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Relationship between admission pulse pressure and clinical outcome during hospitalization among acute stroke patients

Zhong JU[1,2], Huan ZHANG[1], Weijun TONG[1], Tan XU[1], Yanfen ZHANG[3], Ning WANG[1] and Yonghong ZHANG[1]

[1]Department of Epidemiology, School of Radiation Medicine and Public Health of Medical College, Soochow University, Suzhou, China ; [2]Department of Neurology, First People's Hospital of Kerqin District, Tongliao, Inner Mongolia, China ; [3]Department of Neurology, Tongliao Municipal Hospital, Tongliao, Inner Mongolia, China

Abstract

Background and purpose : There are currently no data on the relationship between admission pulse pressure (PP) level and short term clinical outcome among acute stroke patients in the Chinese population. We studied the association between admission PP and in-hospital death or dependency among acute stroke patients in Inner Mongolia, China.

Methods : A total of 2,178 acute ischemic stroke, 1604 intracerebral hemorrhage and 156 subarachnoid hemorrhage patients were included in the present study. Blood pressure and other study variables were collected within the first 24-hours of admission. Study outcome (death or dependency) was evaluated by trained neurologists during hospitalization. The associations between admission PP and study outcome were analyzed by using multiple logistic model.

Results : PP at admission was not significantly associated with study outcome in acute ischemic stroke and subarachnoid hemorrhage. On the other hand, PP was significantly and positively associated with odds of study outcome in acute intracerebral hemorrhage. Compared to those with PP < 50 mmHg, multivariate-adjusted odds ratio (95% confidence interval) of study outcome was 1.545 (1.111-2.148) among intracerebral hemorrhage patients with PP ≥ 70 mmHg (p = 0.01).

Conclusion : Increased PP was significantly and positively associated with poor clinical outcome among patients with acute intracerebral hemorrhage, but not acute ischemic stroke and subarachnoid hemorrhage, in Inner Mongolia, China.

Key words : Pulse pressure ; stroke ; mortality ; dependency.

Introduction

Stroke is the leading cause of death and long-term disability worldwide (WHO, 2003). In China, Stroke is the third leading cause of death for male and the second one for female (He *et al.*, 2005), the morbidity and mortality of stroke were higher in China compared to the other countries (Wu *et al.*, 2001). The incidence and proportion of hemorrhagic stroke, especially, is much higher in the Chinese population than in western populations (Zhang *et al.*, 2003).

Hypertension is an independent and modifiable important risk factor for stroke. Some observational studies demonstrated a positive association between elevated blood pressure (BP) and poor outcome among acute stroke patients (Britton and Carlsson, 1990 ; Dandapani *et al.*, 1995 ; Robinson *et al.*, 2001 ; Ahmed and Wahlgren, 2001). It is well known that BP is usually characterized by its pulsatile (Pulse pressure, PP, i.e. the difference between systolic and diastolic BP) and steady components (mean arterial pressure, MAP). Some studies showed that increased PP was a risk factor of incidence of stroke (Lee *et al.*,1999 ;Vaccarino *et al.*, 2001), and increased PP was also an independent predictor of death and other poor outcome among acute stroke patients (Vemmos *et al.*, 2004 ; Aslanyan *et al.*, 2004 ; Grabska *et al.*, 2009). Despite the fact that stroke is a leading cause of death and disability in China, there are currently no data on the relationship between admission PP level and short term clinical outcome among acute stroke patients in the Chinese population. The purpose of the present study is to examine the association between admission PP level and clinical outcome including death and dependency among acute stroke patients in Inner Mongolia, China.

