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The Systolic Blood Pressure Intervention Trial (SPRINT)

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Intensive blood pressure control appears to be effective and safe in patients with peripheral artery disease: The Systolic Blood Pressure Intervention Trial (SPRINT)

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High blood pressure (BP) is the strongest modifiable risk factor for cardiovascular disease and is highly prevalent among individuals with peripheral artery disease (PAD) (1-3). While patients with atherosclerotic cardiovascular conditions experience considerable morbidity and mortality, the risk is particularly high among those with PAD (4). However, data regarding the effects of strict BP-goals in the setting of PAD are lacking. We leveraged data from the randomized, controlled, open-label Systolic Blood Pressure Intervention Trial (SPRINT) to assess whether the benefits and potential risks of intensive BP-control extended to patients with PAD, and whether baseline PAD modified treatment effect (5).

The full SPRINT clinical data set was acquired from the National Heart, Lung, and Blood Institute's Biologic Specimen and Data Repository Information Coordination Center. A waiver for secondary data use was granted by the Brigham and Women's Hospital Institutional Review Board. In SPRINT, 9,361 high-risk individuals without diabetes or prior stroke, aged ≥ 50 years, with a systolic BP 130-180 mmHg were randomized to intensive (systolic BP target < 120 mmHg; $n=4678$) or standard BP-control (systolic BP target 135-139 mmHg; $n=4683$) (5). The primary outcome was the composite of acute coronary syndromes, stroke, acute decompensated heart failure, or death from cardiovascular causes. We used Cox proportional-hazards regression to determine the efficacy and safety of intensive versus standard BP-control in patients with and without self-reported lower extremity PAD at baseline. Subgroup heterogeneity was examined using the likelihood-ratio test.

Of 9361 participants, 503 (5.3%) had baseline PAD (intensive group 250 (5.3%) versus standard group 253 (5.4%); $P=0.90$). The presence of PAD was associated with male sex ($P<0.001$), older age ($P<0.001$), current or former smoking ($P<0.001$), use of more antihypertensives ($P<0.001$), lower total cholesterol ($P<0.001$), lower high-density lipoprotein cholesterol ($P=0.005$), higher serum creatinine ($P<0.001$), and higher urine albumin-to-creatinine ratio ($P<0.001$). Median follow-up durations were 3.2 years (range 0-4.6 years) and 3.3 years (range 0-4.8 years) for patients with and without PAD, respectively. After adjusting for differences in baseline characteristics, PAD was independently associated with a higher risk of both the primary outcome (hazard ratio 1.61, 95% confidence interval: 1.23-2.12; $P<0.001$) and composite serious adverse events (hazard ratio 1.49, 95% confidence interval: 1.32-1.69; $P<0.001$). However, the presence of PAD did not significantly modify the efficacy and safety of intensive versus standard BP-control ($P\geq 0.05$) (**Figure 1**). Owing to the higher baseline risk in PAD patients, the absolute risk reductions of the primary outcome, death from cardiovascular causes, and death from any cause appeared larger in participants with PAD. Conversely, relative and absolute increases in the risk of adverse events with intensive BP-control were generally higher in those with PAD (**Figure 1**). In a sensitivity analysis, the effects of intensive BP-control

among patients with prevalent clinical cardiovascular disease largely resembled those found for individuals without a history of cardiovascular disease (**Figure 2**).

Our post hoc analysis of SPRINT showed a higher risk of both efficacy and safety outcomes among patients with PAD. While we did not detect any significant heterogeneity in relative risk differences with intensive versus standard BP-control, patients with PAD seemed to experience numerically greater absolute risk reductions of the efficacy outcomes as well as greater absolute risk increases of the safety outcomes, with intensive treatment. Limitations included the small sample size and lack of patients with diabetes as well as objective measures of PAD.

