High Blood Pressure in Acute Stroke and Subsequent Outcome
A Systematic Review

Mark Willmot, Jo Leonardi-Bee, Philip M.W. Bath

Abstract—High blood pressure (BP) is common in acute stroke and might be associated with a poor outcome, although observational studies have given varying results. In a systematic review, articles were sought that reported both admission BP and outcome (death, death or dependency, death or deterioration, stroke recurrence, and hematoma expansion) in acute stroke. Data were analyzed by the Cochrane Review Manager software and are given as odds ratios (ORs) or weighted mean differences (WMDs) with 95% confidence intervals (CIs). Altogether, 32 studies were identified involving 10 892 patients. When all data were included, death was significantly associated with an elevated mean arterial BP (MABP) OR, 1.61; 95% CI, 1.12 to 2.31) and a high diastolic BP (DBP) OR, 1.71; 95% CI, 1.33 to 2.48). Combined death or dependency was associated with high systolic BP (SBP) OR, 2.69; 95% CI, 1.13 to 6.40) and DBP (OR, 4.68; 95% CI, 1.87 to 11.70) in primary intracerebral hemorrhage (PICH). Similarly, high SBP (+11.73 mm Hg; 95% CI, 1.30 to 22.16), MABP (+9.00 mm Hg; 95% CI, 0.92 to 17.08), and DBP (+6.00 mm Hg; 95% CI, 0.19 to 11.81) were associated with death or dependency in ischemic stroke. Combined death or deterioration was associated with a high SBP (OR, 5.57; 95% CI, 1.42 to 21.86) in patients with PICH. In summary, high BP in acute ischemic stroke or PICH is associated with subsequent death, death or dependency, and death or deterioration. Moderate lowering of BP might improve outcome. Acute BP lowering needs to be tested in 1 or more large, randomized trials. (Hypertension. 2004;43:18-24.)

Key Words: stroke, thrombotic ■ stroke, hemorrhagic ■ blood pressure ■ morbidity ■ mortality

High blood pressure (BP >140/90 mm Hg, as defined by the World Health Organization) occurs in acute stroke in up to 75% of cases.1,2 Subsequently, BP settles over a period of about a week, although ~40% of patients remain hypertensive. The causes of this pathophysiologic response are multifactorial and are related to preexisting high BP, activation of the neuroendocrine systems (sympathetic nervous system, renin-angiotensin axis, and glucocorticoid system), increased cardiac output, and “white coat hypertension.”3–7

It has been suggested that high BP is associated with a poor outcome after acute stroke, although the results of observational studies have given conflicting results. Some authors have even demonstrated better outcomes in patients with high initial BP.8,9 Data from the International Stroke Trial (IST) confirmed that the risk of early death and late death or dependency was independently associated with increasing systolic BP (SBP) in 17 398 patients.10 We report here a systematic review of observational studies of BP and outcome and assess the relation between the two.

Methods

Study Identification
Published observational studies that reported baseline BP and outcome (death, death or dependency, death or deterioration) or mechanisms for poor outcome (recurrent stroke, hemorrhagic transfusion, development of cerebral edema, or hematoma expansion) in acute (<7 days) stroke were sought. Systematic searches of EMBASE and PUBMED were made by M.W. The search strategy used 10 key words: blood pressure, hypertension, outcome, prognosis, death, mortality, recovery, stroke, cerebrovascular, and acute. Additional studies were found from reference lists of identified articles and reviews.11–13 Disability or dependency was typically measured with the Barthel Index or Rankin Scale; deterioration was defined as worsening on a stroke neurologic impairment scale, eg, National Institutes of Health stroke scale, or where an ordinal scale (eg, “improved,” “unchanged,” or “worse”) was used. Publications were excluded if they were a randomized trial (these tend not to enroll consecutive patients and might therefore have a biased sample), gave insufficient data, used other outcomes, or were duplicate articles. Decisions on inclusion and exclusion of studies were made by M.W. and P.M.W.B.

Data Extraction
Two authors (M.W. and J.L.-B.) independently extracted data; discrepancies were resolved by P.M.W.B. Studies with dichotomous data were analyzed separately from those with continuous data. Within both types, the studies were subdivided by outcome measure (death, death or dependency, death or deterioration, stroke recurrence, cerebral edema, or hematoma expansion) and by BP measurement (SBP, diastolic BP (DBP), or mean arterial BP (MABP)). The articles were then arranged by stroke type (primary intracerebral hemorrhage [PICH], ischemic stroke, or mixed). Figures 1A and 1B show typical forest plots and illustrate the layout of studies.

