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 mm Hg compared with those with SBP <160 mm Hg 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,5,9 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
a first-ever ischemic stroke and the risk of a recurrent stroke, cardiac events, or death from any cause.

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. 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 heavily 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 Treatment criteria. Hypertension was defined according to World Health Organization criteria: SBP ≥140 mm Hg, DBP ≥90 mm Hg, or patient being on antihypertensive treatment.

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, 105–109, I11, 113, 120–128, 130–152, 160–168, and I70–I79 were screened and diagnoses verified from original patient records when possible. Dates and causes of deaths came from Statistics Finland. The reliability and quality of these registers have previously been validated.

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 cardiovascular 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 parameters. Chi-square tests were used to compare categorical variables. Student’s t and Mann–Whitney U tests allowed comparisons of normally distributed continuous and non-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 percentiles. 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 mm Hg 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

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</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (n=862)</td>
<td>Yes (n=142)</td>
</tr>
<tr>
<td>Admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>141 (125–160)</td>
<td>140 (124–160)</td>
</tr>
<tr>
<td>DBP</td>
<td>865 (78–97)</td>
<td>85 (76–92)</td>
</tr>
<tr>
<td>PP</td>
<td>58 (24)</td>
<td>57 (17)</td>
</tr>
<tr>
<td>MAP</td>
<td>107 (23)</td>
<td>105 (18)</td>
</tr>
<tr>
<td>24-hour</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>134 (120–150)</td>
<td>132 (120–150)</td>
</tr>
<tr>
<td>DBP</td>
<td>80 (72–90)</td>
<td>80 (70–90)</td>
</tr>
<tr>
<td>PP</td>
<td>53 (21)</td>
<td>53 (16)</td>
</tr>
<tr>
<td>MAP</td>
<td>100 (22)</td>
<td>99 (16)</td>
</tr>
<tr>
<td>Δ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔSBP</td>
<td>8 (4–21)</td>
<td>7 (4–20)</td>
</tr>
<tr>
<td>ΔDBP</td>
<td>5 (3–14)</td>
<td>5 (1–15)</td>
</tr>
<tr>
<td>ΔPP</td>
<td>2.5 (7–15)</td>
<td>2 (7–14)</td>
</tr>
<tr>
<td>ΔMAP</td>
<td>5.3 (3–16)</td>
<td>5 (3–15)</td>
</tr>
</tbody>
</table>

Data are shown as median=interquartile range or mean (SD). Δ indicates BP 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 \( \leq 18 \) 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 \( \geq 160 \) 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 \( \geq 100 \) 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 \( \geq 160 \) 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 autoregulation\(^26\); 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 stroke\(^23\) because it could be harmful\(^25\) 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.\(^5\) 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

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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 percentiles. DBP indicates diastolic blood pressure; and SBP, systolic blood pressure.
and cholesterol levels, and had less history of diabetes melli-
tus.6 It, thus, seems to be important in the young to emphasize 
also on the lifestyle modifications, such as obesity, diabetes 
mellitus, hyperlipidemia, and smoking in preventing recurrent 
strokes.

Our study has limitations because it was conducted in a re-

trospective manner without predefined study protocol for the 
BP measurements, and pre-event BP levels were not available. 
The cohort also represents a solely white population, and thus, 
the results may not be directly generalizable to other ethnic 
populations with a different profile of BP.

The strengths of the study include the large number of 
patients enrolled and the ability to stratify the impact of the 
antihypertensive use. The patients were prospectively 
assessed with standardized measures over a 13-year period. 
Given the wide catchment area for our stroke unit, the reg-

istry has likely captured most young stroke patients, and 
because of the surveillance system for medication, recurrent 
events and deaths have likely been near complete over the 
median of a 9-year follow-up, with limited referral or out-

come assessment bias.

The study highlights the prognostic importance of hyper-
tension at the time of the initial stroke, in terms of a rela-
tionship with recurrent events, with only 30% of patients on 
antihypertensive therapy within 3 months. Given the near 
linear association of BP levels and the risk of recurrent vas-
cular events, this study highlights an unmet need where all 
young patients with acute stroke should take BP-lowering 
medication irrespective of initial BP levels. Although the 
young have stroke risk factors differing from the elderly, 
this article reemphasizes the importance of BP control in the 
long-term, and that hypertension in the acute stroke phase 
highlights a need for intensive BP-lowering therapy because 
of its prognostic prediction in terms of major recurrent car-
diovascular events. In our cohort with a mean age of 44 
years, 1 in 7 had a recurrent stroke, and 1 in 5 died, over the 
subsequent several years.

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. A 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.

