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Association Between Low Blood Pressure and Clinical Outcomes in Patients With Acute Ischemic Stroke

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Background and Purpose—Low blood pressure is uncommon in patients with acute ischemic stroke (AIS). We assessed the association between baseline low blood pressure and outcomes in patients with AIS.

Methods—Post hoc analysis of the PASS (Preventive Antibiotics in Stroke Study). We compared patients with AIS and low (<10th percentile) baseline systolic blood pressure (SBP) to patients with normal SBP (≥10th percentile <185 mm Hg). The first SBP measured at the Emergency Department was used. Outcomes included in-hospital mortality, major complications <7 days of stroke onset, and functional outcome at 90 days (modified Rankin scale score). We used regression analysis to calculate (common) odds ratios and adjusted for predefined prognostic factors.

Results—Two thousand one hundred twenty-four out of 2538 patients had AIS. The cutoff for low SBP was 130 mm Hg (n=212; range, 70–129 mm Hg). One thousand four hundred forty patients had a normal SBP (range, 130–184 mm Hg). Low SBP was associated with an increased risk of in-hospital mortality (8.0% versus 4.2%; adjusted odds ratio [aOR], 1.58; 95% CI, 1.13–2.21) and complications (16.0% versus 6.5%; aOR, 2.56; 95% CI, 1.60–4.10). Specifically, heart failure (2.4% versus 0.1%; aOR, 17.85; 95% CI, 3.36–94.86), gastrointestinal bleeding (1.9% versus 0.1%; aOR, 26.04; 95% CI, 2.83–239.30), and sepsis (3.3% versus 0.5%; aOR, 5.53; 95% CI, 1.84–16.67) were more common in patients with low SBP. Functional outcome at 90 days did not differ (shift towards worse outcome: adjusted common odds ratio, 1.24; 95% CI, 0.95–1.61).

Conclusions—Whether it is cause or consequence, low SBP at presentation in patients with AIS was associated with an increased risk of in-hospital mortality and complications, specifically heart failure, gastrointestinal bleeding, and sepsis. Clinicians should be vigilant for potentially treatable complications.

Clinical Trial Registration—URL: https://www.controlled-trials.com. Unique identifier: ISRCTN66140176. **(*Stroke*. 2020;51:338-341. DOI: 10.1161/STROKEAHA.119.027336.)**

Key Words: blood pressure ■ hospital ■ mortality ■ risk ■ sepsis ■ stroke

Most patients with acute ischemic stroke (AIS) have elevated blood pressure (BP) at presentation, which often declines spontaneously in the following days.[1] Several studies that examined the association between BP and outcome after AIS found a U-shaped relationship, with both lower and higher BP associated with an increased risk of poor outcome.[1–3] However, most of these studies mainly focused on high BP. Recently, the ENCHANTED trial (Enhanced Control of Hypertension and Thrombolysis Stroke Study) found that intensive BP lowering resulted in a lower risk of intracranial hemorrhage, but this did not translate into a better functional outcome at 90 days.[4] The association between spontaneous low BP and outcome after AIS has not been thoroughly assessed, which was the aim of our study.

Methods

We included all patients with AIS from the PASS (Preventive Antibiotics in Stroke Study).[5] We used the first BP measured at the Emergency Department with an automatic BP monitor for all analyses. All patients or their legal representatives provided written informed consent. The study protocol was approved by the Institutional Review Board of the Academic Medical Center (Amsterdam, the Netherlands) and the research board of each participating center. Further details of the methods are provided in the online-only Data Supplement. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Outcomes of the study were in-hospital mortality, major complications within 7 days of stroke onset (defined as any thrombotic event, progressive stroke, symptomatic intracranial hemorrhage, major extracranial bleeding, sepsis, and heart failure; for definitions see the online-only Data Supplement) and functional outcome at 3 months (measured with the modified Rankin Scale score).

Statistical Analysis

After evaluation, systolic BP (SBP) showed the strongest association with functional outcome with a shift towards poor functional outcome for patients with an SBP lower and higher than 164 mm Hg: adjusted

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common odds ratio, 1.08 per 10 mm Hg decrease; 95% CI, 1.02–1.14 and adjusted common odds ratio, 1.05 per 10 mm Hg increase; 95% CI, 0.99–1.10. SBP was, therefore, used in all subsequent analyses (Figure 1 and Figures I and II in the online-only Data Supplement). We compared patients with low SBP (SBP<10th percentile) versus normal SBP values (≥10th percentile <185 mm Hg) versus high (SBP ≥185 mm Hg). The normal SBP group was used as reference group. The 10th percentile was chosen as it identifies a subgroup of patients with low SBP within the PASS study population. The 185 mm Hg was used as this is the upper threshold value for intravenous thrombolysis. An exploratory analysis of the lower second percentile was also conducted.

