Systolic Blood Pressure Control and Mortality After Stroke in Hypertensive Patients

Peter M. Okin, MD; Sverre E. Kjeldsen, MD; Richard B. Devereux, MD

Background and Purpose—Hypertensive patients with electrocardiographic left ventricular hypertrophy are at increased risk of all-cause and cardiovascular death. Lowering blood pressure (BP) after stroke reduces the risk of recurrent stroke, but recent data suggest that lower systolic BP (SBP) measured 5 years after stroke is associated with increased mortality. Whether lower SBP is associated with increased short-term mortality after stroke in hypertensive patients is unclear.

Methods—All-cause and cardiovascular mortality were examined in relation to average on-treatment SBP after stroke in 541 hypertensive patients with electrocardiographic left ventricular hypertrophy randomly assigned to losartan- or atenolol-based treatment who had new strokes during follow-up. Patients with on-treatment SBP<144 mm Hg (lowest tertile) and SBP>157 (highest tertile) were compared with patients with average SBP between 144 and 157.

Results—During 2.02±1.65 years mean follow-up after incident stroke, 170 patients (31.4%) died, 135 (25.0%) from cardiovascular causes. In multivariate Cox analyses, adjusting for significant univariate predictors of mortality, compared with average SBP between 144 and 157, an average SBP<144 was a significant predictor of all-cause (hazard ratio, 1.81; 95% confidence interval, 1.20–2.73) and cardiovascular mortality (hazard ratio, 1.60; 95% confidence interval, 1.02–2.54), whereas patients who had an average SBP>157 had no significant increased risk of death.

Conclusions—Lower achieved SBP (<144 mm Hg) is associated with a significantly increased risk of cardiovascular and all-cause mortality after initial stroke in hypertensive patients during short-term follow-up. Further study is required to determine ideal SBP goals after stroke.

Clinical Trial Registration—URL: http://clinicaltrials.gov/. Unique identifier: NCT00338260. (Stroke. 2015;46:2113-2118. DOI: 10.1161/STROKEAHA.115.009592.)

Key Words: blood pressure ▪ electrocardiography ▪ hypertension ▪ hypertrophy ▪ stroke

Obsessional, population-based studies demonstrate that higher blood pressure (BP) is strongly linked to increased cardiovascular risk and cardiovascular and all-cause mortality and that there is a particularly strong association between higher BP and the risk of stroke. In addition, the benefit of BP reduction for stroke reduction is well-established. Although more intensive antihypertensive therapy aimed at greater BP reduction or lower achieved BP has produced mixed results with outcomes other than stroke, with a potential increased risk of all-cause mortality, post hoc analyses of prior studies suggest that lower achieved systolic BP (SBP) and greater lowering of SBP with treatment are associated with greater reductions in stroke risk, with no apparent lower threshold of achieved SBP down to 120 mm Hg.

In contrast, the relationship between BP and outcomes after a stroke is less clear. Although BP lowering after stroke reduces the risk of recurrent stroke, findings on the effectiveness and safety of greater BP reduction or lower achieved SBP for optimal prevention of stroke recurrence are inconclusive, with some data that poststroke average SBP in the very low normal range (<120 mm Hg) may be associated with increased risk of recurrent stroke and death. However, there has been a relative paucity of data on the relationship of lower achieved SBP after stroke to mortality.

A recent analysis of long-term survivors of stroke found that, compared with a reference SBP of 131 to 141 mm Hg, low SBP (<120 mm Hg) measured 5 years after stroke was associated with an increased risk of all-cause mortality and the composite end point of recurrent stroke, myocardial infarction, or death over the ensuing 5 years. In contrast, neither patients with slightly lower SBP (121–130 mm Hg) or higher SBP (142–210 mm Hg) were at increased risk of dying or the composite end point. However, whether lower levels of SBP are associated with increased short-term mortality after stroke in hypertensive patients undergoing treatment is unclear.