In cases where articles quoted several BP measurements, the earliest readings were used. Outcomes after the longest follow-up
period were used when present at multiple time points. Some articles
gave outcome data for several BP strata (eg, mortality with SBP <140 mm Hg, 141 to 180 mm Hg, and >180 mm Hg).\textsuperscript{14} In such
instances, the data were dichotomized into a high-BP and a com-
bined normal/low-BP group by using a cut point nearest to
150 mm Hg because outcome might be best at this level.\textsuperscript{10} Likewise,
publications with DBP or MABP in several strata were dichotomized
as close as possible to 90 mm Hg and 110 mm Hg, respectively.
Additionally, some articles gave continuous BP data in
grouped (eg, SBP for patients with ‘improved,’ ‘unchanged,’ or ‘worse’
neurologic status). These studies were incorporated into the review
after the data were transformed into 2 groups (eg, combined
‘improved’/‘unchanged’ and ‘worse’). This was achieved by gen-
erating pseudo-random BP data (assuming a normal distribution for
BP) and then merging this before recalculating an overall combined
mean BP and SD.

Analysis
Data were analyzed with the Cochrane Collaboration Review Man-
ger (version 4.1) software. Dichotomous data are given as odds ratio
(OR) and 95% confidence interval (CI) and as weighted mean
difference (WMD) with 95% CI for continuous data. These were
calculated with a random-effects model, and statistical heterogeneity
was assessed with a $\chi^2$ test. We explored the causes of heterogeneity
by using sensitivity analyses based on type of stroke. Publication
bias was assessed with the Egger asymmetry test\textsuperscript{15} (STATA function
Metabias) on dichotomous outcome data. Significance was set at
$P<0.05$.

Results
A flow diagram illustrating the search process is given in
Figure 2. Altogether, 32 studies with a total of 10 892 patients
(median size, 184) were included (Table 1). Eleven of these
focused on PICH and 5 on ischemic stroke, and the rest
included patients with either type of stroke. Another 64
studies were excluded; 35 did not provide BP and/or outcome
data in a suitable form, 26 did not assess BP within 7 days of
onset, and 3 were duplicate publications.

BP was recorded at admission in 18 of the included
articles. The method used was given in only 9 studies; 5 used
‘clinic’ BP measurement, 3 used both ‘clinic’ BP measure-
ment and ambulatory BP monitoring, and 1 used ambulatory
BP monitoring alone. The criteria used to define high BP
varied considerably: SBP thresholds ranged from 150 to
200 mm Hg,\textsuperscript{16–18} MABP levels of 140 to 145 mm Hg,\textsuperscript{16,19} and

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
\textbf{Comparison: 01 Death} & \textbf{Outcome: 03 Diastolic BP} & & &
\hline
\textbf{Study} & \textbf{High BP} & \textbf{Normal/low BP} & \textbf{OR (95%CI Random)} & \textbf{OR (95%CI Random)}
\hline
01 Intracerebral haemorrhage & & & &
\hline
Tennant 1949 & 14/44 & 8/31 & 1.34(0.46,3.74) &
\hline
Dandapani 1995 & 15/37 & 12/90 & 2.16(0.66,5.43) &
\hline
Subtotal(95%CI) & 29/81 & 29/91 & 1.74(0.66,3.14) &
\hline
Test for heterogeneity $\chi^2$=0.46 df=4 p=0.58 & & & &
\hline
Test for overall effect $z$=1.59 p<0.11 & & & &
\hline
03 Mixed strokes & & & &
\hline
Acheson 1971 & 151/425 & 16/72 & 1.93(1.07,3.48) &
\hline
Moda-Mulieri 1995 & 128/282 & 41/95 & 1.09(0.69,1.75) &
\hline
Marquardt 1989 & 93/134 & 123/237 & 2.13(1.34,2.29) &
\hline
Marshall 1989 & 67/181 & 90/167 & 2.03(1.52,2.63) &
\hline
Subtotal(95%CI) & 423/922 & 279/571 & 1.71(1.24,2.36) &
\hline
Test for heterogeneity $\chi^2$=3.01 df=3 p=0.19 & & & &
\hline
Test for overall effect $z$=3.26 p<0.001 & & & &
\hline
Total(95%CI) & 491/1063 & 293/852 & 1.71(1.33,2.18) &
\hline
Test for heterogeneity $\chi^2$=5.27 df=5 p=0.26 & & & &
\hline
Test for overall effect $z$=2.25 p<0.00002 & & & &
\hline
\end{tabular}
\caption{A, Forest plot of OR for death in "high" vs "low/normal" DBP. B, Forest
plot of WMD (mm Hg) for SBP in dead or dependent patients compared with
good outcome.}
\end{table}
DBP between 90 and 115 mm Hg. One article did not specify the criteria used for defining high BP; this study was analyzed with the publications that dichotomized according to MAPB. In addition, studies allocated subjects to the high-BP group when SBP, DBP, or both exceeded certain threshold values. These articles were also analyzed with publications that dichotomized according to MAPB.

