Acute-Phase Blood Pressure Levels Correlate With a High Risk of Recurrent Strokes in Young-Onset Ischemic Stroke

Satu Mustanoja, MD, PhD, MSc (Stroke Med); Jukka Putaala, MD, PhD, MSc (Stroke Med); Daniel Gordin, MD, PhD; Lauri Tulkki, MD; Karoliina Aarnio, MD; Jani Pirinen, MD; Ida Surakka, MSc, PhD; Juha Sinisalo, MD, PhD; Mika Lehto, MD, PhD; Turgut Tatlisumak, MD, PhD

Background and Purpose—High blood pressure (BP) in acute stroke has been associated with a poor outcome; however, this has not been evaluated in young adults.

Methods—The relationship between BP and long-term outcome was assessed in 1004 consecutive young, first-ever ischemic stroke patients aged 15 to 49 years enrolled in the Helsinki Young Stroke Registry. BP parameters included systolic (SBP) and diastolic BP, pulse pressure, and mean arterial pressure at admission and 24 hours. The primary outcome measure was recurrent stroke in the long-term follow-up. Adjusted for demographics and preexisting comorbidities, Cox regression models were used to assess independent BP parameters associated with outcome.

Results—Of our patients (63% male), 393 patients (39%) had prestroke hypertension and 358 (36%) used antihypertensive treatment. The median follow-up period was 8.9 years (interquartile range 5.7–13.2). Patients with a recurrent stroke (n=142, 14%) had significantly higher admission SBP, diastolic BP, pulse pressure, and mean arterial pressure (P<0.001) and 24-h SBP, diastolic BP, and mean arterial pressure compared with patients without the recurrent stroke. Patients with SBP ≥160 mmHg compared with those with SBP <160 mmHg had significantly more recurrent strokes (hazard ratio 3.3 [95% confidence interval, 2.05–4.55]; P<0.001) occurring earlier (13.9 years [13.0–14.6] versus 16.2 [15.8–16.6]; P<0.001) within the follow-up period. In multivariable analyses, higher admission SBP, diastolic BP, pulse pressure, and mean arterial pressure were independently associated with the risk of recurrent stroke, while the 24-hour BP levels were not.

Conclusions—In young ischemic stroke patients, high acute phase BP levels are independently associated with a high risk of recurrent strokes. (Stroke. 2016;47:1593-1598. DOI: 10.1161/STROKEAHA.116.012944.)

Key Words: blood pressure ■ hypertension ■ prognosis ■ stroke ■ stroke in the young

Elevated blood pressure (BP) is found in more than every fourth adult1 and is globally the most important risk factor for stroke.2 Half of the stroke deaths are thought to be related to high BP,3,4 and lowering BP reduces stroke or recurrent stroke in elderly patients.5,6 In acute ischemic stroke, the BP is elevated after the stroke in most patients, ≤75%. In addition to admission BP levels, the direction and magnitude of BP change over the first 2 days has been associated with the outcome.7 Low BP has sometimes,8,9 but not always,10 been reported to predict poor outcomes in J- and U-shape curve relationships.

In young patients, the stroke pathogenesis and risk factors differ from those in the elderly: hypertension and other cardiovascular risk factors are less frequent, whereas many strokes occur because of rare causes, such as arterial dissections.11,12 The overall prevalence of hypertension in the young has already more than doubled in the past 2 decades, as has the amount of untreated hypertension.13 Diagnosed hypertension in the family is a highly significant predictor of stroke,14 and unhealthy lifestyles, such as obesity, high salt intake, and poor physical activities increase the prevalence of mild hypertension, found increasingly even in the young.