Therefore, the purpose of the present post hoc analysis of data from the Losartan Intervention For Endpoint reduction (LIFE) study was to examine the relationship of average on-treatment SBP after incident stroke to subsequent all-cause and cardiovascular mortality in hypertensive patients.
with electrocardiographic left ventricular hypertrophy (LVH) and determine whether lower achieved average SBP (<144 mmHg) and higher achieved SBP (>157 mmHg) are associated with higher short-term mortality compared with an average SBP between 144 and 157 mmHg after adjusting for other predictors of mortality in this population.

Methods

Subjects
The LIFE study19,20 enrolled hypertensive patients with electrocardiographic LVH by Cornell product21 or Sokolow-Lyon voltage criteria22 on a screening electrocardiogram in a prospective, double-blind study large enough (n=9193) to demonstrate an appreciable reduction in mortality and morbidity events with use of losartan as opposed to atenolol. Eligible patients were men and women aged 55 to 80 with previously untreated or treated essential hypertension with mean BP in the range 160 to 200/95 to 115 mmHg after 1 and 2 weeks on placebo. There were 541 patients who had an incident stroke during routine LIFE study follow-up that terminated in 2001 (263 women and 278 men; mean age, 70±7 years). Strokes were characterized as atherothrombotic in 403 patients (74.5%), embolic in 84 patients (15.5%), and hemorrhagic in 54 patients (10.0%).

Treatment Regimens
Blinded treatment was begun with losartan, 50 mg, or atenolol, 50 mg, daily and matching placebo of the other agent with a target BP of 140/90 mmHg or lower. During clinic visits at frequent intervals for the first 6 months and at 6-month interval thereafter, study therapy could be uptitrated by addition of hydrochlorothiazide, 12.5 mg, followed by increase in blinded losartan or atenolol to 100 mg per day. In patients whose BP was still not controlled, additional open-label upward titration of hydrochlorothiazide and, if necessary, institution of therapy with a calcium channel blocker or additional other medications (excluding β-blockers, angiotensin-converting enzyme inhibitors, or AT₁-receptor antagonists) was added to the double-blind treatment regimen.20

Electrocardiography
Hard copy electrocardiographs were interpreted at a core laboratory by experienced readers blinded to clinical information as previously reported in detail.11,11,20 QRS duration was measured to the nearest 4 ms in all 12 leads and R-wave amplitudes in leads aVL, V5, and V6 and S-wave amplitudes in leads V1 and V3 were measured to the nearest 0.5 mm (0.05 mV). The product of QRS duration times the Cornell voltage combination (R<sub>v1</sub>+S<sub>v5</sub>) with 6 mm [0.6 mV] added in women23–25 was used to identify electrocardiographic LVH.

End Point Determination
Incident stroke and cardiovascular death, components of the LIFE trial primary composite end point of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke, were determined according to previously defined criteria.20 These end points and all-cause mortality were ascertained and then verified by an expert end point committee as previously described.19,20 Recurrent strokes were not adjudicated.

Statistical Methods
Data management and analysis were performed with SPSS version 22 software. Data are presented as mean±SD for continuous variables and proportions for categorical variables. Patients were classified into 3 groups according to average on-treatment SBP after stroke: <144 mmHg (lowest tertile); between 144 and 157 mmHg; and >157 mmHg (highest tertile). Differences in prevalence between SBP groups were compared using χ² analyses and mean values of continuous measurements were compared using 1-way ANOVA. Baseline measurements refer to those made at LIFE study baseline,19 not at the time of incident stroke.

The risk of all-cause and cardiovascular mortality in patients with average SBP<144 mmHg and average SBP>157 mmHg were compared with patients with average in-treatment SBP between 144 and 157 mmHg using Cox proportional hazards models in which SBP group was included as a standard covariate. Multivariable Cox models included other univariate predictors of mortality in this population: age, sex, history of prior stroke, heart failure, or atrial fibrillation as standard covariates and in-treatment diastolic BP, heart rate, Cornell product LVH, and calcium channel blocker use as time-varying covariates. Kaplan–Meier curves were plotted to illustrate rates of all-cause and cardiovascular mortality as functions of average in-treatment SBP group and were compared using log-rank analyses. For all tests, a 2-tailed P value < 0.05 was required for statistical significance.

