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# Periodic Limb Movements During Sleep and Prevalent Hypertension in the Multi-Ethnic Study of Atherosclerosis

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## Abstract

Periodic limb movements during sleep (PLMS) are associated with immediate increases in blood pressure. Both PLMS and hypertension have different distributions across racial/ethnic groups. We sought to determine if PLMS is associated with hypertension among various racial/ethnic groups. 1,740 men and women underwent measurement of blood pressure and polysomnography with quantification of PLMS. Hypertension was defined as systolic blood pressure (SBP)≥140, diastolic BP≥90, or taking anti-hypertensive medication. For those taking anti-hypertensives, an estimated pre-treatment SBP value was derived based on observed SBP and medication type/dose. Measures of PLMS, PLMS index (PLMI) and PLMS arousal index (PLMAI), were the main explanatory variables. Hypertension and SBP were modeled with logistic and multivariable regression adjusted for age, sex, body mass index, cardiovascular risk factors, lifestyle/habitual factors, apnea-hypopnea index, and race/ethnicity.

In the overall cohort, prevalent hypertension was modestly associated with PLMI (10-unit) (OR 1.05 [95% CI 1.00,1.10]) and PLMAI (1-unit) (1.05 [1.01,1.09]) after adjusting for confounders. Association in the overall cohort was influenced by large effect sizes in African-Americans, in whom the odds of prevalent hypertension increased by 21% [1%,45%] for 10-unit PLMI increase and 20% [2%,42%] for 1-unit PLMAI increase. In African-Americans, every 1-unit PLMAI increase was associated with SBP 1.01 mmHg higher (1.01 [0.04,1.98]). Associations between PLMS and blood pressure outcomes were also suggested among Chinese-Americans but not in Caucasians or Hispanics. In a multiethnic cohort of community dwelling men and women, prevalent hypertension and SBP are associated with PLMS frequency in African-Americans.

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CONFLICTS OF INTEREST
There are no conflicts of interest to disclose.

**Keywords**

Periodic limb movements during sleep; PLMS; hypertension; race; blood pressure; ethnicity

## INTRODUCTION

Periodic limb movements during sleep (PLMS) are repetitive, forceful contractions of leg and foot muscles often associated with arousal from sleep, affecting 7.6% of middle-aged adults and 45% of community-dwelling elderly.[1,2] The motor phenomenon of PLMS occurs in up to 80% of persons suffering from the neurosensory condition, restless legs syndrome (RLS), but can also occur in persons with hypertension and even in the normal elderly.[3-5] Once thought to be primarily a sleep-related peculiarity, PLMS recently has been recognized as associated with cardiovascular disease, at least in elderly and health-compromised populations.[5-7] Pathophysiologic mechanisms which link PLMS and cardiovascular disease are not well understood, but hypertension may play a role. Individual movements of a PLM cluster are associated with discrete elevations in blood pressure on the order of 20 systolic and 10 diastolic mmHg.[8,9] When considering daytime hypertension, there is no clear association with PLMS; however, this question has not been adequately studied.

Hypertension itself is a robust predictor of cardiovascular disease across all ages and racial/ethnic groups.[10] Meta-analyses of blood pressure lowering trials suggest that reduction of heightened blood pressure by 10 mmHg systolic decreases incident coronary heart disease by one-fifth and cerebrovascular disease by one-third.[11] For this reason, it is important to identify secondary causes of hypertension which can be treated to optimize blood pressure and cardiovascular risk.

There is racial/ethnic variation in the prevalence of PLMS, RLS, and hypertension. PLMS occurs in up to 9% of middle-aged European-Americans, and 4% of similarly aged African-Americans.[1,12] RLS is most common in Caucasians, intermediate in Mexican-Hispanics, and least common in Sub-Saharan Africans.[13,14] Conversely, hypertension affects 60% of African-Americans, 44% of Hispanic-Americans, and 42% of Caucasian-Americans.[15] For these reasons, it is important to examine the association between PLMS and hypertension in a multiethnic population, and to determine if either race/ethnicity or RLS influences this association.

To address whether PLMS is associated with hypertension, we analyzed data from the Multi-Ethnic Study of Atherosclerosis (MESA) Sleep ancillary study. MESA is a large U.S. population-based study of Caucasian, African-American, Hispanic and Chinese adults, designed to examine racial/ethnic, age, and gender variation in cardiovascular outcomes. Recently, a subset of MESA participants underwent comprehensive sleep assessment in the MESA Sleep ancillary study. Using these data, we tested our hypothesis that frequency of PLMS with and without arousal would be cross-sectionally associated with daytime hypertension and blood pressure. We also explored whether race/ethnicity or RLS modified any relationship between PLMS and hypertension.

# METHODS

## Study Population

The MESA prospective cohort includes 6,814 men and women (45-64 years at baseline) initially recruited in 2000-2002 from 6 U.S. communities (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles, CA; Manhattan, NY; St. Paul, MN). The primary objective of MESA is to investigate risk factors for cardiovascular disease in a racially/ethnically diverse community population, free of cardiovascular disease at baseline.[16] 5 clinic examinations have taken place, the most recent occurring between 2010 and 2011, being attended by 4,716 original MESA participants. Of these individuals, 4,077 were approached shortly after the 5$^{th}$ clinic exam to take part in the MESA Sleep ancillary study, of which 2,060 participated. Compared to participants in MESA Exam 5 who did not undergo the sleep exam, participants in the sleep exam were slightly younger (68.4 vs 71.0 yrs), less likely to be white (36.1% vs 44.5%), and less likely to be smokers (7.1% vs. 8.4%). However, they were comparable in regards to gender, BMI, physician diagnosed sleep apnea, asthma, diabetes, and prior myocardial infarction. Institutional Review Boards from each study site approved the conduct of this study and written informed consent was obtained from all participants. Excluded were individuals with incomplete information on PLMS and RLS, leaving 1,740 participants in the final analytic sample.

## Polysomnography

Between 2010 and 2013, unattended in-home polysomnography was conducted using the Compumedics Somte System (Compumedics, Abbostville, Australia) with recording of 3 EEG channels ($C_4$-$M_1$, $O_z$-$C_z$, $F_z$-$C_z$), bilateral electrooculogram, chin EMG, thoraco-abdominal respiratory inductance plethysmography; airflow (nasal-oral thermocouple and nasal pressure transduction); ECG; bilateral leg movements (piezoelectric sensors) , and finger pulse oximetry. Recordings were transmitted to the Brigham and Women's centralized reading center and data were scored by trained technicians using standardized criteria.[17,18] Apneas were identified by near absence of airflow for ≥10 seconds. Hypopneas were identified by ≥30% breathing amplitude reduction lasting ≥10 seconds when followed by ≥3% oxygen desaturation or arousal. The apnea-hypopnea index (AHI) was calculated as the total number of apneas and hypopneas per hour of sleep. Arousals were scored when EEG frequency increased ≥3 seconds and were summarized as the total number of arousals per hour of sleep (arousal index).

