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Relationship between Four Blood Pressure Indexes and Ischemic Stroke in Patients with Uncontrolled Hypertension

Hui-Juan Zuo*, Yun Lin, Jin-Wen Wang, Li-Qun Deng

Abstract

Objectives: Hypertension was the most important risk factor for ischemic stroke. In China, three fourths of treated hypertensive didn't meet the standard of control. We analyzed the relationship between systolic blood pressure, diastolic blood pressure, pulse pressure and mean arterial pressure and Ischemic stroke in patients with uncontrolled hypertension.

Methods: In this cross-sectional survey, subjects with uncontrolled hypertension aged above 35 years were recruited from the general medicine clinic of Beijing Anzhen Hospital and its affiliated community health centers from March to December 2012.

Results: WAfter adjusted for 7 covariates, each index was significantly correlated with ischemic stroke according to the result of single index model. SBP ≥ 150 mmHg, DBP ≥ 100 mmHg, high textile and quartile PP and high quartile MAP were associated with higher risk of ischemic stroke. When SBP and DBP or SBP and MAP were introduced into the model together, no significant difference was noted across categories of DBP and MAP, DBP and PP were introduced into the model together, no significant difference was noted across categories of DBP. Four indexes were introduced to the multifactorial model, only SBP entered into the model. Compared with SBP <140 mmHg, relative risk of stroke was 2.777 (95% CI: 1.356~5.688) for SBP between 150-159 mmHg, 2.116 (95% CI: 1.0384.314) for SBP ≥ 160 mmHg. SBP showed the biggest area under ROC curves, which is 64.3%.

Conclusions: SBP is associated with higher risk of ischemic stroke in patients with uncontrolled hypertension than other three blood pressure indexes. The risk of ischemic stroke would decrease when SBP was less than 150 mmHg.

Keywords: Hypertension; Blood pressure control; Ischemic stroke; Recurrent stroke

Introduction

Stroke is the leading cause of death in China nowadays. In recent years, changes have occurred in the incidence and subtype of stroke. A follow-up study of the incidence of stroke from 1982 to 2000 in 10 communities across China suggested that the incidence of ischemic stroke was significantly higher than that of hemorrhagic stroke [1]. Results from the ongoing Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) project in Beijing indicated that from 1984 to 2004 the incidence of hemorrhagic stroke declined by 1.7%, but the incidence of ischemic stroke increased by 8.7% annually [2]. With the percentage of intracerebral hemorrhage and undetermined stroke declining, the percentage of ischemic stroke was increasing (70%) [3].

Hypertension is the most important risk factor for ischemic stroke. The cerebral arterial wall will be hardened and intima will be thickened because of long-term of hypertension. Hypertension also can cause atherosclerosis or accelerate its' development. When the vessel lumen is stenosis or cerebral thrombosis is made, patients will suffer from ischemic stroke. Now, the prevalence of adult hypertension was 18.8% in China, and the estimated number of patients with hypertension was 266 million, 24.7% of them were treated, and the control rate was 25% for the treated patients [4]. It meant that most patients didn't meet the standard of control; they were likely to be higher risk of stroke.

Decrease of blood pressure (BP) could reduce the incidence of stroke significantly, the risk of cardiovascular disease increased by 100% for controlled hypertension, and by 237% for uncontrolled hypertension [5]. Some studies recruited subject with or without hypertension from community. They focused on the relationship between two or four BP indexes with stroke. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) are common predictive factor for cardiovascular diseases [6-8]. Pulse pressure (PP) and mean arterial pressure (MAP) are valuable pathophysiological factors of peripheral vascular resistance and major arterial flexibility. Both of them are also widely used in predicting cardiovascular diseases [9-11]. Evidence showed that blood pressure indexes could be used singly or in combination for predicting stroke. Nevertheless, most studies focused on population with or without hypertension, few studies applied four indexes to predict ischemic stroke for patients with uncontrolled hypertension. Therefore, we collected data of patients with uncontrolled hypertension and analyzed the association between four indexes and ischemic stroke, in order to provide suggestion on stroke prevention for such patients.