Intergroup comparisons were analyzed with χ^2 test, independent *T* test, or Mann-Whitney *U* test. We used multivariable ordinal and logistic regression analysis to calculate (common) odds ratios for all outcomes and adjusted for predefined prognostic factors. When no event occurred in one of the groups, we added 0.5 to all 4 cells of the 2×2 table for the unadjusted analyses.[6]

Results

Of 2538 patients included in PASS, 2124 had AIS and were included in the analyses. Two hundred and twelve patients were in the low SBP group (cutoff 130 mm Hg), 1440 (67.8%) in the normal SBP group, and 472 (22.2%) in the high SBP group (Figure III in the online-only Data Supplement). Patients in the low SBP group had higher National Institutes of Health Stroke Scale at baseline (median 6 versus 5; *P*=0.001) and more often had cardioembolic stroke (33.0% versus 24.0%; *P*=0.016), see Table I in the online-only Data Supplement.

In-hospital mortality was higher in the low SBP group (8.0% versus 4.2%; adjusted odds ratio [aOR], 1.58; 95% CI, 1.13–2.21; Table). Patients in the low SBP group also more often suffered from complications within 7 days after stroke onset (16.0% versus 6.5%; aOR, 2.56; 95% CI, 1.60–4.10). Specifically, patients with low SBP had a higher risk of heart failure (2.4% versus 0.1%; aOR, 17.85; 95% CI, 3.36–94.86), major extracranial bleeding (all gastrointestinal hemorrhages: 1.9% versus 0.1%; aOR, 26.04; 95% CI, 2.83–239.30), and sepsis (3.3% versus 0.5%; aOR, 5.53; 95% CI, 1.84–16.67). There was no difference in symptomatic intracranial hemorrhage between the groups.

After adjustment, there was a trend towards worse functional outcome at 90 days in patients with low SBP (adjusted common odds ratio, 1.24; 95% CI, 0.95–1.61; Figure 2). Outcomes of patients in the second percentile (SBP<110 mm Hg) did not differ from those in the 10th percentile, except for a higher rate of heart failure (12.2% versus 2.4%; *P*=0.008, Table II in the online-only Data Supplement). When patients in the high SBP group were compared with the normal SBP group, there were no statistically significant differences for any of our outcome measures (Table).

Discussion

We found that patients with AIS and low SBP had a higher risk of in-hospital mortality and major complications early after admission when compared with patients with normal SBP.