Individual leg movements were scored if there was a clear amplitude increase from baseline and lasted 0.5-5 seconds. To be considered periodic, a minimum of four movements needed to occur in succession 5-90 seconds apart.[18] Leg movements following respiratory events were excluded unless they were part of a 4 (or more) movement cluster with at least 2 movements occurring independently of respiratory events. Computed were periodic limb movement index (PLMI), total number of periodic leg movements per hour of sleep; and periodic limb movement arousal index (PLMAI), total number of periodic leg movements per hour of sleep in which arousal occurred within 3 seconds of the PLM. Inter- and intra-scorer reliability for PLMI was high (intra-class correlation coefficients 0.93-0.98).

## Exposure and Outcome Data

The main exposure variables were PLMI and PLMAI which were examined continuously in logistic and linear multivariable models. Sensitivity analyses were carried out with the exposure variables in categories; PLMI: (1) <5, (2) ≥5 and <30, (3) ≥30; PLMAI: (1) <1, (2) ≥1 and <5, (3) ≥5.

Blood pressure was based on measurements from MESA exam 5 which occurred a median of 300 days before polysomnography. Blood pressure was measured in triplicate at 2-minute intervals using an automated oscillometric device (Dinamap MonitorPro 100, GE Healthcare, Milwaukee, WI). The second and third readings were averaged to yield systolic ($SBP_{measured}$) and diastolic blood pressure ($DBP_{measured}$). Antihypertensive drug use was determined by medication inventory. Antihypertensive drug classes included: beta-blockers, diuretics, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, alpha-blockers, calcium channel blockers or other peripheral vasodilators. Prevalent hypertension was considered if a participant was taking anti-hypertensive medication or if JNC VII hypertension criteria (SBP≥140 or DBP≥90) were met.[19]

A large proportion of participants were taking anti-hypertensive medications. For these participants, we estimated pre-treatment blood pressure values using previously described methods.[20,21] In brief, the blood pressure imputation model was derived from pre- and post-blood pressures from a subset of new anti-hypertensive drug users, and included data were on-treatment blood pressures, age, gender, race/ethnicity, body mass index (BMI), diabetes, total and HDL cholesterol, smoking, anti-hypertensive medication class, and two-way interactions between gender, race/ethnicity, and medication type. From these procedures, ten imputed blood pressure data sets were created and averaged separately for systolic and diastolic blood pressures to yield $SBP_{imputed}$ and $DBP_{imputed}$, respectively.

## Covariate Data

Other information was also collected during MESA clinic exam 5. Questionnaires documented information concerning demographics, medical history, medication use, physical activity, education, income, depression, atrial fibrillation, diabetes, smoking, and alcohol use. Diabetes was defined by fasting glucose ≥126 mg/dL or medical treatment with insulin/oral hypoglycemic.[22] Depression symptoms were measured using the Center for Epidemiologic Studies Depression scale.[23] Smoking status was categorized as never, former, and current. Alcohol use was categorized as current or not current. Education was categorized into three groups: high school or less, some college, and bachelor's/graduate degree. Income was categorized into four groups: <$25,000/year, $25,000-$39,999/year, $40,000-$74,000/year, and >$75,000/year. Physical Activity was assessed using the MESA Typical Week Physical Activity Survey. Reported time spent performing several physical tasks in a typical week were multiplied by the metabolic equivalent level and summed to create a physical activity score.[24] Waist to hip ratio was calculated as waist circumference/hip circumference, and BMI as weight(kg)/height(m)$^2$.

RLS was assessed with one main question and three additional sub-questions. The main question was (1) ‘Do you ever experience a desire to move your legs because of discomfort

or disagreeable sensations in your legs?'. Three sub-questions were answered only if the response to this main question was 'yes'. The sub-questions were: (1a) 'Do you sometimes feel the need to move to relieve the discomfort, for example by walking, or rubbing your legs?'; (1b) 'Are these symptoms worse when you are at rest, with at least temporary relief by activity?'; (1c) 'Are these symptoms worse later in the day or at night?' Response choices to each of the four questions were identical: 'No', 'Yes' and 'Don't know'. Participants were considered to have RLS, only if all four questions were answered 'Yes'.

### Statistical Analysis

Participant characteristics were compared across PLMI and PLMAI categories using chi-square tests for categorical variables and ANOVA for continuous variables. The effects of PLMI and PLMAI on the odds of hypertension were analyzed using multiple logistic regression; results are presented as odds ratios (OR) with 95% confidence intervals [CI]. Odds of hypertension were presented for every 10-units of PLMI and 1-unit of PLMAI, reflecting meaningful changes across the relevant distribution of these variables. Multivariable regression modeled $SBP_{imputed}$ and $DBP_{imputed}$; $SBP_{measured}$ was considered as an outcome in sensitivity analysis among those not taking anti-hypertensive medication. PLMI and PLMAI were treated both as continuous and categorical variables. Covariates were added to the models in stages: unadjusted, minimally adjusted, and fully adjusted. Minimally adjusted models controlled for gender, age, and BMI. Fully adjusted models added race/ethnicity, education, income, smoking status, alcohol use, atrial fibrillation, diabetes, depression scale, physical activity scale (log transform), AHI, and arousal index.

To allow for the possibility of different effects by race/ethnicity, the unadjusted and minimally adjusted models were stratified by race/ethnicity through interaction terms. The sample sizes in some races/ethnicities were not large enough to accommodate fully adjusted stratified models, so only PLMI/PLMAI and minimally adjusting covariates were allowed racial/ethnic heterogeneity. The effects of the other covariates in the full model were combined over the different races/ethnicities. For the continuous responses, the residual variance was allowed to differ by race/ethnicity, and Satterthwaite denominator degrees of freedom were used for T and F tests. The interaction terms between PLMI/PLMAI and race/ethnicity were jointly tested for statistical significance to determine if race/ethnicity modified the relationship between PLMI/PLMAI and the response. To determine if RLS was associated with hypertension, multiple logistic regression was carried out with RLS diagnosis as the main exposure variable both with and without PLMI or PLMAI in the models.

