Elevated blood pressure (BP) is commonly observed during an acute ischemic stroke and is often higher in patients with a history of hypertension. After acute stroke, elevated BP usually returns to normal within a few days. Elevated BP during an acute ischemic stroke might be either advantageous by improving cerebral perfusion to the ischemic tissue or detrimental by exacerbating edema and hemorrhagic transformation of the ischemic tissue. If BP elevation during acute stroke perfuses jeopardized brain tissue around the infarcted area, it should be associated with favorable prognosis.

The association between admission BP and clinical outcomes in patients with acute stroke has been investigated; however, results have been contradictory. A number of studies have found that elevated in-hospital BP during an acute ischemic stroke was associated with worse clinical outcomes. Several studies observed a U-shaped relationship between admission BP and clinical outcomes, whereas others found no relationship at all. Most studies have used casual BP levels and a short follow-up. It is well known that casual BP may not accurately reflect true BP levels, therefore, 24-hour ambulatory BP monitoring (24H BPM) was found more appropriate for this purpose.

A recent study noted an increasing proportion of very elderly subjects among hospitalized patients with acute stroke. Awareness of the impact of BP levels during acute stroke on the short- and long-term outcome is crucial for the management of these patients. We, therefore, designed a study to evaluate the impact of admission BP levels assessed by casual BP measurements and 24H BPM on short- and long-term outcome in very elderly stroke patients.

Key Words: acute stroke • ambulatory blood pressure monitoring • elderly • mortality


Avraham Weiss, MD*; Yichayaou Beloosesky, MD*; Ron S. Kenett, PhD; Ehud Grossman, MD

Background and Purpose—The prognostic value of blood pressure (BP) levels during acute stroke has not been adequately studied. Most studies do not use continuous BP measurements, and patients are followed only for a short period. We designed a study to assess, with 24-hour BP monitoring (24H BPM), the impact of BP levels during the first day of stroke, on the short-term functional status and long-term mortality in elderly patients.

Methods—We studied 177 patients with acute stroke (89 men), mean age 84±6 years. BP was measured on admission and 24H BPM was recorded within 24 hours of admission. After 7 days, patients were assessed for functional status according to the modified Rankin Scale and were subsequently followed up for mortality ≤5 years (mean, 2.07±1.48).

Results—After 7 days, functional status improved and modified Rankin Scale decreased from 4.2 to 3.7. Follow-up analysis disclosed that 71 patients (27 men and 44 women) had died. Mortality rate was higher in women (50% versus 30%; P<0.01) and in patients with a history of congestive heart failure. Only average systolic BP, recorded by 24H BPM, predicted short-term functional status and long-term mortality. Cox proportional hazards model analysis demonstrated that age, sex, congestive heart failure, and average systolic BP >160 mm Hg, recorded by 24H BPM, were associated with increased mortality.

Conclusions—High systolic BP recorded by 24H BPM on the first day of stroke was found to be associated with unfavorable short-term functional status and long-term mortality in elderly patients. (Stroke. 2013;44:2434-2440.)
who could not continue to take antihypertensive medications, patients with atrial fibrillation, patients with inaccurate 24H BPM, patients who received thrombolysis, and those with a hypertensive crisis (>220/120 mm Hg) who received immediate intravenous antihypertensive treatment. All patients continued their prehospitalization antihypertensive treatment. The study was approved by the local ethics committee and all patients or their next of kin signed an informed consent.

**Study Design**

BP and heart rate were measured on admission. The reported values were the average of 2 measurements taken 1 minute apart. However, when the 2 systolic measurements differed by >5 mm Hg, additional measurements were taken until 2 similar values were obtained, which were then included in the analysis. 24H BPM was recorded within 24 hours (3–24 hours) of admission. The average time interval between the commencement of symptoms and initiation of 24H BPM was 12.8 hours (range, 6–28 hours).

