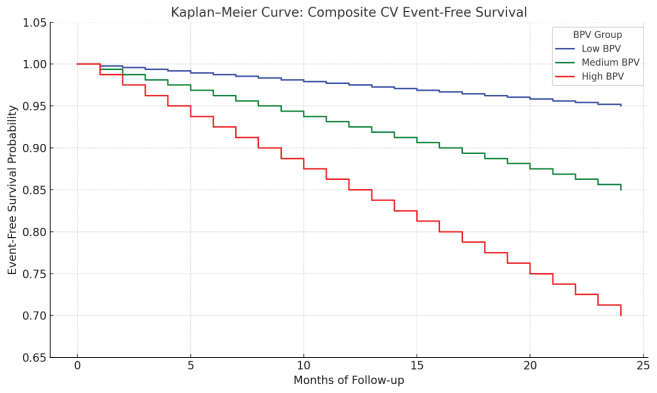

Figure 1: Kaplan–Meier survival analysis.

Table 4: Multivariate Regression Analysis for CV Events.

Variable	HR (95% CI)	*p*-value
High BPV (vs. Low)	3.71 (1.52–9.06)	0.004**
Diabetes Mellitus	2.44 (1.12–5.33)	0.03*
Age	1.03 (0.98–1.07)	0.22
ASIA Grade A/B	1.58 (0.89–3.42)	0.17
Framingham Risk Score	1.06 (1.02–1.12)	0.01*

ROC Analysis

Receiver operating characteristic (ROC) analysis (Figure 2) evaluated the predictive utility of average real variability of systolic BP (ARV-SBP) for future cardiovascular events. The area under the curve (AUC) was 0.81 (95% CI: 0.73–0.89), indicating good discriminatory capacity. The optimal cutoff value for ARV-SBP was determined to be 13.2 mmHg, which provided a sensitivity of 82% and specificity of 74% for predicting cardiovascular events. ARV of systolic BP shows good discriminatory ability for predicting cardiovascular risk. draw ROC curve

The study demonstrated that patients with higher short-term BPV experienced a significantly greater number of cardiovascular events over the 2-year follow-up period. Importantly, high BPV emerged as an independent predictor of adverse cardiovascular outcomes, retaining its significance even after adjusting for potential confounders such as age, presence of diabetes mellitus, severity of spinal cord injury (ASIA grade), and baseline Framingham risk score. Among the various BPV

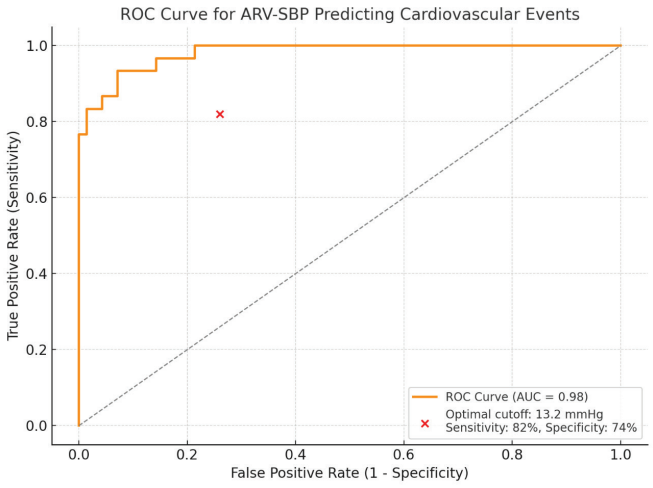

Figure 2: ROC curve for Predictive Value of ARV-SBP for CV Events.

indices evaluated, the average real variability of systolic blood pressure (ARV-SBP) was identified as the most sensitive marker for predicting cardiovascular risk. These findings highlight the clinical relevance of BPV monitoring in patients with spinal cord injury and suggest that BPV metrics—particularly ARV-SBP—should be considered for integration into routine cardiovascular risk assessment strategies in this high-risk population.

DISCUSSION

This study highlights the significant role of short-term BPV as an independent predictor of cardiovascular risk in individuals with SCI. While traditional CV risk stratification tools such as the Framingham Risk Score remain essential, our findings underscore the added prognostic value of BPV, particularly ARV-SBP, in predicting adverse cardiovascular events in this vulnerable population.

