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The Systolic Blood Pressure Intervention Trial (SPRINT)

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Intensive blood pressure control in patients with a history of heart failure: the Systolic Blood Pressure Intervention Trial (SPRINT)

The Systolic Blood Pressure Intervention Trial (SPRINT) found that intensive versus standard blood pressure (BP) control reduced cardiovascular morbidity and mortality in high-risk patients.[1] Effects were consistent among patients with and without prevalent cardiovascular disease. Patients with heart failure may benefit from intensive BP control by slowing the adverse cardiac remodelling associated with high BP. Conversely, some studies have suggested better outcomes among patients with heart failure who have higher BP.[2] Therefore, it remains unknown whether a history of heart failure modifies the risks and benefits of intensive BP control.

SPRINT randomized 9361 individuals who were ≥50 years of age, at high cardiovascular risk, and had a systolic BP of 130–180 mmHg to intensive or standard BP control.[1] Pertinent exclusion criteria included diabetes, prior stroke, and known symptomatic heart failure within the past 6 months or a left ventricular ejection fraction <35%. The primary endpoint was the composite of acute coronary syndromes, stroke, acute decompensated heart failure, or death from cardiovascular causes. The principal safety endpoint was composite serious adverse events. We used multivariable Cox proportional hazards regression to determine the risk of efficacy and safety events in patients with baseline heart failure. We then calculated the efficacy and safety of intensive versus standard BP control in patients with and without baseline heart failure and examined subgroup heterogeneity using the likelihood-ratio test. A waiver for secondary use of the SPRINT data set was obtained from the Brigham and Women's Hospital Institutional Review Board.

Of the 9361 participants, 326 (3.5%) reported a history of heart failure. The prevalence did not significantly differ between patients randomized to intensive versus standard BP control [166 (3.6%) vs. 160 (3.4%); $P = 0.73$]. Median follow-up duration was 3.26 years (range 0–4.77 years). A history of heart failure was independently associated with the primary endpoint (adjusted hazard ratio: 2.34; 95% confidence interval: 1.75–3.13; $P < 0.001$) and with composite serious adverse events (adjusted hazard ratio: 1.41; 95% confidence interval: 1.21-1.64; $P < 0.001$). No significant interactions were detected for any of the endpoints (*Table 1*). Patients with a history of heart failure had higher risks and greater absolute risk reductions in several efficacy endpoints, including the primary endpoint and all-cause death. The risk of safety endpoints was also higher in patients with heart failure, but mostly similar between the intensive and standard groups (*Table 1*).

Our study showed a greater risk of both efficacy and safety events among individuals with heart failure, but no significant differences in the risk–benefit profile of intensive BP control. Effects were virtually identical in patients with vs. those without heart failure. Nevertheless, data regarding the exact phenotype, disease severity, or functional status of individuals with heart failure were not available. It seems likely that a significant proportion of these patients had heart failure with mildly reduced ejection fraction, heart failure with preserved ejection fraction (HFpEF), or heart failure with recovered ejection fraction, and our data support the class I guideline recommendation to control BP in patients with HFpEF.[3] Other limitations were the small sample size, exclusion of other specific high-risk conditions, and that heart failure was self-reported. In conclusion, a specific subgroup of patients with heart failure faces excess risks of clinical adverse events but appears to benefit from intensive BP control to attenuate this risk. Future prospective clinical trials are needed to establish optimal BP targets in HFpEF.

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M.V. has received research grant support or served on advisory boards for American Regent, Amgen, AstraZeneca, Bayer AG, Baxter Healthcare, Boehringer Ingelheim, Cytokinetics, Lexicon Pharmaceuticals, Relypsa, and Roche Diagnostics; had speaker engagements with Novartis and Roche Diagnostics; and participates in clinical endpoint committees for studies sponsored by Galmed and Novartis.

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Table 1 Efficacy and safety events with intensive vs. standard blood pressure control in patients with and without heart failure

Endpoint	Patients with heart failure ($n = 326$)			Patients without heart failure ($n = 9035$)			
	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)	*P*-value for interaction
All participants	166	160		4512	4523		
Primary endpoint	22 (13.3%)	34 (21.3%)	0.58 (0.34–0.99)	221 (4.9%)	285 (6.3%)	0.77 (0.65–0.92)	0.33
Secondary endpoints							
Myocardial infarction	3 (1.8%)	8 (5.0%)	0.34 (0.09–1.29)	94 (2.1%)	108 (2.4%)	0.87 (0.66–1.15)	0.16
Other acute coronary syndrome	3 (1.8%)	5 (3.1%)	0.56 (0.13–2.35)	37 (0.8%)	35 (0.8%)	1.06 (0.67–1.68)	0.40
Stroke	6 (3.6%)	6 (3.8%)	0.92 (0.30–2.85)	56 (1.2%)	64 (1.4%)	0.87 (0.61–1.25)	0.92
Acute decompensated heart failure	12 (7.2%)	18 (11.3%)	0.61 (0.29–1.27)	50 (1.1%)	82 (1.8%)	0.61 (0.43–0.86)	>0.99
Death from cardiovascular causes	5 (3.0%)	7 (4.4%)	0.66 (0.21–2.08)	32 (0.7%)	58 (1.3%)	0.55 (0.36–0.85)	0.76
Death from any cause	12 (7.2%)	18 (11.3%)	0.62 (0.30–1.29)	143 (3.2%)	192 (4.2%)	0.74 (0.60–0.92)	0.64
Primary endpoint with death from any cause	26 (15.7%)	42 (26.3%)	0.55 (0.34–0.90)	306 (6.8%)	381 (8.4%)	0.80 (0.69–0.93)	0.17
Composite serious adverse events	97 (58.4%)	90 (56.3%)	1.01 (0.76–1.35)	1696 (37.6%)	1646 (36.4%)	1.04 (0.97–1.11)	0.83
Emergency department visit or serious adverse events							
Hypotension	13 (7.8%)	6 (3.8%)	2.07 (0.79–5.44)	145 (3.2%)	87 (1.9%)	1.68 (1.29–2.19)	0.71
Syncope	8 (4.8%)	7 (4.4%)	1.08 (0.39–2.97)	155 (3.4%)	106 (2.3%)	1.47 (1.15–1.88)	0.53
Bradycardia	11 (6.6%)	8 (5.0%)	1.29 (0.52–3.21)	93 (2.1%)	75 (1.7%)	1.24 (0.92–1.68)	0.95
Electrolyte abnormality	8 (4.8%)	8 (5.0%)	0.92 (0.34–2.45)	169 (3.8%)	121 (2.7%)	1.40 (1.11–1.77)	0.43
Injurious fall	18 (10.8%)	19 (11.9%)	0.86 (0.45–1.64)	316 (7.0%)	313 (6.9%)	1.01 (0.86–1.18)	0.59
Acute kidney injury or renal failure	18 (10.8%)	13 (8.1%)	1.30 (0.63–2.64)	186 (4.1%)	107 (2.4%)	1.75 (1.38–2.22)	0.41
Orthostatic hypotension alone	40 (24.1%)	42 (26.3%)	0.74 (0.47–1.41)	737 (16.3%)	815 (18.0%)	0.89 (0.81–0.98)	0.37
Orthostatic hypotension with dizziness	4 (2.4%)	2 (1.3%)	1.87 (0.34–10.21)	58 (1.3%)	69 (1.5%)	0.83 (0.58–1.17)	0.50

BP, blood pressure.

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