Results

Patient Characteristics in Relation to Average SBP Group

Baseline clinical and demographic characteristics of patients in relationship to average in-treatment SBP group are shown in Table 1. Patients across average SBP groups differed significantly with respect to sex, race, and serum total cholesterol, but were similar with respect to other baseline characteristics.

BP and electrocardiographic LVH measurements at baseline and changes in these measurements between baseline and last in-study determination in relation to average SBP group are shown in Table 2. As might be expected based on group definitions, baseline SBP increased in a step-wise fashion across increasing on-treatment SBP group, but there were no differences in baseline diastolic BP, Cornell product, Sokolow-Lyon voltage, or heart rate. Similarly, based on group definition, reductions in systolic and diastolic pressure differed significantly across groups, with the greatest reductions among patients with the lowest average in-treatment SBP and the smallest reductions in BP in patients with the highest average SBP during follow-up. Change in heart rate also differed significantly across SBP groups, but there were no significant differences in the magnitude of regression of electrocardiographic LVH by either Cornell product or Sokolow-Lyon voltage across SBP groups.

Average In-Treatment SBP and Mortality

During a mean follow-up of 2.0±1.7 years after first stroke, 170 patients (31.4%) died, 135 (25.0%) from cardiovascular causes. The relationships of cardiovascular and all-cause mortality to average in-treatment SBP group are shown in Table 3 and Figures 1 and 2. Compared with SBP of 144 to 157, SBP<144 was associated with significantly higher all-cause mortality and SBP>157 with significantly higher cardiovascular and all-cause mortality rates (Figure 1). Comparison of Kaplan–Meier survival curves (Figure 2) confirm that SBP>157 was associated with the highest unadjusted rates of cardiovascular and all-cause mortality, SBP<144 with intermediate rates and SBP between 144 and 157 mmHg with the lowest rates of cardiovascular and all-cause mortality. In univariate Cox analyses, compared with average in-treatment SBP of 144 to 157, patients with an average SBP<144 mmHg
had an increased risk of all-cause mortality and patients with average SBP>157 an increased risk of cardiovascular and all-cause mortality. In multivariate Cox analyses, adjusting for other univariate predictors of poststroke mortality in this population (age, sex, history of prior stroke, heart failure, or atrial fibrillation entered as standard covariates and in-treatment diastolic BP, heart rate, Cornell product LVH, and calcium channel blocker use entered as time-varying covariates), an average SBP<144 was a significant predictor of cardiovascular and all-cause mortality, whereas an average SBP>157 was not associated with significantly increased adjusted risk of either all-cause or cardiovascular death compared with an average SBP of 144 to 157. Of note, including randomized treatment allocation, body mass index or use of hydrochlorothiazide during the study in the multivariable Cox models did not change these results (data not shown).

Because early deaths immediately after stroke among patients with low average SBP could possibly reflect undetected underlying disease or frailty conditions (reverse causation bias), additional multivariate analyses were performed restricted to deaths occurring >90 days after initial stroke. In this subset of the population, average in-treatment SBP<144 remained significantly associated with an increased risk of all-cause mortality after adjusting for other potential predictors of death (hazard ratio, 1.89; 95% confidence interval, 1.04–3.13; P=0.037) and average SBP>157 with no significant increased risk of death (hazard ratio, 1.42; 95% confidence interval, 0.77–2.57). Finally, the predictive value of average SBP was not significantly associated with an increased risk of cardiovascular death (hazard ratio, 1.42; 95% confidence interval, 0.99–2.02).

