Article

Correlation between Preoperative Blood Pressure Variability and Carotid Sinus Reaction after Internal Carotid Artery Stenting

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AIM: To investigate the relationship between blood pressure variability (BPV) 24 hours before internal carotid artery stenting and post-procedural carotid sinus reaction (CSR), with an emphasis on identifying BPV indexes that predict the implementation of carotid artery stenting (CAS) and the subtype of CSR.

METHODS: A total of 105 patients who completed 24-hour ambulatory blood pressure monitoring and underwent CAS from August 2019 to February 2024 in the First Affiliated Hospital of Bengbu Medical College were included in this study. Patients were divided into CSR and non-CSR groups. The CSR group was further divided into three subgroups according to the type of CSR that occurred: namely hypotensive, bradycardic, and mixed types. Prior to stent placement, changes in ambulatory blood pressure were monitored using a fully automated non-invasive portable blood pressure monitor for 24 hours before the procedure, and the individual metrics in BPV were compared.

RESULTS: CSR occurred in 69 patients (65.71%) and the remaining 36 patients did not experience CSR (34.29%). Among the patients with CSR, 46 (66.67%) experienced hypotensive CSR, 9 (13.04%) had bradycardic CSR, and 14 (20.29%) mixed-type CSR. The age, history of hypertension, coronary artery disease, and history of smoking were significantly higher in the CSR group than in the non-CSR group (p = 0.007, p = 0.002, p = 0.046, p = 0.007, respectively). Age, hypertension, and history of smoking were the risk factors for CSR. A statistically significant difference in triglyceride levels was found between the three subgroups of CSR ($p < 0.05$); however, triglycerides had no significant effect on the type of CSR subgroups (all $p > 0.05$). A series of preoperative BPV indexes, like the maximum systolic blood pressure (SBP), SBP's max-min difference, mean, standard deviation (SD), coefficient of variation (CV), and degree of variability (SV) of the 24-hour SBP, were significantly correlated with the occurrence of CSR ($p < 0.05$). Further analysis revealed that SBP's max-min difference, SD, CV, and SV of 24-hour SBP were independent predictors of CSR. The bradycardic CSR was significantly correlated with the maximum diastolic blood pressure (DBP), minimum DBP, and 24-hour mean DBP, when compared to the hypotensive CSR ($p < 0.05$). The mixed-type CSR was significantly correlated with the maximum DBP and minimum DBP, when compared to the bradycardic CSR ($p < 0.05$).

CONCLUSIONS: The indexes of BPV 24 hours before internal carotid artery stenting correlate with the occurrence and types of CSR. Therefore, BPV can be used as a predictor of the occurrence and specific type of CSR after internal carotid artery stenting.

Keywords: cerebral infarction; carotid stenosis; blood pressure variability; internal carotid artery stenting; carotid sinus reaction

Introduction

Cerebral infarction is caused by blood circulation disorder, leading to softening and necrosis of brain tissue, which produces various corresponding symptoms of neurological deficits [1]. This pathological condition is associated with extremely high morbidity, disability and mortality rates. Carotid artery stenosis is recognized as a major risk factor for cerebral infarction, accounting for and 30%–60% of cerebral infarctions in clinical settings [2]. Carotid stent implantation is widely used in the clinical treatment of carotid artery stenosis, and this minimally invasive procedure is recognized for causing less trauma, having a better safety profile, and being more effective [3,4]. Nevertheless, carotid artery stenting (CAS) may trigger many complications, especially carotid sinus reaction (CSR) leading to hypotension, bradycardia, syncope and other symptoms, which not only affects the patient's prognosis, but also engenders disability and death [5]; therefore, accurate prediction of CSR occurrence is important for optimizing treatment strategies for CAS.

Blood pressure variability (BPV) refers to fluctuations in blood pressure over time, and high preoperative BPV has been recognized as a predictor of adverse clinical outcomes in a variety of diseases [6]. Patients with high preoperative BPV may have unstable autonomic nervous system func-

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tion, and prolonged exposure to this state may result in altered pressure receptor sensitivity [7]. Wang *et al.*'s study [8] found that elevated systolic blood pressure (SBP) variability was associated with cardiac and cerebral dysfunction. The aim of this study is to analyze the preoperative 24-hour ambulatory BPV in patients treated with CAS and to identify potential factors that can predict the occurrence of postoperative CSR, which offer insights into continuous optimization of preoperative BPV in an early stage and reduction of the occurrence of postoperative CSR [9].