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

2. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Executive summary: heart dis-

4. Vazquez G, Suri MF, Lakshminarayan K, Meoni MZ, Ezzeddine M, Qureshi AI. Prevalence of elevated blood pressure in adult patients pre-

5. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 ran-

domised trials in the context of expectations from prospective epidemiolo-

gical studies. BMJ. 2009;338:b1665.
6. Towfighi A, Markovic D, Ovbiagile B. Consistency of blood pres-

7. Nttaios G, Lambrou D, Michel P. Blood pressure change and outcome in acute ischemic stroke: the impact of baseline values, previous hyper-

9. Leonard-Bee J, Bath PM, Phillips SJ, Sandercor PA; IST Collaborative 

Group. Blood pressure and clinical outcomes in the International Stroke 

10. Bangalore S, Messerli FH, Wun CC, Zuckerman AL, DeMicco D, Kostis 


11. Putaala J, Haapaniemi E, Kaste M, Tatlisumak T. How does number of 


Artery Dissection and Ischemic Stroke Patients (CADISP) Group. Association of vascular risk factors with cervical artery dissec-

1544. doi: 10.1161/CIRCULATIONAHA.110.000125.

MR, et al. Isolated systolic hypertension in young and middle-aged 

adults and 31-year risk for cardiovascular mortality: the Chicago Heart 

al. Estimating the magnitude of genetic factors by calculating the genetic


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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>15-37 (257)</th>
<th>38-44 (284)</th>
<th>45-47 (248)</th>
<th>48-49 (215)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male</td>
<td></td>
<td>133 (52)</td>
<td>175 (62)</td>
<td>172 (69)</td>
<td>147 (68)</td>
<td>&lt;0.001</td>
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<td>NIHSS</td>
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<td>3 (2-7)</td>
<td>3 (1-6)</td>
<td>3 (2-8)</td>
<td>3 (2-9)</td>
<td>0.096</td>
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<tr>
<td>BP, admission</td>
<td></td>
<td>SBP, mmHg</td>
<td>130 (120-146)</td>
<td>140 (123-158)</td>
<td>151 (135-170)</td>
<td>150 (130-170)</td>
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<tr>
<td></td>
<td></td>
<td>DBP, mmHg</td>
<td>80 (70-90)</td>
<td>86 (76-97)</td>
<td>90 (80-101)</td>
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<td></td>
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<td>53 (20)</td>
<td>56 (22)</td>
<td>61 (24)</td>
<td>63 (27)</td>
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<tr>
<td></td>
<td></td>
<td>MAP</td>
<td>98 (20)</td>
<td>106 (23)</td>
<td>112 (24)</td>
<td>112 (23)</td>
</tr>
<tr>
<td>BP, 24 hours</td>
<td></td>
<td>SBP, mmHg</td>
<td>123 (116-135)</td>
<td>134 (120-150)</td>
<td>140 (124-160)</td>
<td>140 (126-160)</td>
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<tr>
<td></td>
<td></td>
<td>DBP, mmHg</td>
<td>75 (70-90)</td>
<td>80 (75-96)</td>
<td>86 (80-100)</td>
<td>89 (80-100)</td>
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<tr>
<td></td>
<td></td>
<td>PP</td>
<td>50 (19)</td>
<td>53 (17)</td>
<td>57 (21)</td>
<td>59 (24)</td>
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<td>106 (20)</td>
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<tr>
<td>ΔBP</td>
<td></td>
<td>ΔSBP</td>
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<td></td>
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<td>ΔDBP</td>
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<td>2 (2-13)</td>
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<td></td>
<td></td>
<td>ΔPP</td>
<td>3 (6-13)</td>
<td>1 (7-12)</td>
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<td>4.2 (3.3-16)</td>
<td>7.3 (1.6-17)</td>
<td>5.3 (3-16)</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 (%).
青年缺血性卒中急性期血压水平与高复发风险相关

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 Putsaala, MD, PhD, MSc (Stroke Med); Daniel Gordin, MD, PhD; Lauri Tulkki, MD; Karolima Arnino, MD; Jani Pirinen, MD; Ida Surakka, MSc, PhD; Juha Sinisalo, MD, PhD; Mika Lehto, MD, PhD; Turgut Tatlisumak, MD, PhD

背景和目的：卒中急性期血压升高与不良预后相关，然而，血压水平对青年卒中中的影响尚未得到评估。

方法：选取赫尔辛基青年卒中登记研究中连续入组的 1004 例首次缺血性卒中患者，年龄 15 ~ 49 岁，评估血压与长期预后的关系。血压参数包括入院和 24 h 的收缩压、舒张压和平均动脉压。在长期随访中以复发性卒中作为主要终点事件。调整人口特征和既往存在的合并症，采用 Cox 回归模型评估与预后相关的独立血压参数。

结果：1004 例患者中（63% 男性），393 例（39%）卒中发生前即有高血压，358 例（36%）应用了降压治疗。平均随访时间为 8.9 年（四分位距 5.7~13.2），卒中复发患者（n = 142，14%）入院时的收缩压、舒张压、脉压、平均动脉压（P<0.001）和 24 h 收缩压、舒张压、平均动脉压明显高于无复发卒中患者。收缩压 ≥160 mmHg 的患者较收缩压 <160 mmHg 的患者随访期间卒中复发更多（风险比 [hazard ratio, HR] 为 3.3 [95%CI, 2.05~4.55]；P<0.001），且复发时间更早 [13.9 年 (13.0~14.6) 比 16.2 年 (15.8~16.6)；P<0.001]。在多变量分析中，入院时更高的收缩压、舒张压、脉压和平均动脉压是卒中复发的独立危险因素，而 24 h 血压水平则不是。

