ORIGINAL ARTICLE

Race, Plasma Renin Activity, and Morning Blood Pressure Surge—Results From the Dietary Approaches to Stop Hypertension Trial

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BACKGROUND
The association of preawake (difference between pre- and postwaking blood pressure (BP)) and sleep-through surge (difference between sleeping nadir and postwaking BP) with cardiovascular events is unclear. Examination of factors associated with surge may provide novel insights. We examined the association of race, which associates with nocturnal dipping, and plasma renin activity (PRA) with preawake and sleep-through surge among individuals on a controlled diet.

METHODS
We performed a post hoc analysis of 323 subjects from the Dietary Approaches to Stop Hypertension trial who had available 24-hour BP data and who ingested a control diet during a 3-week run-in period. Linear regression models were fit to estimate the association of race and PRA with preawake and sleep-through surge.

RESULTS
Of the 323 individuals, 55% were black, 53% were men, and the average age was 45 years. After controlling for other factors, black race was associated with a 3.2 mm Hg lower preawake and a 3.7 mm Hg lower sleep-through surge compared with nonblacks. In nonblacks, higher PRA was associated with greater preawake surge only. There was no association of PRA with either preawake or sleep-through surge in blacks. Additional adjustment for dipping status resulted in attenuation of the race–surge associations.

CONCLUSIONS
Black race is associated with lower preawake and sleep-through surge compared with nonblacks, but the effect is partially attenuated by dipping status. Higher PRA appears to be associated with a higher preawake surge in nonblacks only. Further research should address if morning surge is definitively associated with clinical outcomes in racial subgroups, independent of dipping.

Keywords: blood pressure; DASH; hypertension; racial differences; renin.

doi:10.1093/ajh/hpt031

Blood pressure (BP) increases abruptly (surge) upon wakening, a phenomenon associated with heightened activity of the sympathetic nervous system and alpha-mediated vasoconstriction.[1, 2] Various definitions have been proposed for morning surge, including preawake surge (the difference between pre- and postwaking BPs) and sleep-through surge (the difference between the nadir nighttime and postwaking BPs).[3] There are conflicting reports with regard to the association of higher morning systolic BP (SBP) surge with the development of adverse clinical outcomes.[4–7]

Despite blacks having a higher burden of hypertension-associated disease,[8–10] a prior report has documented less (rather than greater) sleep-through BP surge among black individuals.[11] However, this finding may have been confounded by a variety of factors, including diet, which is known to have a potent role in the determination of BP.[12] In addition, previous studies have not evaluated whether proposed racial differences in surge are related to plasma renin activity (PRA), which is known to follow a diurnal pattern (greater in the second half of sleep)[13, 14] and is usually lower in blacks than nonblacks.[15]

To further investigate these associations, we performed post hoc analyses of individuals who consumed a controlled diet in the Dietary Approaches to Stop Hypertension (DASH) trial. We hypothesized that racial differences in morning surge would persist in the presence of a controlled diet and that PRA may contribute to the racial differences in morning surge.

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Initially submitted November 13, 2012; date of first revision February 12, 2013; accepted for publication February 12, 2013; online publication March 8, 2013.

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METHODS

Study population

The DASH Trial was a multicenter, randomized, controlled study designed to investigate the effect of 3 dietary interventions on BP.[12] All centers had individual institutional review board approval, and all participants provided written informed consent. The present analyses were deemed exempt by the Partners Institutional Review Board.