Materials and Methods

Study Subjects

Data of 105 patients who underwent internal CAS after completing 24-hour ambulatory blood pressure monitoring from August 2019 to February 2024 in the First Affiliated Hospital of Bengbu Medical College were collected.
Inclusion criteria of this study are as follows:

(1) Symptomatic carotid artery stenosis with >50% stenosis. Stenosis was measured with the North American Symptomatic Carotid Endarterectomy Test (NASCET) [10] consistently in this sample. According to the NASCET standard measurement method: Stenosis rate (%) = (B – A)/B × 100, where A is the residual tube diameter and B is the normal internal diameter of the internal carotid artery in the far segment of the stenosis. According to the measurement results of the NASCET method, the degree of carotid artery stenosis was divided into four levels: (i) Mild stenosis: <30% inner arterial diameter reduction; (ii) Moderate stenosis: 30%–69% arterial internal diameter reduction; (iii) Severe stenosis: 70%–99% inner arterial diameter reduction; (iv) Complete occlusion: pre-occlusion state with stenosis >99%. The stenosis also encompasses manifestations like transient ischemic attack or non-disabling stroke.
(2) Asymptomatic carotid stenosis with >70% stenosis, progressive stenosis after follow-up, and symmetric occlusion with >70% stenosis of asymptomatic carotid artery stenosis.
(3) Clear consciousness and premorbid Modified Rankin Score (MRS) score <1.
(4) Simple, single or unilateral stent implantation in the internal carotid artery.
(5) Exclusion of cerebral hemorrhage or other intracranial diseases.

Exclusion criteria of this study include:

(1) Intellectual disability or Modified Rankin Score (MRS) score >3.
(2) A history of cardiac infarction in the preceding 2 weeks.
(3) Uncontrolled malignant hypertension or malignant hypotension.
(4) Comorbid severe cardiac, hepatic, or renal disease.
(5) Elderly patients with a life expectancy of <1 year.
(6) Having multiple stent implants.
(7) Comorbid systemic infections.

This study has been approved by the Bengbu Medical College Ethics Review Committee (Approval No. 2022kj-190) and was conducted in strict adherence to the Declaration of Helsinki. Informed consent was obtained from the patients themselves or their guardians.

Research Methodology

General demographic and clinical data were collected from patients who underwent internal CAS in the First Affiliated Hospital of Bengbu Medical College. General information such as age, gender, height, weight, body mass index (BMI), hypertension, diabetes mellitus, coronary heart disease, hyperlipidemia, smoking, and alcohol consumption was collected. Smoking, in this study, was defined as former smokers who smoked more than 10 packs per year or within 2 years; those who never smoked or smoked less than 1 cigarettes per day were classified as non-smokers. Drinker was defined as people consuming alcohol at least once or more times a week for half a year, whereas non-drinkers were defined as those who never drank alcohol or drank alcohol less than once per week. Regarding ambulatory blood pressure monitoring and indicators of BPV, a fully automatic non-invasive portable ambulatory blood pressure monitor was used. During measurement, the cuff of the monitor was tied to the arm and connected to the instrument for 24 hours before the patient underwent internal CAS. Daytime monitoring was conducted during the 06:00–22:00 period, with a total of 45 measurements, while nighttime monitoring time was performed during the 22:00–06:00 period, with a total of 13 measurements; in total, 58 blood pressure measurements were completed in 24 hours. The BPV indexes were recorded respectively [11]: maximum SBP, minimum SBP, 24-hour mean SBP, SBP's max-min difference, maximum diastolic blood pressure (DBP), minimum DBP, 24-hour mean DBP, DBP's max-min difference, standard deviations (SD) corresponding to 24-hour SBP and DBP, coefficient of variation (CV), and degree of variability (SV) [12].

$$\text{Standard deviation} = \sqrt{1/(n-1)\sum_{i=1}^{n-1}\left(BP_i - BP_{\text{mean}}\right)^2};$$
$$\text{Coefficient of variation (\%)} = \text{SD}/\text{BP mean} \times 100;$$
$$\text{Degree of variability} = \sqrt{1/(n-1)\sum_{i=1}^{n-1}\left(BP_{i+1} - BP_i\right)^2}$$

Surgical Approach of the Carotid Artery Stent Implantation

Preoperatively, all patients with symptomatic carotid artery stenosis underwent at least 3 days of dual-antibody therapy containing aspirin 100 mg/d, clopidogrel 75 mg/d and ator-

Table 1. Comparison of general information between the CSR and non-CSR groups.