**Data Collection**

Data were obtained from the patients’ medical records and included clinical evaluation findings performed on each subject at the time of hospital admission, standard physical examination results, and a detailed medical history. Functional status was determined on admission and 1 week after hospitalization, according to the modified Rankin Scale (mRS). The following variables were recorded: BP,

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Males</th>
<th>Females</th>
<th>P Value (M vs F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>177</td>
<td>89</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>84±6</td>
<td>83±6</td>
<td>85±6</td>
<td>0.07</td>
</tr>
<tr>
<td>BMI, w/h²</td>
<td>26.4±4.6</td>
<td>26.1±3.9</td>
<td>26.8±5.3</td>
<td>0.35</td>
</tr>
<tr>
<td>Casual admission SBP, mm Hg</td>
<td>150.7±24.2</td>
<td>147.6±21.6</td>
<td>153.9±26.3</td>
<td>0.087</td>
</tr>
<tr>
<td>Casual admission DBP, mm Hg</td>
<td>77.6±15.06</td>
<td>77.7±13.9</td>
<td>77.5±16.2</td>
<td>0.96</td>
</tr>
<tr>
<td>Casual admission HR, bpm</td>
<td>75.9±6</td>
<td>75.5±12.3</td>
<td>76.3±12.9</td>
<td>0.68</td>
</tr>
<tr>
<td>Average 24H SBP, mm Hg</td>
<td>146.1±21.3</td>
<td>144.1±21.1</td>
<td>148.1±21.5</td>
<td>0.211</td>
</tr>
<tr>
<td>Average 24H DBP, mm Hg</td>
<td>73.2±11.2</td>
<td>73.9±12.1</td>
<td>72.7±10.3</td>
<td>0.481</td>
</tr>
<tr>
<td>Average 24H HR, bpm</td>
<td>71.2±12.9</td>
<td>68.9±12.9</td>
<td>73.5±12.9</td>
<td>0.017</td>
</tr>
<tr>
<td>SBP variability (SD)</td>
<td>16.4±5.3</td>
<td>15.8±4.6</td>
<td>16.8±5.8</td>
<td>0.146</td>
</tr>
<tr>
<td>DBP variability (SD)</td>
<td>11.3±9.0</td>
<td>11.3±10.1</td>
<td>11.4±7.8</td>
<td>0.934</td>
</tr>
</tbody>
</table>

**Type of stroke**

- Hemorrhagic: 19 (10.7%) 9 (10.1%) 10 (11.4%) 0.788
- Thromboembolic: 143 (80.8%) 70 (78.7%) 73 (82.9%) 0.289
- Undetermined: 15 (8.5%) 10 (11.2%) 5 (5.7%) 0.182

**Functional status on admission**

- Average mRS: 4.2±1.09 4.01±1.07 4.4±1.08 0.016
- Mild handicap (mRS, 0–1): 3 (1.7%) 1 (1.1%) 2 (2.3%) 0.554
- Moderate handicap (mRS, 2–3): 38 (21.8%) 27 (30.3%) 11 (12.8%) 0.003
- Severe handicap (mRS, 4–5): 133 (76.4%) 60 (68.2%) 73 (84.9%) 0.008

**Associated diseases and risk factors**

- Smoking: 48 (28%) 35 (42%) 13 (15%) <0.001
- Hypertension: 126 (74.1%) 62 (73.8%) 64 (74.4%) 0.652
- Ischemic heart disease: 58 (34%) 36 (42.9%) 22 (25.3%) 0.014
- Congestive heart failure: 47 (27.5%) 24 (28.6%) 23 (26.4%) 0.901
- Arrhythmia: 31 (18%) 15 (18%) 16 (18%) 0.816
- Previous stroke: 48 (28%) 21 (31%) 27 (25%) 0.288
- Diabetes mellitus: 59 (34.5%) 33 (39.3%) 26 (29.9%) 0.286
- Chronic renal failure: 28 (16.5%) 17 (20.5%) 11 (12.6%) 0.227
- Dyslipidemia: 67 (39.4%) 34 (41%) 33 (38%) 0.923

**Medications**

- Calcium antagonists: 43 (25%) 19 (22%) 24 (28%) 0.357
- ß-Blockers: 71 (41%) 38 (45%) 33 (38%) 0.480
- Diuretics: 60 (35%) 24 (28%) 36 (41%) 0.068
- ACEI/ARB: 75 (44%) 35 (41%) 40 (46%) 0.409
- ß-Blockers: 30 (17%) 25 (29%) 5 (6%) <0.001
- Aspirin: 84 (49%) 43 (51%) 41 (47%) 0.818

24H indicates 24-hour; ARB, angiotensin receptor blocker; ACEI, angiotensin-converting enzyme inhibitor; BMI, body mass index; DBP, diastolic blood pressure, F, female; HR, heart rate, M, male; mRS, modified Rankin Scale; and SBP, systolic blood pressure.
heart rate, age, height, weight, ethnic origin, and prescribed medications. Comorbid conditions were also identified from the medical records.