The design of the trial has been described previously.[12] Briefly, a total of 459 adult subjects aged ≥22 years were enrolled in 5 separate cohorts over a 2-year period. Ambulatory BP was measured in the last 4 cohorts only (n = 362). Criteria for study inclusion included a screening systolic BP of <160 mm Hg and diastolic BP of 80–95 mm Hg without use of antihypertensive medications. Major exclusion criteria were poorly controlled diabetes mellitus, hyperlipidemia, a cardiovascular event within the prior 6 months, renal insufficiency (estimated glomerular filtration rate < 60 ml/min/1.73m^2 or serum creatinine > 1.5 mg/dl for men or > 1.3 mg/dl for women), chronic disease that could potentially interfere with participation in the trial, pregnancy or breast-feeding, body mass index > 35 kg/m^2, antihypertensive medication use, unwillingness to cease vitamin supplements or calcium/magnesium–containing antacids, and alcohol intake > 14 drinks per week. A designated a priori goal was to recruit two-thirds of the subjects from a racial or ethnic minority.

Trial design

The trial was conducted in 3 phases—screening, run-in, and intervention. In the screening phase, participants continued their normal diet. During the 3-week run-in period all participants were fed a control diet low in fruits, vegetables, and dairy but high in total and saturated fat (similar to typical dietary intake in the United States). The sodium content of the control diet was approximately 3 g/day. Adherence was assessed by self-report, direct observation, and 24-hour urine sodium evaluation. Further details on the DASH Trial have been published previously.[12,16,17]

Ambulatory BP measurements

Ambulatory recordings for the last 4 recruited cohorts only were acquired at the end of run-in (during the 3rd week of the controlled typical US diet) using the Space Labs 90207 device (Space Labs, Redmond, Washington). BP acquisition was programmed to occur every 30 minutes over a period of at least 24 hours. We excluded those with abnormal sleep/wake cycles (defined as going to sleep between 4 AM and 6 PM or waking up before 4 AM or after noon)[18] and those with missing data (>2 hours without readings) critical to the calculation of morning surge. In addition, we excluded individual readings obtained within 10 minutes of a prior reading and restricted BP data to a maximum of 24 hours. Finally, we excluded those with <75% acceptable readings (SBP of 70–240 mm Hg; DBP of 40–150 mm Hg) throughout the monitoring period. The final cohort for this study consisted of 323 individuals.

Other measurements

Demographic variables (age, sex, race), baseline weight, height, alcohol intake, smoking history, estimated annual income, and anthropometric variables were recorded at baseline. In addition, clinic BPs were recorded twice, 30 seconds apart, at each of 3 screening visits and 4 visits during the last week of the run-in period. These readings were taken by trained staff using a random-zero mercury sphygmomanometer and an appropriately sized cuff after subjects had been seated quietly for 5 minutes.[12] At each of these visits, the 2 BPs were averaged. Baseline clinic BP was calculated as the average reading over these 7 visits.

Exposures and outcomes

The primary exposures of interest for this study were self-reported race (black vs. nonblack) and PRA. PRA was measured by radioimmunoassay from stored venous blood samples collected from each individual after an overnight fast after being seated upright for at least 90 minutes. Because of a highly right-skewed distribution, PRA was log-transformed for all regression analyses.

The primary outcomes of interest were morning preawake and sleep-through SBP surge. Preawake SBP surge was defined as the difference between the mean SBP during the 2 hours immediately after waking and the mean SBP during the 2 hours immediately before waking. Sleep-through SBP surge was defined as the difference between the mean SBP during the 2 hours immediately after waking and the mean SBP during the nighttime hour that included the lowest (nadir) SBP.[3,19,20] Preawake and sleep-through SBP surge were calculated using the individual sleep and wake periods that each participant recorded in their diary during the ambulatory BP monitoring. Consistent with prior reporting from this study, daytime BPs were calculated as the mean of the values recorded between 8 AM and 6 PM; nighttime BPs were recorded as the mean of values recorded between 10 PM and 6 AM.[18]

Statistical analysis

Continuous variables were examined graphically and recorded as means (± SDs) for normally distributed data or medians (with interquartile ranges) for nonnormally distributed data. Comparisons were made using *t* tests, Wilcoxon rank sum tests, analysis of variance, or Kruskal–Wallis tests, as appropriate. Categorical variables were examined by frequency distribution and recorded as proportions, and comparisons were made using the χ^2 test.