Subject and Method

Method and subject

In this cross-sectional survey, uncontrolled hypertension aged above 35 years were recruited from general medicine clinic of Beijing Anzhen Hospital and its affiliated community health centers from March to December 2012. All the participants have a history of hypertension over 6 months, and have received antihypertensive medication treatment for at least 6 months. Subjects who suffered from ischemic stroke before hypertension were excluded; subjects with secondary hypertension and white coat hypertension also were excluded. The decision to investigate

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for secondary causes of hypertension may be made when

(1) The young and the old subjects with hypertension.

(2) Blood pressure responded poorly to drug treatment (resistant hypertension).

(3) Blood pressure began to rise after being previously well controlled (first checks should be made for non-compliance).

(4) There was sudden onset of hypertension. We asked patients to provide findings of their kidney exams because the most common causes include renal parenchymal and vascular disease. The patients were excluded when their secondary hypertension was diagnosed. If they had not any relevant information about diagnosis or exclusion of secondary hypertension, they were not selected into this study. We also excluded white coat hypertension (WCH). Patients reported that home BP measurements were normal but office BP ≥ 140/90 mmHg, which should considered WCH. Home BP measurement or ambulatory blood pressure monitoring (ABPM) recordings could help to exclude WCH. WCH should be diagnosed when office BP ≥ 140/90 mmHg at least three occasions, with normal 24 h (<130/80 mmHg), day ABPM <135/85 mmHg, and home BP (average of several readings) <135/85 mmHg. Patients with WCH were excluded. If they had not the value of home BP measurement or ABPM, they were not selected into this study.

BP measurement

BP was measured twice in the clinic with an interval of 5-10 minutes. The average of both measurements was recorded. Uncontrolled hypertension was defined as patients with average SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and patients reported most of the blood pressure values (75%) were not up to the standard in the last year home BP measurement and/or office BP measurement. PP = SBP-DBP, based on interquartile range, PP were divided into four groups, which were ≤ 47, 48~59, 60~69, and ≥ 70 mmHg. MAP =1/3(SBP+2DBP). Based on interquartile range, MAP were divided into four groups, which were ≤ 104, 105~109, 110~117, and ≥ 118 mmHg. Based on the average of both measurements, SBP were divided into four groups, which were <140, 140 ~149, 150 ~159, and ≥ 160 mmHg. DBP were divided into four groups, which were <90, 90 ~ 94, 95 ~ 99, ≥ 100 mmHg.

History of ischemic stroke

History of ischemic stroke was defined as patients have diagnosed ischemic stroke before, when they suffered ischemic, they had symptoms of numbness, abnormal speech, transitional blindness, vertigo, nausea, deviated eyes and mouth, hemiplegia, dribbling, and etc; Examined with brain CT or MRI: And diagnosed with ischemic stroke by a neurologists before (include cerebral thrombosis or lacunar infarction). If patients met the rest two criterions, they were identified having history of ischemic of stroke.

Other factors

Other factors were obtained via survey, such as age, gender, hypertension family history, diabetes history, history of smoking, alcohol consumption, overweight and obesity. Hypertension family history was defined as participants' relatives (brothers/sisters or parents) diagnosed hypertension. Diabetes was defined as being treated for diabetes or having a fasting blood sugar >6.1 mmol/L and being diagnosed diabetes by doctor. Current smoker was defined as patient smoke currently and the sum of cigarettes continuous or cumulative was over 100. Current alcohol consumption was defined as patient dinked alcohol more than once a week on average, and consumption of liquor was over 50ml, or beer over 300 ml, or wine over 100 ml. BMI=Weight (Kg)/ Height (m)2, overweight Plus obesity: BMI ≥ 24 kg/m2.

Statistical analysis

The statistical analysis was performed with SPSS software for Windows (version 18.0; SPSS, Inc., Chicago, IL, USA). Chi-square test was used to compare difference in proportions of different group; Logistic regression analyses were conducted to test the association between SBP, DBP, PP and MAP and Ischemic stroke. Stroke was dependent variable, covariates included the following: gender, age, family history, overweight and obesity, diabetes, cigarettes smoking and alcoholic drinking.