Variable	CSR group (n = 69)	Non-CSR group (n = 36)	$t/Z/\chi^2$	p
Age	69.28 ± 8.87	64.50 ± 7.56	2.572	0.007
Gender			1.279	0.258
Male	53 (76.81%)	31 (86.11%)		
Female	16 (23.19%)	5 (13.89%)		
BMI	22.66 (21.13, 24.22)	23.88 (22.99, 25.67)	–1.868	0.062
Hypertension	59 (85.51%)	21 (58.33%)	9.630	0.002
Diabetes	22 (31.88%)	12 (33.33%)	0.023	0.880
Coronary heart disease	14 (20.29%)	2 (5.56%)	3.976	0.046
Triglyceride	1.30 (0.86, 1.77)	1.37 (0.91, 1.55)	–0.223	0.823
Cholesterol	3.48 (2.85, 4.41)	3.24 (2.80, 3.63)	–1.488	0.137
Smoking history	42 (60.87%)	12 (33.33%)	7.181	0.007
Drinking history	14 (20.29%)	5 (13.89%)	0.654	0.419

Abbreviations: CSR, carotid sinus reaction; BMI, body mass index.

Table 2. Binary logistic regression analysis results.

Variable	B	S.E.	Wald	p	OR	95% CI	
						Lower limit	Upper limit
Age	0.078	0.035	4.966	0.025	1.081	1.009	1.158
Hypertension	2.067	0.809	6.531	0.011	7.904	1.619	38.590
Coronary heart disease	1.554	0.889	3.053	0.081	4.730	0.828	27.035
Smoking history	2.771	0.829	11.164	0.001	15.973	3.144	81.150

Abbreviations: OR, odds ratio; CI, confidence interval; S.E., standard error.

Table 3. Comparison of general information among the three subgroups of CSR.

Variable	Hypotensive CSR (n = 46)	Bradycardic CSR (n = 9)	Mixed-type CSR (n = 14)	H-value/χ^2	p
Age	72.00 (65.00, 76.00)	71.00 (68.25, 77.25)	69.00 (62.00, 74.00)	1.713	0.425
Gender				2.272	0.321
Male	39 (84.78%)	6 (66.67%)	10 (71.43%)		
Female	7 (15.22%)	3 (33.33%)	4 (28.57%)		
BMI	22.31 (20.76, 24.22)	22.98 (21.42, 24.09)	23.39 (22.03, 27.68)	2.369	0.306
Hypertension	41 (89.13%)	7 (77.78%)	11 (78.57%)	1.465	0.481
Diabetes	17 (36.96%)	3 (33.33%)	2 (14.29%)	2.550	0.279
Coronary heart disease	12 (26.09%)	1 (11.11%)	1 (7.14%)	2.921	0.232
Triglyceride	1.20 (0.78, 1.68)	1.75 (1.53, 2.22)	1.45 (1.15, 2.30)	6.754	0.034
Cholesterol	3.30 (2.78, 4.42)	3.72 (3.13, 5.10)	4.29 (2.85, 4.36)	1.817	0.403
Smoking history	27 (58.70%)	5 (55.56%)	10 (71.43%)	0.853	0.653
Drinking history	11 (23.91%)	2 (22.22%)	1 (7.14%)	1.890	0.389

Note: p-values of intergroup comparisons of triglyceride are as follows: hypotensive vs bradycardic p = 0.088; hypotensive vs mixed-type p = 0.237; bradycardic vs mixed-type p = 1.000.

Abbreviations: CSR, carotid sinus reaction; BMI, body mass index.

vastatin 40 mg/d within 2 weeks after the onset of symptoms of cerebral infarction. Under local anesthesia, the guide catheter was placed by puncture through the femoral artery. During the operation, the patients were treated with heparin, and a long sheath or guide catheter was placed at the proximal end of the affected common carotid artery and sent into the brain protection device. The stenosis rate and length of stenosis were calculated according to the NASCET criteria, and a suitable balloon was measured for pre-dilatation. Subsequently, a suitable stent was placed into the stenotic segment, and then the brain protection device and the guide catheter were withdrawn after the review of the contrast medium. Heart rate, blood pressure and oxygen saturation were measured during the operation. After the operation, the patients were treated with dual-antibody therapy for 3 months, and then switched to aspirin (100 mg/d) or clopidogrel (75 mg/d) alone according to their drug resistance profile for long-term maintenance.

Table 4. Multivariate logistic regression analysis results.