The associations of race with preawake and sleep-through SBP surge were estimated by fitting unadjusted and adjusted linear regression models. Adjusted associations were estimated in hierarchical models that included terms for potential confounding covariables that were not felt to plausibly lie on causal pathways. Model 1 was adjusted for race (black vs non-black), sex (male vs female), age and clinical site; Model 2 was additionally adjusted for baseline weight, height, alcohol intake (0, 1–2, >2 drinks per week), annual income (<$30,000, $30–59,000, >$59,000),

sub-scapular skin-fold thickness and smoking history (≥100 or <100 cigarettes in lifetime); Model 3 was adjusted for the same variables as Model 2, with the addition of mean ambulatory 24-hour blood pressure. Linearity of continuous variables was inspected graphically and by comparative model fit diagnostics. The associations of $\log_e$PRA with preawake surge and sleep-through surge were examined in a similar fashion within black and nonblack subgroups. In exploratory models, nocturnal dipping status (dipper (nocturnal BP dip >10%) vs. nondipper) was added to the list of covariables in model 3.

Nominal 2-sided P values < 0.05 were considered statistically significant. Analyses were performed using STATA 10.0MP (STATA, College Station, TX).

RESULTS

Characteristics at the end of the run-in period

The mean age of the cohort was 45.1 ± 10.4 years; 53.2% were men; 55.1% were black. Black subjects were more likely to be female, were younger, were of shorter stature, had greater subscapular skin-fold thickness, consumed fewer alcoholic beverages per week, and had lower income than nonblack subjects. No significant differences were noted in baseline weight, smoking history, or 24-hour urinary sodium excretion between groups (Table 1).

There were no differences in standard office SBP, mean 24-hour ambulatory SBP, or daytime or nighttime ambulatory SBP according to race at the end of the run-in period. Black individuals had significantly less nocturnal dipping than nonblacks and demonstrated less preawake SBP surge (11.2 vs. 14.3 mm Hg; P = 0.01) and less sleep-through SBP surge (17.5 vs. 21.4 mm Hg; P = 0.001) compared with nonblacks (Table 2). Blacks also had lower absolute (0.52, IQR = 0.22–0.89 vs. 1.18, IQR = 0.59–2.22) and log-transformed PRA (−0.70 ± 0.90 vs. 0.14 ± 0.88) than nonblacks at the end of the run-in period (P < 0.001 for both).

Association of race with preawake SBP surge

Black race was significantly associated with less preawake surge in unadjusted (-3.2 mm Hg; P = 0.01) and fully adjusted models (model 3: −3.2 mm Hg; P = 0.03) (Table 3). Upon additional adjustment for $\log_e$PRA in the fully adjusted model, the association of race with preawake surge became attenuated (−2.6 mm Hg vs. nonblacks; P = 0.09), suggesting that PRA may be a pathway intermediate of the association of race with preawake surge.

Association of PRA with preawake surge according to race

In further analyses, the association of $\log_e$PRA was examined in black and nonblack subgroups separately. In nonblacks, each unit increase in $\log_e$PRA was associated with a 3.4 mm Hg greater preawake surge (P = 0.01) in fully adjusted models (model 3). In blacks, each unit increase in $\log_e$PRA was nonsignificantly associated with a 0.9 mm Hg greater preawake surge (P = 0.35).