## RESULTS

### Overall Characteristics

1,740 participants had a mean age of 68.3±9.1 years and 46.0% (n=801) were male. Table 1 shows demographic, anthropomorphic, and health characteristics of the overall cohort and the cohort stratified by PLMI and PLMAI categories. Participants in high compared to low PLMI and PLMAI categories were older with no difference in BMI. The majority of participants fall in the lowest PLMI and PLMAI categories; 16.8% with PLMI≥30 and 9.1%

withPLMAI≥5. Participants with hypertension were disproportionately represented in the PLMI≥30 and PLMAI≥5 groups (Table 1). Having PLMI≥30 was equally prevalent in Caucasians, Hispanics and Chinese-Americans, affecting 18.8%, 20.1%, and 19.1%, respectively, but less prevalent in African–Americans (10.5%). Having PLMAI≥5 in Chinese-American, Caucasian, Hispanic, and African-American groups was 12.1%, 11.4%, 8.3%, and 5.6%, respectively.

## Models For Hypertension

Nearly 60% of the overall cohort was hypertensive (Table 1). As shown in Table 2, the unadjusted frequencies of hypertension differed significantly among races/ethnicities with African-Americans having highest and Chinese-Americans having lowest frequencies ($p<0.0001$). When subset to race/ethnicity, prevalence of hypertension increased with increasing PLMI or PLMAI category in Chinese-Americans but not other groups (Table 2).

For the overall cohort, PLMI, considered as a continuous index, showed a weak association with hypertension in unadjusted analyses (Table 3). When stratifying by race/ethnicity, there were associations between PLMI and hypertension in unadjusted models for African-Americans, Chinese-Americans and Caucasians (Table 3) which were also apparent when hypertension frequency was examined by PLMI category (Table 2). In adjusted analyses, the association between PLMI and hypertension persisted only in African-Americans in whom every increase of PLMI by 10-units was associated with a 21% increased odds of hypertension (OR 1.21 [CI 1.01,1.45; p=0.02]) (Table 3). The p-value for interaction of race and PLMI was 0.19.

For PLMAI modeled continuously in the overall cohort, there were significant associations between PLMAI and hypertension in unadjusted and fully adjusted models (Table 3). In race/ethnicity-specific models, there were significant associations between PLMAI and hypertension for African-Americans, Chinese-Americans and Caucasians (Table 3). After full adjustment for multiple potential confounders, a significant relationship between PLMAI and hypertension remained only for African-Americans in whom a 1-unit PLMAI increase was associated with a 20% increased odds of hypertension (1.20 [1.02,1.42; p=0.005]). In Chinese-Americans, there was a marginal association between PLMAI and hypertension after adjusting for multiple confounders; for every 1-unit PLMAI increase, the odds of hypertension increased 10% (p=0.08). The p-value for interaction of race/ethnicity and PLMAI for hypertension was 0.07.

When modeling PLMI and PLMAI as categorical exposures, similar although less significant associations were observed compared to models using continuous exposure variables. Associations were strongest in African-Americans (data not shown). When considering a potential relationship between RLS and hypertension (without PLMI or PLMAI), there was no association between the presence of RLS symptoms and hypertension in unadjusted (1.23 [0.98,1.55; p=0.07]), minimally adjusted (1.21 [0.95,1.55; p=0.13]) or fully adjusted models (1.15 [0.89,1.49; p=0.30]). When the cohort was stratified by race/ethnicity, there was no association between RLS and hypertension in any racial/ethnic group (data not shown). Additionally, inclusion of RLS in the models that included PLMI or

PLMAI did not appreciably influence the associations between PLMI or PLMAI with hypertension (data not shown).

### Systolic Blood Pressure

In the overall cohort, $SBP_{imputed}$ was associated with PLMI and PLMAI only in unadjusted models (Table 4). In models adjusted fully for multiple potential confounders, neither PLMI nor PLMAI were associated with $SBP_{imputed}$ in Caucasians, Hispanics, or Chinese-Americans (Table 4). In African-Americans, there was a significant association between PLMAI and $SBP_{imputed}$; for every 1-unit PLMAI increase, $SBP_{imputed}$ was 1.01 mmHg [0.04,1.98] higher. Also in African-Americans, there was a marginal but non-significant association between PLMI and $SBP_{imputed}$ (p=0.09). The p-value for interaction of race and PLMAI when considering $SBP_{imputed}$ was 0.27.

Mean $SBP_{imputed}$ differed significantly among the races, with African-Americans having the highest and Caucasians the lowest values (p<0.0001) (Table 2). In the overall cohort, $SBP_{imputed}$ was highest in both PLMI≥30 and PLMAI≥5 groups, but these differences were not statistically significant. $SBP_{imputed}$ was significantly different among PLMI (p=0.02) or PLMAI (p=0.01) categories only in Chinese-Americans, where high PLMI or PLMAI category was associated with highest $SBP_{imputed}$ (Table 2).There was a trend toward increased $SBP_{imputed}$ in higher PLMAI categories for African-Americans.

In sensitivity analysis restricted to those not taking anti-hypertensive medication (n=802), $SBP_{measured}$ was associated with both PLMAI and PLMI after considering multiple potential confounders in African-Americans and Chinese-Americans. In African-Americans for every 10-unit PLMI increase, $SBP_{measured}$ was 2.47 mmHg higher [1.25,3.69; p<0.0001]; and for every 1-unit PLMAI increase, $SBP_{measured}$ was 3.71 mmHg higher [1.69,5.72; p=0.0004]. In Chinese-Americans, for every 10-unit increase in PLMI, $SBP_{measured}$ was 1.31 mmHg higher [0.13,2.50; p=0.03]; and for every 1-unit increase in PLMAI, $SBP_{measured}$ was 1.45 mmHg higher [CI 0.17,2.72; p=0.03].

### Diastolic Blood Pressure

Mean imputed diastolic blood pressure ($DBP_{imputed}$) differed significantly among the races/ethnicities with African-Americans having the highest and Caucasians the lowest $DBP_{measured}$ (p<0.0001) (Table 2). $DBP_{imputed}$ did not differ according to PLMI or PLMAI category (Table 1) in the overall cohort, or cohort stratified by race/ethnicity.

$DBP_{imputed}$ in the overall cohort was not associated with PLMI or PLMAI in unadjusted or adjusted models (data not shown). In race/ethnicity-specific models of $DBP_{imputed}$, there was no significant association with PLMI or PLMAI in any race/ethnicity group but there were marginal associations in both African-Americans and Chinese-Americans. In African-Americans, after adjusting for multiple confounders, $DBP_{imputed}$ was associated with PLMI; every 10-unit PLMI increase, $DBP_{imputed}$ was 1.26 mmHg higher [−0.21,2.72; p=0.09]. In Chinese-Americans after adjusting for multiple confounders, every 1-unit PLMAI increase, $DBP_{imputed}$ was 0.45 mmHg higher [−0.06,0.96; p=0.08]. In sensitivity analysis, for Chinese-Americans in fully adjusted models, having PLMAI≥5 compared to PLMAI<1 was associated with $DBP_{imputed}$ 5.74 mmHg higher [0.62,10.86; p=0.03].