### Table 1. Study Baseline Demographic and Clinical Characteristics in Relation to Average In-Treatment SBP

<table>
<thead>
<tr>
<th>Variables</th>
<th>SBP&lt;144 mmHg (n=179)</th>
<th>SBP 144–157 mmHg (n=183)</th>
<th>SBP&gt;157 mmHg (n=179)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>69.9±6.8</td>
<td>69.5±6.3</td>
<td>71.1±6.5</td>
<td>0.055</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>48.0</td>
<td>39.9</td>
<td>58.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Race, % black</td>
<td>8.9</td>
<td>2.7</td>
<td>8.4</td>
<td>0.032</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>22.9</td>
<td>21.9</td>
<td>19.6</td>
<td>0.731</td>
</tr>
<tr>
<td>History of ischemic heart disease, %</td>
<td>26.8</td>
<td>23.0</td>
<td>20.1</td>
<td>0.322</td>
</tr>
<tr>
<td>History of myocardial infarction, %</td>
<td>10.1</td>
<td>9.8</td>
<td>8.4</td>
<td>0.840</td>
</tr>
<tr>
<td>History of stroke, %</td>
<td>8.4</td>
<td>11.5</td>
<td>13.4</td>
<td>0.311</td>
</tr>
<tr>
<td>History of heart failure, %</td>
<td>2.2</td>
<td>1.6</td>
<td>4.5</td>
<td>0.226</td>
</tr>
<tr>
<td>History of atrial fibrillation, %</td>
<td>8.9</td>
<td>8.7</td>
<td>12.8</td>
<td>0.348</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>21.8</td>
<td>21.3</td>
<td>20.7</td>
<td>0.967</td>
</tr>
<tr>
<td>Prior antihypertensive treatment, %</td>
<td>74.9</td>
<td>78.1</td>
<td>81.6</td>
<td>0.307</td>
</tr>
<tr>
<td>Randomized treatment, % losartan</td>
<td>45.8</td>
<td>46.4</td>
<td>36.3</td>
<td>0.094</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.3±5.2</td>
<td>27.9±4.6</td>
<td>27.5±4.2</td>
<td>0.482</td>
</tr>
<tr>
<td>Serum glucose, mmol/L</td>
<td>6.34±2.66</td>
<td>6.35±2.36</td>
<td>6.22±2.60</td>
<td>0.782</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.87±1.17</td>
<td>6.05±1.09</td>
<td>6.19±1.18</td>
<td>0.040</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.45±0.43</td>
<td>1.36±0.40</td>
<td>1.52±0.41</td>
<td>0.880</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>92.7±21.7</td>
<td>91.7±18.9</td>
<td>91.0±23.1</td>
<td>0.782</td>
</tr>
<tr>
<td>UACR, mg/mmol per L</td>
<td>12.4±5.2</td>
<td>10.7±30.5</td>
<td>11.4±25.2</td>
<td>0.482</td>
</tr>
</tbody>
</table>

HDL indicates high density lipoprotein; SBP, systolic blood pressure; and UACR, urine albumin/creatinine ratio.

### Table 2. Study Baseline and Change From Study Baseline to Last In-Study Measurement of Blood Pressure, Heart Rate, and Electrocardiographic Left Ventricular Hypertrophy in Relation to Average In-Treatment SBP

<table>
<thead>
<tr>
<th>Variables</th>
<th>SBP&lt;144 mmHg (n=179)</th>
<th>SBP 144–157 mmHg (n=183)</th>
<th>SBP&gt;157 mmHg (n=179)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline measurements</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>172±14</td>
<td>178±13</td>
<td>186±13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>97±9</td>
<td>99±9</td>
<td>97±11</td>
<td>0.249</td>
</tr>
<tr>
<td>Cornell product, mm·ms</td>
<td>2869±924</td>
<td>2945±1323</td>
<td>3113±1041</td>
<td>0.106</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage, mm</td>
<td>31.4±10.8</td>
<td>31.9±11.2</td>
<td>33.1±11.0</td>
<td>0.327</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>74.3±10.7</td>
<td>74.6±11.9</td>
<td>73.0±10.9</td>
<td>0.348</td>
</tr>
<tr>
<td>Change from baseline to last measurement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>−37.4±19.4</td>
<td>−32.7±21.6</td>
<td>−24.5±23.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>−19.7±11.1</td>
<td>−18.0±12.1</td>
<td>−13.8±12.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cornell product, mm·ms</td>
<td>−246±1027</td>
<td>−279±783</td>
<td>−238±848</td>
<td>0.901</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage, mm</td>
<td>−5.1±8.8</td>
<td>−3.6±8.0</td>
<td>−3.5±8.5</td>
<td>0.121</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>−4.8±12.2</td>
<td>−6.5±13.8</td>
<td>−1.9±14.1</td>
<td>0.004</td>
</tr>
</tbody>
</table>

