

If blood pressure rises upon standing, so may risk for heart attack

March 17 2022



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Among young and middle-aged adults with high blood pressure, a substantial rise in blood pressure upon standing may identify those with a higher risk of serious cardiovascular events, such as heart attack and stroke, according to new research published today in the American Heart Association's peer-reviewed journal *Hypertension*.



"This finding may warrant starting blood-pressure-lowering treatment including medicines earlier in patients with exaggerated blood pressure response to standing," said Paolo Palatini, M.D., lead author of the study and a professor of internal medicine at the University of Padova in Padova, Italy.

Nearly half of Americans and about 40% of people worldwide have high blood pressure, considered to be the world's leading preventable cause of death. According to the American Heart Association's 2022 <u>heart</u> disease statistics, people with hypertension in mid-life are five times more likely to have impaired cognitive function and twice as likely to experience reduced executive function, dementia and Alzheimer's disease.

Typically, systolic (top number) blood pressure falls slightly upon standing up. In this study, researchers assessed whether the opposite response—a significant rise in systolic blood pressure upon standing—is a risk factor for heart attack and other serious cardiovascular events.

The investigators evaluated 1,207 people who were part of the HARVEST study, a prospective study that began in Italy in 1990 and included adults ages 18-45 years old with untreated stage 1 hypertension. Stage 1 hypertension was defined as systolic blood pressure of 140-159 mm Hg and/or diastolic BP 90-100 mm Hg. None had taken blood pressure-lowering medication prior to the study, and all were initially estimated at low risk for major cardiovascular events based on their lifestyle and medical history (no diabetes, renal impairment or other cardiovascular diseases). At enrollment, participants were an average age of 33 years, 72% were men, and all were white.

At enrollment, six blood pressure measurements for each participant were taken in various physical positions, including when lying down and after standing up. The 120 participants with the highest rise (top 10%) in



blood pressure upon standing averaged an 11.4 mm Hg increase; all increases in this group were greater than 6.5 mm Hg. The remaining participants averaged a 3.8 mm Hg fall in systolic blood pressure upon standing.

The researchers compared heart disease <u>risk factors</u>, laboratory measures and the occurrence of major cardiovascular events (heart attack, heartrelated chest pain, stroke, aneurysm of the aortic artery, clogged peripheral arteries) and chronic kidney disease among participants in the two groups. In some analyses, the development of atrial fibrillation, an arrhythmia that is a major risk factor for stroke, was also noted. Results were adjusted for age, gender, parental history of heart disease, and several lifestyle factors and measurements taken during study enrollment.

During an average 17-year follow-up 105 major cardiovascular events occurred. The most common were <u>heart attack</u>, heart-related chest pain and stroke.

People in the group with top 10% rise in blood pressure:

- were almost twice as likely as other participants to experience a major cardiovascular event;
- did not generally have a higher risk profile for cardiovascular events during their initial evaluation (outside of the exaggerated blood pressure response to standing);
- were more likely to be smokers (32.1% vs. 19.9% in the nonrising group), yet physical activity levels were comparable, and they were not more likely to be overweight or obese, and no more likely to have a family history of cardiovascular events;
- had more favorable cholesterol levels (lower total cholesterol and higher high-density-lipoprotein cholesterol);
- had lower systolic blood pressure when lying down than the other



group (140.5 mm Hg vs. 146.0 mm Hg, respectively), yet blood pressure measures were higher when taken over 24 hours.

After adjusting for average blood pressure taken over 24 hours, an exaggerated blood pressure response to standing remained an independent predictor of adverse heart events or stroke.

"The results of the study confirmed our initial hypothesis—a pronounced increase in blood pressure from lying to standing could be prognostically important in young people with high blood pressure. We were rather surprised that even a relatively small increase in standing blood pressure (6-7 mm Hg) was predictive of major cardiac events in the long run," said Palatini.

In a subset of 630 participants who had stress hormones measured from 24-hour urine samples, the epinephrine/creatinine ratio was higher in the people with a rise in standing blood pressure compared to those whose standing blood pressure did not rise (118.4 nmol/mol vs. 77.0 nmol/mol, respectively).

"Epinephrine levels are an estimate of the global effect of stressful stimuli over the 24 hours. This suggests that those with the highest blood pressure when standing may have an increased sympathetic response [the fight-or-flight response] to stressors," said Palatini. "Overall, this causes an increase in average blood pressure."

"The findings suggest that blood pressure upon standing should be measured in order to tailor treatment for patients with <u>high blood</u> <u>pressure</u>, and potentially, a more aggressive approach to lifestyle changes and blood-pressure-lowering therapy may be considered for people with an elevated [hyperreactor] blood pressure response to standing," he said.

Results from this study may not be generalizable to people from other



ethnic or racial groups since all study participants reported white race/ethnicity. In addition, there were not enough women in the sample to analyze whether the association between rising standing <u>blood</u> <u>pressure</u> and adverse heart events was different among men and women. Because of the relatively small number of major adverse cardiac events in this sample of young people, the results need to be confirmed in larger studies.

Co-authors are Lucio Mos, M.D.; Francesca Saladini, M.D.; and Marcello Rattazzi, M.D. Authors' disclosures are listed in the manuscript.

More information: *Hypertension* (2022). www.ahajournals.org/doi/10.116 ... TENSIONAHA.121.18579

Provided by American Heart Association

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