A patient was identified with hypertension if antihypertensive medications had been prescribed or a BP recording >140/90 mm Hg on ≥2 repeated measurements was noted before hospitalization. Diabetes mellitus was defined as the presence of hyperglycemic agents or a recording of fasting blood glucose of ≥7.0 mmol/L on ≥2 measurements before hospitalization. Renal failure was defined as serum creatinine of >132.6 μmol/L on ≥2 measurements.

**Twenty-Four Hour BP Monitoring**

24H BPM was performed by the Oscar2 24-hour ABP (SunTech Medical Inc, Morrisville, NC). The monitor was mounted on the left arm or the paralyzed arm if patients had right hemiparesis or hemiplegia. A mercury sphygmomanometer was initially attached to the monitor through a Y connector to ensure conformity between the 2 modes of measurements. The initial measurement was considered as the patient’s manual BP. BP was measured every 20 minutes during the day and evening (from 6:00 to 22:00) and every 30 minutes at night (from 22:00 to 6:00). An acceptable 24H BPM recording for our study should have had ≥50 acceptable measurements. The average systolic BP (SBP) and diastolic BP were calculated for 24 hours and separately for day and night. SD as an index of BP variability was calculated for 24 hours and separately for day and night. Until December 1, 2011, data on mortality were available for all participants from the Ministry of Internal Affairs registry.

**Statistical Analysis**

Data were presented as mean±SD. Patients were categorized into 2 groups according to predefined average SBP during the first 24H BPM. Group 1 included patients with an average SBP ≤160 mm Hg and group 2 included patients with an average SBP >160 mm Hg. Paired t test was used to analyze the differences between admission casual BP and BP levels recorded by 24H BPM. Unpaired t test was used to determine significant differences between those with and without elevated BP (in groups 1 and 2). A proportional hazard Cox regression was used to analyze impact of variables on survival. A nonparametric Kaplan–Meier analysis was conducted and presented using survival curves accounting for right censoring of survival data postadmission. A binary logistic regression was used to identify factors affecting a reduction of mRS posthospitalization. All calculations were performed with MINITAB version 16.2.

**Results**

**Patient Characteristics**

One hundred and seventy-seven patients with acute stroke (89 men), mean age 84±6 (range, 70–99) years, participated in the study and underwent 24H BPM within the first 24 hours of hospitalization. Most patients had experienced an ischemic stroke, were severely handicapped on admission, and had hypertension, dyslipidemia, diabetes mellitus, or ischemic heart disease (Table 1). Women tended to be older and were more handicapped on admission than men and were also less likely to have a history of smoking and ischemic heart disease (Table 1). Most patients received β blockers, renin-angiotensin system blockers, and diuretics (Table 1). Women used less α blockers, but tended to use more diuretics than men.

**Admission BP Levels**

Admission casual BP before commencing 24H BPM was 151±24 (range, 113–208)/78±15 (range, 45–125) mm Hg. During the 24H BPM, 17 (9.6%) patients received no antihypertensive treatment, 16 (9%) received 1 antihypertensive drug, 33 (18.6%) received 2 antihypertensive drugs, and 111 (62.7%) patients received ≥3 antihypertensive drugs.

The average 24H BPM was 146±21/73±11 mm Hg. In 45 patients (25%) the average 24-hour SBP was >160 mm Hg. Antihypertensive treatment during the 24H BPM was similar in patients with an average 24-hour SBP ≤160 mm Hg and in those with an average SBP ≥160 mm Hg (Table 2). Patients with an average 24-hour SBP >160 mm Hg were more often

![Table 2. Patient Characteristics According to Initial Blood Pressure Levels](image-url)
women, had worse functional status on admission, and more often had diabetes mellitus (Table 2).