DBP indicates diastolic blood pressure; and SBP, systolic blood pressure.
in-treatment SBP<144 mm Hg for all-cause mortality was similar in relevant subsets of the population, with nonsignificant interaction terms with sex (P=0.383), age stratified at 65 years (P=0.404), history of atrial fibrillation (P=0.714), and randomized treatment arm (P=0.847).

**Discussion**

This study demonstrates that, among hypertensive patients with incident strokes, compared with intermediate average SBP levels control during treatment (SBP 144–157 mm Hg), lower achieved SBP (<144 mm Hg) during antihypertensive treatment was associated with a significantly increased risk of cardiovascular and all-cause mortality in multivariable analyses. In contrast, an average SBP>157 was not associated with a significantly increased adjusted risk of either cardiovascular or all-cause mortality. These findings suggest that treating hypertensive patients with electrocardiographic LVH to lower SBP goals after a stroke to potentially reduce recurrent stroke risk may be associated with an increased risk of death.

Prior studies have demonstrated that lowering BP has a clear benefit on reducing incident stroke, and that greater decreases in SBP are associated with greater reductions in stroke risk, with no apparent lower threshold of achieved SBP down to 120 mm Hg. However, the benefit and safety of more intensive BP lowering to lower achieved BP for incident outcomes other than stroke remains uncertain, with a potential for hazard as noted by the increased mortality risk with lower achieved SBP in the overall LIFE study population and the diabetic subgroup of hypertensive patients with coronary disease participating in the International Verapamil SR-Trandolapril Study (INVEST) study.

Although treatment of hypertension in patients after a stroke also reduces the risk of recurrent stroke, findings on the effectiveness and safety of a lower achieved SBP or greater BP reduction for optimal prevention of stroke recurrence are less clear and there are only limited data on mortality. Among patients with recent lacunar stroke, randomized treatment to a SBP target of <130 versus 130 to 149 mm Hg was associated with a nonsignificant reduction for all stroke (hazard ratio, 0.81; 95% confidence interval, 0.64–1.03) and no significant change in all-cause mortality during 3.7 years mean follow-up. In a post hoc analysis of the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) trial, adjusted annual incidence of recurrent stroke varied significantly across groups defined by SBP reductions of ≥20, 10 to 19, 0 to 9, and <0 mm Hg, but this was driven primarily by a reduction in intracerebral hemorrhage, with incidence of recurrent stroke of an ischemic cause only weakly related to change in SBP. Importantly, there was no evidence of an increased risk of recurrent stroke associated with larger SBP reductions, but mortality was not examined. A post hoc observational analysis of the Prevention Regimen for Effectively Avoiding Second Strokes (PROFESS) trial examined recurrent stroke and mortality in relation to different levels of mean achieved SBP in patients with recent noncardioembolic ischemic stroke. Compared with SBP in the high normal range (130 to <140 mm Hg), mean SBP levels during follow-up in the

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**Table 3. Univariate and Multivariable Cox Regression Analyses to Assess the Relation of Outcomes to Average In-Treatment SBP**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SBP&lt;144 mm Hg</th>
<th>SBP 144–157 mm Hg</th>
<th>SBP&gt;157 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>1.47</td>
<td>1.66</td>
<td>2.27</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.93–2.33</td>
<td>1.10–2.50</td>
<td>1.47–3.50</td>
</tr>
<tr>
<td>P Value</td>
<td>0.103</td>
<td>0.015</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HR</td>
<td>1.60</td>
<td>1.81</td>
<td>1.42</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.02–2.54</td>
<td>1.20–2.73</td>
<td>0.91–2.23</td>
</tr>
<tr>
<td>P Value</td>
<td>0.041</td>
<td>0.005</td>
<td>0.123</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; CV, cardiovascular; HR, hazard ratio; and SBP, systolic blood pressure.