Death was the most commonly reported outcome measure (survival status present in 7242 patients, 66.5%). There were fewer data for combined death or dependency (1290, 11.8%) and combined death or deterioration (1196, 11.0%). These outcomes were assessed with validated stroke scales in 7 articles (Rankin score, Scandinavian Neurological Stroke Scale, National Institutes of Health Scale). The other studies used either non-validated scales or qualitative assessments, such as discharge disposition. Patient follow-up varied considerably between 6 days and 6 years, although most articles chose to measure outcome at discharge from hospital. Potential mechanisms of poor outcome were reported in 4 articles. Three looked at PICH (708, 6.5%) and assessed the relation between BP and hematoma expansion; the other study investigated early recurrence in ischemic stroke (1273, 11.7%). No studies assessed cerebral edema or hemorrhagic transformation.

There was no publication bias (Egger test \( P = 0.21 \)) in articles reporting SBP and mortality data. When stroke as a

### TABLE 1. Included Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Stroke Type</th>
<th>BP Timing</th>
<th>BP Method</th>
<th>BP Data</th>
<th>Outcome Measure</th>
<th>Outcome Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acheson et al18</td>
<td>497</td>
<td>M</td>
<td>Admission</td>
<td>Not given</td>
<td>D</td>
<td>Death</td>
<td>4.6 years (mean)</td>
</tr>
<tr>
<td>Allen et al20</td>
<td>148</td>
<td>M</td>
<td>Admission, 24 hours</td>
<td>Not given</td>
<td>C</td>
<td>Death or dependency</td>
<td>2 and 6 months</td>
</tr>
<tr>
<td>Armario et al23</td>
<td>49</td>
<td>IS</td>
<td>Admission and daily</td>
<td>Not given</td>
<td>C</td>
<td>Death or dependency</td>
<td>Discharge</td>
</tr>
<tr>
<td>Bhalla et al20</td>
<td>72</td>
<td>M</td>
<td>&lt;1 day, 7 days</td>
<td>Manual, ABPM</td>
<td>C</td>
<td>Death or dependency</td>
<td>1 week</td>
</tr>
<tr>
<td>Britton et al30</td>
<td>388</td>
<td>M</td>
<td>Admission</td>
<td>Manual</td>
<td>D</td>
<td>Death; death or dependency</td>
<td>Discharge</td>
</tr>
<tr>
<td>Brott et al16</td>
<td>103</td>
<td>PICH</td>
<td>&lt;3 hours</td>
<td>Not given</td>
<td>C</td>
<td>Hematoma growth</td>
<td>&lt;4 hours</td>
</tr>
<tr>
<td>Carlberg et al14</td>
<td>916</td>
<td>M</td>
<td>Admission</td>
<td>Manual</td>
<td>D</td>
<td>Death</td>
<td>30 days</td>
</tr>
<tr>
<td>Dandapani et al18</td>
<td>87</td>
<td>PICH</td>
<td>Admission</td>
<td>Not given</td>
<td>D</td>
<td>Death; death or dependency</td>
<td>30 days</td>
</tr>
<tr>
<td>Dawson et al20</td>
<td>92</td>
<td>IS</td>
<td>&lt;3 days</td>
<td>Manual, ABPM</td>
<td>C</td>
<td>Death or dependency</td>
<td>30 days</td>
</tr>
<tr>
<td>Dunne et al22</td>
<td>40</td>
<td>Cerebellar PICH</td>
<td>Admission</td>
<td>Not given</td>
<td>D</td>
<td>Death or deterioration</td>
<td>6 days</td>
</tr>
<tr>
<td>Fogelholm et al19</td>
<td>141</td>
<td>IS (brainstem)</td>
<td>&lt;24 hours</td>
<td>Not given</td>
<td>C</td>
<td>Death</td>
<td>46.5 months (median)</td>
</tr>
<tr>
<td>Fogelholm et al20</td>
<td>282</td>
<td>PICH</td>
<td>&lt;24 hours</td>
<td>Manual</td>
