

Research Article

# Ambulatory Arterial Stiffness Index and circadian blood pressure variability



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## Abstract

The manner in which the circulation accommodates each heartbeat may underlie blood pressure (BP) variability. We used the Ambulatory Arterial Stiffness Index (AASI), which reflects this ventricular–vascular interaction, in untreated individuals with prehypertension and Stage 1 hypertension to evaluate two different measures of BP variability using the brachial pulse pressure (PP) obtained over 24 hours. We enrolled 64 untreated adults with systolic BP between 130–159 mm Hg and diastolic values of <100 mm Hg who underwent 24-hour ambulatory BP monitoring with calculation of 24-hour AASIs. Variability in brachial PP was determined using the standard deviation of the measurements over 24 hours and the average real variability. The 24-hour AASI correlated with both measures of 24-hour PP variability ( $P < .001$  for both). Subdividing the 24-hour stiffness index into daytime and nighttime components showed modest differences in their relationship to PP variability, with the daytime being significantly different from 24-hour AASI and the standard deviation of the brachial PP consistently having a higher correlation to the AASI when compared with the average real variability. These observations may be useful to understand differences in variability measures of BP measurements, such as PP, to measures like the AASI as reported in longitudinal studies. *J Am Soc Hypertens* 2015;9(9):705–710. © 2015 American Society of Hypertension. All rights reserved.

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## Introduction

An increase in blood pressure (BP) variability is associated with adverse cardiovascular outcomes.<sup>1–3</sup> However, the physiological mechanisms that underlie such variability remain unclear. Increased arterial stiffness is one potential mechanism because it is more difficult to maintain a steady mean arterial pressure via fluctuations in systemic vascular resistance when arterial stiffness is likely to magnify the pressure effects of small fluctuations in stroke volume. In

addition, a stiffer vessel may not “report” the degree of stretch in a baroreceptor like those found in the carotid sinus resulting in less autonomic input to dampen BP.<sup>4,5</sup>

The measurement of arterial stiffness has several approaches. These include methods such as a noninvasive estimate of pulse wave velocity<sup>6</sup> which reflect stiffness in large vessels like the aorta or methods that analyze the interaction between the diastolic and systolic pressures over a period of observation (typically 24 hours) using regression approaches like the Ambulatory Arterial Stiffness Index (AASI).<sup>7</sup> Methods such as the AASI may provide more insight into the nonlinear relationship between distending pressure and BP<sup>8</sup> over the course of 24 hours because AASI captures data over the course of a day and a night, as opposed to pulse wave velocity which captures data supine at a single moment.

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There are several methods that quantify variability. A commonly used method is the simple calculation of the standard deviation (SD) around the mean BP value. A second method is the calculation of the average real variability (ARV).<sup>9</sup> ARV may be more suitable when assessing BP variability more than a 24-hour period because it reflects changes on a measurement-by-measurement basis and is not subject to the limitation of the SD which measures dispersion around a single mean value and is enhanced when patients show a normal “dipping” pattern characterized by daytime readings which are higher than nighttime BP readings.<sup>9</sup>

In this study, we examined the relationships between AASI and BP variability in an untreated sample of subjects with prehypertension and Stage 1 hypertension. We measured BP variability using the SD and the ARV of 24-hour pulse pressure (PP) measurements in our cohort, and we evaluated the variability measures within the day versus nighttime segments. We examined variability within the PP as our BP metric because PP is felt to be the most relevant standard clinic BP measure related to arterial stiffness.<sup>10</sup> Our objective in this study was to examine variability measures of the brachial PP profile over 24 hours, as well as within the daytime and nighttime settings, and to determine if two different ways of measuring variability generate similar results. Furthermore, we sought to examine how well measures of variability within the PP were related to the AASI during the full 24 hours, as well as during the day and night segments.

## Methods

### Participants

Participants included 64 adults between the ages of 22 and 69 years with untreated systolic BP in the range of 130–160 mm Hg and diastolic BP <100 mm Hg. We excluded people with current use of any medications or dietary supplements that could affect BP, body mass index >40 kg/m<sup>2</sup>, presence of diabetes mellitus, presence of cardiovascular disease, autonomic neuropathy, current tobacco use, renal insufficiency defined as an estimated glomerular filtration rate of less than 60 mL/min/1.73 m<sup>2</sup>, >10 alcoholic drinks per week in women and >15 alcoholic drinks per week in men, pregnancy, or postpartum <3 months.

Participants were recruited by flyers placed in the hospital and university campus and by advertisements placed in local papers and online advertising using craigslist. The University of Pennsylvania Institutional Review Board approved this single center study, and all subjects provided written, informed consent. The study was registered at the Clinical Trials Web site as NCT00328666. These participants were originally recruited as part of a study comparing the efficacy of various BP lowering interventions.<sup>11</sup> In this

article, we report only cross-sectional data before any intervention.

### Study Protocol

Screening BP and heart rate were measured in the morning after a 12-hour fast using a Accutorr Plus (Datascop, Mahwah, NJ, USA) device with an appropriate sized cuff after individuals were seated for 5 minutes. Three readings were obtained, separated by 1-minute intervals and the average of these readings determined eligibility.<sup>11</sup>

Eligible subjects returned to the Clinical & Translational Research Center for an inpatient stay during which time an ambulatory blood pressure monitor (ABPM) recording was performed over 24 hours using Spacelabs model 90207 monitors (Issaquah, WA, USA). The ABPM was programmed to measure BP every 20 minutes from 6 AM to 10 PM and every 30 minutes between 10 PM and 6 AM. ABPM data were determined to be satisfactory if there were at least 48 (80%) acceptable readings (systolic blood pressure between 70 and 280 mm Hg and diastolic blood pressure between 40 and 150 mm Hg) between 6 AM and 12:00 midnight and six acceptable readings between midnight and 6 AM. During their time in the Clinical & Translational Research Center, subjects were allowed to be ambulatory ad lib.

### PP Calculation

The PP was calculated for each measurement as (systolic BP – diastolic BP).

### AASI Calculation

We calculated AASI as 1 minus the regression slope of the diastolic on the systolic BP using the ABPM data as reported by others.<sup>7,8,12</sup> Subjects kept a diary in which sleep and waking times were recorded. AASI was calculated for each subject using 24-hour data, as well as the self-reported daytime and nighttime data for PP, calculated as the systolic minus the diastolic pressure for each measurement.

### Variability Calculations

We calculated the SD of the 24 hours and the daytime and nighttime PP values using standard statistical procedures available within Stata version 12 (StataCorp, College Station, TX, USA). ARV was calculated using a template developed within Microsoft Excel by two of the authors (K.M.D. and P.V.). The template was developed using the formula for ARV proposed by Mena [1] where N represents the number of BP readings in an ambulatory BP monitoring data set for a subject.<sup>9</sup>

$$ARV = \frac{1}{N-1} \sum_{k=1}^{N-1} |BP_{k+1} - BP_k| \quad [1]$$

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