*Adjusted for other univariate predictors of mortality: age, sex, history of prior stroke, heart failure, or atrial fibrillation entered as standard covariates, and in-treatment diastolic blood pressure, heart rate, Cornell voltage duration product left ventricular hypertrophy and calcium channel blocker use entered as time-varying covariates.

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**Figure 1.** Cardiovascular and all-cause mortality rates (per 100 patient years) after stroke according to average on-treatment systolic blood pressure (SBP) group. *P<0.05, **P<0.001 vs systolic blood pressure 144–157 mm Hg.
very low normal (<120 mmHg), high (140 to <150 mmHg), or very high (≥150 mmHg) range were associated with an increased risk of recurrent stroke in multivariate Cox analyses. In addition, all-cause mortality rates were highest in the very low normal and very high SBP groups, but no adjusted analyses were performed. A recent analysis of 5-year survivors of stroke found that, compared with a reference SBP of 131 to 141 mmHg, low SBP (≤120 mmHg) measured 5 years after stroke was associated with an increased risk of all-cause mortality and the composite end point of recurrent stroke, myocardial infarction, or death over the ensuing 5 years, but did not independently assess recurrent stroke risk. In contrast, neither patients with slightly lower SBP (121–130 mmHg) or higher SBP (142–210 mmHg) were at increased risk of dying or the composite end point.8

This study extends these observations to a population of 541 hypertensive patients with electrocardiographic LVH who had an incident stroke during follow-up of the LIFE study. During a mean of 2 years follow-up after their stroke, patients with mean on-treatment SBP levels in the lowest tertile of this group (<144 mmHg) were at significantly higher risk of cardiovascular and all-cause mortality. These findings were independent of the possible impact of other univariate predictors of mortality in this population, including standard cardiovascular risk factors, on-treatment diastolic BP, heart rate, and Cornell product LVH, and were similar in relevant subsets of the population. Importantly, the strong association between average SBP<144 and both cardiovascular and all-cause mortality persisted when early deaths occurring ≤90 days after the incident stroke were excluded, suggesting that neither reverse causality nor underlying frailty played a role in this relationship and further that this was not because of the previously observed association of increased early mortality after stroke with immediately poststroke decreased SBP levels.

Study Limitations
Several limitations of this study warrant review. First, this is a post hoc analysis of a previously conducted randomized clinical trial that did not randomize patients to different SBP control groups. This could lead to possible sources of confounding because of differences between the SBP groups both at baseline and during the trial. Although we control for known, measured differences between groups and for the possible effects on outcomes of other univariate predictors of mortality in this population, multivariable analyses may not fully adjust for these differences and cannot adjust for other potential factors that were not measured. As a consequence, whether low achieved SBP may be a marker of existing disease as opposed to causative of increased mortality risk cannot be definitively addressed using this approach. However, neither incident myocardial infarction nor heart failure, either of which could potentially result in a lower SBP and also be associated with mortality, were significant univariate predictors of mortality in this population. Second, use of electrocardiographic LVH criteria to select patients for LIFE increased the baseline risk of the population, suggesting that caution should be used in generalizing these findings to hypertensive patients at lower risk. Finally, we were unable to assess the relationship of these SBP levels to recurrent stroke in this population.

Implications
The present findings suggest that treatment of hypertension producing an average SBP <144 mmHg may be associated with an increased risk of cardiovascular and all-cause mortality during relatively short-term follow-up in survivors of stroke. These findings support the potential increased mortality associated with lower levels of SBP during a similar 2.5 years of follow-up after stroke in the PROFESS trial and the association of lower SBP measured 5 years after stroke with subsequent mortality in the North East Melbourne Stroke Incidence Study (NEMESIS). The absence of randomized, controlled trial–based evidence for a target value of lower attained SBP during long-term follow-up post stroke has been, in part, the impetus for the recently designed European Society of Hypertension-Chinese Hypertension League Stroke in Hypertension Optimal Treatment (SHOT) trial which will compare 3 different SBP targets in hypertensive patients with a recent stroke or transient ischemic attack for prevention of recurrent stroke, cardiovascular outcomes, dementia, and death.