Table 1. Baseline characteristics according to racial background[a]

Characteristics	Total cohort	Racial Background		P value[b]
		Nonblack	Black	
No.	323	145	178	
Men, %	53.2	71.0	38.8	<0.001
Age, years	45.1 ± 10.4	46.8 ± 11.6	43.7 ± 9.2	0.01
Baseline weight, kg	82.2 ± 14.9	81.9 ± 14.9	82.4 ± 14.9	0.73
Height, cm	170.9 ± 9.4	172.7 ± 9.5	169.5 ± 9.2	0.003
Subscapular skin-fold thickness, cm	22.6 ± 8.4	19.9 ± 7.4	24.9 ± 8.4	<0.001
Annual income, $				<0.001
<30,000	32.2	20.0	42.1	
30,000–59,000	43.0	44.8	41.6	
>59,000	24.8	35.2	16.3	
Alcohol, drinks/week				0.002
None	61.6	51.7	69.7	
1–2	20.7	23.5	18.5	
>2	17.7	24.8	11.8	
Smoked ≥100 cigarettes ever, %	39.3	35.2	42.7	0.17
Urine sodium, mg/day	3152 ± 1,098	3219 ± 1,070	3091 ± 1,123	0.32

[a]Continuous variables are expressed as means ± SDs.
[b]P value for difference; significance testing by t test for continuous variables and χ^2 test for categorical variables.

Table 2. Systolic blood pressure parameters at end of run-in period according to racial background[a]

Mean BP parameter, mm Hg	Total cohort	Racial background		*P* value[b]
		Nonblack	Black	
Office SBP[c]	131 ± 11	131 ± 11	131 ± 11	>0.90
24-hour ASBP	131 ± 11	131 ± 11	131 ± 11	>0.90
Daytime ASBP[d]	137 ± 12	138 ± 12	137 ± 21	0.23
Nighttime ASBP[e]	122 ± 12	121 ± 12	123 ± 12	0.17
Mean awake SBP	137 ± 11	137 ± 11	136 ± 11	0.41
Mean sleep SBP	120 ± 12	118 ± 12	121 ± 11	0.06
Nocturnal decline in ASBP[f]	15 ± 9	17 ± 10	14 ± 8	<0.001
Preawake SBP surge[g]	13 ± 10	14 ± 11	11 ± 10	0.01
Sleep-through SBP surge[h]	19 ± 11	21 ± 11	17 ± 10	0.001

Abbreviations: ASBP, ambulatory systolic blood pressure; BP, blood pressure; SBP, systolic blood pressure.
[a]Continuous variables are expressed as means ± SDs.
[b]*P* value for difference; significance determined by *t* test.
[c]Average SBP over 3 screening visits and 4 separate days during the last week of run-in.
[d]Average SBP between 8 AM and 6 PM.
[e]Average SBP between 10 PM and 6 AM.
[f]Average daytime SBP minus average nighttime SBP.
[g]Average SBP in 2 hours postwakening minus average SBP in 2 hours prewakening
[h]Average SBP in 2 hours postwakening minus average SBP in nighttime hour with lowest SBP.

Table 3. Unadjusted and adjusted associations of race (black vs. nonblack) with preawake and sleep-through morning systolic blood pressure surge

Model	Mean difference for black vs. Nonblacks	
	Preawake surge, mm Hg	Sleep-through surge, mm Hg
Unadjusted	−3.2 (−5.4 to −0.9) *P* = 0.01	−3.9 (−6.2 to −1.6) *P* = 0.001
Model 1	−3.0 (−5.6 to −0.4) *P* = 0.02	−3.2 (−5.9 to −0.5) *P* = 0.02
Model 2	−3.1 (−5.9 to −0.3) *P* = 0.03	−3.6 (−6.5 to −0.7) *P* = 0.02
Model 3	−3.2 (−6.0 to −0.3) *P* = 0.03	−3.7 (−6.6 to −0.9) *P* = 0.01

Linear regression models were fit with effect estimates presented as beta coefficient (95% confidence intervals) and *P* value for difference. Model 1 was adjusted for race (black vs. non-black), sex (male vs. female), age, and clinical site. Model 2 was additionally adjusted for baseline weight, height, alcohol intake (0, 1–2, >2 drinks per week), annual income (<$30,000, $30,000–$59,000, >$59,000), subscapular skin-fold thickness, and smoking history (≥100 or <100 cigarettes in lifetime). Model 3 was adjusted for the same variables as model 2, with the addition of mean ambulatory 24-hour blood pressure.