### Short-term Follow-up

After a week of hospitalization, SBP decreased from 174.2±10.6 to 161.2±17.7 in those with an average SBP >160 mmHg and from 136.6±14.5 to 133.1±15.6 in those with an average SBP ≤160 mmHg. The mRS decreased from 4.2±1.1 to 3.7±1.64 (P<0.01). The average mRS at admission was 4.7 among those with an average SBP >160 mmHg and 4.1 among those with an average SBP ≤160 mmHg (P>0.001). Functional status as determined by the mRS improved in 82 patients, deteriorated in 20, and remained unchanged in the rest. Average SBP as measured by 24H BPM and a history of congestive heart failure, but not casual SBP or BP variability, were inversely associated with 1 week of favorable functional outcome (Table 3).

### Long-term Mortality

During the follow-up period of 5 years (mean, 2.07±1.48), 71 patients died. Patients who died were more often women, had a higher rate of congestive heart failure and previous stroke, a higher 24-hour SBP and diastolic BP, and a higher average 24-hour heart rate than those who survived (Table 4). BP variability and casual BP were the same in those who survived and those who died (Table 4).

Average 24-hour SBP >160 mmHg, was associated with mortality (Figure). Multivariate analysis using the Cox proportional hazard regression showed that age, sex, history of congestive heart failure, and elevated initial 24-hour average SBP were associated with long-term mortality (Table 5).

### Discussion

In the present study, we showed that in very elderly patients with acute stroke, elevated admission SBP as measured by 24H BPM, but not admission casual SBP, was associated with unfavorable short-term functional status and long-term mortality. It is well known that BP levels are commonly elevated during acute stroke and fall spontaneously during subsequent days.3,4 Most studies were based on casual measurements and included only a few very old patients.3,4,19 The advantages of 24H BPM compared with casual BP values is that more measurements are yielded over time, information on BP load and variability are generated and the white coat effect and observer bias are eliminated. 24H BPM enables the usage of a smaller sample and receiving of accurate information. Several studies have used 24H BPM to assess BP during acute stroke, however, only a few very old patients were included. There was no long-term follow-up.3,20–25

In the present study, we examined very old patients with acute stroke and used both admission casual BP levels and 24H BPM. Previous studies have demonstrated contradictory results regarding the effect of admission BP levels on outcomes in patients with acute stroke.5,13,14,19–26

All studies evaluated a short-term (maximum 6 months) outcome. We did not observe any effect of admission BP levels on short- or long-term outcome, which may be related to the older age of our study group or to the fact that admission BP did not represent true BP levels. Several studies evaluated stroke features and functional outcome in very elderly patients.
but did not report admission BP levels and the effect of BP levels on outcome.27–31

Recently, Soares et al36 observed in 115 elderly patients with acute stroke, that initial SBP ≥140 mm Hg was associated with 6 months of dependency or death. However, their patients were younger than our cohort (mean age, 78.6 versus 84 years). Indeed, Kerr et al32 claimed that a stress response does not seem to be the principal cause of BP elevation during stroke. However, we recently demonstrated that casual BP measurements overestimate BP level measures with 24H BPM and that the higher the casual BP, the greater the difference between casual and 24H values.33

Thus, stress response seems to contribute to BP elevation during acute stroke. The increase in BP may actually play a protective role in acute stroke by maintaining perfusion to the ischemic penumbra.

Yong and Kaste34 found elevated BP (SBP, ≥140 or diastolic BP, ≥90 mm Hg) in 79.5% of patients in the European Cooperative Acute Stroke Study-I trial. The authors used repeated manual BP measurements during the first 24 hours poststroke, and included relatively young patients (mean age, <67.2 years).

In the present study, we used automatic BPM and defined elevated BP when the average 24-hour SBP was >160 mm Hg. This level was used because BP levels of <160 mm Hg may be considered acceptable with very old subjects.35 In the recent Hypertension in the Very Elderly Trial, patients who were ≥80 years of age were randomized to receive either active treatment or matching placebo if they had a sustained SBP of ≥160 mm Hg.35

According to this definition, only 25% had elevated BP during the first 24 hours of acute stroke. The rate of elevated BP during acute stroke in our study was lower than the rate described by others.23,36,37 The low rate of elevated BP during acute stroke may be because of the older age of our patients, and the fact that we used 24H BPM.38 It is possible that very old subjects exhibit a smaller protective increase in BP during acute stroke.