Model 1: unadjusted for any covariates.

Model 2: adjusted for gender, age and family history.

Model 3: adjusted for all the 7 covariates. Accuracy of four factors in predicting stroke was conducted by the area under ROC curves. All reported p values were two-tailed and p values less than 0.05 were considered statistically significant.

Results

Descriptive and stroke prevalence

Among the 3909 patients (1932 male, 1977 female) the mean age were 58.9 years (SD = 11.2, range 35-96). Table 1 displays the main characteristics of study population. 144 (3.68%) suffered from stroke. Participants with PP over 70 mmHg or with MAP over 117 mmHg or with SBP range from 150 to 159 mmHg were more likely higher prevalence than other participants. Table 2 displays the prevalence of stoke across categories of four predictors.

Single index and stroke

Table 3 displays the odds ratios and 95% CIs of prevalence of stroke across categories of single index. Using the lowest quartile PP group and MAP group as the reference category, high tertile and quartile PP and high quartile MAP were associated with significantly higher risk of ischemic stroke after adjusted for full covariates. Using SBP <140 mmHg and DBP <90 mmHg as the reference group respectively, SBP >150 mmHg and DBP ≥ 110 mmHg was associated with a significantly higher risk of stroke prevalence respectively.

Two indexes combination and stroke

Table 4 displays the odds ratios and 95% CIs of SBP combination with DBP or MAP and DBP combination with PP for predicting stroke by model 3. When SBP and DBP or SBP and MAP were introduced into the model together, no significant difference in stroke risk was noted across categories of DBP and MAP. DBP and PP were introduced into the model together; no significant difference in stroke risk was noted across categories of DBP.

Multivariate Regression Analysis of PP, MAP, SBP and DBP

All the covariates and the four indexes were introduced to the regression model, using the method of stepwise regression, only SBP of the four indexes entered into the model. Compared with SBP >140 mmHg, the odds ratio was 1.386(95% CI: 0.670 ~2.866)for SBP between 140-149 mmHg, 2.777(95%CI: 1.356~5.688)for SBP between 150-159 mmHg, 2.116(95% CI: 1.038 ~4.314)for SBP ≥ 160 mmHg.

Characteristics	Number	Percentage
Gender (male)	1932	49.9
Age group 35-44	418	10.7
45-54	1044	26.7
55-64	1084	27.7
≥65	1363	34.7
Family history of hypertension	1158	29.6
Current alcohol consumption	1025	26.2
Current smoker	1030	26.3
Overweight plus Obesity	2752	70.4
Diabetes	468	12.0
PP group(mmHg) ≤47	992	25.4
48~59	1177	30.1
60~69	812	20.8
≥70	928	23.7
MAP group(mmHg)≤104	924	23.6
105~109	963	24.6
110~117	1077	27.6
>117	945	24.2
SBP group(mmHg)<140	725	18.5
140-149	1310	33.5
150-159	764	19.5
≥160	1110	28.4
DBP group(mmHg)<90	1323	33.8
90-94	1164	29.8
95-99	575	14.7
≥100	847	21.7

Table 1: Characteristics of study population

Area under ROC Curves of four indexes

Figure 1 displays the area under ROC curve. The area under ROC curve for SBP was 0.643 (95% CI: 0.578~0.708, P>0.001), for DBP was 0.547 (95% CI: 0.466~0.628 P=0.203), for PP was 0.605 (95% CI: 0.544~0.666, P=0.005), for MAP was 0.599 (95% CI: 0.523~0.674, P=0.008).

Discussion

The results showed, each index was associated with higher risk ischemic stroke, but joint application of two indexes was not superior to a single index, only SBP entered into multiple regression models. After analyzed step by step, SBP showed the strongest association with ischemic stroke, and had the largest area under ROC curves. The risk of ischemic stroke increased when SBP was above 150 mmHg.