Association of race with sleep-through SBP surge

Black race was significantly associated with less sleep-through SBP surge in unadjusted (−3.9 mm Hg vs. nonblacks; $P = 0.001$) and fully adjusted models (−3.7 mm Hg vs. nonblacks; $P = 0.01$), as shown in Table 3. Upon additional adjustment for $\log_e$PRA in the fully adjusted model (model 3), the association of race with preawake surge was slightly attenuated (−3.2 mm Hg vs. nonblacks; $P = 0.049$).

Associations of PRA with sleep-through surge according to race

No significant association of $\log_e$PRA with sleep-through surge was noted in either nonblack (2.0 mm Hg per unit increment in $\log_e$PRA; $P = 0.13$) or black subgroups (1.0 mm Hg per unit increment in $\log_e$PRA; $P = 0.31$).

Influence of nocturnal dipping on race–surge associations

In exploratory models, the effect of nocturnal dipping on the race–surge relationship was assessed by inclusion of dipping status (dipper vs. nondipper) as an additional covariable to model 3. The effect estimates for black vs. nonblack with respect to both preawake (−2.3 mm Hg, 95% confidence interval (CI) = −4.9 to 0.3 mm Hg; $P = 0.09$) and sleep-through surge (−3.0 mm Hg, 95% CI = −5.7 to −0.2 mm Hg; $P = 0.03$) were somewhat attenuated, suggesting that at least part (but not all) of the blunted surge in blacks may be related to less nocturnal dipping.

With respect to the association of PRA with preawake and sleep-through surge, there were no qualitative differences in findings after addition of dipping status to the fully adjusted models: greater PRA remained significantly associated with greater preawake surge in the nonblack

subgroup only (2.6 mm Hg per unit increment in $\log_e$PRA; $P = 0.03$).

DISCUSSION

To our knowledge, this is the first study to examine the association of race and PRA with preawake and sleep-though SBP surge in individuals who participated in a controlled dietary intervention. We found that (i) blacks had significantly less preawake and sleep-through SBP surge than non-blacks; (ii) racial differences in preawake surge were attenuated after controlling for PRA and dipping status; and (iii) higher PRA was associated with greater preawake morning SBP surge in nonblacks but not in blacks.

Racial differences have been previously reported in relation to morning BP surge, but there were important limitations associated with these studies. Haas *et al.* found that blacks had 3.8 mm Hg less sleep-through SBP surge than nonblacks in unadjusted analyses ($P = 0.01$). However, upon adjustment for sex, age, and body mass index, the estimated difference attenuated to 2.5 mm Hg and was no longer statistically significant. The lack of a controlled diet and limited information regarding potential demographic confounders were significant limitations of that study.[11] Similarly, Neutel *et al.* reported that blacks had less preawake surge than nonblacks in a post hoc analysis of the PRISMA I and II studies; however in this analysis, blacks constituted only 5% of the overall cohort and again a controlled diet was not enforced.[21]

In our analyses, we found that blacks had lower preawake and sleep-through SBP surge compared with nonblacks after consumption of a controlled diet for a 3-week period. However, addition of $\log_e$PRA to the fully adjusted model lead to significant changes in the effect estimates for the association of race with both preawake and sleep-through surge, suggesting that PRA (based on prior knowledge of racial differences) may be a pathway intermediate of the race–surge relationship. This prompted us to consider the association of PRA with morning surge in black and nonblack subgroups. In these analyses, we found no association between PRA and sleep-through SBP surge in either black or nonblack subgroups. However, we did find evidence for a significant association between greater PRA and greater preawake surge in nonblacks only. Although limited by power and the use of cross-sectional data, these findings may suggest that non–renin-mediated pathways may be important in the determination of sleep-through surge regardless of racial background, whereas renin-mediated pathways may be more important in the determination of preawake surge in nonblack individuals only.