Type	Variable	B	S.E.	Wald	p	OR	95% CI	
							Lower limit	Upper limit
Bradycardia CSR	Triglyceride	0.109	0.204	0.287	0.592	1.116	0.748	1.665
Mixed-type CSR	Triglyceride	0.035	0.210	0.028	0.866	1.036	0.687	1.563

Note: Hypotensive CSR served as the reference category.

Abbreviations: CSR, carotid sinus reaction; OR, odds ratio; CI, confidence interval; S.E., standard error.

Table 5. Comparison of basic 24-hour BPV indexes between CSR and non-CSR groups.

Indicator	CSR group (n = 69)	Non-CSR group (n = 36)	t/Z	p
Maximum DBP	86.42 ± 10.25	84.75 ± 7.68	0.859	0.392
Minimum DBP	73.10 ± 7.96	73.11 ± 8.07	–0.006	0.995
DBP's max-min difference	10.00 (8.00, 20.00)	10.00 (5.00, 18.00)	–0.951	0.342
Mean DBP	79.85 ± 8.30	79.35 ± 6.96	0.305	0.761
SD of DBP	4.76 (3.30, 9.43)	4.31 (2.50, 8.38)	–0.895	0.371
CV of DBP	5.70 (4.25, 11.53)	5.77 (3.54, 10.57)	–0.793	0.428
SV of DBP	5.97 (3.85, 11.55)	6.12 (4.05, 11.89)	–0.300	0.764
Maximum SBP	154.09 ± 14.88	143.11 ± 12.33	3.794	<0.001
Minimum SBP	130.00 (120.00, 140.00)	128.00 (115.25, 137.50)	–0.875	0.382
SBP's max-min difference	22.00 (13.50, 31.50)	11.00 (7.00, 22.25)	–3.399	0.001
Mean SBP	141.09 ± 11.98	135.95 ± 10.68	2.161	0.033
SD of SBP	10.10 (6.32, 14.02)	5.10 (3.16, 10.71)	–3.359	0.001
CV of SBP	7.22 (4.67, 9.98)	3.83 (2.44, 7.00)	–3.349	0.001
SV of SBP	13.03 (8.62, 19.06)	6.26 (3.96, 10.53)	–4.058	<0.001

Abbreviations: CSR, carotid sinus reaction; SD, standard deviation; CV, coefficient of variation; SV, degree of variability; SBP, systolic blood pressure; DBP, diastolic blood pressure; BPV, blood pressure variability.

Statistical Methods

Data were statistically analyzed using SPSS software (version 27.0; IBM SPSS Corporation, Chicago, IL, USA), and the normality of all variables was tested using the Shapiro-Wilk test. Normally distributed data are expressed as mean ± standard deviation, while those that do not conform to normal distribution are presented as median and interquartile range (Q1, Q3). Categorical data are expressed as count and percentage. Independent samples t-test or one-way analysis of variance (ANOVA) was used for comparison of normally distributed data between two or three groups. The Mann-Whitney U test or Kruskal-Wallis test was used for comparison of non-normally distributed data between two or three groups. The chi-square test was used for comparison of categorical data. Correlations of normally distributed data were analyzed using Pearson's correlation test, and those of non-normally distributed data were analyzed by Spearman's correlation test. Binary logistic regression test was used to explore the influencing factors of CSR, whereas multivariate logistic regression test was utilized to explore the influencing factors of different subtypes of CSR. Differences were considered statistically significant when $p < 0.05$.

Table 6. Multivariate analysis of covariance of 24-hour BPV indexes.

Indicator	Covariance statistic	
	Tolerance value	VIF
Maximum SBP	0.033	30.548
SBP's max-min difference	0.008	120.777
Mean SBP	0.045	22.190
SD of SBP	0.003	308.182
CV of SBP	0.006	169.657
SV of SBP	0.069	14.515

Abbreviations: SD, standard deviation; CV, coefficient of variation; SV, degree of variability; VIF, variance inflation factor; SBP, systolic blood pressure.

Results

Comparison of General Information

Comparison of General Information between CSR and Non-CSR Groups

Among the 105 patients included, 69 patients (65.71%) had CSR and 36 patients (34.29%) did not have CSR. The age of the CSR group subjects was significantly different from that of the non-CSR group subjects ($p < 0.05$). The history of hypertension, coronary heart disease, and smoking were also significantly different between the two groups (all $p < 0.05$). The variables that are not significantly different

Table 7. Correlation analysis of covariance indicators.

