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## When Blood Pressure Increases with Standing: Consensus Definition for Diagnosing Orthostatic Hypertension

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### Context

When changing from the supine to the standing position approximately 500–1000 ml blood is pooled below the diaphragm and hydrostatic pressure forces fluids from the intravascular to the interstitial compartment. These changes impose a major hemodynamic burden on the cardiovascular system. Baroreflex-mediated withdrawal of cardiac parasympathetic activity and sympathetic activation maintain standing blood pressure in healthy persons. Orthostatic hypotension occurs when these counterregulatory mechanisms fail. Conversely, some patients have a paradoxical increase in upright blood pressure to hypertensive levels, presumably due to sympathetic activation overshoot. This orthostatic hypertension is not a benign condition because it is associated with increased cardiovascular morbidity and mortality independently of traditional risk factors.<sup>1,2</sup> Yet, there has not been a uniform definition of orthostatic hypertension and the entity is not covered in current hypertension guidelines. Because diagnostic criteria vary profoundly between studies, data on epidemiology, associated health risks, and management of orthostatic hypertension in the existing literature is difficult to interpret.

### Discussion

#### Definition

An international expert panel suggested pragmatic definitions for an exaggerated orthostatic pressor

response and for orthostatic hypertension.<sup>3,4</sup> An exaggerated orthostatic pressor response was defined as sustained increase in systolic blood pressure by at least 20 mmHg when changing from the supine to the standing position regardless of absolute blood pressure while standing. Orthostatic hypertension was defined as an exaggerated orthostatic pressor response associated with systolic blood pressure of at least 140 mmHg while standing. An increase in systolic blood pressure by 20 mmHg corresponds is approximately two standard deviations above the population mean in the Malmö Preventive Project<sup>5</sup> and the Malmö Offspring Study.<sup>6</sup> Diastolic blood pressure was not included in the definition because increases in diastolic blood pressure with standing can be normal and are difficult to interpret, particularly in patients with elevated standing heart rate. The panel decided to differentiate between an exaggerated orthostatic pressor response and orthostatic hypertension because individuals with blood pressure in the normal range could otherwise be labeled as hypertensive. The panel recognized that we lack empirical data to determine if these definitions predict increased cardiovascular risk.

#### Epidemiology and associated risks

An exaggerated orthostatic pressor response or orthostatic hypertension has been observed in 5–30% of participants in epidemiological surveys or clinical trials.<sup>3,4</sup> However, the lack of a uniform definition

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makes it difficult to compare studies, Individuals with increased age, obesity, preexisting arterial hypertension, diabetes mellitus, and the postural tachycardia syndrome (POTS) are more likely to experience orthostatic hypertension.

### Testing for orthostatic hypertension

When diagnosing an exaggerated orthostatic pressor response or orthostatic hypertension, blood pressure measurements with a brachial cuff suffice. Pulse rate should be recorded given the association between an exaggerated orthostatic pressor response and POTS. The panel suggested that supine blood pressure and heart rate be measured after five minutes supine rest. If possible, standing blood pressure and heart rate should be measured after 1, 3 and 5 minutes and 3 and 5 minutes measurements could be averaged. For screening purposes, a single measurement after 3 minutes standing may suffice. Testing should be repeated on a different day to confirm the diagnosis as is standard practice for diagnosis of essential hypertension. Seated to upright measurements could also be considered for screening purposes, however, the approach may reduce diagnostic sensitivity. Beat-by-beat blood pressure measurements or head-up tilt testing are usually not required for clinical purposes but may have utility in scientific investigations.

### Therapeutic considerations

The panel concluded that there is no evidence that individuals with an exaggerated orthostatic pressor response and normotensive blood pressure require therapy. However, these individuals may be at increased for progression to arterial hypertension later in life. In patients with hypertensive blood pressure only when standing (isolated orthostatic hypertension), ambulatory blood pressure monitoring may help to assess average blood pressure and test for altered diurnal blood pressure patterns. Indeed, extreme nighttime blood pressure dipping and masked morning hypertension may be observed in patients with orthostatic hypertension.<sup>2,7</sup> Finally, in individuals with orthostatic hypertension who are also hypertensive in the seated and supine position, anti-hypertensive medications should be prescribe according to current hypertension guidelines. However, some antihypertensive medications, particularly diuretics, may exacerbate sympathetic activation with standing and thereby worsen orthostatic hypertension.

### Conclusion

Blood pressure measurements in the supine and in the upright position, while considered routine part of a physical examination in patients with cardiovascular disease, are rarely conducted in clinical practice. Abnormalities in blood pressure responses to standing, be it orthostatic hypotension or orthostatic hypertension identify patients at an increased cardiovascular risk and may affect therapeutic decisions. Yet, more research on mechanisms, epidemiology, and clinical management of patients with orthostatic hypertension is required. A consensus definition for an exaggerated orthostatic pressor response and orthostatic hypertension is an important step to make future research more comparable and applicable in the clinic.

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IB is a consultant for Theravance Biopharma, Takeda Inc., and Amneal Pharmaceuticals, and has a patent for an automated abdominal binder to treat orthostatic hypotension. He is supported by NIH grants R01HL149386 and R01HL161095

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