Hypertension in Acute Ischemic Stroke

A Compensatory Mechanism or an Additional Damaging Factor?

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Background: In acute ischemic stroke, a transient blood pressure (BP) elevation is common, but the best management is still unknown. Therefore, we investigated retrospectively the relationship between BP after ischemic stroke and neurological outcome (evaluated by means of the National Institutes of Health Stroke Scale score at day 7).

Methods: The medical records of 92 consecutive patients with acute ischemic stroke, aged 47 to 96 years, were examined. Blood pressure was measured on admission, 4 times during the first 24 hours, 3 times daily for the first 4 days, and twice daily on day 7 (or at discharge). Antihypertensive treatment was given according to American Heart Association guidelines.

Results: The region damaged by the stroke was total anterior in 16 patients (17%), partial anterior in 30 (33%), lacunar in 34 (37%), and posterior circulation in 12 (13%). Stroke pathogenesis was cardioembolic in 28 (30%), atherothrombotic in 29 (32%), and lacunar in 34 (37%). The systolic BP range was 140 to 220 mm Hg; diastolic BP, 70 to 110 mm Hg. Initial BP was higher in the group with lacunar infarction than in the other groups (P<.05). The patients with the best outcome had the highest BP during the first 24 hours. The neurological outcome was strongly influenced by baseline stroke severity (NIH Scale score) and admission BP. Better initial neurological conditions and higher initial BP resulted in better neurological outcomes.

Conclusions: The outcome of stroke is influenced by the type of stroke and initial BP. Lacunar stroke and the highest BP on admission carry the best prognosis, whereas the reverse is true for posterior circulation infarction and low BP. We found no evidence that, within the present BP range, hypertension is harmful and that its lowering is beneficial.

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tomography of the brain (Siemens Emotion CT scan; Siemens AG, Erlangen, Germany) in each patient on admission or 48 to 72 hours from the clinical onset.

The pathogenesis of stroke was assessed using the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification, which distinguishes the following 7 subtypes of ischemic stroke: large-vessel atherothrombotic (LVA); cardioembolic (CE); small-vessel (lacunar infarct [LACI]); acute with another cause; acute with unknown cause because the workup is incomplete; acute with unknown cause despite completion of the workup; and acute with unknown cause because more than 1 likely cause exists and the single most likely cause cannot be determined.

The region damaged by ischemic stroke was identified with the Oxfordshire Community Stroke Project (OCSP) classification, which identifies the following 4 groups according to the clinical features: total anterior circulation infarct (TACI), partial anterior circulation infarct (PACI), lacunar infarct (LACI), and posterior circulation infarct (POCI).

Blood pressure was measured every 15 minutes for 1 hour in the ED, starting most often 1 to 6 hours after stroke onset (median, 3 hours); twice on admission to the inpatient clinic, after a median interval of 2 hours; every 6 hours during the first 24 hours of the hospital stay; 3 times daily for the first 4 days of hospital stay; and twice on day 7 (or at discharge). Each measurement was obtained with a mercury sphygmomanometer at least twice by the physician in charge of the patient, and the lowest value was recorded. For the analysis of the results, we considered BP in the ED, on admission to the inpatient clinic, the mean of the first 24-hour measurements, the mean of days 2 to 4 BP measurements, and the value at discharge or on day 7.

Hypertension was defined as supine BP higher than 140/90 mm Hg according to the World Health Organization–International Society of Hypertension guidelines. Antihypertensive therapy after day 7.

During the first 24 hours after stroke, at the discretion of the admitting physician and in accordance to the American Heart Association guidelines, especially in comatose patients, and takes into consideration eye opening and best verbal and motor reactions. The score decreases with severity of stroke.

At baseline and day 7, we obtained a disability index using the Rankin Modified Scale and an index of daily living activity using the Barthel Index.

The study was approved by the local institutional review board.

We used paired and unpaired t tests, bivariate and multiple linear regression analysis, analysis of variance (ANOVA), and χ² test when required. We used the Tukey correction for multiple comparisons. The results are reported as mean ± SD.

Seventy-two patients (79%) were previously hypertensive, but almost half of these (35) had never been treated for hypertension. Previous cerebrovascular events were reported in 32 patients.

The OCSP classification disclosed TACI in 17%, PACI in 33%, LACI in 37%, and POCI in 13% (Table 1). The TOAST classification showed CE genesis in 30%, LVA disease in 32%, LACI in 37%, and carotid dissection in 1% (Table 2). Age, smoking, and history of hypertension and diabetes were not different among groups according to the OCSP and TOAST classifications. During the hospital stay, all patients received antithrombotic therapy, and 26 patients (28%) were switched to oral anticoagulant therapy after day 7.