	Maximum SBP		SBP's max-min difference		Mean SBP		SD of SBP		CV of SBP		SV of SBP	
	r	*p*	r	*p*	r	*p*	r	*p*	r	*p*	r	*p*
Maximum SBP	—	—	0.539**	<0.001	0.896**	<0.001	0.547**	<0.001	0.439**	<0.001	0.543**	<0.001
SBP's max-min difference	0.539**	<0.001	—	—	0.169	0.085	0.995**	<0.001	0.987**	<0.001	0.953**	<0.001
Mean SBP	0.896**	<0.001	0.169	0.085	—	—	0.185	0.059	0.058	0.558	0.184	0.061
SD of SBP	0.547**	<0.001	0.995**	<0.001	0.185	0.059	—	—	0.988**	<0.001	0.958**	<0.001
CV of SBP	0.439**	<0.001	0.987**	<0.001	0.058	0.558	0.988**	<0.001	—	—	0.953**	<0.001
SV of SBP	0.543**	<0.001	0.953**	<0.001	0.184	0.061	0.958**	<0.001	0.953**	<0.001	—	—

Note: ** Correlation is significant at a confidence level (two-test) of 0.01.

Abbreviations: SD, standard deviation; CV, coefficient of variation; SV, degree of variability; SBP, systolic blood pressure.

Table 8. Multivariate logistic regression analysis of 24-hour blood pressure data.

Combination	Indicator	B	S.E.	Wald	*p*	OR	95% CI	
							Lower limit	Upper limit
Combination 1	Mean SBP	–0.033	0.019	2.925	0.087	0.967	0.931	1.005
	SD of SBP	–0.107	0.043	6.166	0.013	0.899	0.826	0.978
Combination 2	Mean SBP	–0.039	0.019	4.154	0.042	0.961	0.925	0.998
	CV of SBP	–0.141	0.058	5.895	0.015	0.868	0.775	0.973
Combination 3	Mean SBP	–0.031	0.020	2.588	0.108	0.969	0.933	1.007
	SV of SBP	–0.100	0.034	8.441	0.004	0.905	0.846	0.968
Combination 4	Mean SBP	–0.034	0.019	3.081	0.079	0.966	0.930	1.004
	SBP's max-min difference	–0.047	0.019	6.194	0.013	0.954	0.919	0.990

Abbreviations: SD, standard deviation; CV, coefficient of variation; SV, degree of variability; SBP, systolic blood pressure; OR, odds ratio; CI, confidence interval; S.E., standard error.

Table 9. Comparison of blood pressure data between the three CSR subgroups.

Indicator	Hypotensive CSR (n = 46)	Bradycardic CSR (n = 9)	Mixed-type CSR (n = 14)	F/H-value	*p*
Maximum DBP	88.00 (82.00, 92.00)	67.00 (66.50, 89.50)^{a}	89.00 (81.75, 98.00)^{b}	8.605	0.014
Minimum DBP	74.39 ± 6.92	64.56 ± 6.93^{a}	74.36 ± 8.83^{b}	7.022	0.002
DBP's max-min difference	11.50 (8.00, 20.25)	8.00 (5.00, 19.00)	9.00 (6.00, 17.75)	1.614	0.446
Mean DBP	81.00 (77.31, 86.06)	65.00 (63.25, 78.75)^{a}	78.75 (74.94, 84.25)	11.557	0.003
SD of DBP	4.98 (3.39, 9.30)	3.32 (2.16, 7.13)	4.07 (2.75, 11.76)	2.997	0.223
CV of DBP	5.99 (4.42, 10.97)	5.31 (3.35, 8.79)	5.74 (3.50, 13.96)	1.301	0.522
SV of DBP	6.38 (3.82, 11.50)	3.87 (3.37, 11.47)	5.58 (3.92, 13.92)	0.960	0.619
Maximum SBP	156.35 ± 13.87	146.67 ± 18.76	151.43 ± 14.59	1.923	0.154
Minimum SBP	131.87 ± 12.63	122.44 ± 20.43	129.00 ± 12.20	1.823	0.170
SBP's max-min difference	23.50 (14.75, 32.25)	24.00 (11.50, 37.00)	15.50 (12.00, 29.00)	1.250	0.535
Mean SBP	143.13 ± 11.40	134.08 ± 16.23	138.89 ± 9.26	2.548	0.086
SD of SBP	11.39 (6.82, 14.37)	11.40 (5.31, 16.16)	7.12 (5.89, 12.81)	1.187	0.552
CV of SBP	7.55 (4.91, 9.97)	7.22 (3.83, 12.98)	5.19 (4.39, 9.18)	0.779	0.677
SV of SBP	13.15 (8.64, 18.85)	13.40 (7.36, 22.10)	10.01 (8.25, 19.10)	0.297	0.862

Note: ^{a} $p < 0.05$ vs hypotensive CSR group; ^{b} $p < 0.05$ vs bradycardic CSR group.

