

Background

The benefits of improved systolic blood pressure (BP) control on stroke, coronary heart disease, and heart failure are well-established, yet its effect on overall cerebral small vessel disease (SVD), a major contributor to cognitive decline and dementia, remains uncharacterized. We examined the association between intensive BP control and longitudinal change in SVD burden in a randomized clinical trial.

Methods

We conducted a post-hoc analysis of the Systolic Blood Pressure Intervention Trial (SPRINT), a multicenter randomized clinical trial across 27 US sites. A total of 442 hypertensive individuals aged ≥ 50 years without diabetes or prior stroke completed multisequence brain MRI at baseline and at a median of 3.9 years (interquartile range, 3.6–4.1) after randomization. Participants were randomly assigned to an intensive systolic BP target of <120 mmHg ($n=245$) or a standard systolic BP target of <140 mmHg ($n=197$). The primary outcome was longitudinal change in a global SVD factor designed to capture overall SVD-related vascular brain injury by integrating multiple complementary SVD endophenotypes – including periventricular white matter hyperintensities, white matter free water, and basal ganglia perivascular spaces.

Results

Participant baseline characteristics by treatment group are presented in Table 1. Greater attained systolic BP lowering was associated with progressively larger reductions in SVD burden compared with increased BP, demonstrating a clear dose-response relationship ($\beta_{0-10\text{mmHg}} = -0.083$ [95%CI, $-0.137, -0.029$]; $\beta_{10-20\text{mmHg}} = -0.103$ [$-0.156, -0.05$]; $\beta_{>20\text{mmHg}} = -0.154$ [$-0.216, -0.092$]) – Figure 1. Consistent with this graded effect, participants randomized to the intensive BP treatment group experienced a significantly greater reduction in SVD burden compared with those in the standard BP treatment group ($\beta_{\text{intensive treatment}} = -0.066$ [95%CI, $-0.106, -0.026$], corresponding to a standardized mean difference [Cohen's d] of -0.395 [$-0.616, -0.174$] between groups) – Figure 2.

Conclusions

Among hypertensive adults, targeting a systolic BP of <120 mmHg, compared with <140 mmHg, resulted in a greater reduction in SVD burden. Notably, even modest systolic BP reductions of ≤ 10 mmHg conferred measurable brain benefits, while larger BP reductions yielded gradually greater protection against SVD progression. These findings support BP lowering as a promising strategy for preserving vascular brain health and potentially mitigating SVD-related stroke and cognitive risk.

	Standard treatment (n = 197)	Intensive treatment (n = 245)
<i>Demographic and vascular characteristics</i>		
Age, mean (SD), years	67.4 (8.3)	68.8 (8.5)
Sex, n (%)	Men	132 (67%)
	Women	65 (33%)
Race/ethnicity, n (%)	Black	57 (29%)
	Hispanic	13 (6.6%)
	White	123 (62%)
	Other	4 (2.0%)
Systolic blood pressure, mean (SD), mmHg	138.8 (15.5)	136.2 (16.8)
Diastolic blood pressure, mean (SD), mmHg	78.6 (12.3)	76.3 (10.8)
Intracranial volume, mean (SD), mm ³	1,419,003 (137,492)	1,400,771 (137,382)
<i>SVD indicators</i>		
Periventricular WMH, median (IQR), mm ³	2,437.0 (1,186.0, 4,514.0)	2,183.9 (961.3, 4,780.8)
Mean WM free water, mean (SD)	0.232 (0.038)	0.233 (0.040)
Basal ganglia PVS, mean (SD), count	94.7 (34.4)	98.6 (37.9)

Figure 1: Multiple-indicator latent change score model examining the association between attained systolic blood pressure (SBP) reduction and change in small vessel disease (SVD) burden. SVD is modeled as a latent construct, measured by periventricular white matter hyperintensities (WMH), white matter (WM) free water, and basal ganglia perivascular spaces (PVS) at baseline (t0) and follow-up (t1). The model includes direct effects of baseline age and follow-up time on each MRI indicator to account for age-related differential item functioning. Latent SVD change is defined as the difference in SVD between t1 and t0. Dummy variables representing incremental SBP reductions from baseline are modeled as predictors of latent SVD change, with SBP increase as the reference group. Arrow values represent regression coefficients (or covariances for double-headed arrows). Asterisks indicate statistically significant parameter estimates at $p < 0.05$ (*), $p < 0.01$ (**), and $p < 0.001$ (***).

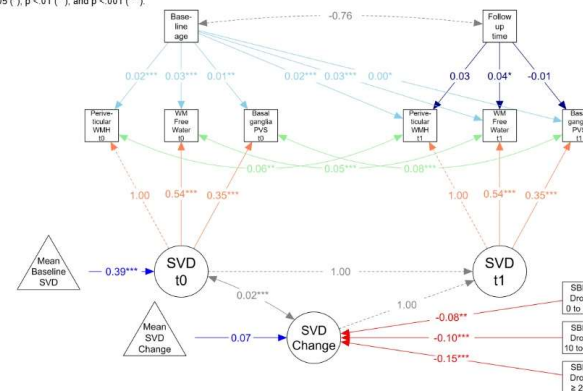


Figure 2: Multiple-indicator latent change score model examining the effect of treatment assignment on small vessel disease (SVD) burden. SVD is modeled as a latent construct, measured by periventricular white matter hyperintensities (WMH), white matter (WM) free water, and basal ganglia perivascular spaces (PVS) at baseline (t0) and follow-up (t1). The model includes direct effects of baseline age and follow-up time on each MRI indicator to account for age-related differential item functioning. Latent SVD change is defined as the difference in SVD between t1 and t0. Intensive BP treatment group membership is modeled as a predictor of latent SVD change. Arrow values represent regression coefficients (or covariances for double-headed arrows). Asterisks indicate statistically significant parameter estimates at $p < 0.05$ (*), $p < 0.01$ (**), and $p < 0.001$ (***).