Each index was associated with higher risk ischemic stroke according to the result of single index model. SBP ≥ 150 mmHg, DBP ≥ 100 mmHg, high tertile and quartile PP and high quartile MAP were associated with higher risk of ischemic stroke. Those results were consistent with previous study. SBP and DBP were continuously independently positively correlated with incidence of stroke and coronary disease regardless of gender [6]. Review of 61 global prospective studies found that risk of cerebrovascular disease doubled with an increase of SBP by 20 mmHg or DBP by 10 mmHg [7]. A prospective cohort study [8] in China found, after adjustment for other Covariates, systolic BP was a stronger predictor of CVD risk compared to diastolic BP. Okada [12] and Baba [13] found that PP can independently predict risk of stroke. Zhang L [14] inspired that MAP can be applied as an independent predictor of stroke for patients with uncontrolled hypertension.

Generally speaking, joint application of several indicators was superior to a single indictor for predicting the risk of stroke. SBP combination with DBP or MAP and DBP combination with PP were suggest ideal joint. Inoue [17] found that SBP combined with MAP was superior to DBP combined with PP for predicting the risk of stroke. But our results showed when SBP and DBP or SBP and MAP were introduced into the model together; no significant difference in stroke risk was noted across categories of DBP and MAP. DBP and PP were introduced into the model together; no significant difference in stroke risk was noted across categories of DBP. The results meant joint application of two indexes was not superior to a single index. Some studies also utilized the four indexes to predict stroke. Minra [15] found a strong association between SBP/MAP and cardiovascular mortality rates, the association was stronger than that of DBP, and PP showed the weakest association. Miura K [16] found, for male in age of 65-74 yrs, SBP showed the strongest association, while for female, MAP showed the strongest association. In this study, four blood pressure

Variables	Stroke Patients NO.	Prevalence (%)	χ^2	*P*- Value
PP group(mmHg)≤ 47	14	1.4	22.503	<0.001
48~59	30	3.7		
60~ 69	51	4.3		
≤ 70	49	5.3		
MAP group(mmHg)≤ 104	29	3.1	12.870	0.005
105~109	25	2.6		
110~117	38	3.5		
>117	52	5.5		
SBP group(mmHg)<140	11	1.5	28.810	<0.001
140-149	34	2.6		
150-159	45	5.9		
≥ 160	54	4.9		
DBP group(mmHg)<90	53	4.0	4.793	0.188
90-94	32	2.7		
95-99	21	3.7		
≥ 100	38	4.5		

Table 2: Prevalence of stroke across categories of the four predictors

	Model 1			Model 2			Model 3		
	OR 95% CI			OR 95% CI			OR 95% CI		
SBP 1	1			1			1		
2	1.731	0.871	3.437	1.273	0.632	2.564	1.385	0.669	2.866
3	4.051	2.078	7.896	2.655	1.333	5.289	2.769	1.351	5.675
4	3.320	1.724	6.393	1.021	1.043	4.017	2.105	1.032	4.294
DBP 1	1			1			1		
2	0.677	0.434	1.058	0.960	0.607	1.519	0.920	0.578	1.464
3	0.908	0.543	1.520	1.267	0.745	2.155	1.220	0.714	2.084
4	1.126	0.735	1.723	1.619	1.036	2.532	1.584	1.008	2.489
PP 1	1			1			1		
2	2.670	1.406	5.071	1.685	0.862	3.294	1.771	0.891	3.524
3	3.156	1.736	5.738	2.398	1.301	4.419	2.497	1.329	4.693
4	3.913	2.145	7.137	2.255	1.178	4.316	2.226	1.141	4.343
MAP 1	1			1			1		
2	0.821	0.477	1.413	0.874	0.506	1.510	0.822	0.471	1.433
3	1.127	0.689	1.842	1.165	0.710	1.914	1.155	0.701	1.905
4	1.793	1.128	2.851	1.823	1.140	2.913	1.708	1.063	2.746