<td>C</td>
<td>Death</td>
<td>28 days</td>
</tr>
<tr>
<td>Fuji et al22</td>
<td>419</td>
<td>PICH</td>
<td>&lt;24 hours</td>
<td>Not given</td>
<td>D</td>
<td>Hematoma growth</td>
<td>&lt;2 days</td>
</tr>
<tr>
<td>Fullerton et al17</td>
<td>206</td>
<td>M</td>
<td>12–48 hours</td>
<td>Not given</td>
<td>C</td>
<td>Death; death or deterioration</td>
<td>6 months</td>
</tr>
<tr>
<td>Harmse et al23</td>
<td>97</td>
<td>M</td>
<td>Admission</td>
<td>Manual</td>
<td>D</td>
<td>Death</td>
<td>Discharge</td>
</tr>
<tr>
<td>Jorgensen et al22</td>
<td>868</td>
<td>M</td>
<td>Admission</td>
<td>Not given</td>
<td>C</td>
<td>Death or deterioration</td>
<td>Day 2, weekly; at discharge</td>
</tr>
<tr>
<td>Kazui et al19</td>
<td>186</td>
<td>PICH</td>
<td>&lt;24 hours</td>
<td>Not given</td>
<td>C</td>
<td>Hematoma growth</td>
<td>&lt;5 days</td>
</tr>
<tr>
<td>Latorre et al22</td>
<td>200</td>
<td>M</td>
<td>Admission</td>
<td>Not given</td>
<td>D</td>
<td>Death</td>
<td>Discharge</td>
</tr>
<tr>
<td>Longo-Mbenza et al24</td>
<td>1032</td>
<td>M</td>
<td>Admission</td>
<td>Not given</td>
<td>C</td>
<td>Death</td>
<td>Discharge</td>
</tr>
<tr>
<td>Marquardt et al23</td>
<td>371</td>
<td>M</td>
<td>Admission, day 1, day 7</td>
<td>Not given</td>
<td>D</td>
<td>Death</td>
<td>5 years</td>
</tr>
<tr>
<td>Marshall et al17</td>
<td>251</td>
<td>M</td>
<td>Admission</td>
<td>Not given</td>
<td>D</td>
<td>Death</td>
<td>6 years</td>
</tr>
<tr>
<td>Mbabu-Mukendi et al21</td>
<td>388</td>
<td>M</td>
<td>Admission</td>
<td>Not given</td>
<td>C</td>
<td>Death</td>
<td>Discharge</td>
</tr>
<tr>
<td>Parayiotou et al23</td>
<td>55</td>
<td>M</td>
<td>&lt;24 hours</td>
<td>ABPM</td>
<td>C</td>
<td>Death</td>
<td>2 years</td>
</tr>
<tr>
<td>Portenoy et al22</td>
<td>112</td>
<td>PICH</td>
<td>Admission</td>
<td>Not given</td>
<td>D</td>
<td>Death or dependency</td>
<td>At last recorded follow-up</td>
</tr>
<tr>
<td>Qureshi et al19</td>
<td>182</td>
<td>PICH</td>
<td>Admission</td>
<td>Manual</td>
<td>D</td>
<td>Death</td>
<td>Discharge</td>
</tr>
<tr>
<td>Rankin et al22</td>
<td>247</td>
<td>M</td>
<td>&lt;7 days</td>
<td>Not given</td>
<td>D</td>
<td>Death</td>
<td>Discharge</td>
</tr>
<tr>
<td>Robinson et al20</td>
<td>136</td>
<td>M</td>
<td>&lt;24 hours</td>
<td>Manual, ABPM</td>
<td>C</td>
<td>Death or dependency; death or deterioration</td>
<td>30 days</td>
</tr>
<tr>
<td>Sacco et al20</td>
<td>1273</td>
<td>IS</td>
<td>&lt;7 days</td>
<td>Not given</td>
<td>D</td>
<td>Recurrent stroke</td>
<td>30 days</td>
</tr>
<tr>
<td>Tennent et al21</td>
<td>107</td>
<td>PICH</td>
<td>Admission</td>
<td>Not given</td>
<td>D</td>
<td>Death</td>
<td>Discharge</td>
</tr>
<tr>
<td>Terayama et al27</td>
<td>1701</td>
<td>PICH</td>
<td>&lt;24 hours</td>
<td>Not given</td>
<td>D</td>
<td>Death</td>
<td>Discharge</td>
</tr>
<tr>
<td>Toni et al21</td>
<td>152</td>
<td>IS</td>
<td>&lt;5 hours</td>
<td>Not given</td>
<td>C</td>
<td>Death or deterioration</td>
<td>Discharge</td>
</tr>
<tr>
<td>Tuhrim et al17</td>
<td>94</td>
<td>PICH</td>
<td>Admission</td>
<td>Not given</td>
<td>D</td>
<td>Death</td>
<td>30 days</td>
</tr>
</tbody>
</table>

