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Intensive vs. standard blood pressure control and vascular procedures: insights from the Systolic Blood Pressure Intervention Trial (SPRINT)

Trial Registration: SPRINT (Systolic Blood Pressure Intervention Trial); ClinicalTrials.gov Identifier: NCT01206062, https://clinicaltrials.gov/ct2/show/NCT01206062.

Hypertension is a risk factor for both the occurrence and rupture of abdominal aortic aneurysms, is present in most individuals with acute aortic dissection, and has been linked with an increased risk of peripheral artery disease (PAD).[1–3] Limited data are available to inform whether lower blood pressure (BP) treatment targets affect the risk of peripheral vascular events. We examined the risk of vascular procedures (as a proxy of progression of PAD) with intensive vs. standard BP control in The Systolic Blood Pressure Intervention Trial (SPRINT).[4]

SPRINT was a randomized, controlled, open-label trial in which 9361 individuals ≥50 years of age, at high cardiovascular risk (cardiovascular disease except stroke, chronic kidney disease, ≥15% 10-year risk of cardiovascular disease based on the Framingham risk score, or age ≥75 years), and without diabetes, were randomized to intensive (systolic BP target <120mmHg; $n = 4678$) or standard BP control (systolic BP target 135–139 mmHg; $n = 4683$).[4] We used Kaplan–Meier analyses and Cox proportional-hazards regression to evaluate the risk of vascular procedures, information on which was obtained during scheduled study visits, with intensive vs. standard BP control. We further examined subgroup heterogeneity for treatment effect using likelihood-ratio test-based interaction analysis on the prespecified subgroups listed in the primary outcome paper as well as baseline PAD. The SPRINT clinical data set is available from the National Institutes of Health Biologic Specimen and Data Repository Information Coordination Center. The Brigham and Women's Hospital Institutional Review Board waived approval for secondary data utilization.

At baseline, 503 (5.3%) participants had a self-reported history of lower limb PAD, with no significant difference between the intensive and standard treatment groups [250 (5.3%) vs. 253 (5.4%); $P = 0.90$]. During a median of 3.3 years (range 0–5.5 years), 174 (1.9%) composite vascular procedures were recorded. Such procedures were significantly more common among individuals with baseline PAD vs. those without [60 (11.9%) vs. 114 (1.3%), hazard ratio 10.23, 95% confidence interval 7.48–13.99]. The risk of composite and most individual vascular procedures was numerically, though not significantly, lower with intensive BP control (*Figure 1* and *Table 1*). Intensive BP control significantly reduced the risk of peripheral vascular surgery, although this event was infrequent [7 (0.1%) vs. 21 (0.4%), hazard ratio 0.33, 95% confidence interval 0.14–0.77]. The effect of intensive BP lowering was not modified by chronic kidney disease, age, sex, race, previous cardiovascular disease, baseline systolic BP, or history of PAD.

In this secondary analysis of the large SPRINT trial, incident composite vascular procedures were numerically reduced with intensive vs. standard BP lowering, and with an effect, estimate mimicking that of the primary efficacy endpoint; however, the difference did not meet statistical significance. While the study was randomized, and analyses were conducted using the intention-to-treat principle, it was not powered for vascular endpoints. The evidence for antihypertensive treatment for limiting the expansion of aortic aneurysms is equivocal, and optimal BP targets are not known.[2] Conversely, more data regarding secondary prevention are available for PAD.[1] A *post hoc* analysis of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) demonstrated a J-shaped relationship between systolic BP and PAD-related events, with an optimum of 120–129 mmHg.[3] A diastolic BP <70 mmHg was also associated with a high risk of PAD-related events. Although that analysis had suggested that lower BP targets in this population may impair blood flow to the lower limb, data regarding baseline PAD were not available. Furthermore, a meta-analysis suggested that BP lowering might even increase maximal walking distance in patients with PAD.[5] In our study, intensive BP control reduced the risk of peripheral vascular surgery to a similar degree among individuals with and without known PAD. However, this was based on a limited number of events, and the treatment group did not significantly affect the risk of peripheral angioplasty or thrombolysis and lower limb amputation. Nevertheless, it seems reasonable to treat individuals with hypertension and PAD in a similarly aggressive manner as supported by SPRINT as those who have hypertension without PAD.[1]