## DISCUSSION

This is the first study to examine the association of PLMS and hypertension across race/ethnic groups. Using objective measures of PLMS, we found that the likelihood of prevalent hypertension and measurements of systolic blood pressure were significantly associated with PLMS frequency, and report the novel finding that associations were strongest among African-Americans. In African-Americans, an increase by 10-units for PLMI and 1-unit for PLMAI was associated with an approximately 20% increased odds of prevalent hypertension. Systolic blood pressure was approximately 1 systolic unit higher for every 1-unit PLMAI increase. When restricting to those not taking antihypertensive medications, both PLMI and PLMAI were significantly associated with systolic blood pressure in African-Americans and Chinese-Americans. Finally, the presence of RLS did not influence relationships between PLMS and blood pressure.

This study represents the largest series to report on PLMS prevalence in different race/ethnic categories. Caucasian, Hispanic, and Chinese-Americans had similar distributions for PLMS with about 20% of each group having PLMI≥30, while a lower percentage of African-Americans had PLMI≥30, about 10%. Similar to previous reports, hypertension prevalence was similar among Caucasian, Hispanic and Chinese-Americans (about 50%), and highest among African-Americans (about 70%).[25]

The Seventh Report of the Joint National Committee on high blood pressure outlined the importance of considering minority groups in assessing risk of hypertension.[19] The multi-ethnic design of MESA allowed us to explore racial/ethnic differences in associations between PLMS and hypertension. Our findings suggest that PLMS are associated with hypertension in middle-aged to older African- and Chinese-Americans but not in Caucasian- and Hispanic-Americans. While the basis for this difference is not clear, pathophysiologic mechanisms of both PLMS and HTN may provide a clue. Mechanisms of hypertension differ according to race/ethnicity. For example, salt sensitivity is more common in African-Americans and Chinese,[26,27] and differences in salt-fluid balance may moderate responses to PLMS. The dopamine system is involved in the reabsorption of salt and water in the intra-renal system and has also been implicated in RLS (to which PLMS is highly correlated).[28,29]

Our findings also provide insight into PLMS-associated blood pressure elevations, with two mechanisms standing out. First, PLMS arise from neuronal generators within the spinal cord, likely in thoracolumbar sections which also house preganglionic sympathetic nerve fibers.[30] Co-activation of leg motor and sympathetic nervous fibers in these areas could result in both PLMS and blood pressure increases. The second means by which PLMS may lead to blood pressure increases is through arousal. Notably, we observed an average increase in SBP of 0.2 mmHg for every 1-unit PLMI, and 1.1 mmHg increase for every 1-unit PLMAI. Both PLMS and arousal, even when occurring alone, are associated with discrete blood pressure increases.[9,31] When PLMS and arousal occur together these increases in blood pressure are greater.[9] This interaction between PLMS and arousal may provide new insight into the relationship between fragmented sleep (i.e. arousal) and the development of hypertension, which has been frequently studied but not clarified.

There are other potential physiologic interactions that are worth mentioning. Since many participants were receiving blood pressure medications, it is important to consider the effects of anti-hypertensive medications on PLMS. In general, PLMS frequency is decreased with dopamine agonsim;[32] pharmacologic effects of antihypertensive medications on PLMS has not been defined and thus is a potential confounder. Obstructive sleep apnea (OSA) often co-occurs with PLMS and is a well-studied independent risk factor for hypertension.[33] The statistical adjustment for AHI may not have fully accounted for this potential physiologic confounder. Finally, the phenomenon of PLMS itself can be seen in a large variety of conditions including RLS, hypertension, neuropathy, and senility.[3-5] The frequency of these conditions varies across racial/ethnic and socio-economic lines, and may also have confounded the results.

In this study, RLS symptoms were not associated with hypertension and did not influence the relationship between PLMS and hypertension. Other large population studies have reported an association between RLS and hypertension in unadjusted models but not in models adjusted for potential confounders.[34,35] In these previous reports, persons with frequent RLS symptoms were most likely to have hypertension. RLS symptom frequency was not assessed in MESA, which may account for the disparate and negative findings regarding RLS.

A challenge in evaluating blood pressure in the community relates to consideration of anti-hypertensive medication effects. We addressed this limitation by using a robust approach for integrating longitudinal blood pressure data and information regarding medication type to impute pre-treatment blood pressure levels.[20,21] Although robust, the imputation methods could have resulted in blood pressure estimates that lacked precision. We also performed sensitivity analysis on $SBP_{measured}$, limited to those not taking anti-hypertensive medication. The latter analysis confirmed the association between SBP and PLMS frequency in African-Americans, and found that in Chinese-Americans, $SBP_{measured}$ was 1.5 mmHg higher for every 10-unit PLMI increase and 1-unit PLMAI increase. These findings indicate that differences in anti-hypertensive use or imputation effects were unlikely to explain associations between hypertension and PLMS.

This study has several strengths. Participants with diverse ethnic and racial backgrounds were studied, providing an opportunity to explore associations across population groups. Participants were not chosen according to predilection for PLMS or hypertension, allowing generalizability to other similarly aged populations. Data were rigorously collected and scored by highly trained and centralized polysomnologists, with high PLMS intra-scorer reliability. Clinic visits and blood pressure measurement were also standardized across institutions.

There are also some limitations to consider. The study was cross-sectional which weakens an argument for causality. Blood pressure, anthropomorphic, and questionnaire data were ascertained a median of 300 days prior to PSG testing. Although the measures of interest are generally quite stable over one year in individuals studied in community settings, this time difference could have contributed to some misclassification of exposure and outcome associations. The diagnosis of hypertension was based upon a point sample of blood

pressure. PLMS were measured using piezoelectric sensors and not standard electromyography. Previously, we had performed in-laboratory validation in 51 subjects where PLMS was assessed concurrently using piezoelectric leg sensors and leg electromyography, and showed a correlation of r=0.81.[36] Also, despite the large overall sample, the number of participants within each race/ethnicity group was limited, reducing the power to detect significant interactions

In summary, PLMS are associated with hypertension and systolic blood pressure, with findings strongest in African-Americans and Chinese-Americans. Given the high prevalence of hypertension in minority groups, these data suggest novel targets for improving blood pressure control. Further research is needed to identify the pathophysiological links between PLMS and hypertension, and to determine whether environmental or genetic factors that vary with ancestry modify these associations.

