Brief Reports

Relationship Between Baseline Blood Pressure Parameters (Including Mean Pressure, Pulse Pressure, and Variability) and Early Outcome After Stroke

Data From the Tinzaparin in Acute Ischaemic Stroke Trial (TAIST)

Chamila Geeganage, PhD; Michael Tracy, MSc; Timothy England, MRCP; Gillian Sare, MRCP; Thierry Moulin, MD; France Woimant, MD; Hanne Christensen, PhD; Peter Paul De Deyn, MD; Didier Leys, MD; Desmond O’Neill, FRCP; E. Bernd Ringelstein, MD; Philip M.W. Bath, FRCP; for TAIST Investigators

Background and Purpose—High blood pressure (BP) in acute stroke is associated independently with a poor outcome. Recent evidence suggests that other hemodynamic parameters may also be associated with outcomes following stroke.

Methods—The relationship between baseline BP, heart rate, and other hemodynamic parameters, and early outcomes were assessed using data from TAIST trial.

Results—Death or neurological deterioration at day 10 was associated, both in unadjusted and adjusted analyses, with systolic BP (adjusted OR, 1.02; 95% CI, 1.01–1.03), mean arterial pressure (OR, 1.02; 95% CI, 1.01–1.04), pulse pressure (OR, 1.02; 95% CI, 1.01–1.03), and BP variability (OR, 1.03; 95% CI, 1.01–1.05). Similar relationships were noted for deterioration alone, and recurrent stroke.

Conclusions—Early death or neurologic deterioration, deterioration, and recurrent stroke are associated independently with high systolic BP, mean arterial pressure, pulse pressure, and BP variability. These measures offer potential therapeutic targets for improving early outcome after acute ischemic stroke. (Stroke. 2011;42:491-493.)

Key Words: acute stroke ■ blood pressure ■ hemodynamics ■ outcome

High blood pressure (BP) in acute stroke is associated independently with a poor outcome.1 Recent evidence suggests that other hemodynamic parameters including pulse pressure (PP), mean arterial pressure (MAP), heart rate, rate pressure product, and BP variability may also be associated with outcomes following stroke.2,3,5 This study explores the possible relationship between BP and other important hemodynamic parameters, with early outcomes using data from TAIST trial.

Patients and Methods

Study Participants

The TAIST trial compared high-dose tinzaparin, medium-dose tinzaparin, and aspirin <48 hours after acute ischemic stroke.6

Hemodynamic Parameters

Baseline systolic BP, diastolic BP, and heart rate were obtained. Systolic BP variability was calculated as SD of systolic BP. PP was calculated as systolic BP minus diastolic BP. MAP was calculated as diastolic BP plus one third PP. PP index was calculated as PP divided by MAP. Rate pressure product was calculated as systolic BP times heart rate.

Early Outcomes at Day 10

Four clinical outcome measures were assessed: death, neurologic deterioration from the initial stroke, death or deterioration, and stroke recurrence.6 Three outcomes on the day-10 computed tomography scan were also assessed: cerebral edema, cerebral bleeding (hemorrhagic transformation, intrainfarct hematoma, additional hematoma, or intraventricular bleeding), and clinicoradiological bleeding (clinical deterioration and cerebral bleeding).

Statistical Methods

The relationships between hemodynamic parameters and early outcomes were studied using binary logistic regression with adjustment for baseline prognostic factors, time to treatment and treatment assignment. Significance was set at P<0.05, and OR and 95% CI were obtained. All analysis was performed using SPSS 16 for Mac (SPSS, Inc.).

Results

Study Participants

Analyses included 1479 patients with acute ischemic stroke. Baseline characteristics were as follows: mean age, 71 years;
54% males; mean systolic BP, 156.4 mm Hg; and diastolic BP 84.6 mm Hg. At day 10, 60 patients had died; 139 suffered neurologic deterioration; 173 died or deteriorated; 26 died after neurologic deterioration; 53 had a recurrent stroke (ischemic or unknown); 215 had cerebral edema; 448 had cerebral bleeding; and 56 had clinico-radiological bleeding.

