Fellows Corner

Blood Pressure Variability: The Basics and Beyond

By Sriram Sriperumbuduri

Blood pressure (BP) is a dynamic entity and, just like many other orders in nature, is affected by variability. Studies have shown variability in an individual’s BP over seconds, minutes, and days. This variability has been found to correlate with morbidity and mortality events. This review is intended to highlight some basic concepts of this entity with a focus on measures of variability and outcomes. The types of BP variability are shown in Table 1 (1).

Indices for measurement of short-term variability

Short-term variation is measured by 24-hour ambulatory BP monitoring (ABPM) through the following indices.

The standard deviation (SD) of 24-hour average BP values is used widely, but its main drawback is that it represents the dispersion of values around the mean but does not account for the order in which BP measurements are obtained. It is sensitive to the low sampling frequency of noninvasive BP monitoring.

The weighted mean of daytime and nighttime values is used because the nighttime fall in BP has more effect on an accurate BP variability assessment. In the study by Bilo et al. (2), the weighted 24-hour SD of BP removed the mathematical interference from the nighttime fall in BP and correlated better with end-organ damage.

The coefficient of variation (CV) is the ratio of the average SD of BP and the mean BP multiplied by 100.

The average real variability (ARV) is a more reliable prognostic indicator than SD because it is sensitive to the order of individual BP measurements. First described by Mena et al. (3) in 2005, ARV represents a reliable index inspired by a total variability concept of real analysis in mathematics. For example, Figure 1 shows that two subjects with different BP measurement sets could have the same SD but different ARVs: clearly, subject b with more variability has a higher ARV than subject a, who has less variability despite a similar SD. Therefore, the SD index may not always reflect data variability.

In their study of 312 subjects, Mena et al. (3) tested the performance of ARV versus SD and showed a statistically significant relative risk of 4.548 for cardiovascular (CV) events in the group with higher BPV with respect to low BPV with ARV. The relative risk for the SD index was not significant statistically. Thus, ARV may be a better measure based on which patients could be treated.

Significance of BP variability

Increased BP variability has been reported to be associated with adverse CV outcomes; hence, there has been a resurgence in studies investigating this area. This is beyond a mere assessment of circadian BP patterns (e.g., nocturnal dipping status, morning surge), which have been known for a while to be associated with adverse outcomes.

In a post hoc analysis of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) (4), which included 25,814 patients, the higher visit-to-visit variability (VVV) of systolic BP to SBP (defined as the SD of SBP measurements over seven visits) was associated with an increased risk for CV disease and mortality. The hazard ratio for SBP variability in a comparison of study participants in the highest versus the lowest quintile of SD (>14.4 mm Hg vs. <6.5 mm Hg) was 1.30 (95% confidence interval [CI], 1.06 to 1.59) for fatal coronary heart disease or nonfatal myocardial infarction, 1.58 (CI, 1.32 to 1.90) for all-cause mortality, 1.46 (CI, 1.06 to 2.01) for stroke, and 1.25 (CI, 0.97 to 1.61) for heart failure.

Vertedich et al. (5) analyzed the association of ambulatory BP variability with mortality and CV events by studying 7112 individuals with untreated hypertension; their mean age was 52 years, and the median follow-up time was 5.5 years. The nighttime systolic BP SD of ≥12.2 mm Hg was associated with a 41% greater risk of CV events, a 55% greater risk of CV death, and a 59% increased risk of all-cause mortality in comparison with an SD of <12.2 mm Hg. The authors suggested that the addition of BP variability to models of long-term outcomes in hypertensive patients would increase the predictive value for long-term outcomes.

Impact of treating BP variability

Inasmuch as both short-term and long-term variability have shown an association with CV events, treating variability might be a beneficial target for CV protection. In the Anglo-Scandinavian Cardiac Outcomes Trial Blood Pressure Lowering Arm (ASCOT-BPLA) trial (6), both VVV and ABPM BP variability were reduced by amlodipine, which likely contributed to the reduced event rate in that group versus atenolol. A study by Hoshino et al. (7) of 31 patients showed the effect of chronotherapy; the administration of amlodipine and olmesartan at bedtime reduced the morning BP surge, corrected the nocturnal BP fall, and improved urine albumin excretion.

Thus, BP variability represents an interesting entity with a wide scope for review and research. Many questions and avenues are still to be explored in this area.

What are the mechanistic explanations for the difference in variability? Would any interventions favorably change this variability, and would these interventions have a beneficial effect on clinical outcomes? More research is needed.

References


Figure 1. Comparison of the two measures of BP variability

The standard deviation (SD) is similar in the two subjects (a) and (b) but the average real variability (ARV) is variable. The calculation is based on the following computer-based formula, from the 24-hour ambulatory BP monitoring data: ARV = \[ N \cdot \left( \frac{1}{2} \cdot \text{SBP} + 1 - \text{BP} \right) \] where N = number of valid BP measurements and K = order of measurements from each subject’s monitoring.
Table 1. Types of BP variability

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<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>TYPE</th>
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<tbody>
<tr>
<td></td>
<td>VERY SHORT TERM</td>
</tr>
<tr>
<td>What is it?</td>
<td>Beat-to-beat changes in BP</td>
</tr>
<tr>
<td>What causes it?</td>
<td>Interaction between RAS, vascular myogenic response, and NO release from endothelium</td>
</tr>
<tr>
<td>How is it measured?</td>
<td>Specialized finger cuffs</td>
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</tbody>
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RAS, renin-angiotensin system; NO, nitric oxide; ABPM, ambulatory BP monitoring; OBPM, office BP monitoring; HBPM, home BP monitoring.

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