## PERSPECTIVES

Periodic limb movements during sleep (PLMS) are repetitively occurring limb movements during sleep that are often associated with arousal from sleep. Individual movements of a PLM cluster are each associated with elevations in blood pressure on the order of 20 systolic millimeters of mercury. Since the prevalence of both PLMS and hypertension differs by race/ethnicity, we wished to determine if PLMS was associated with prevalent hypertension and if this association was modified by race/ethnicity. We found that PLMS are associated with hypertension and systolic blood pressure, with findings strongest in African-Americans and Chinese-Americans. Given the high prevalence of hypertension in minority groups, these data suggest novel targets for improving blood pressure control in these groups.

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## REFERENCES

1. Scofield H, Roth T, Drake C. Periodic limb movements during sleep: population prevalence, clinical correlates, and racial differences. Sleep. 2008; 3:1221–1227. [PubMed: 18788647]
2. Ancoli-Israel S, Kripke DF, Klauber MR, Mason WJ. Fell, Kaplan O. Periodic limb movements in sleep in community-dwelling elderly. Sleep. 1991; 14:496–500. [PubMed: 1798881]
3. Montplaisir J, Boucher S, Poirier G, Lavigne G, Lapierre O, Lespérance P. Clinical, polysomnographic, and genetic characteristics of restless legs syndrome: a study of 133 patients diagnosed with new standard criteria. Mov Disord. 1997; 12:61–65. [PubMed: 8990055]
4. Scofield H, Roth T, Drake C. Periodic limb movements during sleep: population prevalence, clinical correlates, and racial differences. Sleep. 2008; 31:1221–1227. [PubMed: 18788647]

5. Koo BB, Blackwell T, Ancoli-Israel S, Stone KL, Stefanick ML, Redline S. Association of incident cardiovascular disease with periodic limb movements during sleep in older men: outcomes of sleep disorders in older men (MrOS) study. Circulation. 2011; 124:1223–1231. [PubMed: 21859975]
6. Lindner A, Fornadi K, Lazar AS, Czira ME, Dunai A, Zoller R, Veber O, Szentkiralyi A, Kiss Z, Toronyi E, Mucsi I, Novak M, Molnar MZ. Periodic limb movements in sleep are associated with stroke in patients with renal failure. J Sleep Res. 2012; 21:297–307. [PubMed: 21917047]
7. Yumino D, Wang H, Floras JS, Newton GE, Mak S, Ruttanaumpawan P, Parker JD, Bradley TD. Relation of periodic leg movements during sleep and mortality in patients with systolic heart failure. Am J Cardiol. 2011; 107:447–451. [PubMed: 21257013]
8. Siddiqui F, Strus J, Ming X, Lee IA, Chokroverty S, Walters AS. Rise of blood pressure with periodic limb movements in sleep and wakefulness. Clin Neurophysiol. 2007; 118:1923–1930. [PubMed: 17588809]
9. Pennestri MH, Montplaisir J, Colombo R, Lavigne G, Lanfranchi PA. Nocturnal blood pressure changes in patients with restless legs syndrome. Neurology. 2007; 68:1213–1218. [PubMed: 17420405]
10. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002; 360:1903–1913. [PubMed: 12493255]
11. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009; 338:b1665. [PubMed: 19454737]
12. O'Brien LM, Holbrook CR, Faye Jones V, Gozal D. Ethnic difference in periodic limb movements in children. Sleep Med. 2007; 8:240–246. [PubMed: 17368099]
13. Sawanyawisuth K, Palinkas LA, Ancoli-Israel S, Dimsdale JE, Loredo JS. Ethnic differences in the prevalence and predictors of restless legs syndrome between Hispanics of Mexican descent and non-Hispanic Whites in San Diego county: a population-based study. J Clin Sleep Med. 2013; 9:47–53. [PubMed: 23319904]
14. Winkler AS, Trendafilova A, Meindl M, Kaaya J, Schmutzhard E, Kassubek J. Restless legs syndrome in a population of northern Tanzania: a community-based study. Mov Disord. 2010; 25:596–601. [PubMed: 20198689]
15. Mujahid MS, Diez Roux AV, Cooper RC, Shea S, Williams DR. Neighborhood stressors and race/ethnic differences in hypertension prevalence (the Multi-Ethnic Study of Atherosclerosis). Am J Hypertens. 2011; 24:187–193. [PubMed: 20847728]
16. Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, Greenland P, Jacob DR Jr, Kronmal R, Liu K, Nelson JC, O'Leary D, Saad MF, Shea S, Szklo M, Tracy RP. Multi-ethnic study of atherosclerosis: objectives and design. Am J Epidemiol. 2002; 156:871–881. [PubMed: 12397006]
17. Redline S, Sanders MH, Lind BK, Quan SF, Gottlieb DJ, Bonekat WH, Rapoport DM, Smith PL, Kiley JP. Methods for obtaining and analyzing unattended polysomnography data for a multicenter study. SHHS Research Group. Sleep. 1998; 21:759–767. [PubMed: 11300121]
18. Iber, C.; Ancoli-Israel, S.; Chesson, AL. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. 1st ed.. American Academy of Sleep Medicine; Westchester, IL: 2007.
19. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003; 42:1206–1252. [PubMed: 14656957]
20. McClelland RL, Kronmal RA, Haesslaer J, Blumenthal RS, Goff DC. Estimation of risk factor associations when the response is influenced by medication use: An imputation approach. Statistics Med. 2008; 27:5039–5053.
21. McClelland RL, Jorgensen NW, Post WS, Szklo M, Kronmal RA. Estimating Disparities in Medication Use in Observational Cohort Study: Results from the Multi-Ethnic Study of Atherosclerosis. Pharmacoepidemiology and Drug Safety. 2013; 22:533–541. [PubMed: 23382107]

22. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, Kitzmiller J, Knowler WC, Lebovitz H, Lernmark A, Nathan D, Palmer J, Rizza R, Saudek C, Shaw J, Steffes M, Stern M, Tuomilehto J, Zimmet P. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care. 2003; 26:3160–3167. [PubMed: 14578255]
23. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. Appl Psychol Meas. 1977; 1:385–401.
24. Ainsworth BE, Bassett DR Jr, Strath SJ, Swartz AM, O'Brien WL, Thompson RW, Jones DA, Macera CA, Kimsey CD. Comparison of three methods for measuring time spent in physical activity. Med Sci Sports Exerc. 2000; 32(9 Suppl):S457–S464. [PubMed: 10993415]
25. Kramer H, Han C, Post W, Goff D, Diez-Roux A, Cooper R, Jinagouda S, Shea S. Racial/ethnic differences in hypertension and hypertension treatment and control in the multi-ethnic study of atherosclerosis. Am J Hypertens. 2004; 17:963–970. [PubMed: 15485761]
26. Falkner B, Kushner H. Effect of chronic sodium loading on cardiovascular response in young blacks and whites. Hypertension. 1990; 15:36–43. [PubMed: 2295513]
27. Chen J. Sodium sensitivity of blood pressure in Chinese populations. Curr Hypertens Rep. 2010; 12:127–134. [PubMed: 20424958]
28. Harris RC, Zhang MZ. Dopamine, kidney, and hypertension. Curr Hypertens Rep. 2012; 14:138–143. [PubMed: 22407378]
29. Earley CJ, Kuwabara H, Wong DF, Gamaldo C, Salas R, Brasic J, Ravert HT, Dannals RF, Allen RP. The dopamine transporter is decreased in striatum of subjects with restless legs syndrome. Sleep. 2011; 34:341–347. [PubMed: 21358851]
30. Bara-Jimenez W, Aksu M, Graham B, Sato S, Hallett M. Periodic limb movements in sleep: state-dependent excitability of spinal flexor reflex. Neurology. 2000; 54:1609–1616. [PubMed: 10762502]
31. Davies RJ, Belt PJ, Roberts SJ, Ali NJ, Stradling JR. Arterial blood pressure responses to graded transient arousal from sleep in normal humans. Appl Physiol. 1993; 74:1123–1130. 1985.
32. Becker PM, Jamieson AO, Brown WD. Dopaminergic agents in restless legs syndrome and periodic limb movements of sleep: response and complications of extended treatment in 49 cases. Sleep. 1993; 16:713–716. [PubMed: 7909374]
33. Warnes H, Dinner DS, Kotagal P, Burgess RC. Periodic limb movements and sleep apnoea. J Sleep Res. 1993; 2:38–44. [PubMed: 10607069]
34. Winkelman JW, Shahar E, Sharief I, Gottlieb DJ. Association of restless legs syndrome and cardiovascular disease in the SHHS. Neurology. 2008; 70:35–42. [PubMed: 18166705]
35. Winkelman JW, Finn L, Young T. Prevalence and correlates of restless legs syndrome symptoms in the Wisconsin Sleep Cohort. Sleep Med. 2006; 7:545–552. [PubMed: 16740407]
36. Claman DM, Redline S, Blackwell T, Ancoli-Israel S, Surovec S, Scott N, Cauley JA, Ensrud KE, Stone KL. Prevalence and correlates of periodic limb movements in older women. J Clin Sleep Med. 2006; 2:438–445. [PubMed: 17557474]

## NOVELTY AND SIGNIFICANCE

What is new?

In this study, we found that the frequency of PLMS is associated with hypertension and systolic blood pressure, especially in the African-and Chinese-American populations. After adjusting for multiple potential confounders, PLMS frequency both with and without arousal was associated with significant increases in measured systolic blood pressure.

What is relevant?

Minority groups, particularly African-Americans, have a very high prevalence of hypertension. In this study, it was interesting that African-Americans were least likely (compared to other racial/ethnic groups) to have PLMS, but when PLMS was present in African-Americans, it was most predictive of prevalent hypertension. It will be important to determine if this strong association between PLMS and hypertension in African-Americans is consistent with mechanisms of hypertension which also differ by race/ethnicity, such as greater salt sensitivity in African-Americans. Given the high prevalence of hypertension in minority groups, these data suggest novel targets for improving blood pressure control in these groups.

Summary

PLMS frequency both with and without arousal is associated with prevalent hypertension and systolic blood pressure in African- and Chinese-Americans.

**Table 1**

Distributions of Participant Characteristics by PLMI/PLMAI

| Participant Characteristics | Overall (n=1740) | PLMI<5 (n=1001) | 5≤ PLMI<30 (n=446) | PLMI≥30 (n=293) | PLMAI<1 (n=1218) | 1≤PLMAI<5 (n=364) | PLMAI≥5 (n=158) |
|---|---|---|---|---|---|---|---|
| Age (years) | 68.3±9.1 | 66.9±8.5 | 69.0±9.4 | 71.8±9.2 | 67.3±8.7 | 69.8±9.5 | 72.4±9.4 |
| Sex, male, n(%) | 801(46.0) | 442(44.2) | 197(44.2) | 162(55.3) | 549(45.1) | 177(48.6) | 75(47.5) |
| Race (% PLMcat, % race) | - | - | - | - | - | - | - |
| Caucasian, n(%) | 624(35.9) | 311(31.1,49.8) | 196(44.0,31.4) | 117(39.9,18.8) | 385(31.6,61.7) | 168(46.2,26.9) | 71(44.9,11.4) |
| Black, n(%) | 484(27.8) | 333(33.3,68) | 100(22.4,20.7) | 51(17.4,10.5) | 395(32.4,79.5) | 62(17.0,13.4) | 27(17.1,5.6) |
| Hispanic, n(%) | 433(24.9) | 241(24.1,55.7) | 105(23.5,24.2) | 87(29.7,20.1) | 300(24.6,69.3) | 97(26.7,22.4) | 36(22.8,8.3) |
| Chinese, n(%) | 199(11.4) | 116(11.6,58.3) | 45(10.1,22.6) | 38(13.0,19.1) | 138(11.3,69.3) | 37(10.2,18.6) | 24(15.2,12.1) |
| BMI, $kg/m^2$ | 28.7±5.6 | 29.0±5.7 | 28.2±5.5 | 28.4±5.5 | 28.8±5.6 | 28.4±5.7 | 28.4±5.4 |
| Waist:Hip | 0.94±0.08 | 0.93±0.08 | 0.93±0.08 | 0.95±0.07 | 0.93±0.08 | 0.93±0.08 | 0.94±0.07 |
| Physical Activity (PAS) | 2848±3242 | 2875±3188 | 2837±3358 | 2769±3255 | 2901±3217 | 2653±3249 | 2884±3416 |
| Education | - | - | - | - | - | - | - |
| High School or less | 538(30.9) | 300(30.0) | 136(30.5) | 102(34.8) | 359(29.5) | 132(36.3) | 47(29.8) |
| College/Associate | 512(29.4) | 313(31.3) | 123(27.6) | 76(25.9) | 376(30.9) | 92(25.3) | 44(27.9) |
| Bachelor's/Graduate | 690(39.7) | 388(38.8) | 187(41.9) | 115(39.3) | 483(39.7) | 140(38.5) | 67(42.4) |
| Smoking Status, n(%) | - | - | - | - | - | - | - |
| Never | 812(46.7) | 481(48.1) | 212(47.5) | 119(40.6) | 580(47.6) | 156(42.9) | 76(48.1) |
| Past | 801(46.0) | 429(42.9) | 209(46.9) | 163(55.6) | 538(44.2) | 186(51.1) | 77(48.7) |
| Current | 127(7.3) | 91(9.1) | 25(5.6) | 11(3.8) | 100(8.2) | 22(6.0) | 5(3.2) |
| Drink Alcohol, n(%) | 754(43.3) | 420(42.0) | 200(44.8) | 134(45.7) | 516(42.4) | 165(45.3) | 73(46.2) |
| Depression, n(%) | 252(14.5) | 147(14.7) | 70(15.7) | 35(12.0) | 188(15.4) | 43(11.8) | 21(13.3) |
| Atrial Fibrillation, n(%) | 71(4.1) | 36(3.6) | 20(4.5) | 15(5.1) | 47(3.9) | 15(4.1) | 9(5.7) |
| Diabetes, n(%) | 351(20.2) | 209(20.9) | 84(18.8) | 58(19.8) | 257(21.1) | 64(17.6) | 30(19.0) |
| Anti-hypertensive, n (%) | 938(53.9) | 515(51.5) | 245(54.9) | 178(60.8) | 637(52.3) | 202(55.5) | 99(62.7) |
| Hypertension, n(%) | 1034(59.4) | 574(57.3) | 262(58.7) | 198(67.6) | 704(57.8) | 221(60.7) | 109(69.0) |
| Clinic 5 SBP (mmHg) | 122.4±19.8 | 122.5±19.8 | 121.0±19.4 | 124.4±20.1 | 122.3±19.8 | 121.6±18.7 | 125.5±21.6 |
| Imputed SBP (mmHg) | 129.8±19.6 | 129.1±19.6 | 129.3±20.1 | 133.2±18.8 | 129.2±19.8 | 129.6±18.6 | 135.0±20.2 |
| Clinic 5 DBP (mmHg) | 68.1±9.9 | 68.5±9.7 | 67.3±9.9 | 67.8±10.4 | 68.2 ± 9.7 | 67.6±10.0 | 68.2±10.7 |
| Imputed DBP (mmHg) | 72.0±9.1 | 72.1±9.1 | 71.5±9.3 | 72.3±9.0 | 72.0±9.1 | 71.5±9.1 | 73.0±9.0 |