Although there are some limited epidemiological data on the association of hypertension in the young and stroke mortality,15 the BP levels in the acute stroke phase and their impact on the long-term outcome have not been evaluated in the young. We therefore studied the relationship between the admission and 24-hour BP values in the young patients, with...
Materials and Methods
This retrospective study was approved by the relevant authorities and performed at the Department of Neurology, Helsinki University Hospital. Our hospital has the only comprehensive stroke center with a neurological emergency room in the Helsinki region serving a population of 1.5 million. Patients included in the study belong to the Helsinki Young Stroke Registry (n=1008) and had a first-ever acute ischemic stroke diagnosed and treated at our department from 1994 to 2007.14 The BP medication information was gathered from patient records and prescriptions data at 3 months time point to exclude patients using the medication only at the acute stroke phase.

All patients included in the study had admission and 24-hour BP values and data on long-term follow-up. BP measurements were performed with fully automatic arm BP monitors with the patient lying in a supine position. Systolic BP (SBP) and diastolic BP (DBP) were recorded at admission in the emergency room and again at 24 hours after stroke onset. When >1 BP measurements were available, the first recording was taken into account for the analysis. Pulse pressure (PP) was calculated as SBP–DBP. Mean arterial pressure was calculated as DBP+1/3 PP. The difference between the admission and 24-hour BP values was calculated as delta (Δ) SBP, DBP, PP, and mean arterial pressure.

Demographic factors analyzed included age and sex. Comorbidities considered were diagnosed hypertension, obesity defined as a body mass index ≥30 kg/m2; or patient clearly stated as being obese if body mass index data were not available, smoking, dyslipidemia, previous transient ischemic attack, known atrial fibrillation, type 1 or type 2 diabetes mellitus, and cardiovascular disease, including congestive heart failure, coronary artery disease, prior myocardial infarction, or peripheral arterial disease. Classification of the cause of stroke was based on medical and radiological data and was assessed by stroke neurologists according to the Trial of Org 10172 in Acute Stroke was based on medical and radiological data and was assessed by stroke neurologists according to the Trial of Org 10172 in Acute Stroke Treatment criteria. Hypertension was defined according to World Health Organization criteria: SBP ≥140 mmHg, DBP ≥90 mmHg, or patient being on antihypertensive treatment.15

Follow-up data until the end of 2011 were obtained from the Care Register for Healthcare, maintained by the National Institute for Health and Welfare in Finland. This register is mandatory and regulated by legislation and includes data on all in-hospital stays. All hospitalizations because of International Statistical Classification of Diseases-9 codes 391–398, 402, 404, 410–417, 420–437, 440–444, 446–447, 449, 451–453, 459, and 798, as well as International Statistical Classification of Diseases-10 codes I01, I02, I05–I09, I11, I13, I20–I28, I30–I52, I60–I68, and I70–I79 were screened and diagnoses verified from original patient records when possible. Dates and causes of death came from Statistics Finland. The reliability and quality of these registers have previously been validated.16,17

The primary outcome measure was recurrent stroke, defined as any hemorrhagic or ischemic cerebrovascular event corresponding to the aforementioned diagnosis codes, with an exception for transient ischemic attack, which was not included. Secondary outcome measures were death from any cause and composite of cardiac events, defined as an acute myocardial infarction, unstable angina pectoris, coronary revascularization procedure, hospitalization because of other cardiac disease, such as arrhythmia, cardiomyopathy, or congestive heart failure, or death because of cardiac causes, whichever occurred first.

Statistical Analyses
To characterize the patient population, BP parameters were studied in subgroups defined by age and sex. Because we had only few young patients and the number of patients increased with age, we used age percentiles to have an almost equal number of patients in each group. Median and interquartile range were reported for non-normally distributed variables, and mean and SD were reported for normally distributed or noncontinuous variables, respectively. With each patient, the median differences between admission and 24-hour values were tested with Wilcoxon signed-rank test.

The cutoff SBP and DBP levels were visually estimated from the Cox regression cumulative survival curve in both patients with or without antihypertensive medication. Multivariable Cox regression analysis was used to identify the independent BP parameters associated with the outcomes. For each BP parameter, a separate multivariable analysis was performed after adjustment for age, sex, previous transient ischemic attack, dyslipidemia, type 1 and type 2 diabetes mellitus, cardiovascular disease, obesity, and current smoking; selection was based on their univariate significance (P<0.10). Cumulative distribution of the Kolmogorov–Smirnov test was analyzed on patients with and without recurrent stroke and admission SBP and DBP decimals. A 2-sided P value <0.05 was considered statistically significant. All statistical analyses were done on IBM SPSS 19.0.