A theoretical concern in patients with PAD is the exacerbation of limb ischemia with excessive BP-lowering (2,3,6). However, while some studies have suggested an association between low BP and PAD-related events, others have found a reduction in cardiovascular events with antihypertensive treatment (3). Furthermore, in our study, the risk of adverse events with intensive BP-control was relatively higher in the PAD group. Balancing the efficacy and safety of intensive versus standard BP-control in this vulnerable patient population is, therefore, challenging. Nevertheless, the possible mortality benefit with a strict BP-target among patients with PAD is worth noting. Conclusively, we agree with contemporary guideline recommendations that patients with hypertension and PAD should be treated in a similar fashion to patients with hypertension without PAD (1).

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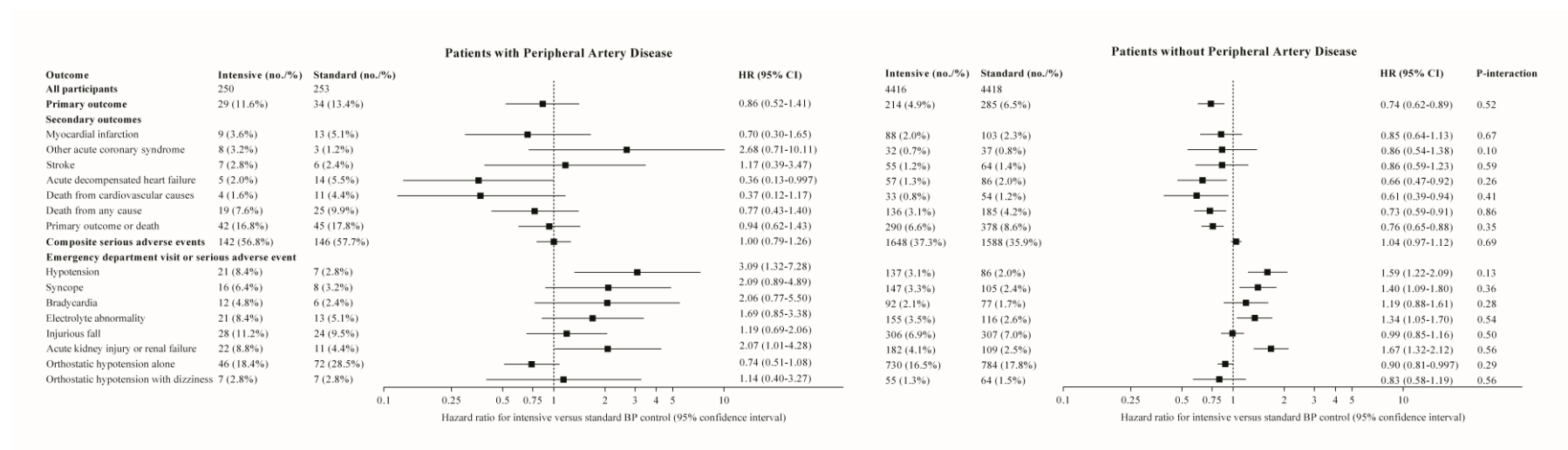
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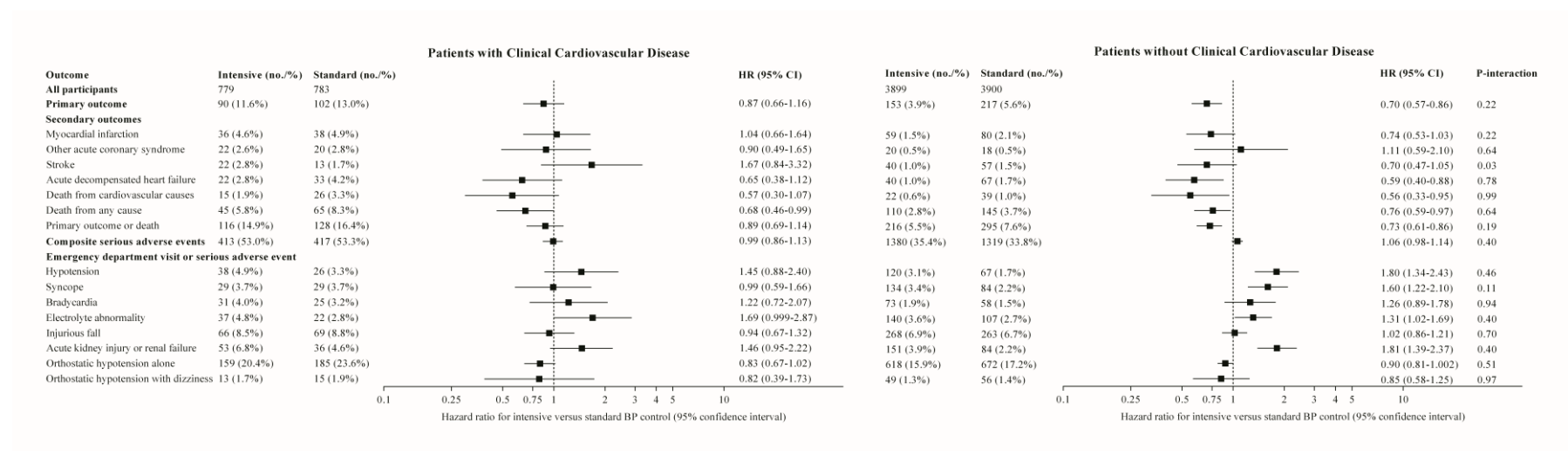
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Figure 1. Efficacy and safety events with intensive versus standard blood pressure control in patients with and without peripheral artery disease.