Abbreviations: SD, standard deviation; CV, coefficient of variation; SV, degree of variability; DBP, diastolic blood pressure; SBP, systolic blood pressure.

between the two groups include gender, BMI, triglyceride, cholesterol, diabetes mellitus, and history of alcohol consumption (all $p > 0.05$) (Table 1).

Binary Logistic Regression Analysis

Incorporate the significant factors from Table 1, including age, hypertension, coronary heart disease, and smoking history, into a binary logistic regression analysis. The results showed that age, hypertension and smoking history were factors influencing CSR ($p < 0.05$) (Table 2).

Comparison of General Information among the Three CSR Subgroups

Among the 69 patients with CSR, 46 (66.67%) were hypotensive, 9 patients (13.04%) were bradycardic, and 14 patients (20.29%) were of mixed-type CSR. Statistical dif-

Table 10. Multivariate logistic regression analysis of influencing factors for the three CSR subtypes.

Type	Indicator	B	S.E.	Wald	p	OR	95% CI	
							Lower limit	Upper limit
Bradycardic CSR	Maximum DBP	0.179	0.153	1.372	0.242	1.196	0.886	1.614
	Minimum DBP	0.134	0.190	0.495	0.482	1.143	0.787	1.660
	Mean DBP	–0.576	0.318	3.271	0.071	0.562	0.301	1.049
Mixed-type CSR	Maximum DBP	0.294	0.115	6.602	0.010	1.342	1.072	1.680
	Minimum DBP	0.376	0.174	4.641	0.031	1.456	1.034	2.049
	Mean DBP	–0.708	0.282	6.312	0.012	0.493	0.284	0.856

Note: Hypotensive CSR served as the reference category.

Abbreviations: CSR, carotid sinus reaction; OR, odds ratio; CI, confidence interval; S.E., standard error.

Table 11. Multivariate analysis of covariance of 24-hour blood pressure data.

Variable	Covariance statistic	
	Tolerance value	VIF
Maximum SBP	0.162	6.186
SBP's max-min difference	0.023	43.012
Mean SBP	0.211	4.740
SD of SBP	0.029	34.185
CV of SBP	0.036	27.573
SV of SBP	0.129	7.722

Abbreviations: SD, standard deviation; CV, coefficient of variation; SV, degree of variability; VIF, variance inflation factor; SBP, systolic blood pressure.

ferences were found between the three subgroups of CSR with respect to triglycerides ($p < 0.05$). A series of factors such as age, gender, BMI, cholesterol, hypertension, diabetes mellitus, coronary artery disease, history of smoking, and history of alcohol consumption were found not to be statistically different between the three subgroups of CSR ($p > 0.05$) (Table 3).

Multivariate Logistic Regression Analysis

Using the three CSR subgroups as the dependent variable and the factor presenting significant difference in Table 3 (triglycerides) as the independent variable, the multivariate logistic regression analysis showed that triglyceride levels had no significant deterministic effect on the subtypes of CSR, using the hypotensive CSR subtype as the reference category (all $p > 0.05$) (Table 4).

Comparison of Basic Ambulatory Blood Pressure Indexes and Blood Pressure Variability

Correlation and Functional Prediction Analysis of Basic 24-Hour BPV Indexes with CSR Occurrence

Maximum SBP, SBP's max-min difference, mean, SD, CV, and SV of 24-hour SBP were significantly different between the CSR group and the non-CSR group ($p < 0.05$). Minimum SBP, maximum DBP, minimum DBP, DBP's max-min difference, mean, SD, CV, SV of 24-hour DBP were found not to be statistically different between the CSR group and the non-CSR group ($p > 0.05$) (Table 5).