On admission to the ED, 71 patients (77%) had elevated BP. Blood pressure in relation to the OCSP and TOAST classifications is reported in Table 3 and Table 4. In general, it was higher in patients with LACI than in the other groups.

Sixty-four patients (70%) were admitted with a mild (NIH Scale score, <15), 20 (22%) with a moderate (NIH Scale score, 15-28), and 8 (9%) with a severe neurological impairment (NIH Scale score, >28). The severity of stroke, as assessed by the NIH Scale score, GCS, and Barthel and Rankin measures, is reported in Table 5 and Table 6 according to the OCSP and TOAST classifications. Analysis of the differences among groups showed a more severe neurological impairment in POCI and less severe in LACI. We found no correlation between mean BP (MBP) on admission and NIH Scale score in the whole group or in the separate stroke subtype groups (data not shown).

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During the first 24 hours after stroke, at the discretion of the admitting physician and in accordance to the American Heart Association guidelines, antihypertensive therapy after day 7.
sive therapy was started or increased in 21 patients, tapered or stopped in 29, and unchanged in 23, compared with prestroke therapy. Nineteen patients did not receive any antihypertensive drug. In those who received no antihypertensive drug, systolic and diastolic BP increased after the first evaluation in the ED and reached the highest value within the first 24 hours, mostly after 3 hours (Figure 1). After the first 24 hours from admission, BP progressively declined in all patients, and by day 7 no significant differences could be detected among treated and nontreated patients (Figure 1). At day 7, the degree of neurological damage was mild (NIH Scale score, 1-14) in 66 patients (32 with LACI, 18 with LVA stroke, and 16 with CE stroke) and moderate (NIH Scale score, 15-27) in 12 (1 with LACI, 5 with LVA stroke, and 6 with CE stroke), whereas 13 had severe damage (NIH Scale score, ≥28) or died (1 with LACI, 6 with LVA stroke, and 6 with CE stroke). One patient with carotid dissection is not included in this analysis. The neurological outcome differed according to the type and severity of stroke (P<.001).

In those discharged alive, the mean NIH Scale score decreased from 11±9 on admission to 7±8 on day 7 (P<.01). A significant improvement of mean NIH Scale score was seen in patients with PACI (from 10±5 to 7±6; P<.01), LACI (from 7±7 to 4±3; P<.01), and LVA stroke (from 14±11 to 12±11; P<.05). The total in-hospital mortality rate was 13% (7 patients with TACI and 5 with POCI), with 5 deaths (5%) during the first 7 days of the hospital stay. In those with the best outcome (NIH Scale score, 1-14), systolic and diastolic BP were higher than in the other groups during the first 24 hours after stroke onset (Figure 2).

On bivariate linear regression, the neurological outcome was significantly correlated with the initial NIH Scale score (r=0.81; P<.001), age (r=0.27; P<.05), and admission MBP (r=−0.24; P<.05). Therefore, we conducted multiple regression analysis with neurological outcome (NIH Scale score) as the dependent variable and initial NIH Scale score, age, and admission MBP as independent variables. The ANOVA was significant (F=53.56; P<.001), and the outcome was strongly, independently, and positively correlated to the baseline NIH Scale score (β=.786) and inversely correlated to admission MBP (β=−.14), but unrelated to age. That is, lower

<table>
<thead>
<tr>
<th>TOAST Classification</th>
<th>Mean ± SD Age, y</th>
<th>No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardioembolic (n = 28)</td>
<td>80.1 ± 9.4</td>
<td>5 (18)</td>
</tr>
<tr>
<td>LACI (n = 34)</td>
<td>75.2 ± 10.7</td>
<td>8 (24)</td>
</tr>
<tr>
<td>LVA (n = 29)</td>
<td>78.8 ± 9.4</td>
<td>13 (45)</td>
</tr>
</tbody>
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Abbreviations: LACI, lacunar infarct; LVA, large-vessel atherothrombotic; TOAST, Trial of Org 10172 in Acute Stroke Treatment.ª

ªOne patient with carotid dissection is not included in the analysis.