Abbreviations: CI = confidence interval; HR = hazard ratio.

Figure 2. Efficacy and safety events with intensive versus standard blood pressure control in patients with and without clinical cardiovascular disease.

Abbreviations: CI = confidence interval; HR = hazard ratio.

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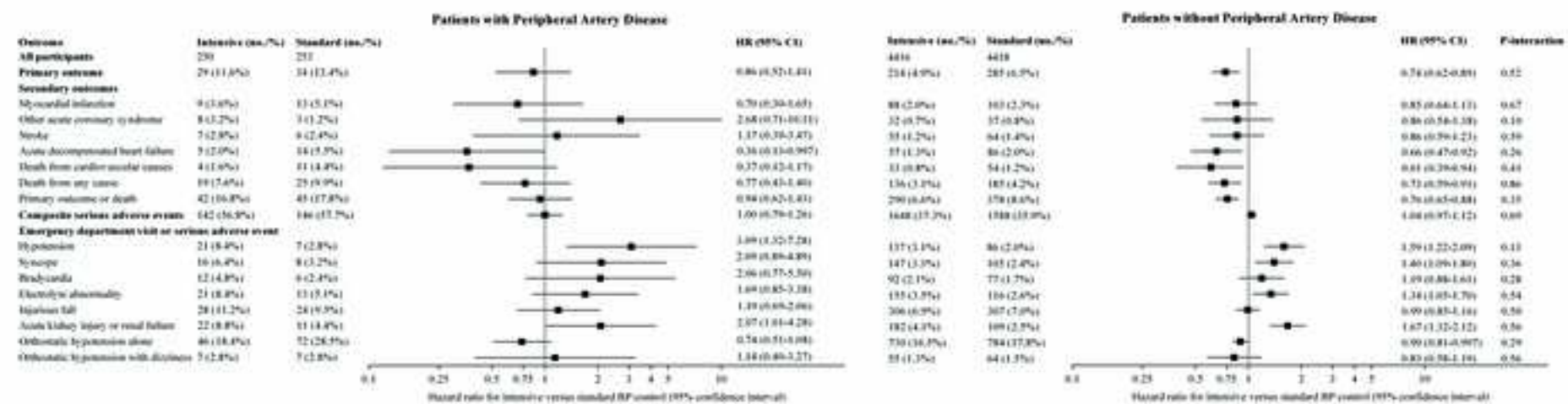


Figure 2