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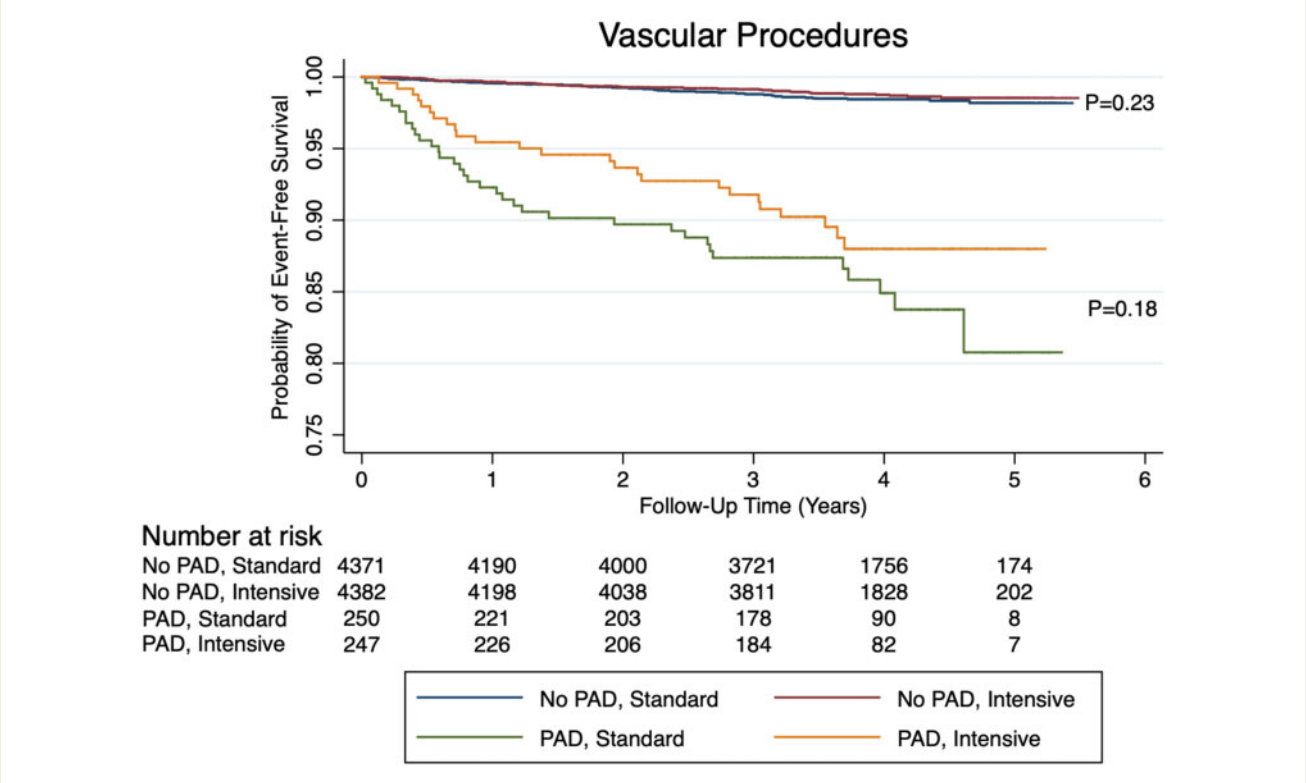

Figure 1 Kaplan–Meier survival curve showing the risk of vascular procedures with intensive vs. standard blood pressure control in patients with and without peripheral artery disease. PAD, peripheral artery disease.

Table 1 The risk of incident composite and individual vascular procedures in patients with and without peripheral artery disease.

Procedure	Patients with peripheral artery disease			Patients without peripheral artery disease		
	Intensive BP control (no. of patients)	Standard BP control (no. of patients)	Hazard ratio (95% confidence interval)	Intensive BP control (no. of patients)	Standard BP control (no. of patients)	Hazard ratio (95% confidence interval)
All participants	250	253		4416	4418	
Any vascular procedure (composite)	25	35	0.70 (0.42–1.18)	51	63	0.80 (0.55-1.15)
Carotid angioplasty	1	3	0.33 (0.03–3.18)	5	3	1.64 (0.39-6.87)
Carotid endarterectomy	3	6	0.48 (0.12–1.93)	14	21	0.66 (0.33-1.29)
Peripheral angioplasty	11	16	0.68 (0.32–1.46)	20	22	0.90 (0.49-1.64)
Peripheral vascular surgery	5	10	0.50 (0.17–1.46)	2	11	0.18 (0.04-0.81)
Lower limb amputation	2	3	0.66 (0.11–3.96)	3	1	2.97 (0.31-28.52)
Surgical or vascular procedure for AAA	4	1	3.96 (0.44–35.43)	8	13	0.60 (0.25-1.46)
Surgical or vascular procedure for TAA	0	0	–	4	1	3.92 (0.44-35.09)
Surgical or vascular procedure for other problem	3	1	2.92 (0.30–28.05)	3	2	1.47 (0.25-8.81)

AAA, abdominal aortic aneurysm; BP, blood pressure; TAA, thoracic aortic aneurysm.

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