Currently, the diagnosis and treatment of hypertension is based mainly on average blood pressure (BP) values over a period of time. However, BP is dynamic and varies over time, often depending on physical activity, such as increasing BP during exercise and a decrease in BP during sleep. As such, BP is not fully captured by its mean value of a series of measurements. Moreover, excessive BP variability has been shown to be detrimental to vascular health, as it has been associated with markers of (sub)clinical organ damage, such as (micro-)albuminuria [1] and increased arterial stiffness [2], as well as cardiovascular events and mortality [3]. Importantly, these associations were independent of high mean BP, indicating that increased BP variability does harm beyond an elevated mean BP.

Interestingly, researchers have defined various forms of harmful BP variability: variability over a series of BP readings that is increased short-term (beat-to-beat or over 24 h) to long-term (over days, weeks, years) BP variability, or specific patterns in a 24-h BP profile, such as nocturnal nondipping, increased morning BP surge or orthostatic hypertension and hypotension [4]. Excessive BP changes during postural changes may be especially important, as most individuals change from a supine or sitting position to a standing position over 40 times a day [5].

In this issue of the *Journal of Hypertension*, Nolde et al. [6] provide an interesting insight into the association between postural BP changes and arterial stiffness. They studied a cohort of 200 patients referred to a tertiary hypertension clinic and evaluated the association between postural BP changes and arterial stiffness. The authors measured BP in a sitting position and after 1 min standing upright, and considered change in BP of more than 10 mmHg as compared with the seated BP to be abnormal: orthostatic hypertension was defined as a BP decrease of 10 mmHg after standing. Arterial stiffness was measured using carotid-to-femoral pulse wave velocity (cfPWV). They found that the association between postural BP changes and cfPWV followed a U-shaped curve: both orthostatic hypertension and hypotension were associated with greater arterial stiffness, independent of important confounders, such as age, type 2 diabetes and mean 24-h BP. In unadjusted analyses, cfPWV was 1.4 and 1.1 m/s higher in the orthostatic hypertension and hypotension group, respectively, as compared to those with stable BP after 1 min standing upright. Such high cfPWV values are quite impressive, as these high degrees of arterial stiffness are equivalent to approximately 10–15 years of vascular ageing [7].

At first sight, this U-shaped association between postural BP changes and arterial stiffening may perhaps seem somewhat surprising. However, it becomes more understandable when looking at the order of sequences of what comes first: orthostatic hypertension/hypotension or arterial stiffening?

With regard to orthostatic hypertension, one may on the one hand hypothesize that a sudden surge in BP may cause arterial stiffening by putting greater mechanical stress on the arterial wall, which in turn deteriorates its elastin components. If these BP surges occur more often, it may be even more damaging to the vessel wall than a high mean BP. In fact, this concept has been revisited multiple times and has been named ‘stress fatigue theory’ in earlier studies [8,9], and is derived from the field of mechanical engineering: ‘high cycle fatigue’. Examples are found readily in everyday life: bending a paperclip very often breaks much easier than when only applying constant stress. Actual structural ruptures due to cyclic stress do not occur often in arterial walls, as their structural properties will change into stiffer arteries that can withstand the cyclic stress via an increased extracellular matrix deposition and enhanced vascular smooth cell proliferation [10]. On the other hand, reverse causality is also plausible: arterial stiffening may cause orthostatic hypertension due to the decreased buffering capacity of the large arteries, which will increase pulse pressure [11] and may lead to a BP overshoot in combination with the compensatory heart rate increase whilst standing up. Moreover, as these mechanisms seem equally biologically plausible, it is entirely feasible that both are
simultaneously true, which leads to a vicious circle of increased BP surges and arterial stiffening. With regard to orthostatic hypotension, reverse causality is also plausible. On the one hand, carotid artery stiffening may cause orthostatic hypotension via decreased sensitivity of the stretch-sensitive baroreceptors [12]. As a result, when standing up, the initial drop in BP may not be sensed appropriately by the carotid baroreceptors due to impaired relaxation of the vessel wall, and thereby cause prolonged periods of hypotension. However, in the study by Nolde et al. [6] cfPWV was measured, which is a marker of aortic stiffness, and measurements of carotid stiffness were unfortunately not available. Carotid stiffness may represent other structural changes and another degree of vascular health. Indeed, the aorta and carotid artery change differently over time due to their inherent structures: the aorta has a mixed muscular and elastic vessel wall, whereas the carotid artery has an elastic vessel wall [13]. In addition, increased carotid artery stiffness is associated with cardiovascular events, independently of aortic stiffness [14]. On the other hand, orthostatic hypotension itself may not directly cause arterial stiffening, but it does lead to increase BP variability. The constant fall and subsequent rise of BP after standing up could eventually cause the aforementioned ‘high cycle fatigue’ and arterial stiffening.

