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COMMENTARY

Home monitoring is the optimal method for assessing blood pressure variability

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Blood pressure is a continuous variable with dynamic characteristics and considerable inherent fluctuation that is predominantly affected by physical and, to a lesser extent, mental activity. The assessment of the blood pressure abnormality and the classification of hypertension are traditionally made on the average of multiple measurements taken in the office or by 24-hour ambulatory or self-home monitoring, whereas the blood pressure fluctuations, which often rise well above the average blood pressure level, are usually regarded as 'random' and 'noise,' and are thus ignored.[1]

OFFICE BLOOD PRESSURE VARIABILITY

The concept of blood pressure variability, according to which for the same mean blood pressure level increased variability puts additional stressor effect on the cardiovascular system, resulting in increased risk of target organ damage, is being investigated in the last 25 years.[1] Recently, blood pressure variability has gained significant attention due to the publication of retrospective analyses of the Anglo-Scandinavian Cardiac Outcomes Trial Blood Pressure Lowering Arm (ASCOT-BPLA) data by Rothwell *et al.* These analyses showed, first, that systolic blood pressure variability and the maximum systolic blood pressure are strong predictors of stroke independent of the mean blood pressure[2] and, second, that different antihypertensive drugs might differently affect blood pressure variability, influencing their contribution to cardiovascular protection.[3] The NHANES study confirmed the relationship between systolic blood pressure variability and an all-cause mortality in the general population.[4]

Interestingly, the abovementioned studies assessed visit-to-visit blood pressure variability on the basis of repeated measurements in office visits,[2–4] whereas the original studies that raised the issue of the clinical relevance of blood pressure variability were based on 24-hour reading-to-reading variability that was assessed by intra-arterial monitoring.[5] In contrast, in this issue of the Journal, Ushigome *et al.*[6] investigated day-to-day blood pressure variability based on 14-day self-home blood pressure measurements. This study of 858 patients with type 2 diabetes showed that home blood pressure variability is associated with macroalbuminuria independently of other known risk factors.[6] Thus, all three of the established blood pressure measurement methods (office, ambulatory and home) have been successfully used to demonstrate the detrimental effects of blood pressure variability on the cardiovascular system (Table 1).

INHERENT AND SPONTANEOUS BLOOD PRESSURE VARIABILITY

The amplitude and frequency of the blood pressure fluctuations of an individual over a given time period have two components. The first is the inherent blood pressure variability, which is regulated by the complex interactions between central and reflex neural mechanisms, as well as the vasoactive hormones and arterial wall stiffness of the individual. The second component is the spontaneous blood pressure variability, which is due to acute response to environmental stress as the individual faces the challenges of daily activities. The former reflects the normal function of the cardiovascular control systems of the individual, whereas the latter is largely affected by the intensity of the physical and mental activities in which the individual is engaged during the particular blood pressure-monitoring period. It might be argued that, specifically for the assessment of blood pressure variability, a measurement methodology with a standardized posture and activity (for example, office, home and nocturnal ambulatory blood pressure) might be more appropriate than awake ambulatory blood pressure measurement, because in the latter, the variable intensity of activity during the day might largely affect the reliability and reproducibility of the blood pressure variability. Thus, by reducing spontaneous variability, home and nocturnal blood pressure monitoring might be superior to awake ambulatory monitoring for the assessment of the inherent variability. Indeed, when office, home and ambulatory blood pressure variability was assessed in the same patients (calculating the s.d. of the mean value), the closest associations were found between home and asleep or between home and office systolic blood pressure variability measurements (coefficient r 0.42 and 0.44, respectively).[7]

HOME BLOOD PRESSURE VARIABILITY

In addition to the abovementioned results by Ushigome *et al.*[6] in diabetic patients, two previous studies have investigated blood pressure variability based on self-home measurements.[8,9] In a recent paper by Matsui *et al.*[8] studying untreated hypertensive patients, the maximum systolic blood pressure value from 14-day home monitoring was more closely related to cardiac and vascular damage than the average home blood pressure. More importantly, the maximum home blood pressure was independently predictive of target organ damage, even beyond average home blood pressure.[8] Moreover, in the Ohasama general population outcome study,

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Table 1 Features of variability assessed by different blood pressure measurement methods

