

AHA Hypertension 2022 Abstract

Effects of Orthostatic Hypotension on Intensive Blood Pressure Treatment with respect to Cardiovascular Disease and All-Cause Mortality: An Individual-Level Meta-analysis

Stephen P Juraschek, MD, PhD, Jiun-Ruey Hu, MD, MPH, Jennifer L Cluett, MD, Anthony M Ishak, PharmD, Carol Mita, MLIS, Lewis A. Lipsitz MD, Lawrence J Appel, MD, MPH, Nigel S Beckett MB, ChB, Ruth L. Coleman, MSc, William C. Cushman, MD, Barry R Davis, MD, PhD, Greg Grandits, MS, Rury R. Holman, FRCP, Edgar R Miller 3rd, MD, PhD, Ruth Peters, PhD, MSc, Jan A. Staessen, MD, PhD, Addison A. Taylor, MD, PhD, Jackson T Wright Jr, MD, PhD, Kenneth J Mukamal, MD, MPH, MA

Characters: 1445 [max 1450]

Background In a recent individual level meta-analysis, intensive versus standard blood pressure (BP) treatment reduced participants' risk of orthostatic hypotension (OH). Whether OH modified the relationship between intensive treatment and risk of cardiovascular disease (CVD) or death is unknown.

Methods We performed an individual participant data meta-analysis, updating a previous systematic review of MEDLINE, EMBASE, and CENTRAL databases through May 13, 2022, which included randomized trials of BP pharmacologic treatment (more intensive BP goal or active agent) on CVD or death. CVD events were adjudicated and included coronary heart disease, stroke, and congestive heart failure. OH was defined as a drop in SBP ≥ 20 mmHg and/or DBP ≥ 10 mmHg after changing positions from seated to standing. Ultimately, 8 trials were identified with OH and outcomes data. Effects were examined overall and by trial type (BP goal or active agent), using Cox proportional hazard models adjusted for age and sex.

Results There were 27,974 participants followed for median 4 years (mean age 69.5 ± 10.7 yrs; 48.5% female; 8.6% with OH). Baseline OH was associated with a higher risk of CVD or death (HR 1.24; 95% CI: 1.10, 1.39). More intensive BP treatment or active therapy lowered risk of CVD or death among those without OH at baseline (HR 0.82; 95% CI: 0.76, 0.88) and with OH at baseline (HR 0.79; 95% CI: 0.63, 0.98). Effects did not differ by baseline OH (*P*-interaction 0.78) (**Table**).

Conclusion While baseline OH was associated with CVD or death, it did not increase the risk of CVD or death from intensive treatment. OH prior to the initiation of intensive therapy should not be viewed as a reason to avoid BP treatment.

Table. Effects of an intensive treatment goal or active agent versus a standard treatment goal or placebo on risk of cardiovascular disease or death from any cause

	No Orthostatic Hypotension		Orthostatic Hypotension		P-interaction
	n/N	HR (95% CI)	n/N	HR (95% CI)	
Intensive Goal Trials					
AASK	923/986	0.96 (0.84, 1.09)	96/100	0.95 (0.63, 1.43)	0.96
ACCORD	130/1220	0.87 (0.62, 1.24)	15/101	0.52 (0.18, 1.47)	0.46
SPRINT	858/8542	0.81 (0.71, 0.93)	90/674	0.80 (0.53, 1.21)	0.89
SPS3	243/2097	0.82 (0.63, 1.05)	41/238	1.10 (0.59, 2.04)	0.39
Pooled	2154/12845	0.87 (0.80, 0.95)	242/1113	0.88 (0.68, 1.14)	0.92
Active Agent Trials					
HYVET	71/3509	0.40 (0.24, 0.67)	8/336	0.17 (0.02, 1.35)	0.43
SHEP	130/4041	0.44 (0.30, 0.63)	16/554	0.37 (0.12, 1.16)	0.77
SYS-EUR	412/4342	0.75 (0.62, 0.91)	45/332	0.73 (0.41, 1.32)	0.99
TOMHS	46/843	0.73 (0.39, 1.35)	5/59	0.40 (0.06, 2.53)	0.51
Pooled	659/12735	0.63 (0.54, 0.74)	74/1281	0.56 (0.35, 0.89)	0.75
Overall	2813/25580	0.82 (0.76, 0.88)	316/2394	0.79 (0.63, 0.98)	0.78

Hazard ratios (95% CI) were determined using Cox proportional hazard models. Individual trial estimates were adjusted for age and sex. Pooled estimates are adjusted for age, sex, and study. n/N represents number of deaths/total population at risk. I^2 for heterogeneity of (1) baseline OH with the outcome was 0% ($P = 0.59$), (2) intensive treatment among participants without OH and the outcome was 72% ($P = 0.001$), (3) standard treatment among participants with OH was 0% ($P = 0.44$), and (4) the pooled interaction-term was 0% ($P = 0.93$).