| Participant Characteristics | Overall (n=1740) | PLMI<5 (n=1001) | 5≤ PLMI<30 (n=446) | PLMI≥30 (n=293) | PLMAI<1 (n=1218) | 1≤PLMAI<5 (n=364) | PLMAI≥5 (n=158) |
|---|---|---|---|---|---|---|---|
| RLS Symptoms, n(%) | 424(24.4) | 228(22.8) | 122(27.4) | 74(25.3) | 281(23.1) | 109(30.0) | 34(21.5) |
| Apnea-hypopnea index | 24.0±19.4 | 24.9±20.5 | 22.7±18.0 | 22.7±17.2 | 24.2±19.8 | 22.0±17.8 | 26.5±19.0 |
| PLMI | 13.8±23.5 | 0.7±1.3 | 14.5±7.0 | 57.3±26.7 | 3.9±9.3 | 27.6±21.8 | 58.2±33.7 |
| PLMAI | 1.5±3.3 | 0.10±0.3 | 1.8±2.0 | 5.8±5.7 | 0.1±0.3 | 2.4±1.1 | 9.8±5.4 |
| Arousal index | 22.3±11.9 | 21.9±12.2 | 22.4±11.1 | 23.2±12.1 | 21.1±11.8 | 22.7±10.6 | 30.7±12.2 |

For binary outcomes, data expressed as number and frequency.

For continuous variables, data expressed as mean±standard deviation.

P-values for continuous variables are from an ANOVA and Chi-square for binary variables.

BMI=Body mass index; DBP=diastolic blood pressure; PAS=Physical Activity score (reported time spent performing physical tasks in a week multiplied by metabolic equivalent); SBP=systolic blood pressure