<table>
<thead>
<tr>
<th>OCSP Classification</th>
<th>Mean ± SD BP, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>TACI (n = 16)</td>
<td>160 ± 22 Systolic (ED) 79 ± 13 Diastolic (ED) 165 ± 27 Systolic (AD) 88 ± 17 Diastolic (AD)</td>
</tr>
<tr>
<td>PACI (n = 30)</td>
<td>165 ± 26 Systolic (ED) 85 ± 14 Diastolic (ED) 169 ± 28 Systolic (AD) 90 ± 13 Diastolic (AD)</td>
</tr>
<tr>
<td>LACI (n = 34)</td>
<td>170 ± 30 Systolic (ED) 90 ± 11† Diastolic (ED) 181 ± 34‡ Systolic (AD) 96 ± 14 Diastolic (AD)</td>
</tr>
<tr>
<td>POCI (n = 12)</td>
<td>148 ± 46 Systolic (ED) 84 ± 18 Diastolic (ED) 153 ± 42 Systolic (AD) 87 ± 21 Diastolic (AD)</td>
</tr>
</tbody>
</table>

Abbreviations: AD, admission to the inpatient clinic; BP, blood pressure; ED, emergency department. Other abbreviations are explained in the footnote to Table 1.

†P<.05 vs TACI.
‡P<.001 vs POCI.

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<td>Cardioembolic (n = 28)</td>
<td>157 ± 29 Systolic (ED) 84 ± 14 Diastolic (ED) 162 ± 28 Systolic (AD) 91 ± 14 Diastolic (AD)</td>
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<td>170 ± 30 Systolic (ED) 90 ± 11† Diastolic (ED) 181 ± 34‡ Systolic (AD) 96 ± 14‡ Diastolic (AD)</td>
</tr>
<tr>
<td>LVA (n = 29)</td>
<td>163 ± 33 Systolic (ED) 81 ± 15 Diastolic (ED) 167 ± 34 Systolic (AD) 86 ± 18 Diastolic (AD)</td>
</tr>
</tbody>
</table>

Abbreviations are explained in the first footnotes to Tables 2 and 3.

†P<.05 vs LVA.
‡P<.05 vs cardioembolic and LVA.
neurological impairment and higher initial BP resulted in better neurological outcomes.

The present study shows that after an acute ischemic stroke, the clinical outcome is mostly dependent on the type and severity of stroke presentation and the level of BP during the first 24 hours after the acute event. The patients with the highest BP on admission, within the range of 140 to 220 mm Hg for systolic and 70 to 110 mm Hg for diastolic BP, presented the best neurological outcomes. This applies in particular to patients with LACI, whereas patients with POCI, who presented with the lowest BP, had the poorest prognosis.

A transient BP increase after an acute ischemic stroke has already been reported in previous studies and is also evident in the present series among the patients who were never treated with antihypertensive drugs. The BP reached its plateau within the first 24 hours after stroke and waned within the first week. Hypertension has been suggested to be associated with a poor outcome, because it may favor the development of cerebral infarction, cerebral edema, or hemorrhagic transformation of the ischemic area. However, to our knowledge, none of the previous studies took into consideration the different pathogenesis and site of stroke.

In our series, the highest BP in the ED and during the first 24 hours after admission was seen in the patients with LACI. These patients had the less severe neurological damage at presentation and at day 7, most likely owing to the small size of the cerebral infarction. An LACI is a focal neurological deficit in the territory of a single penetrating artery. Its main mechanisms are a lipohyalinotic occlusion of the midportion of a penetrating artery, secondary to long-standing hypertension and/or diabetes, or to atherothrombotic occlusion at the origin of the vessel.

The patients with stroke caused by LVA and CE disease had a lower BP and a more severe neurological impairment at baseline and day 7, compared with those with LACI. Among these stroke subtypes, those with the worse neurological outcome had a lower BP during the first days of observations than those with a better outcome. Hypertension plays a major role in the long-term atherogenic process leading to LVA, vessel stenosis, and occlusion due to thrombus formation and artery-to-artery embolism. Cardiac embolism derives from the migration of a thrombus that can totally or partially occlude a vessel. In both stroke subtypes, we have no evidence that in the acute phase, lower BP results in better clinical outcomes. Rather, the reverse appears to be true.

Collectively, from the analysis of the patients with LACI and those with LVA and CE stroke, we can con-
clude that within the range of 140 to 220 mm Hg for systolic and 70 to 110 for diastolic BP, higher BP results in better clinical outcomes. This finding suggests that, in the acute phase of stroke, hypertension represents probably only a compensatory mechanism to maintain cerebral perfusion, and that its failure is associated with a poor outcome. Therefore, the neurological outcomes of patients with ischemic stroke are highly unlikely to be improved by BP reduction with antihypertensive treatment within the above-mentioned range.