Unlike casual admission BP levels, average elevated SBP recorded by 24H BPM was associated with an unfavorable short- and long-term outcome. In the short-term (7 days), elevated BP was associated with low functional status, and in the long-term follow-up it was associated with increased all-cause mortality. It seems that 24H BPM better reflects the BP burden than admission BP observed during the first few hours. Elevated average 24H SBP levels may reflect the severity of the stroke. Indeed, patients with elevated SBP were more often women and more often on admission tended to exhibit a higher SBP and unfavorable outcomes. However, the effect of elevated SBP on short- and long-term outcomes remained significant even after adjustment for age and sex.

To the best of our knowledge, our study is the only one that has used 24H BPM in very elderly patients who were followed up for 5 years. Previous studies have followed up patients for only 90 to 180 days. In most studies, elevated admission 24H BPM was associated with poor short-term outcome. Robinson et al39 observed in a group of 136 patients with acute stroke, that only 24-hour admission and not casual SBP predicted 7-day outcomes. Similarly, Rodríguez-García et al40 demonstrated in 434 patients with ischemic stroke that an average SBP >160 mm Hg measured by 24H BPM, was associated with poor outcome. However, they evaluated only short-term outcome, and their study population was younger than the patients included in our study.

Our study has expanded the present knowledge regarding the prognostic value of elevated SBP measured by 24H BPM during acute stroke in very elderly patients and long-term mortality. We showed that elevated SBP measured by 24H BPM during the first day of acute stroke is associated with long-term mortality.

Yong et al37 found that lower mean levels of systolic or diastolic BP during the first 72 hours were independent predictors of favorable outcome at 90 days. In their study, BP was repeatedly manually measured every 2 hours within the first 20 hours and then every 4 hours between 20 and 72 hours after admission. By using this method, one cannot eliminate the white coat effect. Variability may represent to some extent patients’ stress, whereas by using 24H BPM, the stress effect is suppressed and the variability between the measurements better represents the true variability.

Several studies have reported that BP variability predicts outcome.34,37,41 We did not find an association between BP variability during the first 24 hours and short- and long-term outcome. In patients with acute stroke treated with intravenous thrombolysis, high BP variability led to a poor outcome.41

Table 5. Multivariate Analysis of Factors Associated With Mortality in a Cox Proportional Hazard Survival Model

<table>
<thead>
<tr>
<th>Variable</th>
<th>Risk Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 1.06*</td>
<td>1.1</td>
<td>1.11</td>
<td></td>
</tr>
<tr>
<td>Sex 2.15*</td>
<td>1.24</td>
<td>3.83</td>
<td></td>
</tr>
<tr>
<td>Smoking 1.72</td>
<td>0.93</td>
<td>3.13</td>
<td></td>
</tr>
<tr>
<td>History of hypertension</td>
<td>1.32</td>
<td>0.76</td>
<td>2.44</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2.47*</td>
<td>1.49</td>
<td>4.02</td>
</tr>
<tr>
<td>Average 24H SBP 1.01*</td>
<td>1.00</td>
<td>1.02</td>
<td></td>
</tr>
</tbody>
</table>

24H SBP indicates 24-hour systolic blood pressure; and CI, confidence interval.

*P<0.05.
However, the authors did not use 24H BPM, and included only patients who received thrombolysis. The difference between our results and the results of Yong et al. and Kellert et al. may be explained by the different methods of BP measurements and by the index of variability used. We used the simple index of SD, whereas others used a more complicated equation, which is less practical in daily life. It is also possible that BP variability may have a reduced effect on outcome in very elderly patients.

Our study has several limitations. First, we included very few patients with intracerebral hemorrhage, and in some of our patients (8.5%) the type of stroke was undetermined. Nevertheless, the effect of BP on outcome remained the same when we analyzed data only in patients with thromboembolic stroke. Second, data relating to drug treatment and BP control after discharge were unavailable; therefore, we were unable to comment on the effect of treatment on long-term mortality. Third, data regarding long-term functional outcome were unavailable; therefore, we were unable to analyze the effect of SBP levels on long-term functional status.

Conclusions

The present study revealed that in the very elderly an increase in 24-hour BP levels after acute stroke is associated with poor outcome. Whether BP should be reduced pharmacologically throughout the acute stroke period, warrants a randomized double-blind placebo-controlled prospective study.

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Disclosures

None.

References


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