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# Discrepant relationships between admission blood pressure and mortality in different stroke subtypes

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ABSTRACT

The relationship between blood pressure(BP) and clinical outcome in patients with acute stroke is still controversial. The present study aimed to elucidate the impact of admission blood pressure on mortality in patients with acute stroke of different subtypes. Data were from ChinaQUEST (QUality Evaluation of Stroke Care and Treatment), a multicenter, prospective hospital registry study in 37 cities across China. A total of 6427 patients were admitted within 24 h of onset and after following up for 12 months, 5501 were included in the final analysis. Multivariate Cox regression model were used in data analysis. A "U-curve shaped" relationship was observed between admission systolic or diastolic BP and mortality at 12 months in the overall study population. Compared to first quartile, the Hazard ratio (HR) for the systolic BP of top quartile was 1.444 (95%CI 1.854–1.636), while the HR was 0.692 (95%CI 0.802–0.930) for the second quartile. Similar associations were observed when we applied admission diastolic BP. In subgroup analysis, the U-shaped effect was remained only in patients with intracranial hemorrhage (ICH). The HR for the systolic BP of top quartile was 2.274 (95%CI 1.878–2.755), while the HR was 0.751 (95%CI 0.571–0.986) for the second quartile. Moreover, admission diastolic BP of top quartile was significantly associated with elevated risk of death for patients with ischemic stroke caused by small vessel diseases (LACI)(HR 1.470; CI 1.040–2.078). In addition, we found a heterogeneity of the admission BP distribution among different subtypes, which may explain the "U-curve" effect.

## 1. Introduction

A transient initially increase of blood pressure (BP) occurred in three quarters of patients with acute stroke and usually declines spontaneously within the first few days after admission [1,2].Whether the post-stroke hypertension was a physiological response to maintain perfusion of ischemic penumbra because of impaired auto regulation or a sigh of the poor outcome was still controversial [3,4]. Some studies have suggested that high BP on admission was associated with increased stroke mortality [5–7], poor functional outcome and stroke recurrence, although this was not confirmed in other studies [3,8,9]. On the contrary, other studies have reported that low systolic BP may be associated with poor outcome [7,10]. The variable proportions of each stroke subtypes of subjects among studies may resulted in the conflicting conclusions. However, there were scarcely any investigations that have focused on different effects of admission BP on different subtypes of acute stroke. In the present study, patients were classified based on pathogenic mechanisms as large vessel atherosclerotic stroke (LVA), small vessel or lacunar infarct (LACI), cardioembolic stroke(CE), intracranial hemorrhage (ICH) and stroke of other etiology (e.g. retinal

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infarct, venous infarct, carotid dissection) or undetermined according to TOAST classification [11]. On the other hand, by the Oxfordshire Community Stroke Project(OCSP) classification [12], patients were classified into following groups including total anterior circulation syndrome(TACS), partial anterior circulation syndrome(PACS), lacunar infarction syndrome(LACS), and posterior circulation syndrome(POCS).

The purpose of the present post hoc analysis of the ChinaQUEST study was to elucidate the impact of admission blood pressure on poor outcomes in different subtypes of acute stroke during 12 months follow-up. Moreover, we compared the admission BP distribution among different stroke subtypes.

## 2. Subjects and method

### 2.1. Subjects

ChinaQUEST (QUality Evaluation of Stroke Care and Treatment) is a multicenter, prospective hospital (n = 62, 14 Level 2 and 48 Level 3 hospitals of varying size: < 500 beds [26%], 500 to 1000 beds [34%], and > 1000 beds [40%]) registry study in 37 cities in China, as previously described [13,14]. Over a 5 month period in 2006, consecutive patients in China with an acute stroke within 24 h of onset were enrolled and assessed at the time of discharge, 3 months, and 12 months post-stroke. Data were collected by trained local staff according to a standardized protocol, and then transferred to a secure website located at The George Institute for Global Health in Sydney, Australia. This study was approved by the ethics committees of Peking University First Hospital (Beijing), Ruijin Hospital (Shanghai), Prince of Wales Hospital (Hong Kong), and The University of Sydney. Good Clinical Practice guidelines in accordance with the Declaration of Helsinki were used, and the privacy of patients was strictly protected.

### 2.2. Explanatory and outcome variables

Baseline information was predominantly obtained by face-to-face interviews with patients and proxies or through medical record review. Follow-up details were obtained by telephone interviews. Death information was ascertained from family or through medical records, police records, or other sources. Supine blood pressure was measured by trained nurses at the upper arm on admission using an automated cuff or a mercury sphygmomanometer, and BP values were defined as the average values of three measurements. Demographic data (age, gender), medical history(hypertension, atrial fibrillation, diabetes mellitus, previous stroke, transient ischemic attack, coronary heart disease, including myocardial infarction, angina and heart failure) and vascular risk factors(current smoker, regular drinker), and current medications(antiplatelets, anticoagulants, antihypertensives, antidiabetics, and lipid-lowering drug) were evaluated in this study.