As for the pathogenesis of stroke-related hypertension, various authors have hypothesized that it is induced by lesions of particular cerebral areas causing an impaired neurogenic cardiovascular control and dysautoregulation. In our study, we observed a transient BP increase in all types of stroke (PACI, TACI, LACI, POCI, cortical, and subcortical), which thereby does not support the hypothesis that a particular localization is preferentially associated with hypertension. Furthermore, POCI has been associated with increased BP secondary to baroreflex failure, but this is not confirmed in the present series, where patients with POCI presented with the lowest BP. Other mechanisms of stroke-related hypertension include mental stress, increased sympathetic drive, and reflex response to cerebral ischemia, but we did not address these.

Some authors have reported that a careful and gradual BP reduction may improve the neurological outcome, but whether this applies to all stroke subtypes is still unknown. Others have shown that a reduction (with administration of β-blockers or calcium channel blockers) of high BP and an increase (with administration of diaspirin cross-linked hemoglobin) of low BP in acute stroke worsen the neurological outcome. In all of the studies concerning the impact of antihypertensive therapy on the clinical outcome of stroke, no distinction was made among the different stroke subtypes, and this may have obscured significant differences in the role of hypertension and its treatment.

Blood pressure gradually and spontaneously fell during the hospital stay in all subgroups, and this finding casts doubts on the need to use antihypertensive drugs to lower BP in patients with acute stroke, at least in those with systolic BP within the range of 140 to 220 mm Hg and diastolic BP within the range of 70 to 110 mm Hg at onset. Rordorf et al have proposed that BP should be pharmacologically increased in patients with hypotension and changing neurological symptoms. A pharmacologically induced elevation of BP might have been useful in some patients with PACI, TACI, and POCI with low BP on admission, but no such treatment was used in our study, and no conclusion can be drawn in this matter.

Some limitations of the present study have to be addressed. First, we have considered only the short-term neurological outcome, but it has been shown that the major changes in the NIH Scale score occur during the first few days and are unlikely to worsen or improve after this time. Second, we did not monitor BP continuously, and since it has been shown that acute stroke is associated with increased BP variability, we may have missed some BP peaks and troughs. Third, the American Heart Association guidelines recommend that in case of BP values above 220/120, labetalol hydrochloride should be given. In our study, no such cases were seen, and therefore we have no data on the effect of pharmacologically induced reduction of very high BP on prognosis.

Figure 1. Systolic and diastolic blood pressure (BP) at different times during hospital stay according to the antihypertensive therapy administered by the attending physicians, who were asked to follow American Heart Association guidelines. Antihypertensive drug therapy was started or increased compared with prestroke therapy in 21 patients, tapered or stopped in 29, and not changed in 23. Nineteen patients received no treatment. Data are expressed as mean±SD. ED indicates emergency department; AD, admission in the inpatient clinic.

Figure 2. Systolic and diastolic blood pressure (BP) during the hospital stay according to the clinical outcome, as assessed by the National Institutes of Health Stroke Scale (NIH Scale) and mortality at day 7. The degree of neurological damage was mild (NIH Scale score, 1-14) in 66 patients (32 with lacunar infarct [LACI]; 18 with large-vessel atherothrombotic [LVA] stroke; and 16 with cardioembolic [CE] stroke), and moderate (NIH Scale score, 15-27) in 12 (1 with LACI; 5 with LVA stroke; and 6 with CE stroke), whereas 13 had severe neurological damage (NIH Scale score, ≥28) or died (1 with LACI; 6 with LVA stroke; and 6 with CE stroke). One patient with carotid dissection was not included in this analysis. Data are expressed as mean±SD. Asterisk indicates P<.05 vs those with an NIH Scale score of greater than or equal to 28 or dead. Remaining abbreviations are explained in the legend to Figure 1.
over, in the present study, no data are available to indicate also the lowest range of MBP correlated to the poorest outcome.

CONCLUSIONS

Our study confirms a wide physiopathological and clinical heterogeneity of acute stroke. Within the BP range examined (ie, 140-220 mm Hg for systolic and 70-110 mm Hg for diastolic BP), better BP control is highly unlikely to improve the clinical outcome. In most cases, the use of antihypertensive drugs is unnecessary, and the transient BP rise that is common in the acute phase tends to spontaneously fade away after the first 24 hours from onset.

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REFERENCES