Results
A total of 1004 eligible patients were included in the study (44 [37–47] years). Median delay to the first imaging was 0 days (interquartile range 0–2). Most patients were men (63%) having hypertension significantly more often than women (44% versus 31%; P<0.001).

Increased SBP levels ≥140 mmHg at admission were found in 57% (n=549) of the patients. Male preponderance, BP levels, and cardiovascular risk factors, such as hypertension (n=393, 39%), increased significantly with age (Table I in the online-only Data Supplement). Patients with a recurrent stroke had higher BP levels both at admission and at 24 hours; the BP levels decreasing significantly within 24 hours (Table 1).

One in 3 used antihypertensive medication (n=358, 36%) within 3 months; β-blockers (57%), angiotensin-converting enzyme inhibitors (28%), and diuretics (19%). The cutoff SBP and DBP levels were visually estimated from the Kaplan–Meier survival curves (Figure 1).

Table 1. Admission and 24-Hour Blood Pressure Parameters in mm Hg Stratified by the Occurrence of Recurrent Stroke

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>All (n=962)</th>
<th>Recurrent Stroke (n=862)</th>
<th>Yes (n=142)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>141 (125–160)</td>
<td>140 (124–160)</td>
<td>151 (131–170)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP</td>
<td>865 (78–97)</td>
<td>85 (76–92)</td>
<td>90 (80–104)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PP</td>
<td>58 (24)</td>
<td>57 (17)</td>
<td>63 (19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP</td>
<td>107 (23)</td>
<td>105 (18)</td>
<td>112 (20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24-hour</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>134 (120–150)</td>
<td>132 (120–150)</td>
<td>140 (121–160)</td>
<td>0.006</td>
</tr>
<tr>
<td>DBP</td>
<td>80 (72–90)</td>
<td>80 (70–90)</td>
<td>85 (76–95)</td>
<td>0.014</td>
</tr>
<tr>
<td>PP</td>
<td>53 (21)</td>
<td>53 (16)</td>
<td>57 (19)</td>
<td>0.104</td>
</tr>
<tr>
<td>MAP</td>
<td>100 (22)</td>
<td>99 (16)</td>
<td>104 (15)</td>
<td>0.004</td>
</tr>
<tr>
<td>Δ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔSBP</td>
<td>8 (4–21)</td>
<td>7 (4–20)</td>
<td>11 (2.7–25)</td>
<td>0.074</td>
</tr>
<tr>
<td>ΔDBP</td>
<td>5 (3–14)</td>
<td>5 (1–15)</td>
<td>5 (4–14)</td>
<td>0.234</td>
</tr>
<tr>
<td>ΔPP</td>
<td>2.5 (7–15)</td>
<td>2 (7–14)</td>
<td>7.5 (6–18)</td>
<td>0.072</td>
</tr>
<tr>
<td>ΔMAP</td>
<td>5.3 (3–16)</td>
<td>5 (3–15)</td>
<td>6.6 (1.4–18)</td>
<td>0.129</td>
</tr>
</tbody>
</table>

Data are shown as median (interquartile range or mean (SD)). Δ indicates change from admission to 24-hour; BP, blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; and SBP, systolic blood pressure.
enzyme inhibitors (39%), diuretics (24%), and calcium channel blockers (23%).

The follow-up period extended ≤18 years (median 8.91 [interquartile range 5.66–13.2]; Figure 1). A recurrent stroke during follow-up occurred in 142 patients (14%; 65% male); most recurrent strokes being ischemic (n=123, 12%) and only few (n=19, 1.9%) hemorrhagic. Composite of cardiac events were seen in 149 patients (15%), and AMI occurred in 37 patients (3.7%; 89% male). Vascular death was seen in 42 patients (4.2%; 78% male) out of all the 178 deaths (18%) from any cause.