Early Outcomes and Baseline Hemodynamics

Death or neurologic deterioration at day 10 was associated with increased systolic BP, MAP, PP, and systolic BP variability in univariate and multivariate analyses (Table, Figure). Similar relationships were observed for neurologic deterioration alone and recurrent stroke (Table). Computed tomography–based early outcome at day 10 was not associated with baseline BP parameters on multiple variable analyses. However, data from International Stroke Trial reported a possible relationship between BP and fatal cerebral edema.1 In the International Stroke Trial analysis, fatal cerebral edema was an outcome derived from other data and did not depend on clinical or imaging data.

Several caveats must be made about this study. Most importantly, the data come from a randomized controlled trial with specific inclusion and exclusion criteria leading to

### Table. Relationship Between Blood Pressure Parameters and Early Outcomes at Day 10

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Systolic Blood Pressure</th>
<th>Systolic Blood Pressure Variability</th>
<th>Diastolic Blood Pressure</th>
<th>Heart Rate</th>
<th>Mean Arterial Pressure</th>
<th>Pulse Pressure</th>
<th>Pulse Pressure Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (unadjusted)</td>
<td>1.001 (0.989–1.012)</td>
<td>1.012 (0.988–1.039)</td>
<td>1.013 (0.992–1.035)</td>
<td>1.034* (1.015–1.053)</td>
<td>1.007 (0.989–1.026)</td>
<td>0.985 (0.981–1.009)</td>
<td>0.311 (0.051–1.896)</td>
</tr>
<tr>
<td>Death (adjusted)</td>
<td>1.010 (0.995–1.025)</td>
<td>1.013 (0.986–1.041)</td>
<td>1.027 (0.999–1.055)</td>
<td>1.017 (0.993–1.043)</td>
<td>1.022 (0.998–1.047)</td>
<td>1.003 (0.986–1.021)</td>
<td>0.455 (0.047–4.393)</td>
</tr>
<tr>
<td>Deterioration (unadjusted)</td>
<td>1.011 (1.003–1.019)</td>
<td>1.025 (1.009–1.042)</td>
<td>1.007 (0.992–1.021)</td>
<td>1.013 (0.999–1.029)</td>
<td>1.013* (1.000–1.026)</td>
<td>1.014* (1.005–1.023)</td>
<td>3.309* (1.022–10.712)</td>
</tr>
<tr>
<td>Deterioration (adjusted)</td>
<td>1.019 (1.008–1.030)</td>
<td>1.031 (1.009–1.053)</td>
<td>1.010 (0.990–1.030)</td>
<td>1.014 (0.995–1.033)</td>
<td>1.021* (1.003–1.039)</td>
<td>1.023* (1.010–1.035)</td>
<td>6.671* (1.377–32.311)</td>
</tr>
<tr>
<td>Death/deterioration (unadjusted)</td>
<td>1.009* (1.002–1.016)</td>
<td>1.025* (1.009–1.041)</td>
<td>1.010 (0.997–1.023)</td>
<td>1.017* (1.004–1.030)</td>
<td>1.013* (1.001–1.024)</td>
<td>1.016* (1.002–1.018)</td>
<td>1.904 (0.651–5.567)</td>
</tr>
<tr>
<td>Death/deterioration (adjusted)</td>
<td>1.017* (1.007–1.027)</td>
<td>1.030* (1.010–1.052)</td>
<td>1.014 (0.997–1.032)</td>
<td>1.010 (0.993–1.027)</td>
<td>1.022* (1.006–1.038)</td>
<td>1.019* (1.008–1.030)</td>
<td>3.503 (0.852–14.405)</td>
</tr>
<tr>
<td>Recurrence (unadjusted)</td>
<td>1.020* (1.008–1.033)</td>
<td>1.023* (1.001–1.045)</td>
<td>1.016 (0.993–1.039)</td>
<td>1.006 (0.985–1.029)</td>
<td>1.028* (1.006–1.046)</td>
<td>1.021* (1.007–1.034)</td>
<td>6.147* (1.023–36.946)</td>
</tr>
<tr>
<td>Recurrence (adjusted)</td>
<td>1.031* (1.013–1.049)</td>
<td>1.024 (0.997–1.052)</td>
<td>1.025 (0.995–1.057)</td>
<td>1.015 (0.986–1.046)</td>
<td>1.040* (1.012–1.069)</td>
<td>1.028* (1.008–1.044)</td>
<td>7.586 (0.719–80.034)</td>
</tr>
</tbody>
</table>