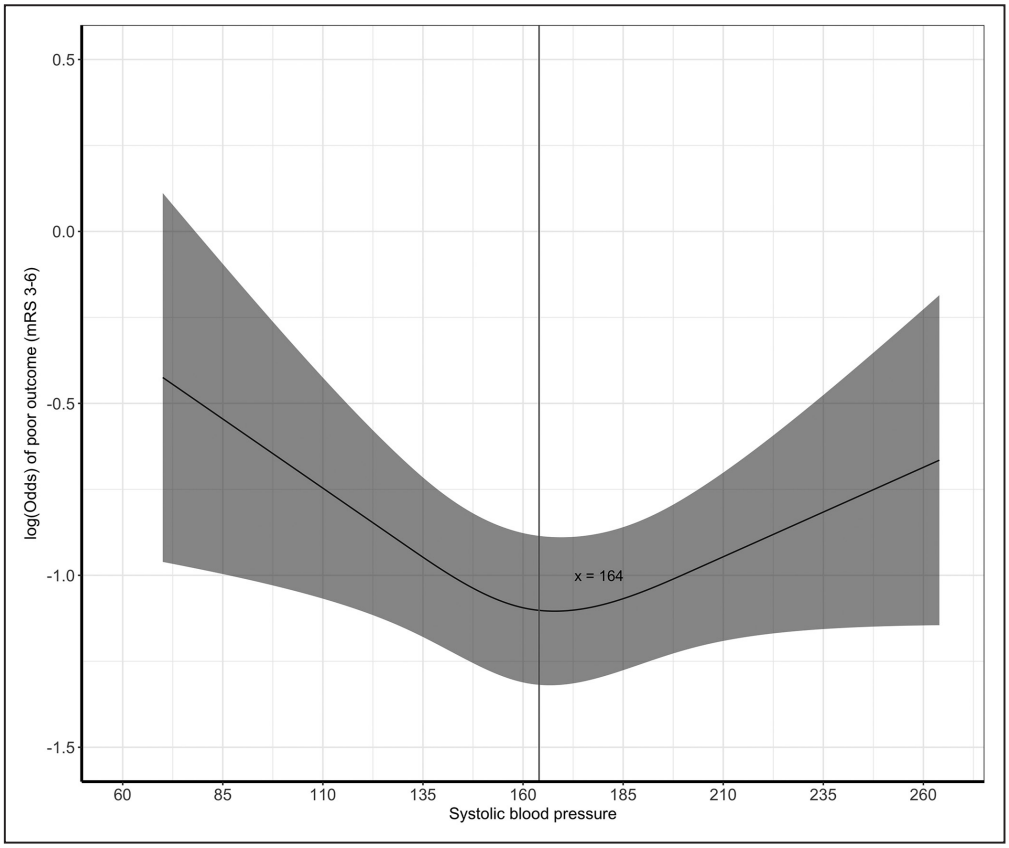

Figure 1. Association between systolic blood pressure (SBP) and log (odds) to achieve poor functional outcome at 90 days (modified Rankin Scale [mRS], 3–6) estimated with multivariable logistic regression. *x* axis shows the SBP in mm Hg, *y* axis shows the linear predictors of the regression model. The nadir is located at 164 mm Hg SBP, and there was a shift towards poor functional outcome for patients with lower and higher SBP: adjusted common odds ratio, 1.08 per 10 mm Hg decrease; 95% CI, 1.02–1.14 and adjusted common odds ratio, 1.05 per 10 mm Hg increase; 95% CI, 0.99–1.10.

Table. Outcomes in SBP Groups

		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
In-hospital mortality			
Low SBP	17/212 (8.0)	1.97 (1.13–3.44)	1.58 (1.13–2.21)*
Normal SBP	61/1440 (4.2)	1.0†	1.0†
High SBP	18/472 (3.8)	0.90 (0.52–1.53)	1.03 (0.75–1.42)*
Cause of death			
Neurological			
Low SBP	9/212 (4.3)	1.78 (0.84–3.76)	1.25 (0.55-2.84)‡
Normal SBP	35/1440 (2.4)	1.0†	1.0†
High SBP	11/472 (2.3)	0.96 (0.48–1.90)	0.80 (0.28–2.27)‡
Septic			
Low SBP	5/212 (2.4)	1.91 (0.70–5.19)	1.61 (0.57–4.54)‡
Normal SBP	18/1440 (1.3)	1.0†	1.0†
High SBP	4/472 (0.8)	0.68 (0.23–2.01)	1.74 (0.41–7.41)‡
Cardiac			
Low SBP	2/212 (0.9)	1.95 (0.40–9.45)	1.72 (0.34–8.61)‡
Normal SBP	7/1440 (0.5)	1.0†	1.0†
High SBP	3/472 (0.6)	1.31 (0.34–5.08)	0.91 (0.13–6.37)‡
Other/unknown			
Low SBP	1/212 (0.5)	6.82 (0.43–109.45)	5.23 (0.30–92.33)‡
Normal SBP	1/1440 (0.1)	1.0†	1.0†
High SBP	0	1.02 (0.04–24.97)	N/A
Any complication within 7 days			
Low SBP	34/212 (16.0)	2.77 (1.81–4.22)	2.56 (1.60–4.10)*
Normal SBP	93/1440 (6.5)	1.0†	1.0†
High SBP	29/472 (6.1)	0.95 (0.62–1.46)	1.17 (0.92–1.49)*
Thrombotic events§			
Low SBP	3/212 (1.4)	2.28 (0.62–8.50)	1.78 (0.47–6.77) ‡
Normal SBP	9/1440 (0.6)	1.0†	1.0†
High SBP	5/472 (1.3)	1.70 (0.57–5.11)	2.07 (0.67–6.37)‡
Progressive stroke			
Low SBP	14/212 (6.6)	1.63 (0.89–2.86)	1.26 (0.67–2.36)‡
Normal SBP	60/1440 (4.2)	1.0†	1.0†
High SBP	18/472 (3.8)	0.91 (0.53–1.56)	1.13 (0.65–1.98)‡
Any major bleeding			
Low SBP	5/212 (2.4)	2.29 (0.83–6.38)	2.01 (0.71–5.73)‡
Normal SBP	15/1440 (1.0)	1.0†	1.0†
High SBP	3/472 (0.6)	0.61 (0.18–2.11)	0.67 (0.19–2.35)‡
sICH			
Low SBP	1/212 (0.5)	0.48 (0.06–3.69)	0.40 (0.05–3.14)‡
Normal SBP	14/1440 (1.0)	1.0†	1.0†
High SBP	3/472 (0.6)	0.65 (0.19–2.28)	0.74 (0.21–2.62)‡
Major extracranial bleeding‖			
Low SBP	4/212 (1.9)	27.67 (3.08–248.80)	26.04 (2.83–239.30)*
Normal SBP	1/1440 (0.1)	1.0†	1.0†
High SBP	0	1.02 (0.04–24.97)	N/A
Heart failure			
Low SBP	5/212 (2.4)	17.37 (3.35–90.10)	17.85 (3.36–94.86)‡
Normal SBP	2/1440 (0.1)	1.0†	1.0†
High SBP	0	0.61 (0.03–12.71)	N/A
Sepsis			
Low SBP	7/212 (3.3)	6.99 (2.43–20.13)	5.53 (1.84–16.67)‡
Normal SBP	7/1440 (0.5)	1.0†	1.0†
High SBP	3/472 (0.6)	1.31 (0.34–5.08)	1.93 (0.47–7.96)‡