Table 3: Odds Ratio (95%CI) of stroke across categories of single index

		β	Se	Wals-χ^2	P	OR	CI95%
SBP+DBP	SBP 1					1	
	2	0.331	0.388	0.729	0.393	1.392	0.651~2.977
	3	0.972	0.378	6.601	0.01	2.643	1.259~5.546
	4	0.606	0.382	2.513	0.113	1.833	0.867~3.875
	DBP 1					1	
	2	0.017	0.248	0.005	0.945	1.017	0.626~1.652
	3	0.200	0.280	0.511	0.475	1.222	0.705~2.117
	4	0.404	0.249	2.624	0.105	1.497	0.919~2.440
SBP+MAP	SBP 1					1	
	2	0.261	0.372	0.493	0.483	1.299	0.626~2.694
	3	0.848	0.387	4.797	0.029	2.334	1.093~4.983
	4	0.346	0.425	0.664	0.415	1.413	0.615~3.247
	MAP 1					1	
	2	-0.230	0.287	0.643	0.423	0.794	0.452~1.395
	3	-0.036	0.281	0.017	0.897	0.964	0.556~1.671
	4	0.429	0.319	1.810	0.179	1.536	0.822~2.870
DBP+PP	DBP 1					1	
	2	0.035	0.248	0.02	0.886	1.036	0.637~1.684
	3	0.348	0.280	1.548	0.213	1.416	0.819~2.449
	4	0.555	0.235	5.569	0.018	1.742	1.099~2.761
	PP 1						
	2	0.665	0.360	3.416	0.065	1.944	0.961~3.935
	3	0.978	0.325	9.062	0.003	2.658	1.406~5.023
	4	0.899	0.353	6.483	0.011	2.457	1.230~4.097

Table 4: Multivariable adjusted Odds Ratio (95%CI) of stroke and two indexes combination

indexes were introduced into the multiple regression models, only SBP showed the significant association with ischemic stroke.

We also analyzed the accuracy of four factors. BP had the largest area among the four indexes, and it was near to 70%, which means a fairly good accuracy. So the result indicated SBP was a good index to predict ischemic stroke.

Zhang L also analyzed the relationship between BP indexes and ischemic stroke in patients with uncontrolled hypertension. In one of his paper, he inspired that MAP could be applied as an independent predictor of stroke for this kind of patients [14]. Another paper applied MAP and PP in predicting ischemic stroke for patients with uncontrolled hypertension, the results showed patients with the highest quartile group of PP or MAP were associated with a significant risk of stroke after adjusted for other covariates, The odds ratio (OR) were 1.479 (95% CI 1.027-2.130) and 2.000 (1.373-2.914) respectively [19].

Our study was the second one based on uncontrolled hypertension. In this study; we analyzed the relationship between single index or two or four indexes combination and stroke then tested the accuracy of the four indexes, the method was superior to other similar study, and got different and simple result after analyzed step by step. Based on the result, GPs could understand what they should do for patients. Also there were some limitations; we could not confirm ischemic stroke was developed after their BP uncontrolled and obtain the causal relationship in this cross-sectional survey. Also it was not a large

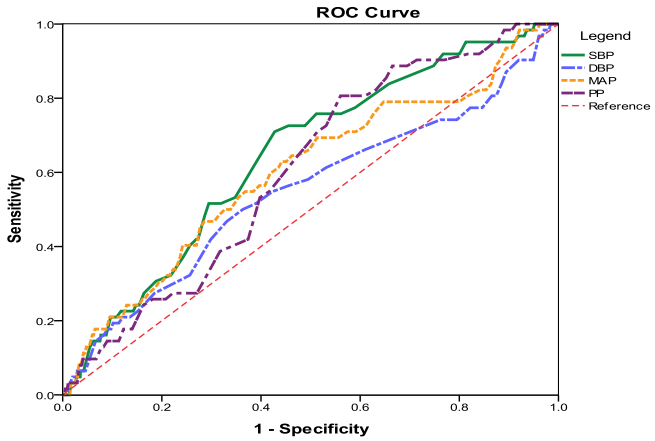

Figure 1: The area under ROC curve

sample survey, so the result of the study needs to be confirmed by large sample prospective study.

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