*Significant result.

Discussion

The results of this study found significant positive associations between death or neurologic deterioration, neurologic deterioration alone, and recurrent stroke at day 10 with baseline systolic BP, MAP, and PP, and systolic BP variability. Similar relationships were observed for neurologic deterioration alone and recurrent stroke at day 10. Analysis of computed tomography–based early outcome showed no significant relationship with baseline BP parameters on multiple variable analyses. However, data from International Stroke Trial reported a possible relationship between BP and fatal cerebral edema.1 In the International Stroke Trial analysis, fatal cerebral edema was an outcome derived from other data and did not depend on clinical or imaging data.

Several caveats must be made about this study. Most importantly, the data come from a randomized controlled trial with specific inclusion and exclusion criteria leading to
selection bias. First, patients with BP >220/120 mm Hg were excluded from TAIST, and hence, no data are available for those with severe hypertension. Second, only patients with baseline modified Rankin Scale ≤2 were included in TAIST trial, and therefore, qualifying stroke events were not severe and disabling. As a result, the strength of relationship between hemodynamic measures and functional outcome may be an underestimate. Third, exclusion of patients with serious comorbid factors, such as myocardial infarction, may have resulted in an under-representation of patients with low BP; this will have affected the ability to identify the “U-shaped” curve relating BP and functional outcome. Fourth, TAIST allowed randomization out to 48 hours from ictus; therefore, some patients with raised BP will have been missed, since BP falls in some individuals during the first 6 hours after stroke.7 Fifth, patients who had hemorrhagic transformation on their baseline scan were excluded, which will have led to a relative under-recruitment of patients with severe stroke. Nevertheless, data in this analysis come from a large, hi-fidelity, double-blind, double-dummy trial where outcomes and computed tomography findings were reviewed by independent adjudicators blinded to treatment allocation.

In summary, this analysis provides new evidence on the relationship between BP parameters with early adverse outcomes in acute ischemic stroke. These measures offer a potential therapeutic target for improving early outcome after acute ischemic stroke.

Acknowledgments
The authors thank LEO Pharma A/S for sharing the TAIST database. The analysis and interpretation were performed independently of LEO Pharma A/S.

Sources of Funding
T.E. was supported by the Medical Research Foundation. G.S. was supported by the British Heart Foundation. P.M.W.B. is a Stroke Association Professor of Stroke Medicine. The funding sources had no involvement in this study.

Disclosures
P.M.W.B. was chief investigator for the TAIST Trial. T.M., F.W., P.D.D., D.L., D.O., E.B.R., and P.M.W.B. were members of the TAIST Trial Steering Committee.

References
Relationship Between Baseline Blood Pressure Parameters (Including Mean Pressure, Pulse Pressure, and Variability) and Early Outcome After Stroke: Data From the Tinzaparin in Acute Ischaemic Stroke Trial (TAIST)
Chamila Geeganage, Michael Tracy, Timothy England, Gillian Sare, Thierry Moulin, France Woimant, Hanne Christensen, Peter Paul De Deyn, Didier Leys, Desmond O'Neill, E. Bernd Ringelstein, Philip M.W. Bath and for TAIST Investigators

Stroke. 2011;42:491-493; originally published online December 23, 2010;
doi: 10.1161/STROKEAHA.110.596163
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/42/2/491

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/