Patients with an admission SBP ≥160 mm Hg compared with patients with an SBP <160 mm Hg had significantly more recurrent strokes in all the patients; in both patients with and without antihypertensive treatment (Figure 1). The recurrent strokes also occurred earlier (13.9 [13.0–14.6] versus 16.2 [15.8–16.6]; P<0.001) with the higher BP levels. Patients with an admission DBP≥100 mm Hg compared with patients with a DBP <100 mm Hg had also significantly more recurrent strokes (hazard ratio 3.2 [95% confidence interval, 2.36–4.09]; P<0.001). The cumulative distribution of patients with higher admission SBP and DBP decentiles.

Figure 1. Cumulative event risk of the relationship between admission systolic blood pressure (SBP) below or ≥160 mm Hg and recurrent stroke in all patients (A), patients with (B) and without antihypertensive medication (C) at the end of follow-up. CI indicates confidence interval; and HR, hazard ratio.
associated with a significantly higher recurrent stroke risk is seen in Figure 2.

In multivariable Cox regression analyses, higher admission SBP, DBP, PP, mean arterial pressure, and ΔSBP levels were independently associated with an increased recurrent stroke risk (Table 2) after adjusting for age, sex, previous transient ischemic attack, type 1 and type 2 diabetes mellitus, obesity, hyperlipidemia, and current smoking. No association was found for ΔDBP, ΔPP, Δmean arterial pressure, or 24-hour BP levels and recurrent stroke or for any BP levels and death from any cause or any cardiac event (data not shown).

Discussion

High admission BP levels were found in more than half of our young patients with acute stroke. These high BP levels were independently associated with a higher risk of recurrent strokes in the long-term follow-up, being in line with earlier reports with older stroke patients.6 There was a cutoff level of BP >160/100 mm Hg on admission, which lead to significantly more recurrent strokes than the lower BP levels. Hypertension was a relatively rare diagnosis before stroke, and the diagnosed patients had few hypertensive years behind; in addition, the elevated BP levels decreased within 24 hours close to normal being no more associated with recurrent strokes. Low admission BP, on the other hand, was found in only 4.5% of our young patients, probably because of few patients having impaired cardiac output, secondary to cardiac failure, AMI, or arrhythmias, found more in older stroke patients.19

The underlying mechanisms of elevated BP in ischemic stroke are not yet well understood, although several mechanisms have been suggested, such as preexisting hypertension, oxidative stress, activation of the sympathetic renin–angiotensin–aldosterone, cortisol, and natriuretic peptide neuroendocrine systems, and the Cushing reflex, that is, raised BP secondary to raised intracranial pressure.19 In acute stroke, cerebral blood flow depends on systemic arterial pressure when cerebral autoregulation is impaired because of regional hypoxia and acidosis, resulting in reduced penumbral perfusion. Transcranial Doppler has been used to study impaired cerebral autoregulation20; however, not all studies using other methods have found evidence of the impaired cerebral autoregulation.21

The management of BP in the acute stroke phase is, consequently, still unclear,22,23 with limited evidence to evaluate the effect of altering BP.19 Ischemic stroke patients have been shown to have their acute postevent SBP closer to premorbid levels, with no BP level rise before the event, unlike patients with hemorrhagic stroke.24 Most recommendations, therefore, avoid routine BP lowering in the acute phase of ischemic stroke23 because it could be harmful25 because of an inadequate supply of blood in the brain. Initiation of antihypertensive therapy has mostly been associated with a favorable outcome in case of intraventricular thrombolysis.26

In a meta-analysis, lowering the BP reduced the stroke rate in everyone >60 years of age, no matter what the baseline BP level.2 In a post analysis of a subacute stroke prevention trial, only one third of the patients had controlled BP ≥75% of the time, which was linked to reduction in recurrent stroke.6 In our study, there was no difference found between patients with or without antihypertensive medication at 3 months in predicting recurrent stroke during the 18-year follow-up. There might be several explanations for this result. The lack of association of BP variability during the acute phase may relate to bed rest and acute therapy. Our patients might have had uncontrolled BP like most patients in the stroke prevention trial, or the young patients getting older might instead have been using more antihypertensive medication later on, after the 3 months. The patients in the stroke prevention trial having controlled BP most of the time were younger, had lower body mass index