Prior physiologic studies reported that PRA appears to be highest in the latter part of sleep and prewakening period.[22] The preawake surge is determined by the difference in BP between the pre- and postwakening periods (both of which occur during the early morning rise in PRA, a time when alpha-mediated vasoconstriction is also greatest).[1] In contrast, the nadir sleeping BP is determined from the period during sleep in which the lowest BP is recorded; this is likely subject to large within and between person variability and likely occurs when the nocturnal PRA is relatively flat. These may be contributing factors as to why we did not find an association between PRA and sleep-through surge.

In our analyses, blacks had lower overall PRA than nonblacks, consistent with numerous prior studies.[23–25] Various theories have been postulated to explain this phenomenon, including polymorphisms of the renin gene,[26] differences in dietary sodium and potassium intake,[27] and inherent differences in control of the renin-angiotensin-aldosterone system.[28] In our analyses, participants were exposed to the same control diet and had no significant differences in measured 24-hour urinary sodium excretion, making diet a less likely explanation for suppressed renin activity among blacks. Differences in urinary potassium excretion according to race have been noted before in this cohort, with blacks having lower urinary potassium excretion at the end of the run-in period;[29] however, lower PRA has also been reported in blacks in the absence of detectable differences in urinary potassium.[25]

In exploratory analyses, we additionally adjusted for nocturnal dipping status in an attempt to ascertain the association of race with surge, independent of dipping. We found that the association of black race with lower preawake and sleep-through surge attenuated after adjustment for dipping but remained significant for sleep-through surge. These finding suggest that at least part of the reason why blacks have lower surge may be related to attenuated nocturnal dipping but that dipping status alone is not sufficient to explain the complete picture.

The major strengths of this study include detailed collection of data in the setting of a randomized, controlled trial, the institution of a controlled dietary intervention for all participants during the run-in phase of the study, and the ability to adjust for potential demographic and socioeconomic confounders. However, there are limitations of this study that merit discussion. The relationship of $\log_e$PRA with SBP surge was assessed in a cross-sectional fashion, and thus it is impossible to make any definite inference on causality. PRA was measured only once at the end of the run-in period, which could potentially lead to misclassification; however, such misclassification would likely be nondifferential in nature and, if anything, bias our estimates toward the null. The sample size was relatively modest, and the presence of residual confounding from incomplete adjustment of considered variables in the setting of an observational study remains a possibility. Finally, because there was only 1 ambulatory reading obtained at the end of the controlled feeding period and because BP is dynamic and variable from day to day, BP surge may likewise be variable.

The true implications of morning BP surge with adverse clinical outcomes have been the topic of much debate and conflicting literature in recent times. For example, some studies have reported an increased risk of ischemic stroke[3] and cerebral hemorrhage[4] and greater mortality with greater morning BP surge,[5] whereas others have not.[6, 7] Because the DASH Trial did not examine clinical outcomes, we were unable to assess the clinical associations of morning BP surge after the institution of a controlled diet. However, we were able to confirm the presence of significant racial differences in preawake and sleep-through SBP surge in individuals participating in a controlled feeding study, with blacks having less morning surge than nonblacks and PRA being

associated with greater preawake surge in nonblacks only. Importantly we noted that these relationships were attenuated upon additional adjustment for dipping status, raising the possibility that the clinical risk associated with attenuated nocturnal dipping in blacks may partially outweigh any potential benefit associated with less morning surge. Future studies should test these associations in other cohorts and definitively address whether greater BP surge is an independent predictor of adverse cardiovascular events.

ACKNOWLEDGMENTS

We thank the DASH Trial investigators and the National Heart Lung and Blood Institute (NHLBI) data repository for the data used in this study. The DASH Trial was performed by the DASH Trial investigators and supported by the NHLBI. This paper was not prepared in collaboration with the investigators of the DASH Trial and does not necessarily reflect the opinions or views of the DASH Trial or the NHLBI.