Subjects and methods

Study participants

Acute stroke patients were recruited from 6 hospitals (Tongliao Municipal Hospital, Teaching

Hospital of Inner Mongolia National University, Kezuohou Banner (County) Hospital, Kezuozhong Banner Hospital, Zalute Banner Hospital, and Keerqin District Hospital) in Tongliao, a prefecture-level city in eastern Inner Mongolia, China. The written informed consent was obtained for all study participants. The 6 hospitals are the only western medicine facilities in this region and serve a population of 2.04 million ; most of whom are of Han or Mongolian ethnicity. All patients with a clinical diagnosis of acute stroke admitted to the 6 hospitals from January 1, 2003 to December 31, 2005 were potentially eligible for the study. However, only those cases confirmed by a computed tomography (CT) scan or magnetic resonance imaging (MRI) were included. All subtypes of stroke, including ischemic stroke (thrombosis, embolism, or lacunar infarction) and hemorrhagic stroke (intracerebral hemorrhage or subarachnoid hemorrhage) were included in this study. A team of investigators including neurologists reviewed the eligibility of study participants. Among 4,369 acute stroke patients admitted to the 6 hospitals during the study period, 3,938 had a CT scan or MRI confirmed ischemic or hemorrhagic stroke and were included in this analysis. A total of 431 patients were excluded from our analysis because of a discharge diagnosis of transient ischemic attack or stroke of undetermined type (n = 373) or lack of a CT scan or MRI test (n=58). This study was approved by Soochow University School of Public Health and Radiation Medicine Ethics Committee.

Data collection

Baseline data were collected within the first 24-hours of hospital admission by in-person interview with patients or their family members (if patients were not able to communicate). Data on demographic characteristics, lifestyle risk factors, medical history, clinical laboratory tests, and imaging data (CT and MRI) were obtained using a standard questionnaire administered by trained staffs. Cigarette smokers were defined as having smoked at least 1 cigarette per day for 1 year or more. The amount and type of alcohol consumed during the past year was collected. Alcohol consumption was defined as consuming one or more alcoholic drinks per day during the last year. Three BP measurements were taken within 30 minutes of admission while the study participants were in the supine position using a standard mercury sphygmomanometer according to a standard protocol (Perloff *et al.*, 1993). The first and fifth Korotkoff sounds were recorded as systolic and diastolic BP, respectively. The mean of 3 BP measures were used in all analysis. PP is defined as the difference between systolic and diastolic BP.

Fast plasma glucose was measured using a modified hexokinase enzymatic method. Total cholesterol, HDL-cholesterol, and triglycerides were analyzed enzymatically on a Beckman Synchron CX5 Delta Clinical System (Beckman Coulter, Inc., Fullerton, CA, USA) using commercial reagents (Allain *et al.*, 1974). LDL-cholesterol levels were calculated by use of the Friedewald equation for the participants who had triglyceride levels < 400 mg/dL : LDL cholesterol = total cholesterol-HDL-cholesterol-triglycerides/5 (Friedewald *et al.*, 1972).

The study outcome included death during hospitalization and dependency on discharge. If a patient died in the hospital, a study staff member recorded the death on the event form and obtained the death certificate. If a patient survived the acute stroke, the study neurologists conduct a comprehensive clinical evaluation on discharge. Dependency was defined as moderate or severe disability using a Modified Rankin's scale > 2 (Rankin, 1957 ; Bonita and Beaglehole, 1988).

Statistical analysis

The mean and standard deviation of continuous variables and proportion of categorical variables on admission were calculated for ischemic stroke, intracerebral hemorrhage and subarachnoid hemorrhage, and both patients without study outcome and patients with study outcome in ischemic stroke, intracerebral hemorrhage and subarachnoid hemorrhage. Patients were grouped by stroke subtype and PP level (< 50 mmHg, 50~69 mmHg and ≥ 70 mmHg). Multivariate logistic regression analysis was used to examine the association between PP and study outcome (death or dependency) adjusted for age, gender, ethnicity (Mongol vs. Han), alcohol consumption, cigarette smoking, physical activity, and history of hypertension, systolic BP, diastolic BP, history of diabetes, and dyslipidemia. Statistical analyses were conducted using SPSS statistical software (version 13.0).