Figure 2. Cumulative distribution of the Kolmogorov–Smirnov test on patients with and without recurrent stroke and admission systolic (A; P<0.001) and diastolic (B; P<0.01) blood pressure deciles. DBP indicates diastolic blood pressure; and SBP, systolic blood pressure.
Conclusions

This study brings new clinically useful information about the impact on outcome of admission BP levels in young adults having acute, first-ever ischemic stroke. In the young ischemic stroke patients, high acute-phase BP levels were independently associated with a high risk of recurrent strokes. There was a cutoff level of BP >160/100 mm Hg at admission, leading to significantly more recurrent strokes than with lower levels.

Sources of Funding

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Disclosures

None.

References


Table 2. Multivariable Cox Regression Analyses on the Association of Blood Pressure Parameters (per 10 mm Hg) and Recurrent Ischemic Stroke

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP admission</td>
<td>1.11 (1.04–1.18)</td>
<td>0.001</td>
</tr>
<tr>
<td>DBP admission</td>
<td>1.16 (1.04–1.29)</td>
<td>0.005</td>
</tr>
<tr>
<td>PP admission</td>
<td>1.11 (1.01–1.21)</td>
<td>0.017</td>
</tr>
<tr>
<td>MAP admission</td>
<td>1.01 (1.00–1.02)</td>
<td>0.001</td>
</tr>
<tr>
<td>ΔSBP</td>
<td>0.99 (0.98–1.00)</td>
<td>0.043</td>
</tr>
<tr>
<td>ΔDBP</td>
<td>0.99 (0.98–1.00)</td>
<td>0.212</td>
</tr>
<tr>
<td>ΔPP</td>
<td>0.99 (0.98–1.00)</td>
<td>0.157</td>
</tr>
<tr>
<td>ΔMAP</td>
<td>0.99 (0.98–1.00)</td>
<td>0.077</td>
</tr>
</tbody>
</table>

Each analysis was adjusted for age, sex, previous transient ischemic attack, type 1 and 2 diabetes mellitus, obesity, hyperlipidemia, and current smoking. The association between each BP variable and outcome after correction for baseline factors were tested separately. Δ indicates the admission BP−24-h BP; BP, blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; and SBP, systolic blood pressure.


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**SUPPLEMENTAL MATERIAL.**

**Supplemental Table I.** Baseline characteristics in four age percentiles.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Age Groups, year range (n)</th>
<th></th>
<th></th>
<th></th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15-37 (257)</td>
<td>38-44 (284)</td>
<td>45-47 (248)</td>
<td>48-49 (215)</td>
<td></td>
</tr>
<tr>
<td>Gender, male</td>
<td>133 (52)</td>
<td>175 (62)</td>
<td>172 (69)</td>
<td>147 (68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NIHSS</td>
<td>3 (2-7)</td>
<td>3 (1-6)</td>
<td>3 (2-8)</td>
<td>3 (2-9)</td>
<td>0.096</td>
</tr>
<tr>
<td>BP, admission</td>
<td>130 (120-146)</td>
<td>140 (123-158)</td>
<td>151 (135-170)</td>
<td>150 (130-170)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>80 (70-90)</td>
<td>86 (76-97)</td>
<td>90 (80-101)</td>
<td>89 (80-100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>53 (20)</td>
<td>56 (22)</td>
<td>61 (24)</td>
<td>63 (27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PP</td>
<td>98 (20)</td>
<td>106 (23)</td>
<td>112 (24)</td>
<td>112 (23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP</td>
<td>123 (116-135)</td>
<td>134 (120-150)</td>
<td>140 (124-160)</td>
<td>140 (126-160)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BP, 24 hours</td>
<td>75 (70-90)</td>
<td>80 (75-96)</td>
<td>86 (80-100)</td>
<td>89 (80-100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>50 (19)</td>
<td>53 (17)</td>
<td>57 (21)</td>
<td>59 (24)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>93 (17)</td>
<td>100 (23)</td>
<td>104 (20)</td>
<td>106 (20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PP</td>
<td>6 (5-19)</td>
<td>5 (4-20)</td>
<td>13 (2-23)</td>
<td>6 (6-23)</td>
<td>0.475</td>
</tr>
<tr>
<td>MAP</td>
<td>6 (3-10)</td>
<td>5 (5-15)</td>
<td>6 (3.7-17)</td>
<td>2 (2-13)</td>
<td>0.110</td>
</tr>
<tr>
<td>ΔSBP</td>
<td>3 (6-13)</td>
<td>1 (7-12)</td>
<td>4 (6-16)</td>
<td>3 (8.5-16)</td>
<td>0.068</td>
</tr>
<tr>
<td>ΔDBP</td>
<td>4.6 (2.3-12)</td>
<td>4.2 (3.3-16)</td>
<td>7.3 (1.6-17)</td>
<td>5.3 (3-16)</td>
<td>0.228</td>
</tr>
</tbody>
</table>

NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, Pulse pressure; MAP, mean arterial pressure. Data are shown as mean (SD), median±IQR or n (%).
**Acute-Phase Blood Pressure Levels Correlate With a High Risk of Recurrent Strokes in Young-Onset Ischemic Stroke**

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**Background and Objective:** Acute-phase blood pressure levels correlate with a high risk of recurrent strokes in young-onset ischemic stroke. The study aimed to evaluate the association between acute-phase blood pressure levels and recurrent strokes, as well as the risk factors associated with these events.

**Methods:** A retrospective analysis was conducted on patients under the age of 50 who experienced a first ischemic stroke between 1994 and 2007. Blood pressure measurements were taken at presentation and 24 hours later. The association between acute-phase blood pressure levels and recurrent strokes was assessed using Cox regression analysis, adjusting for demographic factors, presence of risk factors, and previous stroke history.

**Results:** Among 1004 patients, those with acute-phase blood pressures above 160 mmHg for systolic and 90 mmHg for diastolic pressure were at significantly higher risk for recurrent strokes (hazard ratio, 3.3; 95% confidence interval, 2.05–4.55; P < 0.001) compared to those with lower blood pressures. The risk was higher in patients with higher acute-phase blood pressure levels and lower in those with lower levels. The risk was also higher in patients with higher acute-phase blood pressure levels and lower in those with lower levels.

**Conclusion:** Acute-phase blood pressure levels are associated with a higher risk of recurrent strokes in young-onset ischemic stroke, and these findings highlight the importance of blood pressure control in the acute phase of stroke.

**Keywords:** blood pressure; hypertension; prognosis; stroke; young stroke
统计分析

血压参数根据人口特征在不同年龄和性别的亚组中进行统计分析。中位数和四分位数间距用来描述非正态分布参数。卡方检验比较分类变量。t检验和Mann-Whitney U检验分别用来比较连续正态分布和非正态分布或非连续变量。对每例患者入院时和24 h的血压差值进行Wilcoxon秩和检验。

通过Cox回归生存曲线评估降压或未降压治疗患者SBP和DBP的临界值。应用多变量Cox回归分析确定独立的血压参数与预后相关性。对每个血压参数，分别用多变量分析校正年龄、性别、既往短暂性脑缺血发作、1型和2型糖尿病、冠状动脉疾病、肥胖和吸烟等因素，并基于上述的单变量意义进行选择（P<0.10）。Kolmogorov-Smirnov检验的累积分布用于分析患者有或无卒中复发与入院时的SBP和DBP分布密度的关系。

所有统计分析采用IBM SPSS 19.0软件进行，P值<0.05为差异有显著性。

结果

共有1004例符合人选标准的患者纳入本研究[44(37~47)岁]。首次完成影像学检查的中位时间为0 d(四分位距0~2 d)。多数患者为男性(63%)，且患有高血压比例明显高于女性(44% vs 31%; P<0.001)。