This work was conducted with support from the Scholars in Clinical Science Program of Harvard Catalyst. The Harvard Clinical and Translational Science Center (award No. UL1 RR025758 and financial contributions from Harvard University and its affiliated academic health care centers). The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic health care centers, the National Center for Research Resources, or the National Institutes of Health.

F.R.M. was supported by a Clinical Fellowship Grant from the National Kidney Foundation (2011–13). C.J.M. was supported by an American Society of Nephrology Fellowship Grant (2012–14). J.P.F is supported by the National Institute of Health grant 5R01HL105440 and the American Heart Association grant 2009A050171.

DISCLOSURE

The authors declared no conflict of interest.

REFERENCES

1. Panza JA, Epstein SE, Quyyumi AA. Circadian variation in vascular tone and its relation to alpha-sympathetic vasoconstrictor activity. *N Engl J Med* 1991;325:986–990.
2. Dodt C, Breckling U, Derad I, Fehm HL, Born J. Plasma epinephrine and norepinephrine concentrations of healthy humans associated with nighttime sleep and morning arousal. *Hypertension* 1997;30:71–76.
3. Kario K, Pickering TG, Umeda Y, Hoshide S, Hoshide Y, Morinari M, Murata M, Kuroda T, Schwartz JE, Shimada K. Morning surge in blood pressure as a predictor of silent and clinical cerebrovascular disease in elderly hypertensives: a prospective study. *Circulation* 2003;107:1401–1406.
4. Metoki H, Ohkubo T, Kikuya M, Asayama K, Obara T, Hashimoto J, Totsune K, Hoshi H, Satoh H, Imai Y. Prognostic significance for stroke of a morning pressor surge and a nocturnal blood pressure decline: the Ohasama study. *Hypertension* 2006;47:149–154.
5. Li Y, Thijs L, Hansen TW, Kikuya M,Boggia J, Richart T, Metoki H, Ohkubo T, Torp-Pedersen C, Kuznetsova T, Stolarz-Skrzypek K, Tikhonoff V, Malyutina S, Casiglia E, Nikitin Y, Sandoya E, Kawecka-Jaszcz K, Ibsen H, Imai Y, Wang J, Staessen JA. Prognostic value of the morning blood pressure surge in 5645 subjects from 8 populations. *Hypertension* 2010;55:1040–1048.
6. Israel S, Israel A, Ben-Dov IZ, Bursztyn M. The morning blood pressure surge and all-cause mortality in patients referred for ambulatory blood pressure monitoring. *Am J Hypertens* 2011;24:796–801.
7. Verdecchia P, Angeli F, Mazzotta G, Garofoli M, Ramundo E, Gentile G, Ambrosio G, Reboldi G. Day-night dip and early-morning surge in blood pressure in hypertension: prognostic implications. *Hypertension* 2012;60:34–42.
8. Sacco RL, Boden-Albala B, Gan R, Chen X, Kargman DE, Shea S, Paik MC, Hauser WA. Stroke incidence among white, black, and Hispanic residents of an urban community: the Northern Manhattan Stroke Study. *Am J Epidemiol* 1998;147:259–268.
9. USRDS. *US Renal Data System 2011 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States*. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases: Bethesda, MD, 2011
10. Holmes JS, Arispe IE, Moy E. Heart disease and prevention: race and age differences in heart disease prevention, treatment, and mortality. *Med Care* 2005;43:I33–I41.
11. Haas DC, Gerber LM, Shimbo D, Warren K, Pickering TG, Schwartz JE. A comparison of morning blood pressure surge in African Americans and whites. *J Clin Hypertens (Greenwich)* 2005;7:205–209; quiz 210–211.
12. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997;336:1117–1124.
