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Editorial

Understanding the Augmented Blood Pressure Variability as a Clinical Marker of Cardiovascular Risk and Mortality

Gopal Krushna Pal*

Professor (Senior Scale), Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, INDIA.

High blood pressure is a leading risk factor for cardiovascular (CV) disease.[1] Most studies on CV risk assessment have used mean blood pressure as the indicator of risk, measured either in clinic or "out of office" settings.[2] Nevertheless, blood pressure demonstrates perceptible oscillations in short-term and long-term basis. Blood pressure oscillations during different time scales, known as Blood Pressure Variability (BPV), have become a focus of growing scientific interest. Historically, variability in blood pressure has been viewed as prescribing accurate measurement of mean blood pressure and as a phenomenon to be overcome by improved monitoring. Blood pressure oscillations during different time scales, known as BPV, have become a focus of growing scientific and clinical interest. For at least two decades, this variability has also been recognised as a potential risk factor in its own right.[2] In 2010, an analysis of three cohort studies and two randomised trials found that long-term variability in blood pressure was a predictor of stroke and coronary events in high-risk patients.[2] BPV can be measured at long-term (seasonal variability or visit-to-visit), at mid-term (differences in consecutive days or weeks) or at short-term (day-night differences or changes induced by other daily activities and conditions). An increased BPV, either at long, mid or short-term is associated with a poor cardiovascular prognosis independently of the amount of blood pressure elevation.[3] Nonetheless, there are several aspects of the relationship between BPV, antihypertensive treatment and clinical outcomes that are still unknown in therapeutic targets in clinical practice.

As high blood pressure is one of the most powerful determinants of cardiovascular disease risk, BP assessment should be done properly with all precautions. BP estimates, obtained punctually in the clinic or through measurements in different hours, days or weeks, if found to be high are associated with the risk of cardiovascular events and mortality. However, BP is not a static physiological parameter. It fluctuates most often due to the influence of a large number of internal and external factors. BPV is defined as the BP variation over different time scales that ranges from beat-to-beat of the heart, to hours, days, months to years. The importance of BPV is that such fluctuations are related with the development of organ damage, cardiovascular events and mortality, irrespective of the absolute degree of BP rise.[3] Such situations have fashioned a great attention in understanding of the mechanisms responsible for BPV, the different types of variability and the methods of assessment, as well as possible therapeutical interventions modifying several aspects of BPV.[3]

The types of BPV, their physiological regulation and methods of assessment depend on the time scale contemplated.[3] The short-term BP variability, usually defined as variations occurring in a 24 hr period of time, day-to-day, week-to-week and long-term variability including variations occurring among visits, in different seasons of the year, or even through several years, have different physiological and clinical implications. The physiological regulation of BP variations, as well as its derangements in the variations are complex processes. They constitute a mixture of cardiovascular regulatory mechanisms, as well as behavioural and environmental factors.[3] Several therapeutic interventions both by cardiovascular and non-cardiovascular drugs influence the magnitude BPV. Among the intrinsic mechanisms regulating BPV, baroreflex activity and arterial stiffness are considered to be the most important factors.[4] Short-term variability is highly dependent on the circadian rhythm of activity and sleep and, during sleep BP is particularly affected by sleep disturbances. The adherence to antihypertensive treatment and the duration of action of different antihypertensive drugs clearly influence day-to-day, week-to-week, as well as visit-to-visit variability.[3] Changes in weather and outdoor temperature are the main influencers of seasonal variability. Therefore, the assessment of very-short-term BPV requires continuous monitoring. This can be achieved by intra-arterial recording, or with the use of some non-invasive devices. Its use is usually restricted to monitor patients in intensive care units, emergencies or operation rooms. Continuous ambulatory non-invasive devices using finger plethysmography were developed several years ago, but were impractical for its use in ambulatory patients.[5,6] Short-term BPV is usually assessed by Ambulatory Blood Pressure Monitoring (ABPM) with oscillometric validated cuff devices, measuring BP at repeated intervals, usually from 15 to 30 min.[5] Home Blood Pressure Monitoring (HBPM) is the method of choice for assessing mid-term BPV, such as day-to-day

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or week-to-week changes. It is usually recommended to proceed to a 7-day period of measurement, twice per day, 3 repeated measurements each. The results of this schedule are very close to daytime BP obtained through ABPM.[6] Finally, office BP is usually the method of assessment of visit-to-visit variability or seasonal variability. As BPV is a major determinant of CVD risk and mortality. it is necessary to strictly adhere to a protocol of measurement, which should be always the same. Further, minor deviations can cause important differences in BP, which are not necessarily patient-dependent.[7]

Long-term higher magnitude of variability in blood pressure measured in adults at clinic visits is associated with cardiovascular and mortality outcomes, over and above the effect of mean blood pressure.[7] The mid-term (home monitoring) and short-term (ambulatory monitoring) variability in blood pressure is also associated with all-cause mortality. However, the association with cardiovascular disease outcomes requires with BPV requires further investigation in larger cohorts. Nevertheless, higher visit-to-visit systolic blood pressure variability is associated with increased risk of cardiovascular events in patients with hypertension, irrespective of baseline risk of cardiovascular events. Associations were stronger in younger patients and in those with lower mean systolic blood pressure.[8] Though mechanisms of BP regulation are complex, understanding the processes involved in BP variability is still intricate. Nevertheless, the BPV must be checked to be minimum to ensure a good cardiovascular health, especially in hypertensive patients irrespective of their age and gender.

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***Correspondence:**
Gopal Krushna Pal,
Editor-in-Chief, IJCEP,
Professor (Senior Scale), Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, INDIA.
Email: drgkpal@gmail.com

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