Disclosures
Dr Okin has received grant support from Merck & Co., Inc. and serves as a consultant to Novartis. Dr Kjeldsen has served as a consultant to Bayer, Serodis, and Takeda, and has received honoraria from Bayer, Merck Sharp & Dome, Novartis, and Takeda. Dr Devereux has received grant support, honoraria, and support for travel from Merck & Co, Inc, served on advisory boards for Novartis, Sanofi-Aventis,
References


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Stroke. 2015;46:2113-2118; originally published online June 18, 2015;
doi: 10.1161/STROKEAHA.115.009592
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
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Key Words: blood pressure ■ electrocardiography ■ hypertension ■ hypertrophy ■ stroke

배경과 목적
심전도에서 좌심실 비대를 가진 고혈압 환자에서 모든 원인 및 심혈관 사망의 위험이 증가한다. 뇌졸중 이후 혈압(blood pressure, BP)강하는 뇌졸중 재발의 위험을 줄일 수 있지만, 최근 데이터는 뇌졸중 이후 5년째에 측정한 낮은 수축기 혈압(systolic BP, SBP)이 사망률 증가와 관련이 있었다. 고혈압 환자에서 낮은 SBP가 뇌졸중 이후 단기 사망률의 증가와 관련이 있는지 여부는 명확하지 않다.
방법
Losartan 또는 atenolol을 기본 치료로 무작위 배정되어 추적기
간 중 새로운 뇌졸중이 발생한 심전도에서 좌심실 비대를 가진
541명의 고혈압 환자에서 뇌졸중 이후 평균 치료 중 SBP와 모든
원인 및 심혈관 사망을 조사하였다. 치료 중 SBP<144 mmHg
(가장 낮은 삼분위군) 및 SBP>157 (가장 높은 삼분위군)인 환자
들이 144와 157 사이의 평균 SBP를 가진 환자들과 비교되었다.

결과
초기 뇌졸중 이후 2.02±1.65년의 평균 추적기간 동안, 170명
(31.4%)이 사망하였고, 그들 중 135명(25.0%)이 심혈관 원인이었
다. 유의한 단변량 사망 예측인자를 보정한 다변량 Cox 분석에
서, 144에서 157 사이의 평균 SBP와 비교하여, 평균 SBP<144
는 모든 원인(hazard ratio [HR], 1.81; 95% confidence interval
[Ci], 1.20–2.73) 및 심혈관 사망(HR, 1.60; 95% CI, 1.02–
2.54)의 유의한 예측인자인데 반해, 평균 SBP>157인 환자에서
는 사망 위험이 유의하게 높지 않았다.

결론
낮게 도달된 SBP (<144 mmHg)는 단기 추적기간 동안 고혈압
환자에서 초기 뇌졸중 이후 심혈관 및 모든 원인의 사망률의 유
의한 위험증가와 관련이 있었다. 뇌졸중 이후 이상적인 SBP 목
표를 결정하기 위해서는 추가 연구가 필요하다.

<table>
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<th>Table 3. Univariate and Multivariable Cox Regression Analyses to Assess the Relation of Outcomes to Average In-Treatment SBP</th>
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<td><strong>Outcome</strong></td>
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<tr>
<td>Multivariable Cox models*</td>
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<td>CV mortality</td>
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<td>All-cause mortality</td>
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Ci indicates confidence interval; CV, cardiovascular; HR, hazard ratio; and SBP, systolic blood pressure.
*Adjusted for other univariate predictors of mortality: age, sex, history of prior stroke, heart failure, or atrial fibrillation entered as standard covariates, and in-treatment diastolic blood pressure, heart rate, Cornell voltage duration product left ventricular hypertrophy and calcium channel blocker use entered as time-varying covariates.