入院时SBP水平升高的患者占57%(n=549)。男性比例、血压水平和心血管危险因素如高血压(n=393,39%)均随年龄增长显著增加(在线补充数据表1)。卒中复发的患者入院时和24 h的血压水平更高；所有患者血压在24 h内显著下降(表1)。

1/3的患者(n=358,36%)在发病3个月内应用了降压药物：β-受体阻滞剂(57%)、血管紧张素转换酶抑制剂(39%)、利尿剂(24%)和钙离子拮抗剂(23%)。

研究中最长随访时间为18年[中位数8.91(四分位距5.66~13.2)；图1]。随访期间142例(14%;男性占65%)出现复发性卒中；其中缺血性卒中占12%(n=123)，出血性卒中占19%(n=19)，149例(15%)发生心血管事件，其中37例出现心肌梗死(3.7%;男性占89%)，共有178例(18%)死亡，其中42例(4.2%;男性占78%)因心血管事件死亡。

无论是否应用降压治疗，入院时SBP≥160 mmHg的患者出现复发性卒中明显多于SBP<160 mmHg的患者(图1)，且复发的时间更早[13.9(13.0~14.6) vs 16.2(15.8~16.6)；P=0.001]。入院时DBP≥100 mmHg的患者较DBP<100 mmHg的患者更容易复发卒中[Hazard Ratio=3.62(95%CI, 2.36~5.09)；P<0.001]。入院时收缩压和舒张压较高的患者与更高的卒中复发风险相关(图2)。

在调整了年龄、性别、既往短暂性脑缺血发作、1型和2型糖尿病、肥胖、高脂血症和吸烟等危险因素后，多变量Cox回归分析显示入院时较高的SBP、DBP、PP、平均动脉压和ΔSBP是卒中复发的独立危险因素(表2)。而ΔDBP、ΔPP、Δ平均动脉压或24 h的血压水平与卒中复发不相关，同时，未发现任何血压水平与全因死亡或心脏事件相关（数据未显示）。

讨论

超过半数的青年急性卒中患者在入院时血压升高，长期随访发现高血压是卒中复发的独立危险因素，这与以往老年卒中的相关研究结果一致6。将入院时血压160/100 mmHg作为临界值，高于临界值的表1根据卒中复发与否对入院及24 h BP参数(mmHg)进行分层

表 2 血压参数(每10 mmHg)和复发性缺血性卒中关系的多变量Cox回归分析

<table>
<thead>
<tr>
<th>预后因素</th>
<th>HR (95%CI)</th>
<th>P值</th>
</tr>
</thead>
<tbody>
<tr>
<td>入院时SBP</td>
<td>1.11(1.04~1.18)</td>
<td>0.001</td>
</tr>
<tr>
<td>入院时DBP</td>
<td>1.16(1.04~1.29)</td>
<td>0.005</td>
</tr>
<tr>
<td>入院时PP</td>
<td>1.11(1.01~1.21)</td>
<td>0.017</td>
</tr>
<tr>
<td>入院时MAP</td>
<td>1.17(1.00~1.00)</td>
<td>0.001</td>
</tr>
<tr>
<td>ΔSBP</td>
<td>0.99(0.98~1.00)</td>
<td>0.043</td>
</tr>
<tr>
<td>ΔDBP</td>
<td>0.99(0.98~1.00)</td>
<td>0.212</td>
</tr>
<tr>
<td>ΔPP</td>
<td>0.99(0.98~1.00)</td>
<td>0.157</td>
</tr>
<tr>
<td>ΔMAP</td>
<td>0.99(0.98~1.00)</td>
<td>0.077</td>
</tr>
</tbody>
</table>

注：每个分析调整了年龄、性别、既往短暂性脑缺血发作、1型和2型糖尿病、肥胖、高脂血症和吸烟等危险因素。Δ表示入院时血压减去卒中24 h的血压差值；BP：血压；DBP：舒张压；MAP：平均动脉压；PP：脉压；SBP：收缩压。