Results

A total of 2,178 ischemic stroke, 1,604 intracerebral hemorrhage and 156 subarachnoid hemorrhage patients were included in our analysis. The median time from onset of symptom to admission was 9.3 h (11.1 h for ischemic, 8.9 h for intracerebral hemorrhage, 8.6 h for subarachnoid hemorrhage). Table 1 presents the demographic and clinical characteristics

Table 1

Characteristics of stroke patients at hospital admission

Variables	ischemic	intracerebral hemorrhage	subarachnoid hemorrhage
No	2178	1604	156
Age ($\bar{X}$ ± SD)	61.6 ± 12.0$^{\#\#\circ}$	56.3 ± 11.6°	52.9 ± 12.1
Men(%)	1351 (62.0)$^{\circ\circ}$	984 (61.3)$^{\circ\circ}$	66 (42.3)
Mongol Ethnicity (%)	512 (23.5)$^{\#}$	424 (26.4)$^{\circ}$	49 (31.4)
Cigarette Smoking (%)	528 (24.2)$^{\#}$	325 (20.3)	33 (21.2)
Alcohol Drinking (%)	449 (20.6)	355 (22.1)$^{\circ}$	27 (17.3)
Manual Labor Profession, No. (%)	817 (37.5)$^{\#}$	847 (52.8)	85 (54.5)
History of Hypertension, No. (%)	1193 (54.8)$^{\#\circ}$	952 (59.4)$^{\circ}$	68 (43.6)
History of Diabetes (%)	246 (11.3)$^{\#}$	35 (2.2)	3 (1.9)
Dyslipidemia*, No. (%)	883 (72.5)$^{\#}$	349 (65.7)	37 (66.1)
Family History of Hypertension, No. (%)	109 (5.0)$^{\#}$	112 (7.0)$^{\circ}$	5 (3.2)
Systolic BP ($\bar{X}$ ± SD)	152.1 ± 28.9$^{\#\#}$	174.1 ± 34.4$^{\circ\circ}$	153.8 ± 31.4
Diastolic BP ($\bar{X}$ ± SD)	92.03 ± 16.8$^{\#\#}$	104.9 ± 19.3$^{\circ\circ}$	94.2 ± 18.6
Pulse Pressure ($\bar{X}$ ± SD)	60.07 ± 19.9$^{\#\#}$	69.3 ± 23.8$^{\circ\circ}$	59.6 ± 20.3
Hyperglycemia (%)*	686 (40.1)$^{\#\#}$	625 (54.6)	67 (58.8)

* Dyslipidemia : Total cholesterol ≥ 6.22 mmol/L (240 mg/dl) or LDL ≥ 4.14 mmol/L (160 mg/dl) or HDL < 1.04 mmol/L (40 mg/dl) or triglyceride ≥ 2.26 mmol/L (200 mg/dl). Hyperglycemia : Fast plasma glucose ≥ 6.1.

compared with intracerebral hemorrhage : $^{\#}P < 0.05$, $^{\#\#}P < 0.01$

° compared with subarachnoid hemorrhage : $^{*}P < 0.05$, $^{**}P < 0.01$

of stroke patients at admission by stroke subtypes. Those with acute ischemic stroke were more likely to be older, smoke and have a history of diabetes or dyslipidemia compared with those with intracerebral hemorrhage ; whereas those with acute intracerebral hemorrhage were more likely to be of Mongol ethnicity, have a profession involving manual labor, have both a personal and family history of hypertension, and have higher systolic BP, diastolic BP and PP levels compared with those with ischemic stroke. There was no significant difference in gender or alcohol consumption between patients with acute ischemic and hemorrhagic strokes. Those with acute intracerebral hemorrhage were more likely to be older and male, have alcohol drinking, have both a personal and family history of hypertension, and have higher systolic BP, diastolic BP and PP levels compared with those with subarachnoid hemorrhage.