IS indicates ischemic stroke; M, mixed; C, continuous; D, dichotomous; and ABPM, ambulatory BP monitoring.
whole was assessed, patients with high SBP or DBP were at a 1.5- to 5.0-fold increased risk of dying or combined death or dependency/deterioration (Table 2). Similarly, high MABP was associated with increased odds for combined death and dependency. In patients with poor outcome, judged as death and death or dependency/deterioration, there was a trend for higher SBP/DBP levels of 5/3 mm Hg. Heterogeneity was present in several of these analyses (Table 2), so the data were further examined by stroke type.

Primary Intracerebral Hemorrhage
Increased odds of death and death or disability/deterioration were found in patients with high BP (Table 3). Additionally, MABP was higher in patients who died after PICH (Table 4). The odds of hematoma expansion were increased for patients with high SBP (Table 2).

Ischemic Stroke
Limited data were available for studies specifically including patients with ischemic stroke. SBP/DBP were higher by 12/6 mm Hg in patients who died or became dependent (Table 4). Similarly, ischemic stroke patients had a 2-fold increase in the risk of stroke recurrence when their DBP was elevated (Table 2).

Mixed Stroke Studies
The odds of death were doubled in patients with high DBP. SBP was higher by 6.39 mm Hg in patients who subsequently died (Table 4).

Discussion
High SBP, MABP, and DBP in the acute phase of stroke are associated with a poor outcome, assessed either as death or as combined death or disability, and possibly as combined death.

### TABLE 2. BP in Acute Stroke by Outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies/Subjects</th>
<th>Dichotomous BP</th>
<th>P</th>
<th>Heterogeneity</th>
<th>Continuous BP</th>
<th>P</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SBP</td>
<td></td>
<td></td>
<td>MABP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td>6/1211</td>
<td>1.85 (1.17, 2.93)</td>
<td>&lt;0.01*</td>
<td>0.03*</td>
<td>5/1799</td>
<td>4.81 (−0.98, 10.60)</td>
</tr>
<tr>
<td>MABP</td>
<td></td>
<td>6/1912</td>
<td>1.61 (1.12, 2.31)</td>
<td>0.01*</td>
<td>0.15</td>
<td>5/1983</td>
<td>11.40 (8.21, 14.58)</td>
</tr>
<tr>
<td>DBP</td>
<td></td>
<td>6/1655</td>
<td>1.71 (1.33, 2.18)</td>
<td>&lt;0.01*</td>
<td>0.38</td>
<td>5/1799</td>
<td>−0.05 (−2.56, 2.47)</td>
</tr>
<tr>
<td>Death/disability</td>
<td></td>
<td>6/1811</td>
<td>2.69 (1.13, 6.40)</td>
<td>0.03*</td>
<td></td>
<td>5/691</td>
<td>5.11 (−3.00, 13.22)</td>
</tr>
<tr>
<td>SBP</td>
<td></td>
<td>3/587</td>
<td>1.92 (0.83, 4.44)</td>
<td>0.13</td>
<td>0.05*</td>
<td>1/92</td>
<td>9.00 (0.92, 17.08)</td>
</tr>
<tr>
<td>MABP</td>
<td></td>
<td>1/87</td>
<td>4.68 (1.87, 11.70)</td>
<td>&lt;0.01*</td>
<td></td>
<td>5/691</td>
<td>2.55 (−1.53, 6.62)</td>
</tr>
<tr>
<td>DBP</td>
<td></td>
<td>2/91</td>
<td>1.86 (0.28, 12.50)</td>
<td>0.50</td>
<td>&lt;0.01*</td>
<td>3/1155</td>
<td>−1.04 (−7.59, 5.50)</td>
</tr>
<tr>
<td>Recurrent stroke</td>
<td></td>
<td>1/1273</td>
<td>1.52 (0.80, 2.98)</td>
<td>0.20</td>
<td></td>
<td>3/1155</td>
<td>0.59 (−3.55, 4.73)</td>
</tr>
<tr>
<td>PICH enlargement</td>
<td></td>
<td>2/600</td>
<td>1.93 (1.22, 3.06)</td>
<td>&lt;0.01*</td>
<td>0.43</td>
<td>2/284</td>
<td>7.24 (−2.63, 17.10)</td>
</tr>
<tr>
<td>SBP</td>
<td></td>
<td>1/180</td>
<td>1.14 (0.47, 2.75)</td>
<td>0.80</td>
<td></td>
<td>2/284</td>
<td>0.81 (−4.57, 6.19)</td>
</tr>
</tbody>
</table>