Measurement method	*Advantages—disadvantages*
Office blood pressure (visit-to-visit variability)	Assessed within months or years. Prediction of cardiovascular events, stroke and all cause mortality. Treatment-induced decline related to vascular event prevention. Difficult to standardize in clinical practice.
Ambulatory blood pressure (continuous beat-to-beat variability by intra-arterial method; intermittent reading-to-reading variability by non-invasive method)	Assessed within 24 h (at maximum 15 min intervals). Prediction of target organ damage and cardiovascular risk. Little prognostic ability beyond that provided by mean ambulatory blood pressure or by office blood pressure variability. Not widely available. Not acceptable for repeated use in the long-term follow-up.
Home blood pressure (day-to-day variability)	Assessed within several days. Prediction of target organ damage and stroke (direct comparison with office or ambulatory blood pressure not available). Widely available and well accepted by users/patients for repeated use in long-term follow-up.

an increased level of home blood pressure variability was associated with a significant increase in cardiovascular and stroke mortality.[9]

AMBULATORY BLOOD PRESSURE VARIABILITY

The large amount of blood pressure data obtained by 24-h ambulatory monitoring during routine daily activities appear to give a unique opportunity to investigate blood pressure variability. Interestingly, in the retrospective analysis of the ASCOT-BPLA study, both the office and ambulatory blood pressure variability were lower in the amlodipine group compared with the atenolol group, suggesting that the two measurement methods might provide similar information on the effects of antihypertensive drug treatments on blood pressure variability.[3] However, the visit-to-visit blood pressure variability as assessed by office measurements had a larger effect on vascular events than the reading-to-reading variability assessed by ambulatory blood pressure monitoring.[3] These data are consistent with the results of an international database analysis that included 8938 subjects (International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcome (IDACO)), which showed that the blood pressure variability assessed by the 24-h ambulatory monitoring did not contribute much to risk stratification over and beyond the average ambulatory blood pressure.[10]

It should be noted that the original studies that demonstrated the prognostic value of ambulatory blood pressure variability were based on intra-arterial beat-to-beat blood pressure measurements.[5] Moreover, it has been shown that with non-invasive intermittent ambulatory blood pressure monitors, frequent measurements taken at no longer than 15-min intervals are required to provide an accurate assessment of blood pressure variability.[11] However, in both the ASCOT study[3] and the IDACO database,[10] less frequent ambulatory blood pressure measurements were obtained (30-min intervals for 24 h in the ASCOT study and 15–30 min intervals during the daytime, and 30–60-min intervals during the nighttime in the IDACO study). Thus, in these studies, the potential of non-invasive ambulatory blood pressure monitoring to reveal the clinical significance of blood pressure variability has not been exhausted.

THE OPTIMAL METHOD FOR ASSESSING BLOOD PRESSURE VARIABILITY

It is interesting that visit-to-visit, day-to-day and reading-to-reading blood pressure variability as assessed by office, home and ambulatory blood pressure measurements, respectively, have all been shown to predict cardiovascular event risk (Table 1). However, these different components of blood pressure variability may reflect different mechanisms, are likely to provide different information on cardiovascular regulation, and might have different clinical implications that are still poorly understood.[1]

The assessment of office blood pressure variability in repeated visits, although successful in the context of outcome trials such as the ASCOT[2,3] and the NHANES[4] studies, appears to be impractical for routine clinical use; first, because of poorly standardized office measurements and, second, because of the long time required for multiple visits. Regarding the 24-h ambulatory monitoring, the results of the ASCOT study and the IDACO database have been rather disappointing,[2,3,10] but further studies with more frequent readings must be performed. Moreover, ambulatory monitoring is not widely available and may not be suitable for repeated use in the long-term follow-up. In contrast, self-home blood pressure monitoring is widely available and very well accepted by patients who have made the decision to cover the cost of applying the technique. Thus, in clinical practice, the assessment of blood pressure variability by self-home measurements will probably be more feasible, as well as more reliable and cost-effective than both office and ambulatory blood pressure variability measurements, and more appropriate for repeated assessment in the long-term follow-up of treated hypertension.

BLOOD PRESSURE VARIABILITY IN CLINICAL PRACTICE

Even if agreement is reached among researchers on the optimal measurement method for assessing blood pressure variability (which will probably require a head-to-head comparison of the measurement methods), several fundamental questions remain to be resolved, such as the index that more accurately represents the impact of variability on the cardiovascular system, the optimal measurement schedule that gives a reproducible and reliable assessment of variability, the threshold to define increased variability, the effects of drugs on variability, and the effects of treatment-induced changes in variability on target organ damage and cardiovascular event risk. Until all these research questions are addressed, the blood pressure variability will largely remain a research issue, with little practical value for individual patients. Future prospective observational and interventional hypertension trials should take into account mean blood pressure together with its variability, aiming to resolve the abovementioned questions and to reveal a practical and efficient approach for applying the challenging concept of blood pressure variability in clinical practice.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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