The median duration of hospitalization was 7 days for ischemic stroke, 11 days for intracerebral hemorrhage and 9 days for subarachnoid hemorrhage. 142 stroke patients (39 ischemic – 94 intracerebral hemorrhage and 9 subarachnoid hemorrhage) died during hospitalization and 1506 stroke patients (900 ischemic, 596 intracerebral hemorrhage and 10 subarachnoid hemorrhage) were dependency on discharge. The in-hospital case-fatality rate was higher for acute intracerebral hemorrhage (5.9%) than it was for acute ischemic stroke (1.8%). There was no difference for in-hospital case-fatality rate between intracerebral hemorrhage and subarachnoid hemorrhage (5.8%). However, the dependency rate was higher for those with acute ischemic stroke (41.3%) compared with acute intracerebral hemorrhage (37.2%) and subarachnoid hemorrhage (6.4%).

Among ischemic stroke patients, those with study outcome were more likely to have a history of diabetes compared to those without study outcome, $P < 0.05$, and there were no significant difference for systolic BP, diastolic BP and PP between those with and without study outcome, $P > 0.05$. Among intracerebral hemorrhage patients, those with study outcome were more likely to be older, and have a history of hypertension, higher systolic BP, diastolic BP and PP compared to those without study outcome, $P < 0.05$. Among intracerebral hemorrhage patients, those with study outcome were more likely to be older, and have a history of hypertension, higher systolic BP, diastolic BP and PP compared to those without study outcome, $P < 0.05$. Among subarachnoid hemorrhage patients, there were no significant difference for all characteristics except for age between patients with and without study, all $P > 0.05$ (Table 2) .

There was no significant association between PP levels on admission and study outcomes among patients with acute ischemic stroke and subarachnoid hemorrhage, $p > 0.05$. On the other hand, there was a positive and significant association between admission PP and study outcome among patients with acute hemorrhagic stroke (Table 3). Compared to those with PP < 50 mmHg, multivariate-adjusted odds ratio (95% confidence interval) of study

Table 2

Characteristics of stroke patients without and with study outcome at hospital admission

Variables	Ischemic stroke			intracerebral hemorrhage			subarachnoid hemorrhage		
	Without study outcome	With study outcome	P	Without study outcome	With study outcome	P	Without study outcome	With study outcome	P value
No	1239	939		914	690		137	19	
Age ($\bar{X}$ ± SD)	61.2 ± 12.0	62.1 ± 12.1	0.068	55.9 ± 11.8	56.8 ± 11.3	0.147	52.1 ± 11.8	59.4 ± 12.9	0.015
Men (%)	772 (62.3)	580 (61.8)	0.529	580 (63.5)	404 (58.6)	0.876	57 (41.6)	9 (47.4)	0.482
Mongl Ethnicity (%)	312 (25.2)	200 (21.3)	0.124	258 (28.2)	166 (24.1)	0.354	41 (29.9)	8 (42.1)	0.383
Cigarette Smoking (%)	297 (24.0)	231 (24.6)	0.464	187 (20.5)	138 (20.0)	0.608	27 (19.7)	6 (31.6)	0.218
Alcohol Drinking (%)	248 (20.0)	201 (21.4)	0.250	208 (22.8)	147 (21.3)	0.931	22 (16.1)	5 (26.3)	0.203
History of Hypertension (%)	670 (54.1)	522 (55.6)	0.142	542 (59.3)	410 (59.4)	0.068	60 (43.8)	8 (42.1)	0.938
History of Diabetes (%)	126 (10.2)	120 (12.8)	0.031	22 (2.4)	13 (1.9)	0.621	2 (1.5)	1 (5.3)	0.310
Dyslipidemia (%)*	491 (71.2)	392 (74.2)	0.232	201 (63.4)	148 (69.2)	0.171	34 (66.7)	3 (60.0)	1.000
Manual labor (%?)	455 (36.7)	362 (38.6)	0.158	497 (54.4)	350 (50.7)	0.923	74 (54.0)	11 (57.9)	0.548
Family history of hyperten (%)	56 (4.5)	53 (5.6)	0.176	59 (6.5)	53 (7.7)	0.173	4 (2.9)	1 (5.3)	0.463
Systolic BP, mmHg	152.9 ± 29.1	151.0 ± 28.6	0.116	171.7 ± 34.9	177.7 ± 33.4	0.001	154.03 ± 31.2	151.6 ± 33.8	0.760
Diastolic BP, mmHg	92.5 ± 16.6	91.4 ± 17.1	0.138	103.6 ± 19.0	106.7 ± 19.5	0.001	94.1 ± 18.2	94.8 ± 21.3	0.876
Pulse pressure, mmHg	60.5 ± 20.4	59.6 ± 19.2	0.299	68.1 ± 24.0	70.9 ± 23.3	0.019	59.9 ± 19.8	56.8 ± 24.6	0.607
hyperglycemia*	382 (39.5)	304 (40.8)	0.586	361 (53.1)	264 (56.8)	0.219	59 (57.8)	8 (66.7)	0.758