*P<0.05.

### TABLE 3. Outcome by Type of Stroke for Dichotomous Data

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PICH</th>
<th>Infarct</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Studies/Subjects</td>
<td>OR (95% CI)</td>
<td>P</td>
</tr>
<tr>
<td>Death</td>
<td>3/244</td>
<td>3.55 (1.80, 7.00)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>MABP</td>
<td>3/354</td>
<td>2.26 (1.40, 3.66)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>DBP</td>
<td>2/162</td>
<td>1.74 (0.88, 3.46)</td>
<td>0.11</td>
</tr>
<tr>
<td>Death/disability</td>
<td>1/87</td>
<td>2.69 (1.13, 6.40)</td>
<td>0.03*</td>
</tr>
<tr>
<td>SBP</td>
<td>2/199</td>
<td>2.90 (1.57, 5.36)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>MABP</td>
<td>1/87</td>
<td>4.68 (1.87, 11.70)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>DBP</td>
<td>1/40</td>
<td>5.57 (1.42, 21.86)</td>
<td>0.01*</td>
</tr>
</tbody>
</table>

*P<0.05.
or early deterioration. This observation was present irrespective of stroke type. The result, based on 32 studies involving 10,892 patients, is similar to that found in IST, which found that a high SBP (≥140 mm Hg) was independently related to an increased risk of early death and combined death or dependency in 17,398 patients with acute ischemic stroke. The individual studies that form the basis of this systematic review were generally either positive or neutral for the association between BP and outcome. The neutral findings in some studies probably reflect their small size and therefore, limited statistical power. Three articles found improved outcomes for high SBP and DBP; however, when analyzed with other studies, there was no evidence of a protective effect for high BP.

This review has found evidence for mechanisms that might link high BP to poor outcome. In ischemic stroke, high DBP was associated with a 2-fold increase in risk of early recurrence. SBP was an important determinant of recurrent stroke in IST, wherein an initial SBP of 200 mm Hg or more conferred a >50% higher risk of recurrence than did an SBP of 130 mm Hg. No studies investigating the relation between BP and hemorrhagic transformation or cerebral edema in ischemic stroke fulfilled our inclusion criteria. Nevertheless, evidence that was excluded from the review suggests that an acutely elevated SBP is associated with increased fatal cerebral edema. Also, several studies have observed that high BP promotes hemorrhagic transformation in animal models, although this was not found in the IST. As far as PICH is concerned, patients with high SBP were almost twice as likely to have hematoma expansion. This could support the concept that high BP in the acute phase of hemorrhagic stroke leads to a worse outcome, at least in part, by promoting continued intracerebral bleeding. However, this relation might be confounded by the timing of inclusion, because patients with severe PICH tend to present earlier and are at greater risk of rebleeding.