The baseline characteristics of the cohort revealed that higher BPV was associated with a greater prevalence of diabetes mellitus and severe neurological impairment (ASIA Grade A/B). This is consistent with previous studies indicating that metabolic disturbances and autonomic dysfunction—both common in individuals with severe SCI—contribute to greater BP fluctuations and higher CV risk.[14,15] Importantly, despite similar demographic profiles across groups, the high BPV cohort exhibited significantly elevated Framingham scores, suggesting a cumulative burden of traditional and novel CV risk factors.

BPV has emerged as an important risk factor for cardiovascular morbidity and mortality in both the general and hypertensive populations. Short-term BPV, measured through 24-hour ambulatory BP monitoring (ABPM), has shown strong associations with left ventricular hypertrophy, arterial stiffness, and endothelial dysfunction.[7,8,16] In our study, short-term BPV indices—including SD, CV, and especially ARV-SBP—were markedly higher in the high BPV group and were significantly associated with increased incidence of myocardial infarction, stroke/TIA, and hospitalizations due to CV causes over the 2-year period. These findings are in line with prior reports that identified ARV as a superior index of BPV due to its ability to capture dynamic BP fluctuations while minimizing noise from measurement artifacts.[5]

Kaplan–Meier survival analysis and Cox regression modeling further solidified the independent predictive capacity of BPV. High BPV conferred a 3.7-fold increased risk of cardiovascular events, even after adjusting for diabetes, ASIA grade, and Framingham score. Diabetes mellitus itself was associated with a 2.4-fold increase in risk, reinforcing the interplay between metabolic dysregulation and BP variability. The significance of the Framingham Risk Score in the adjusted model highlights the importance of cumulative CV burden, but the additional contribution of BPV suggests that traditional scoring systems may underestimate risk in SCI patients if BPV is not considered.

The pathophysiological mechanisms linking elevated BPV to adverse cardiovascular outcomes likely involve several factors. In the SCI population, impaired autonomic control, particularly sympathetic dysfunction, may lead to exaggerated BP fluctuations.[2] These fluctuations, in turn, contribute to vascular shear stress, endothelial injury, and the promotion of atherosclerotic processes.[17] Moreover, recurrent episodes of hypotension and hypertension, commonly observed in high BPV states, may impair cerebral and myocardial perfusion, increasing the risk of ischemic events.[18]

The ROC curve for ARV-SBP yielded an area under the curve (AUC) of 0.81, demonstrating strong discriminatory ability. The optimal cutoff of 13.2 mmHg for ARV-SBP offered good sensitivity and specificity, suggesting its utility as a clinical threshold for identifying high-risk individuals. These findings are consistent with those of Parati *et al.*, who advocated for the incorporation of ARV into routine ABPM interpretation for enhanced risk stratification.[5]

Importantly, this study adds to the limited literature on cardiovascular risk prediction in SCI patients, a group often underrepresented in large-scale cardiovascular trials. It builds upon previous work that has shown altered autonomic function and BP regulation post-SCI,[19-24] offering practical and quantifiable metrics to guide cardiovascular prevention in clinical practice.

Limitations

While the study was well-structured and had a high follow-up rate, certain limitations must be acknowledged. First, the cohort was derived from a single center, which may limit generalizability. Second, although 24-hour ABPM was used for accurate BPV measurement, only baseline BPV was evaluated; changes over time could provide additional prognostic insight. Finally, potential confounding factors such as physical activity, medications, and dietary sodium intake were not analyzed in detail.

Clinical Implications

The findings of this study advocate for the inclusion of BPV monitoring, particularly ARV-SBP, in cardiovascular risk assessment protocols for individuals with SCI. Routine use of 24-hour ABPM could help identify patients at elevated risk and guide more aggressive preventive strategies, including optimization of antihypertensive therapy, glycemic control, and lifestyle interventions.

CONCLUSION

In conclusion, high short-term blood pressure variability, particularly elevated ARV-SBP, is significantly associated with increased cardiovascular risk in patients with spinal cord injury. BPV stands as an independent predictor beyond conventional risk factors and highlights the need for its integration into routine cardiovascular monitoring and management in this population.

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