*Dyslipidemia : Total cholesterol ≥ 6.22 mmol/L (240 mg/dl)or LDL ≥ 4.14 mmol/L (160 mg/dl) or HDL < 1.04 mmol/L (40 mg/dl) or triglyceride ≥ 2.26 mmol/L (200 mg/dl). Hyperglycemia : Fast plasma glucose≥ 6.1.

Table 3

Odds ratio and 95% confidence intervals of study outcomes associated with admission Pulse Pressure among patients with acute ischemic stroke and hemorrhagic stroke

	Unadjusted OR (95%CI)	P value	Adjusted OR (95%CI)	P value
Ischemic				
Pulse Pressure level				
< 50 mmHg	1.000 (ref)		1.000 (ref)	
50~69 mmHg	1.147 (0.926 1.421	0.210	1.166 (0.929 1.465	0.185
≥ 70 mmHg	0.992 (0.793 1.240)	0.942 0.945	(0.742 1.203)	0.645
intracerebral hemorrhage				
Pulse Pressure level				
< 50 mmHg	1.000 (ref)		1.000 (ref)	
50~69 mmHg	1.278 (0.934 1.749)	0.125	1.298 (0.925 1.821)	0.132
≥ 70 mmHg	1.582 (1.174 2.131)	0.003	1.545 (1.111 2.148)	0.010
subarachnoid hemorrhagic				
Pulse Pressure level				
< 50 mmHg	1.000 (ref)		1.000 (ref)	
50~69 mmHg	0.436 (0.129 1.477)	0.182	0.406 (0.086 1.911)	0.254
≥ 70 mmHg	0.718 (0.221 2.328)	0.581 0.411	(0.080 2.096)	0.284

#Adjusted for age, gender, ethnicity (Mongol vs. Han), alcohol consumption, cigarette smoking, systolic BP, diastolic BP and history of hypertension, diabetes, and dyslipidemia.

outcome was 1.564 (1.141 2.143) among patients with PP ≥ 70 mmHg, $p < 0.01$.

Discussion

Our study found that in-hospital case-fatality rate was 1.8%, 5.9% and 5.8% in acute ischemic stroke, intracerebral hemorrhage and subarachnoid hemorrhage patients, respectively. A higher case-fatality rate in intracerebral hemorrhage compared with ischemic stroke was reported in previous studies (Bamford *et al.*, 1990 ; Ellekjaer *et al.*, 1997 ; Wong *et al.*,1999). Our study, however, reports a considerably lower case-fatality rate compared with some previous studies (Wong *et al.*, 1999 ; Feigin *et al.*, 2003). We found that the dependency rate was 41.3%

for ischemic stroke, 37.2% and 6.4% for intracerebral hemorrhage and subarachnoid hemorrhage, respectively. Our findings were comparable with those reported from previous studies in China (CAST Collaborative Group, 1997 ; Liu *et al.*, 2007). Regarding case-fatality rate and dependency rate among stroke patients in our study, we have made discussion in our previous paper (Zhang *et al.*, 2008).

