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Research Article

# Racial impact of diurnal variations in blood pressure on cardiovascular events in chronic kidney disease

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## Abstract

Ambulatory blood pressure parameters, nocturnal dipping and morning surge, are associated with cardiovascular outcomes in several populations. While significant variation exists between racial groups in ambulatory blood pressure measurements and the incidence of cardiovascular disease, the effect of race on the associations of dipping and morning surge with cardiovascular outcomes is unknown. In a prospective analysis of 197 African American and 197 Japanese individuals with non–diabetic chronic kidney disease matched by age and renal function, we analyzed the associations of dipping and morning surge with cardiovascular events for both races and assessed whether these relations differed by race. Higher sleep–trough morning surge was independently associated with cardiovascular events in Japanese (hazard ratio, 1.93 per 10 mm Hg; 95% confidence interval, 1.20–3.10) but not in African American participants, with race an effect modifier (*P*–value <.01). Dipping was not associated with cardiovascular events in either racial group. In individuals with chronic kidney disease, the association between morning surge and cardiovascular events appears to be dependent upon race, with higher morning surge a risk factors in Japanese but not in African Americans. J Am Soc Hypertens 2015;9(4):299–306. 

*Keywords:* Ambulatory blood pressure; African Americans; coronary artery disease; Japanese; stroke.

## Introduction

Just as the risk of stroke and other cardiovascular diseases varies by geographic region and race, so too do the risk factors responsible for these diseases.[1–4] While hypertension is universally recognized as a risk factor for cardiovascular disease, there is increased appreciation that diurnal blood pressure characteristics determined by 24–hour ambulatory blood pressure monitoring (ABPM) have potentially greater prognostic value, and that these characteristics differ among racial groups.[5–7]

Two such diurnal characteristics that may predict future cardiovascular events are blood pressure dipping and morning blood pressure surge.[8–10] Reduced nocturnal blood pressure dipping is associated with an increased risk of myocardial infarction, stroke, congestive heart failure, and overall mortality.[11–13] Conversely, increased sleep to awake morning blood pressure surge is related to an increased risk of cardiovascular events in some populations.[9,14,15]

The African American Study of Kidney Disease and Hypertension (AASK) Cohort study trial was conducted by the AASK Investigators with support from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In addition, AASK was supported by the Office of Research in Minority Health. King Pharmaceuticals, Pfizer, AstraZeneca Pharmaceuticals, GlaxoSmithKline, Forest Laboratories, Pharmacia, and Upjohn donated antihypertensive medications. The data from the AASK trial reported here were supplied by the NIDDK Central Repositories. This work does not necessarily reflect the opinions of the AASK study or the NIDDK. Dr McMullan was funded by the ASN Research Fellowship - 2012D000333. Dr Yano was supported by a grant-in-aid from the Foundation for the Development of the Community, and a research grant from Manpei Suzuki Diabetes Foundation.

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Diurnal blood pressure patterns differ between racial groups. As an example, African American and Afro–Caribbean individuals have attenuated nocturnal blood pressure dipping compared with whites, despite similar clinic blood pressures.[7,16,17] In addition, the association of attenuated dipping with surrogate markers for cardiovascular disease is stronger among African Americans than white individuals.[6,17] Likewise, the relation between an increased morning blood pressure surge and cardiovascular events may differ according to race; an increased risk was described in Japanese, but a decreased risk was reported in white populations.[15,18,19]

Individuals with chronic kidney disease (CKD) have not only an increased prevalence of hypertension but also an increased prevalence of abnormal diurnal blood pressure characteristics.[20] As glomerular filtration rate deteriorates, nocturnal blood pressure increases, and many individuals shift from a dipping to a non–dipping pattern; similarly, there is a reduction in morning blood pressure surge among those with CKD.[21]

The prospective association of morning blood pressure surge with cardiovascular events in individuals with CKD is unknown. Likewise, the effect of race on the associations of dipping and morning surge with cardiovascular outcomes has not been reported. Thus, we compared diurnal blood pressure characteristics in a matched population of African American and Japanese individuals with non–diabetic CKD to determine the associations of nocturnal blood pressure dipping and morning blood pressure surge with cardiovascular events, and to determine whether these relations differed by race.

## Methods

### *Study Population*

Three cohorts were combined to create the study population: the Jichi Medical School ABPM study, the Miyazaki ABPM study, and the African American Study of Kidney Disease and Hypertension (AASK) Cohort study. Details of these three cohorts have previously reported.[22,23] Briefly, the Jichi study enrolled 811 hypertensive Japanese participants without pre-existing cardiovascular disease (mean age ± standard deviation, 72.3 ± 9.8 years; 38% male) from 1992 to 1998.[22] The Miyazaki study enrolled 596 hypertensive Japanese individuals (72.9 ± 8.3 years; 42% male) between 2007 and 2009.[22] The AASK cohort study was a 5–year prospective observational study of 795 African American patients with non–diabetic CKD who had completed the AASK trial in 2002.[23] Of the 795 patients followed in the AASK cohort, 646 subjects (60.5 ± 10.1 years) had an initial 24–hour ABPM measurement performed between the years 2002 and 2007.

Due to large baseline differences between the Japanese and African American populations in prevalence of diabetes mellitus, age, and renal function (based on estimated glomerular filtration rate [eGFR]), we matched African Americans and Japanese based upon estimated glomerular filtration rate (eGFR; ±6 mL/min/1.73 $m^2$) and age (±4 years). Among the 493 African American and 569 Japanese individuals with an eGFR <65 mL/min/1.73 $m^2$, 197 pairs (394 total individuals) were identified.

### *ABPM*

Twenty–four hour ABPM was performed in the AASK cohort with the Space–Labs 90,207 Ambulatory BP Device (Redmond, WA) as described previously.[23] In the Jichi and Miyazaki cohorts, the Nippon Colin Co ABPM–630 device (Komaki, Japan) and the A&D TM–2421 and TM–2425 devices (Tokyo, Japan) were used as previously described[9,24] with prescribed anti–hypertensive medication held for 14 days prior to ABPM in the Jichi cohort but continued in the Miyazaki and AASK cohort.[9,23,24] In each cohort, blood pressure was measured every 30 minutes for a 24–hour period, and all participants completed a sleep diary documenting the time they went to bed and the time they rose in the morning. We excluded those individuals whose 24–hour ABPM measurements yielded less than 80% of readings while awake or less than 80% of readings while asleep. In addition, we excluded those who reported going to bed between 6AM and 6PM.

Nocturnal systolic blood pressure was defined as the mean of measurements occurring after going to bed and before awakening, while daytime systolic blood pressure was defined as the mean of readings during the awake period. The morning systolic blood pressure was defined as the mean of systolic blood pressure measurements taken during the first 2 hours after awakening. The sleep nadir systolic blood pressure was defined as the mean of three systolic readings, specifically the lowest night time systolic blood pressure and the systolic blood pressures measured immediately before and immediately after the lowest night time measurement. Using the aforementioned definitions, we calculated nocturnal dipping as previously described and expressed it as a percentage of the daytime systolic pressure ($100 \times [1 - \text{nocturnal systolic blood pressure}] \div$ daytime systolic blood pressure).[9] Sleep–trough morning blood pressure surge (ie, morning surge) was calculated as the morning systolic pressure minus the sleep nadir systolic pressure (Figure 1).[9]

### *Covariates*

Demographic and clinical data were collected on all participants in the cohorts at baseline using standardized