Predictability Analysis of Basic 24-Hour BPV Indexes for CSR Occurrence

After multivariate analysis of covariance, it was found that the tolerance values of maximum SBP, SBP's max-min difference, mean, SD, CV, and SV of 24-hour SBP were <0.1, and the variance inflation factor (VIF) values were all >10, proving that there was covariance in all of these indicators (Table 6). A subsequent correlation analysis found that the maximal SBP was correlated with the other five indexes (all $p < 0.05$); the 24-hour mean SBP was not significantly correlated with the SBP's max-min difference, SD, CV, and SV of 24-hour SBP (all $p > 0.05$); the SBP's max-min difference was significantly correlated with SD, CV, and SV of 24-hour SBP (all $p < 0.05$); the 24-hour SBP SD was significantly correlated with CV and SV of 24-hour SBP (all $p < 0.05$); 24-hour SBP CV was significantly correlated with 24-hour SBP SV (all $p < 0.05$) (Table 7). According to the results in Tables 6,7, in a regression analysis of CSR as the dependent variable, we excluded maximum SBP and sequentially included the 24-hour mean SBP and the other 4 variables in the logistic regression equations. The analysis results showed that SBP's max-min difference, mean SBP, SD, CV, and SV of 24-hour SBP were the independent predictors of CSR ($p < 0.05$) (Table 8).

Differential Comparison of Blood Pressure among the Three CSR Subgroups

The maximum DBP, minimum DBP, and 24-hour mean DBP in the bradycardic CSR group were significantly different from those in the hypotensive CSR group ($p < 0.05$). The maximum DBP and minimum DBP in the mixed-type CSR group were significantly different when compared with those in the bradycardic CSR group ($p < 0.05$). However, there was no significant difference in the comparison of the rest of the blood pressure data among the three CSR subgroups ($p > 0.05$) (Table 9).

Analysis of Significant Factors in Multivariate Logistic Regression of the Three CSR Subtypes

The results of the multivariate logistic regression analysis showed that the maximum DBP ($p = 0.010$, OR: 1.342, 95% CI: 1.072–1.680), minimum DBP ($p = 0.031$, OR: 1.456,

Table 12. Correlations between blood pressure indexes and CSR.

Risk factor	Quantile	Median		Tertiles		Quartile		p
		OR	95% CI	OR	95% CI	OR	95% CI	
Maximum SBP	1.000	1.762	0.268–11.572	0.098	0.004–2.254	0.006	0.000–0.406	0.010
Mean SBP	1.000	1.572	0.261–9.470	14.947	0.777–287.399	35.678	0.968–1315.328	0.195
SV of SBP	1.000	0.102	0.021–0.500	0.040	0.005–0.292	0.433	0.067–2.785	0.004

Abbreviations: CSR, carotid sinus reaction; OR, odds ratio; CI, confidence interval; SV, degree of variability; SBP, systolic blood pressure.

95% CI: 1.034–2.049), and 24-hour mean DBP ($p = 0.012$, OR: 0.493, 95% CI: 0.284–0.856) were the independent predictors of mixed-type CSR (Table 10).

Analysis of Significant Factors in Multivariate Analysis of Covariance of the Three CSR Subtypes

The blood pressure indexes found to be statistically significant ($p < 0.05$) in the multivariate logistic regression analysis were divided into quartiles due to the large differences in their unit changes. The blood pressure data divided into quartiles were subjected to multivariate analysis of covariance, which showed that covariance existed for SBP's max-min difference, SD and CV of 24-hour SBP (Table 11). We excluded the variables with covariance and subjected the remaining variables to binary logistic regression analysis, which showed that maximal SBP and SV of 24-hour SBP were significantly correlated with CSR ($p < 0.05$) (Table 12).

Discussion

Carotid stent implantation is a new and effective treatment for carotid artery stenosis [13]. Liu *et al.*'s study [14] has demonstrated the excellent efficacy of carotid stent implantation in the treatment of carotid artery stenosis, as it reduces the degree of inflammation, oxidative stress, and neurological damage; improves ischemic symptoms and signs of carotid artery stenosis; reduces the degree of stenosis; enhances patients' quality of life and cognition; and promotes postoperative recovery.

Nevertheless, carotid stent implantation has its drawbacks. In particular, the CSR occurring after internal CAS is a major cause of disability and death in patients [15,16]. Ryu *et al.* [17] showed that carotid stent implantation is less invasive, making it an important treatment for carotid artery disease. It is worth noting that some complications could affect the prognosis of CAS. Patients who develop CSR after carotid stent implantation are at an increased risk of perioperative stroke and death and are more likely to be hospitalized for a longer period.

According to Leisch *et al.*'s study [18], CSR occurred in 40% (42/105) of patients, with most of them experiencing both asystole and hypotension. Most patients with short-term asystole and hypotension did not develop any clinical symptoms during CSR. In our study, among the 105 patients who underwent CAS treatment, CAS occurred in 69 patients (65.71%), with hypotensive CSR accounting for 46 cases (66.67%), bradycardic type 9 cases (13.04%) and mixed type 14 cases (20.29%).

