Cerebral small vessel disease and effects of intensive versus standard blood pressure treatment on cardiovascular outcomes and adverse events

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INTRODUCTION AND OBJECTIVE: Cerebral small vessel disease, identified by white matter lesions on brain magnetic resonance imaging (MRI), is common among adults with hypertension and chronic kidney disease. It is also a risk factor for dementia and cognitive impairment. The Systolic Pressure Intervention Trial (SPRINT) demonstrated that intensive versus standard systolic blood pressure lowering (targeting systolic BP <120 mm Hg versus <140 mm Hg, respectively) reduced the progression of cerebral small vessel disease, but there still remains uncertainty about the safety of intensive blood pressure lowering in patients with pre-existing cerebral small vessel disease.

METHODS: We used data from 759 adults participating in the Systolic Pressure Intervention Trial (SPRINT) who completed a baseline MRI to determine the effects of intensive versus standard blood pressure treatment on cardiovascular outcomes and adverse events. We categorized participants by the median abnormal white matter lesion volume. We determined the association of baseline abnormal white matter lesion volume on cardiovascular outcomes and adverse events using Cox proportional hazards models adjusted for age, sex, MRI facility, and intracranial volume.

RESULTS:

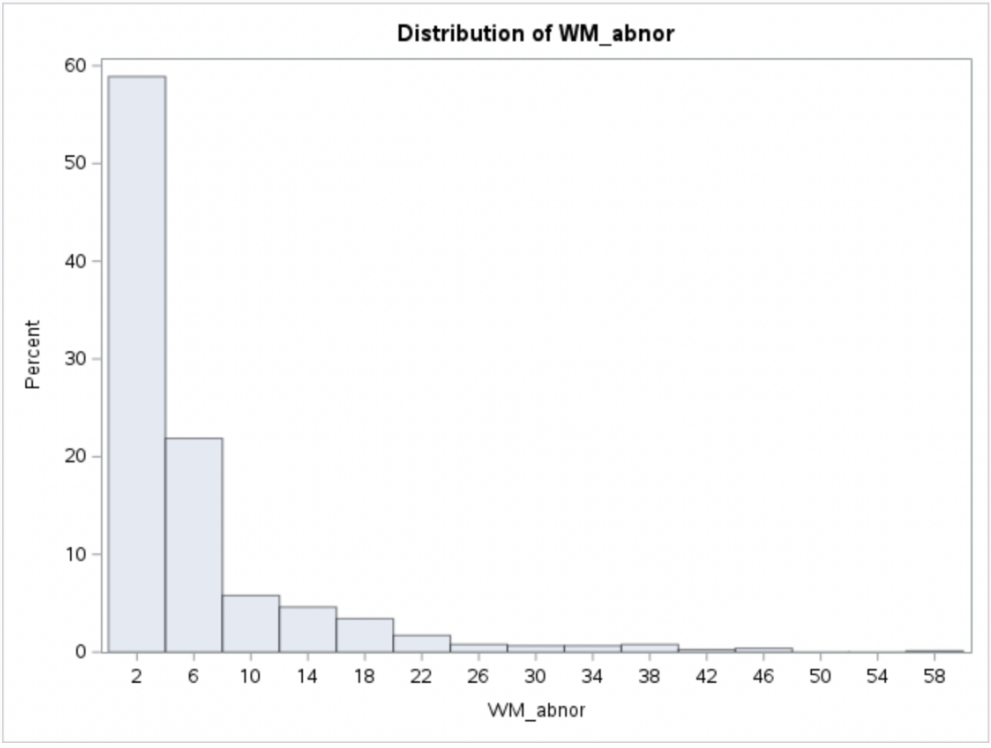
Table 1. Unadjusted frequency of SPRINT outcomes over X years of follow-up, by median of abnormal WMV

	Unadjusted %		**Adjusted HR (95% CI)**	
Characteristics	WMV Tertile 1 WMV<3.20 N=379	WMV Tertile 2 WMV>3.20 N=380	WMV Tertile 1 WMV<3.20 N=379	WMV Tertile 2 WMV>3.20 N=380
Unadjusted %				
SPRINT primary outcome	4.22	10.26	1.0 (Ref)	2.66 (1.43, 4.95)
All-cause mortality	2.90	6.84	1.0 (Ref)	2.24 (1.05, 4.78)
Dementia or Mild cognitive impairment	5.56	11.46	1.0 (Ref)	1.82 (1.02, 3.26)
Syncope	4.13	3.44	1.0 (Ref)	0.71 (0.26, 1.92)
Injurious Fall	9.50	9.54	1.0 (Ref)	0.61 (0.32, 1.16)
Composite kidney outcome	1.85	2.11	1.0 (Ref)	1.25 (0.42, 3.72)

Table 2. SPRINT outcomes over X years of follow-up, by median of abnormal WMV and treatment arm

	Intensive		Standard	
Characteristics	WMV Tertile 1 WMV<3.20 N=379	WMV Tertile 2 WMV>3.20 N=380	WMV Tertile 1 WMV<3.20 N=379	WMV Tertile 2 WMV>3.20 N=380
Unadjusted %				
SPRINT primary outcome	1.0 (Ref)	1.81 (0.79, 4.13)	1.0 (Ref)	3.33 (1.43, 7.72)
All-cause mortality	1.0 (Ref)	2.33 (0.89, 6.13)	1.0 (Ref)	2.21 (0.78, 6.23)
Dementia or Mild cognitive impairment	1.0 (Ref)	3.13 (1.56, 6.28)	1.0 (Ref)	1.22 (0.51, 2.89)
Syncope	1.0 (Ref)	0.92 (0.30, 2.86)	1.0 (Ref)	0.59 (0.13, 2.63)
Injurious Fall	1.0 (Ref)	0.75 (0.34, 1.62)	1.0 (Ref)	1.14 (0.49, 2.68)
Composite kidney outcome	1.0 (Ref)	0.92 (0.31, 2.75)	1.0 (Ref)	27464716 (0,.)

Figure 1. Distribution of abnormal WMV at baseline among SPRINT participants (histogram)



CONCLUSIONS: Adults with a higher volume of abnormal white matter lesions had a higher likelihood of SPRINT primary outcome, all-cause mortality, dementia or mild cognitive

impairment, and adverse kidney events and a lower likelihood of syncope. After adjustment, these effects remained statistically significant for SPRINT primary outcome, all-cause mortality, and dementia or mild cognitive impairment. Analyses stratified by treatment group suggested that intensity of hypertension treatment modified these effects; but the bounds of the 95% confidence intervals were wide and included the possibility of no difference in event rates by volume of white matter lesion and treatment arm.