An important question is the one when BP should be measured during postural changes. In the study by Nolde et al., BP was measured supine and after 1 min standing upright. However, under normal physiological circumstances, the course of BP after standing up is more complex. BP drops quickly after standing up, with a nadir at approximately 6–8 s after standing up [15]. Usually, this drop in BP recovers quickly to baseline values within 20–30 s, often resulting in a small overshoot in BP as compared to supine. This drop in BP occurs in all individuals, but in some individuals, the magnitude in BP drop is so large that it leads to light-headedness due to cerebral hypoperfusion. In more severe cases, this phenomenon is referred to as initial orthostatic hypotension (IOH), which is defined as a drop in BP after standing up of more than 40 mmHg systolic or more than 20 mmHg diastolic as compared to supine. This initial drop in BP cannot be detected using a single BP measurement after 1 min. Moreover, recovery after the initial drop in BP after standing up may be delayed, which may occur more frequently in older/ frail individuals [16]. In these patients, BP recovers more slowly after the initial drop, which also leads to delayed overshoot in BP. If one measures BP only once after 1 min of standing upright, the patient could either still be in the recovery phase (finding a lower BP than supine), may be in the overshoot phase (finding a higher BP than supine), may be somewhere in between recovery and overshoot (finding a BP comparable to supine), or may have been fully recovered to supine BP values (after the overshoot). Thus, the BP one finds with a single measurement strongly depends upon the timing of the measurement and the speed of recovery after the initial drop in BP. As such, one may draw the wrong conclusion on postural BP changes. Hence, we recommend that future studies on the association between postural BP changes and vascular stiffness evaluate the course of BP after standing up more in detail, for example by using noninvasive beat-to-beat-BP devices.

The clinical consequences of the findings of Nolde et al. [6] are not fully evident at this moment. Although increased BP variability and arterial stiffening have been associated with cardiovascular events and mortality, such measurements are not yet routinely used in clinical practice. Although researchers in the cardiovascular field have propagated the use of cfPWV in clinical practice (mainly to pull the trigger for therapeutic intervention of those with intermediate cardiovascular risk [17]), it has not found its way into the clinician’s office yet. However, as Nolde et al. [6] demonstrated, a clinical observation of excessive postural BP changes may also point towards increased arterial stiffness. Therefore, symptoms of orthostatic hypertension or hypotension, such as headache, light-headedness, dizziness or falls, may prompt screening for traditional cardiovascular risk factors, and thereby induce earlier treatment and thus better vascular health on the long run.

In conclusion, excessive postural changes in BP may have clinical relevance with regard to vascular ageing, as both orthostatic hypertension and hypotension are associated with increased arterial stiffness. However, if the clinician chooses to measure BP variability in a patient, he or she is presented with an array of choices: what form of BP variability to measure, postural BP changes, early morning BP surge, nocturnal dipping or beat-to-beat, 24-h, day-to-day or visit-to-visit BP variability? All of these measures have been associated with some form of cardiovascular end-organ damage and events, but a gold standard of BP variability remains elusive. Without a consensus on how all these subtypes of BP variability should be used, actual implementation of BP variability into the clinician’s office will take a long time.

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Conflicts of interest

None.

REFERENCES