结论：急性期血压升高是青年缺血性卒中患者中卒中复发的独立危险因素。

关键词：血压；高血压；预后；卒中；青年卒中

材料和方法

这项回顾性研究由赫尔辛基大学医院神经内科完成，医院拥有赫尔辛基地区唯一的综合卒中中心。研究对象为 1994-2007 年间，赫尔辛基青年卒中登记研究中诊断并治疗的首次急性缺血性卒中患者 1004 例。从患者的记录和处方数据中收集汇总 3 个月应用降压药的信息，排除仅在发病急性期应用降压药治疗的患者。所有纳入研究的患者均具备入院时、24 h 血压和长期随访数据。应用全自动手臂血压仪测量患者仰卧位血压。分别于急诊室和卒中后 24 h 测量患者收缩压 (systolic blood pressuer, SBP) 和舒张压 (diastolic blood pressure, DBP)。脉压 (pulse pressure, PP) 为 SBP 减去 DBP。平均动脉压为 DBP 加 1/3PP。入院时和 24 h 血压的差异用 (Δ)SBP、DBP、PP 和平均动脉压表示。

人口统计因素包括年龄和性别。合并症包括确诊的高血压、肥胖 [定义为体质量指数 ≥ 30 kg/m²，或没有体质指数数据但严重肥胖者]，吸烟、血压异常，既往有短暂性脑缺血发作，心房颤动、1 型或 2 型糖尿病、心肌疾病 (包括充血性心力衰竭, 冠状动脉疾病, 冠状动脉疾病), 冠心病, 以及外周动脉疾病。卒中的病因分类基于医学和影像学资料，由神经科专家依据 Org10172 急性卒中治疗标准试验进行评估。根据世界卫生组织的标准将高血压定义为：SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, 或正在接受降压治疗。随访数据截止到 2011 年底，所有数据来源于医疗保健注册登记处，并由芬兰国家健康与福利研究所维护。依据国际疾病分类第 10 版的编码进行筛选和确诊确认，死亡日期和原因源于芬兰统计局，数据记录的可靠性和质量已得到验证。研究的主要终点事件为卒中复发，除了短暂性脑缺血发作之外的任何出血性或缺血性脑血管事件。次要终点为全因死亡和心脏事件，包括急性心肌梗死、不稳定型心绞痛、冠状动脉血管重建术以及因其他心脏疾病住院，如心律不齐、心肌病、充血性心力衰竭或起因于心脏的死亡。
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。对每例患者入院时和 24 h 的血压差值进行 Wilcoxon 秩和检验。

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 例符合入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 I)。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 178 例 (18%) 死亡，其中 42 例 (4.2%; 男性占 78%) 因血管疾病死亡。

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 [HR=3.2 (95%CI, 2.36~4.09); 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、高脂血症和吸烟等因素后，多变量 Cox 回归分析显示出院时较高的 SBP、DBP、舒张压和平均动脉压是卒中复发的独立危险因素 (表 2)。而 ΔDBP、ΔPP、Δ平均动脉压或在 24 h 的血压水平与卒中复发相关，同时，未发现任何血压水平与全因死亡或者心脏事件相关 (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。将入院时血压 160/100 mmHg 作为临界值，高于临界值的

<table>
<thead>
<tr>
<th>预防因素</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 MPA</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>

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、高脂血症和吸烟等因素。校正基线因素后，对每个血压变量和结局之间的关系分别进行检验。Δ 表示入院时血压减去卒中 24 h 的血压值; HR: 风险比; SBP: 收缩压; DBP: 舒张压; MPA: 平均动脉压; PP: 脉压; MAP: 平均动脉压; SBP: 收缩压。

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。将入院时血压 160/100 mmHg 作为临界值，高于临界值的
能障碍的研究20，而用其他方法的研究尚未发现此方面的证据21。

由于评估血压改变对卒中影响的证据有限19，目前对卒中急性期血压的管理目标尚不明确22,23。与出血性卒中不同，缺血性卒中发病前血压并无明显升高，发病后亦无明显变化24。考虑到脑灌注减少的不利影响25，一般不推荐在卒中急性期进行常规降压治疗26。但是，降压治疗与静脉溶栓的良好预后相关26。

在一项 meta 分析中，不论血压如何，对年龄大于 60 岁的人群，降低血压能够降低卒中的发生率5。另一项亚急性卒中预防试验的分析显示，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6。而本研究的结果显示，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相同，本研究中卒中的血压未能得到有效控制；或者由于卒中患者随着年龄增长在 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，这部分患者有较低的血压和胆固醇水平，且较少有糖尿病史6。因此，青年患者尤其是伴有肥胖、糖尿病、高脂血症、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及到其他不同血压特征的种族中。

本研究的另一种可能的解释是，由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，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，也有效地减少了患者转诊和结局评价的偏差。

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 可作为卒中复发的临界值，高于这一临界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研究提供了有意义的临床信息。

### 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 可作为卒中复发的临界值，高于这一临界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研究提供了有意义的临床信息。