IVT indicates intravenous thrombolysis; mRS, modified Rankin Scale; N/A, not applicable; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; SBP, systolic blood pressure; and sICH, symptomatic intracranial hemorrhage.

*Adjusted for age, sex, prestroke mRS, NIHSS, stroke etiology, history of hypertension, atrial fibrillation, myocardial infarction, diabetes mellitus and prior stroke, IVT treatment.

†Reference category.

‡Adjusted for age and NIHSS.

§Eleven myocardial infarctions, 5 recurrent stroke, 1 gastrointestinal ischemia.

‖All gastrointestinal hemorrhages.

Specifically, heart failure, gastrointestinal bleeding, and sepsis occurred more often in patients with low SBP. The higher rate of early complications did not translate into a statistically significant worse functional outcome at 90 days.

The prognostic value of BP in acute stroke has been previously evaluated. Many studies found U-shaped relationships between BP and outcomes, similar to our study.[1–3] However, the underlying mechanisms for these outcomes seem to differ between high and low BP. Most studies focused on high BP and identified edema and increased risk of symptomatic intracranial hemorrhage as causes for poor functional outcome in these patients.[1,3,7] We found significantly more major extracranial bleeding, heart failure, and sepsis in patients with low SBP. The observed association between low SBP and the risk of these complications, of course, does not necessarily indicate causality. The association could also be the other way around because low SBP could be a marker of these conditions developing. Moreover, patients with low SBP more often received intravenous thrombolysis, which may have contributed to the higher frequency of extracranial bleeding.

Our study has several limitations. First, the PASS was a randomized trial, which might have led to some selection bias in our patient cohort. Still, the inclusion criteria were broad and did not include any restrictions related to BP. Second, computed tomography angiography was not routinely conducted in our cohort. It is, therefore, possible that aortic or carotid dissections causing low BP were missed. Third, serial

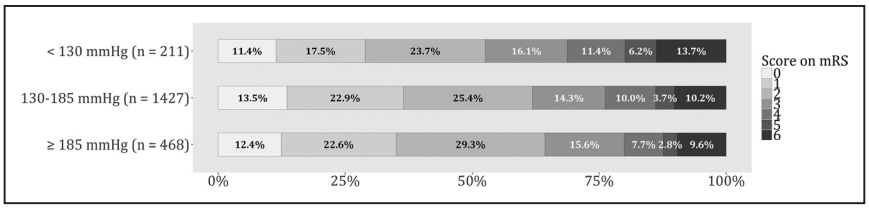

Figure 2. Functional outcome at 90 days (measured with modified Rankin Scale score), missing values n=18. Low vs normal adjusted common odds ratio, 1.24; 95% CI, 0.95–1.61. High vs normal adjusted common odds ratio, 1.09; 95% CI, 0.90–1.33. mRS indicates modified Rankin Scale.

BP measurements would have been of value to study the association between low BP and outcome in more detail. Fourth, there is no clearly defined cutoff for low BP in patients with AIS. Previously identified nadirs of the tipping point in the U-shaped association between BP and outcome also vary between 120 and 180 mm Hg.[2,3] Because of this variability, we decided to use the lowest 10th percentile as a cutoff, which is also, of course, a somewhat arbitrary cutoff.

In conclusion, low SBP at presentation was associated with an increased risk of in-hospital mortality and complications in patients with AIS. Whether low SBP is a cause or consequence of these complications is unknown, but the presence of low SBP should prompt clinicians to look for these conditions.

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Disclosures

None.

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