13. Portaluppi F, Bagni B, degli Uberti E, Montanari L, Cavallini R, Trasforini G, Margutti A, Ferlini M, Zanella M, Parti M. Circadian rhythms of atrial natriuretic peptide, renin, aldosterone, cortisol, blood pressure and heart rate in normal and hypertensive subjects. *J Hypertens* 1990;8:85–95.
14. Gordon RD, Wolfe LK, Island DP, Liddle GW. A diurnal rhythm in plasma renin activity in man. *J Clin Invest* 1966;45:1587–1592.
15. Price DA, Fisher ND. The renin-angiotensin system in blacks: active, passive, or what? *Curr Hypertens Rep* 2003;5:225–230.
16. Vogt TM, Appel LJ, Obarzanek E, Moore TJ, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Cutler JA, Windhauser MM, Lin PH, Karanja NM. Dietary Approaches to Stop Hypertension: rationale, design, and methods. DASH Collaborative Research Group. *J Am Diet Assoc* 1999;99:S12–S18.
17. Karanja NM, Obarzanek E, Lin PH, McCullough ML, Phillips KM, Swain JF, Champagne CM, Hoben KP. Descriptive characteristics of the dietary patterns used in the Dietary Approaches to Stop Hypertension Trial. DASH Collaborative Research Group. *J Am Diet Assoc* 1999;99:S19–27.
18. Jehn ML, Brotman DJ, Appel LJ: Racial differences in diurnal blood pressure and heart rate patterns: results from the Dietary Approaches to Stop Hypertension (DASH) trial. *Arch Intern Med* 2008;168:996–1002.
19. Hering D, Kucharska W, Kara T, Somers VK, Narkiewicz K. Resting sympathetic outflow does not predict the morning blood pressure surge in hypertension. *J Hypertens* 2011;29:2381–2386.
20. Kario K, Yano Y, Matsuo T, Hoshide S, Asada Y, Shimada K. Morning blood pressure surge, morning platelet aggregation, and silent cerebral infarction in older Japanese hypertensive patients. *J Hypertens* 2011;29:2433–2439.
21. Neutel JM, Schumacher H, Gosse P, Lacourciere Y, Williams B. Magnitude of the early morning blood pressure surge in untreated hypertensive patients: a pooled analysis. *Int J Clin Pract* 2008;62:1654–1663.
22. Hurwitz S, Cohen RJ, Williams GH. Diurnal variation of aldosterone and plasma renin activity: timing relation to melatonin and cortisol and consistency after prolonged bed rest. *J Appl Physiol* 2004;96:1406–1414.
23. Levy SB, Lilley JJ, Frigon RP, Stone RA. Urinary kallikrein and plasma renin activity as determinants of renal blood flow. The influence of race and dietary sodium intake. *J Clin Invest*. 1977;60:129–138.

24. He J, Klag MJ, Appel LJ, Charleston J, Whelton PK. The renin-angiotensin system and blood pressure: differences between blacks and whites. *Am J Hypertens.* 1999;12:555–562.
25. He FJ, Markandu ND, Sagnella GA, MacGregor GA. Importance of the renin system in determining blood pressure fall with salt restriction in black and white hypertensives. *Hypertension* 1998;32: 820–824.
26. Barley J, Carter ND, Cruickshank JK, Jeffery S, Smith A, Charlett A, Webb DJ. Renin and atrial natriuretic peptide restriction fragment length polymorphisms: association with ethnicity and blood pressure. *J Hypertens* 1991;9:993–996.
27. Sagnella GA. Why is plasma renin activity lower in populations of African origin? *J Hum Hypertens* 2001;15:17–25.
28. Price DA, Fisher ND, Osei SY, Lansang MC, Hollenberg NK. Renal perfusion and function in healthy African Americans. *Kidney Int* 2001;59:1037–1043.
29. Turban S, Miller ER 3rd, Ange B, Appel LJ. Racial differences in urinary potassium excretion. *J Am Soc Nephrol* 2008;19:1396–1402.