In the present study, we found that the PP level was higher in patients with study outcome than those without study outcome among intracerebral hemorrhage patients, however, there was no significant difference between patients with study outcome and those without study outcome among ischemic stroke and subarachnoid hemorrhage patients. This finding seems to indicate that PP levels at admission correlate to short term outcome of acute intracerebral hemorrhage.

In different clinical settings, PP was well-established marker of cardiovascular risk (Palmer *et al.*, 1992 ; Benetos *et al.*, 1998 ; Safar and Boudier, 2005 ; Paultre and Mosca, 2005). In a general population study, PP predicted cardiovascular but not cerebrovascular mortality (Benetos *et al.*, 1997). Whereas, an epidemiological study indicated that PP was a better predictor of fatal stroke (Mazza *et al.*, 2001). There are some studies (Tuhrim *et al.*, 1988 ; Vemmos *et al.*, 2004 ; Aslanyan *et al.*, 2004) showing positive association between PP during acute phase and outcome of stroke. Tuhrim`s study (Tuhrim *et al.*, 1988) showed that PP was related to the poor outcome in 30 days after onset of intracerebral hemorrhage. Vemmos's study (Vemmos *et al.*, 2004) demonstrated that increased 24-hour PP level was independently associated with higher long-term mortality post stroke. The hazards ratio for 1-year mortality associated with every 10 mm Hg increase in 24 h PP was 1.39 among stroke patients. In Aslanyan's study (Aslanyan *et al.*, 2004), elevated PP in the first 60 hours after onset was associated with poor outcome including mortality and dependency during three months after onset of stroke. Grabska's study (Grabska *et al.*, 2009) showed that elevated PP during the acute phase of ischemic stroke was an independent predictor of poor early outcome at hospital discharge and 30-day mortality. Our study indicated a positive and significant association between PP levels and study outcome (death/dependency) among intracerebral hemorrhage patients. The odds ratio of study outcome was significant in the highest category of PP $\geq$ 70 mm Hg. In our previous paper (Zhang *et al.*, 2008), our findings showed that BP was positively and significantly associated with death during hospitalization and dependency on discharge among patients with hemorrhagic stroke. Therefore, we adjusted for multivariate including systolic and diastolic BP in the present analysis. So we believe that elevated admission PP is also related to in-hospital poor outcome. But our study did not find a positive association between admission PP and study outcome in ischemic stroke and subarachnoid hemorrhage patients.

Just as some other observation study, the admission PP we recorded might be a pathological and physiological reaction to acute stroke and the severity of disease, and it was not sure to represent the general level of PP before onset. Admission PP recorded in our study, as well as in other observational studies, might reflect the pathophysiological responses to acute stroke and the severity of disease. Our study was limited in that it was an observational study. In the whole research process, we didn't systematically monitor the changing of BP and PP, which should be improved in future study to determine the relationship between the changing of PP during hospitalization and clinical outcome at discharge.

In summary, our study found that increased PP was significantly and positively associated with poor outcome among patients with acute intracerebral hemorrhage, but not acute ischemic stroke and subarachnoid hemorrhage. This study suggest that PP is a predictor of poor outcome (death or dependency) during hospitalization for intracerebral hemorrhage patients.

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Yonghong ZHANG, M.D., Ph.D.,
Department of Epidemiology,
School of Radiation Medicine and Public Health of Medical College,
Soochow University,
199 Renai Road,
Industrial Park District,
215123 Suzhou (China).
E-mail : yhzhang@suda.edu.cn