It is now recognized that the wide distribution of vasomotor nerve fibers throughout the systemic vasculature except for capillaries, with arterioles being more numerous than venules and micro arterioles being the most numerous, is the pathological prerequisite for the development of CSR. Vasomotor nerve fibers are categorized into sympathetic and parasympathetic motor nerve fibers, which control vasoconstriction and vasodilation, respectively [19,20]. The beginning part of the carotid artery is an important structure of carotid sinus, which contains the body's pressure receptors. In the process of CAS, the contact of the stent or balloon with the vasodilated carotid sinus causes parasympathetic excitability enhancement, triggering a vagal reflex, reduced contraction of the vascular smooth muscle, decreased peripheral vascular resistance, vasodilatation, a drop in blood pressure, and even shock [21,22]. In addition, the stent also passes through the sinus node and atrioventricular node, slowing down the patient's heart rate, or even causing cardiac arrest [23]. Therefore, exploring whether adjusting preoperative blood pressure and controlling preoperative BPV indexes could reduce the incidence of postoperative CSR became the objective of this study.

In a study by Men *et al.* [24], the SBP variability was shown to be a strong predictor of stroke, independent of mean SBP, and a higher SBP variability possesses a higher predictive value for stroke. Ryu *et al.* [17] showed that 61 out of the 176 patients surveyed (34.7%) developed CSR; an increase in SBP's SD, an index of preoperative BPV in patients who developed CSR, was independently associated with the risk of CSR; SBP's CV was associated with the development of CSR; and an increase in BPV before carotid stent implantation was associated with the risk of CSR after carotid stent implantation. Given these published findings, BPV before carotid stent implantation is a potential predictor of CSR. These findings are also consistent with the results in the current study, in which 69 patients with CSR were found to have statistically significant differences in BPV indexes like maximum SBP, SBP's max-min difference, 24-hour mean SBP, SD of 24-hour SBP, and CV of 24-hour SBP, which are critical factors influencing CSR. This suggests that: (i) changes in preoperative SBP indexes have the most obvious influence on the occurrence of CSR after surgery; (ii) BPV is closely related to the occurrence of CSR; (iii) 24-hour SBP variability plays an important role in the occurrence of CSR. Thus, it can be postulated that reducing the preoperative 24-hour SBP variability of patients can reduce the preoperative BPV of patients, thus reducing the incidence of CSR in postoperative patients.

In contrast to the findings by Ryu *et al*. [17], the present study showed that there were significant differences in terms of maximum DBP, minimum DBP, and 24-hour mean DBP between the bradycardic CSR group and the hypotensive CSR group, and between the mixed-type CSR group and the bradycardic CSR group. This suggests that the variability of preoperative 24-hour DBP has a significant effect on the occurrence of postoperative bradycardia. However, their findings may be inconsistent with our results due to the difference in calculation method or measurement time as well as the different definitions of BPV used. Another limitation of this study is the retrospective, single-center nature of the research design, thus warranting a well-designed prospective, multicenter study to further validate our findings. The mechanisms underlying the close relationship between the variability of preoperative 24-hour DBP and bradycardic CSR occurrence remain to be further analyzed and investigated.

Conclusions

In conclusion, BPV is closely related to the occurrence of postoperative CSR. This finding leads to a postulation that controlling BPV can reduce the occurrence of postoperative CSR; specifically, lowering the preoperative 24-hour SBP variability can reduce the incidence of postoperative hypotension, and lowering the preoperative 24-hour DBP variability can decrease the incidence of postoperative bradycardia. This study presents only a preliminary exploration of the correlation between BPV and CSR. In future, fundamental experiments and multicenter studies involving larger sample size are needed to elucidate the mechanism of the correlation between BPV and CSR occurrence, thereby providing strategic insights into minimizing CSR occurrence in patients undergoing CAS surgery.

Availability of Data and Materials

The data analyzed was available on the request from the corresponding author.

Author Contributions

XXZ and ZYT contributed to the study design. ZYT and LY performed the data. SL and YYL collected and analyzed data. PS and WDQ made statistical analysis. WDQ and XXZ gave the valuable advice on study performance. XXZ made the first draft. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study has been approved by the Bengbu Medical College Ethics Review Committee (Approval No. 2022kj-190) and strictly adheres to the Declaration of Helsinki. The patients themselves or their guardians included in the study have signed the informed consent form.

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Conflict of Interest

The authors declare no conflict of interest.

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