患者卒中复发明显增多。本研究中，高血压在卒中前诊断的较少且时间不长；此外，卒中后升高的血压在24 h内下降并接近正常，与卒中复发没有明显的相关性。另一方面，入院时低血压的青年卒中患者仅占4.5%，可能是因为青年患者中很少有继发于心脏衰竭，急性心肌梗死或心律失常的低血压。入院时低血压在老年卒中患者中更为常见19。

缺血性卒中后血压升高的机制尚不清楚，目前提出的有以下几种机制：如脑血管痉挛、氧化应激、交感神经的异常、血管紧张素、醛固酮系统激活、皮质醇和脑钠肽的神经内分泌系统，以及库欣反应—继发于颅内压增高的高血压19。急性卒中时，局部缺氧和酸中毒，脑血管自动调节功能受损，缺血半暗带区域血流灌注减少，此时，脑血流量则取决于系统动脉压。经颅多普勒超声已经用于脑血管自动调节功能的检测。
能障碍的研究，而应用其他方法的研究尚未发现此方面的证据。

由于评估血压改变对卒中影响的证据有限，目前对卒中急性期血压的管理目标尚不明确。与出血性卒中不同，缺血性卒中发病前血压无明显升高，发病后亦无明显变化。考虑到脑灌注压的不利影响，一般不推荐在卒中急性期进行常规降压治疗。但是，降压治疗与静脉溶栓的良好预后相关。

在一项 meta 分析中，不论基础血压如何，对年龄大于 60 岁的人群，降低血压能够降低卒中的发生率。另一项亚急性卒中预防试验的试验结果表示，仅 1/3 患者的血压在 ≥ 75% 的时间得到控制，降低了卒中复发的危险。而本研究的试验显示，卒中发生后 3 个月是否应用降压药物与卒中复发无明显相关性。这一结果可能有几种解释：首先，本研究未对卒中急性期的患者卧床和治疗与血压变异性的关系进行分析。其次，与上述卒中预防试验的多数患者不同，本研究中患者的基础血压可能未能得到有效控制；或者由于有年轻皮肤随着年龄增加在 3 个月以后应用了更多的降压药物。此外，在卒中预防试验中，血压控制较好的是年轻患者，这部分患者的血压指数在目标范围内，且有较少的发病因素。因此，青年患者尤其是伴有肥胖、糖尿病、高血脂症、吸烟者，改变不良的生活方式同样重要，以预防卒中复发。

本研究的局限性在于这是一项回顾性的研究，因此未在研究前设计血压监测的方案，亦缺少卒中发生的血压数据。此外，研究入组对象仅为白种人，研究结果不能直接推广到其他不同血压特征的种族中。

本研究的优势为样本量大，可以对降压治疗的影响进行分层分析。此外，研究应用标准化方法对患者进行了超过 13 年的前瞻性评估。鉴于本研究卒中单元覆盖区域广，对地区绝大多数青年卒中患者进行了登记。但由于药物监控系统的应用，在 9 年（中位数）的随访中，获得了几乎全部卒中复发和死亡事件的数据，有效地减少了患者转诊和结局评价的偏差。

本研究的结果显示了卒中发生时高血压对卒中复发的重要影响，但研究中只有 30% 的患者在 3 个月内进行了降压治疗。由于血压水平与复发性血管事件的风险呈线性关系，研究者强调控制血压在长期预后中的重要性。此外，通过对重大心血管事件复发预测的研究，卒中急性期的高血压需要进行强化降压治疗。本研究队列平均年龄为 44 岁，1/7 的患者复发卒中，其中 1/5 在随后的数年死亡。

结论
急性期血压升高是青年缺血性卒中患者卒中复发的独立危险因素。入院时血压 160/100 mmHg 可作为卒中复发的警戒值，高于这一警戒值时卒中复发明显增多。这项研究为青年缺血性卒中患者血压对预后的影响提供了有意义的临床信息。