Although this review has demonstrated a positive association between high BP and subsequent events in acute stroke, the findings are limited by several factors. First, there were considerable differences in patient eligibility, case mix (including baseline BP), definition of high BP, measurement and timing of BP, and type and timing of outcome among the studies. This could be considered an advantage, because it means that the relations observed are more likely to be generalizable. However, it might also have led to statistical heterogeneity. To assess whether stroke type was a potential source of heterogeneity in the review, we analyzed ischemic stroke and PICH separately. The relation between outcome and BP tended to be stronger in patients with PICH (OR, 2.26 to 5.57) compared with those with ischemic stroke. Similarly, patients who had a poor outcome had a higher BP if they had PICH (MABP, 11 mm Hg) than ischemic stroke (SBP/DBP, 12/6 mm Hg, equivalent to an MABP of ~8 mm Hg). Nevertheless, these comparisons are indirect and not precise. Other explanations for heterogeneity among the studies are likely, but we were unable to explore these owing to the paucity of data.

A second limiting factor is that we were unable to judge whether the relations that we observed were independent of other factors such as age, premorbid BP status, drug therapy, stroke severity, or timing of BP measurement. A meta-analysis of the studies, based on individual patient data, would be required to investigate this further. This issue is important, because some of the relations might have been different if potential confounding factors had been accounted for. For example, the relation between BP and rebleeding in PICH is probably mostly explained by an interaction between timing of BP measurement and severity. Likewise, high premorbid BP contributes to elevated BP in acute stroke and could contribute, in part, to poor outcome through previous cerebral vascular damage. Third, the strategy of dichotomizing BP, though clinically relevant, might create artificial strata for the analysis. For example, several articles have reported a U-shaped relation between BP and outcome, with the least poor outcome at an SBP of 140 to 160 mm Hg in the IST (judged by the nadir of the U). Hence, studies including a significant proportion of patients with a BP below a cut point of 160 mm Hg might be expected to miss a relation

TABLE 4. Outcome by Type of Stroke for Continuous Data

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PICH</th>
<th>Infarct</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Studies/</td>
<td>WMD (95% CI)</td>
<td>P</td>
</tr>
<tr>
<td>Death</td>
<td>1/131</td>
<td>2.04 (–12.76, 8.68)</td>
<td>0.70</td>
</tr>
<tr>
<td>SBP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MABP</td>
<td>2/1983</td>
<td>11.40 (8.21, 14.58)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>DBP</td>
<td>1/131</td>
<td>2.22 (–8.46, 9.30)</td>
<td>0.50</td>
</tr>
<tr>
<td>Death/disability</td>
<td>2/141</td>
<td>11.73 (1.30, 22.16)</td>
<td>0.03*</td>
</tr>
<tr>
<td>SBP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MABP</td>
<td>1/92</td>
<td>9.00 (0.92, 17.08)</td>
<td>0.03*</td>
</tr>
<tr>
<td>DBP</td>
<td>2/141</td>
<td>6.00 (0.19, 11.81)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Death/deterioration</td>
<td>1/152</td>
<td>3.00 (–6.70, 12.70)</td>
<td>0.50</td>
</tr>
<tr>
<td>SBP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td>1/52</td>
<td>–0.60 (–5.20, 4.00)</td>
<td>0.80</td>
</tr>
</tbody>
</table>

*P < 0.05.
between high BP and poor outcome. Unfortunately, because only 1 article gave sufficient data on low BP in acute stroke, it was not possible to examine how it influenced outcome. Last, it is worth noting a consistent weakness in the observational studies themselves, namely, the lack of reporting on how BP was measured. All studies assessing BP should give information on equipment (manufacturer, model, technique, validation), user (how trained, assessed, and reassessed), and patient (number and site of readings, position).43

**Perspectives**

This article assesses data from all available observational studies and shows that there is a positive association between high BP and poor outcome in acute stroke. This relation might be mediated, at least in part, by early recurrence in patients with ischemic stroke and possibly, by early rebleeding in those with PICH. Although these relations suggest that high admission BP is directly causal, we cannot rule out that this relation was independent of other factors, such as stroke severity or timing of measurements. Nevertheless, because lowering a high BP prevents first and recurrent stroke, it can be hypothesized that moderate lowering of a high BP in acute stroke might similarly reduce early death and deterioration and late death and dependency. Aggressive lowering of BP will do harm through inducing cerebral hypoperfusion. Also, some animal data and limited clinical data support the alternative concept of induced hypertension as a treatment strategy.44,45 Until the results of ongoing randomized, controlled trials are available,46 the management of high BP in acute stroke will remain controversial.

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