### 2.3. Statistical analysis

Continuous variables were displayed as means ( ± standard deviation) and categorical variables as frequency (percentage). Baseline characteristics were compared between different subgroups using the Mann-Whitney *U* test and the Chi-square test for continuous and categorical variables. Mortality from all causes was analyzed at 12 months, and the time since onset of the stroke was used as the time scale. Multivariate Cox proportional hazard models were used to assess the impact of the hypertension stage on survival, with adjustment of risk factors including age, gender, history of stroke, history of coronary heart disease, history of atrial fibrillation, history of heart failure, Glasgow Coma Scale(GCS) score, anti-hypertension medication, antiplatelet medication and use of lipid lowering agents. All P values were two-sided, with $P < 0.05$ considered statistically significant. Candidate covariates included all variables with $P < 0.05$ for association with survival in bivariable analysis. Backward elimination of non-significant variables ($P > 0.1$) was subsequently used to generate a final model in the Cox regression analysis. All statistical analyses were performed using SPSS version 20.0.

**Table 1**
General characteristics of the study population.

| | | Survival | | Death | P value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| No. of patients | 4878 | | 623 | | |
| Age | 63(mean) | 12(SD) | 68(mean) | 12(SD) | < 0.001 |
| Female | 1868 | 38.30 | 259 | 41.6 | 0.132 |
| Current smoking | 1407 | 28.9 | 126 | 20.3 | < 0.001 |
| Regular drinker | 1363 | 27.9 | 117 | 18.8 | < 0.001 |
| Hypertension history | 3563 | 73.0 | 468 | 75.1 | 0.23 |
| Atrial fibrillation history | 228 | 4.7 | 67 | 10.8 | < 0.001 |
| Diabetes mellitus history | 784 | 16.1 | 90 | 14.4 | 0.268 |
| Stroke history | 1281 | 26.3 | 228 | 36.6 | < 0.001 |
| TIA history | 197 | 4.0 | 21 | 3.4 | 0.417 |
| Antihypertensive treatment | 3183 | 65.3 | 359 | 57.6 | < 0.001 |
| Antiplatelet treatment | 3033 | 62.2 | 227 | 36.4 | < 0.001 |
| Lipid-lowering treatment | 1345 | 27.60 | 80 | 12.80 | < 0.001 |
| No. of antihypertensive agent use | | | | | |
| 0 | 1695 | 34.7 | 264 | 42.4 | |
| 1 | 1872 | 38.4 | 206 | 33.1 | |
| 2 | 1010 | 20.7 | 107 | 17.2 | |
| 3 | 271 | 5.6 | 39 | 6.3 | |
| 4 | 30 | 0.6 | 7 | 1.1 | |
| Class of antihypertensive agent use | | | | | |
| ACEI/ARB | 1566 | 32.1 | 167 | 26.8 | |
| CCB | 2415 | 48.7 | 224 | 36.0 | |
| Diuretic | 439 | 9.0 | 100 | 16.1 | |
| β-Blocker | 405 | 8.3 | 74 | 11.9 | |
| Glasgow Coma Scale score | | | | | |
| 3–7 | 151 | 3.1 | 159 | 25.5 | |
| 8–12 | 534 | 10.9 | 167 | 26.8 | |
| 13–15 | 4136 | 84.8 | 283 | 45.4 | |
| Stroke subtype | | | | | |
| LVA | 788 | 16.2 | 146 | 23.4 | |
| LACI | 2786 | 57.1 | 165 | 26.5 | |
| CE | 119 | 2.4 | 45 | 7.2 | |
| ICH | 1054 | 21.6 | 253 | 40.6 | |
| other or undetermined etiology | 131 | 2.7 | 14 | 2.2 | |
| Stroke location | | | | | |
| TACS | 509 | 10.4% | 160 | 25.7% | |
| PACS | 2562 | 52.5% | 282 | 45.3% | |
| LACS | 902 | 18.5% | 45 | 7.2% | |
| POCS | 642 | 13.2% | 90 | 14.4% | |
| Uncertain | 263 | 5.4% | 46 | 7.4% | |

## 3. Results

### 3.1. Baseline characteristics

A total of 6427 patients were screened for enrollment. 345 patients dropped out of the study; 578 patients were excluded because of a lack of BP information; 3 patients were excluded because they were under 18 years of age. A total of 5501 patients were finally included in our analysis and 623 patients died during follow-up. 32 died during time of hospitalization, while 387 patients and 204 patients died during 3 months and 12 months follow-up period, respectively. The detailed demographic characteristics are presented in Table 1. The main causes of death were cerebrovascular diseases (374 cases), following by injuries or other causes(143 cases), infection (62cases) and cardiovascular diseases(42 cases). The mean age of patients who died were 68 years old(SD,12),older than those who survived. Moreover, the atrial fibrillation history, stroke history, use of medications, Glasgow Coma Scale score, and stroke subtype distribution were significantly different