**Table 2**

Hypertension By PLMI/PLMAI Category and Race/Ethnicity

| Participant Characteristics | Overall (n=1740) | PLMI<5 (n=1001) | 5≤PLMI<30 (n=446) | PLMI≥30 (n=293) | p | PLMAI<1 (n=1218) | 1≤PLMAI<5 (n=364) | PLMAI≥5 (n=158) | p |
|---|---|---|---|---|---|---|---|---|---|
| Hypertension, n (% of race) | n (% hypertensive of that race for that PLM category) | | | | | n (% hypertensive for that race/category) | | | |
| Overall (n=1740) | 1034(59.4) | 574/1001 (57.3) | 262/446 (58.7) | 198/293 (67.6) | 0.01 | 704/1218 (57.8) | 221/364 (60.7) | 109/158 (69.0) | 0.02 |
| African-American (n=484) | 359(74.2%) | 240/333 (72.1) | 75/100 (75.0) | 44/51 (86.3) | 0.07 | 285/395 (72.2) | 50/62 (80.7) | 24/27 (88.9) | 0.05 |
| Caucasian (n=624) | 327(52.4%) | 152/311 (48.9) | 105/196 (53.6) | 70/117 (59.8) | 0.12 | 193/385 (50.1) | 90/168 (53.6) | 44/71 (62.0) | 0.17 |
| Hispanic (n=433) | 253(58.4%) | 134/241 (55.6) | 60/105 (57.1) | 59/87 (67.8) | 0.13 | 168/300 (56.0) | 62/97 (63.9) | 23/36 (63.9) | 0.30 |
| Chinese-Americans (n=199) | 95(47.7%) | 48/116 (41.4) | 22/45 (48.9) | 25/38 (65.8) | 0.03 | 58/138 (42.0) | 19/37 (51.4) | 18/24 (75.0) | 0.01 |
| Systolic $BP_{measured}$ (mmHg) | | | | | | | | | |
| Overall | 122.4±19.8 | 122.5±19.8 | 121.0±19.4 | 124.4±20.1 | 0.07 | 122.3±19.8 | 121.6±18.7 | 125.5±21.6 | 0.10 |
| African-Americans | 126.4±19.2 | 125.7±19.1 | 126.4±19.3 | 130.6±19.8 | 0.23 | 126.0±19.2 | 125.3±17.5 | 134.4±21.5 | 0.08 |
| Caucasian | 119.6±19.2 | 120.1±19.6 | 117.8±18.7 | 121.6±18.8 | 0.20 | 119.6±19.5 | 119.2±19.2 | 120.9±17.4 | 0.83 |
| Hispanic | 123.1±20.1 | 123.9±20.5 | 121.8±19.4 | 122.4±19.8 | 0.62 | 123.1±20.6 | 123.4±17.9 | 122.1±21.8 | 0.94 |
| Chinese-Americans | 120.2±20.7 | 116.7±19.2 | 121.5±20.2 | 129.2±23.0 | 0.004 | 117.4±18.6 | 121.1±19.6 | 134.6±27.3 | 0.0007 |
| Diastolic $BP_{measured}$ (mmHg) | | | | | | | | | |
| Overall | 68.1±9.9 | 68.5±9.7 | 67.3±9.9 | 67.8±10.4 | 0.09 | 68.2±9.7 | 67.6±10.0 | 68.2±10.7 | 0.51 |
| African-Americans | 69.7±9.7 | 70.1±9.6 | 69.5±9.1 | 67.5±11.0 | 0.19 | 69.8±9.5 | 68.3±9.7 | 70.8±11.3 | 0.43 |
| Caucasian | 66.8±9.8 | 67.0±9.6 | 66.0±9.9 | 67.4±10.0 | 0.40 | 66.6±9.8 | 67.3±9.8 | 66.4±9.7 | 0.68 |
| Hispanic | 68.0±10.1 | 68.5±9.4 | 67.5±11.3 | 67.5±10.4 | 0.62 | 68.2±9.7 | 67.8±10.8 | 67.0±11.6 | 0.74 |
| Chinese-Americans | 68.4±9.8 | 68.1±10.2 | 68.0±7.7 | 69.9±10.8 | 0.58 | 68.3±9.7 | 66.7±9.5 | 72.1±10.3 | 0.11 |
| Systolic $BP_{imputed}$ (mmHg) | | | | | | | | | |
| Overall | 129.8±19.6 | 129.1±19.6 | 129.3±20.1 | 133.2±18.8 | 0.08 | 129.2±19.8 | 129.6±18.6 | 135.0±20.2 | 0.08 |
| African-Americans | 135.6±17.2 | 134.5±17.1 | 136.2±17.8 | 142.2±15.1 | 0.21 | 135.0±17.3 | 136.3±15.4 | 143.7±17.1 | 0.29 |
| Caucasian | 126.1±19.7 | 125.4±19.7 | 125.6±20.8 | 128.7±17.7 | 0.56 | 125.5±20.2 | 126.2±19.2 | 129.5±18.6 | 0.58 |
| Hispanic | 130.1±19.7 | 129.7±20.4 | 129.0±18.3 | 132.6±19.2 | 0.68 | 129.4±20.1 | 131.0±17.4 | 134.0±19.6 | 0.58 |
| Chinese-Americans | 126.7±21.5 | 122.2±20.0 | 130.2±22.4 | 136.2±21.4 | 0.02 | 123.0±19.6 | 129.8±21.3 | 143.0±24.2 | 0.01 |
| Diastolic $BP_{imputed}$ (mmHg) | | | | | | | | | |
| Overall | 72.0±9.1 | 72.1±9.1 | 71.5±9.3 | 72.3±9.0 | 0.64 | 72.0±9.1 | 71.5±9.1 | 73.0±9.0 | 0.47 |
| African-Americans | 74.8±8.3 | 74.8±8.4 | 75.0±7.7 | 74.2±8.6 | 0.93 | 74.8±8.2 | 74.0±8.4 | 76.3±8.9 | 0.71 |
| Caucasian | 70.3±9.1 | 70.0±8.9 | 70.1±9.5 | 71.3±9.1 | 0.64 | 69.9±9.2 | 70.9±9.2 | 70.9±8.6 | 0.65 |

| Participant Characteristics | Overall (n=1740) | PLMI<5 (n=1001) | 5≤PLMI<30 (n=446) | PLMI≥30 (n=293) | p | PLMAI<1 (n=1218) | 1≤PLMAI<5 (n=364) | PLMAI≥5 (n=158) | p |
|---|---|---|---|---|---|---|---|---|---|
| Hispanic | 71.5±9.1 | 71.7±8.8 | 70.3±10.1 | 72.3±8.5 | 0.53 | 71.5±9.1 | 71.1±9.0 | 72.1±9.2 | 0.91 |
| Chinese-Americans | 71.4±9.6 | 70.5±10.1 | 72.4±7.6 | 73.0±10.0 | 0.47 | 70.7±9.6 | 70.7±9.7 | 76.5±8.1 | 0.09 |

Diastolic $BP_{imputed}$=imputed diastolic blood pressure; Diastolic $BP_{measured}$=measured diastolic blood pressure; Systolic $BP_{imputed}$=imputed systolic blood pressure; Systolic $BP_{measured}$=measured systolic blood pressure;

**Table 3**

Logistic Regression of Hypertension by Periodic Limb Movements Indices

| | | Hypertension; Estimate (95% Confidence Interval) | | | | | |
|---|---|---|---|---|---|---|---|
| | **Group** | **Unadjusted** | **p-value** | **Minimally Adjusted** | **p-value** | **Fully Adjusted** | **p-value** |
| **PLMI (10 unit)** | | | | | | | |
| By Race | Overall | 1.07 (1.02,1.12) | 0.002 | 1.02 (0.98,1.07) | 0.32 | 1.05 (1.00,1.10) | 0.055 |
| | African-American | 1.24 (1.05,1.47) | 0.003 | 1.18 (0.99,1.40) | 0.04 | 1.21 (1.01,1.45) | 0.02 |
| | Caucasian | 1.07 (1.00,1.14) | 0.04 | 1.02 (0.95,1.10) | 0.53 | 1.03 (0.95,1.11) | 0.49 |
| | Hispanic | 1.06 (0.98,1.15) | 0.13 | 1.01 (0.93,1.10) | 0.79 | 1.00 (0.91,1.09) | 1.00 |
| | Chinese-American | 1.18 (1.05,1.34) | 0.005 | 1.10 (0.96,1.25) | 0.16 | 1.10 (0.96,1.25) | 0.16 |
| **PLMAI (1 unit)** | | | | | | | |
| By Race | Overall | 1.05 (1.01,1.08) | 0.003 | 1.02 (0.99,1.06) | 0.23 | 1.05 (1.01,1.09) | 0.02 |
| | African-American | 1.22 (1.03,1.43) | 0.003 | 1.16 (0.99,1.35) | 0.02 | 1.20 (1.02,1.42) | 0.005 |
| | Caucasian | 1.05 (1.00,1.10) | 0.03 | 1.03 (0.98,1.08) | 0.30 | 1.03 (0.989,1.09) | 0.21 |
| | Hispanic | 1.03 (0.97,1.09) | 0.39 | 0.99 (0.93,1.06) | 0.82 | 1.00 (0.93,1.07) | 0.96 |
| | Chinese-American | 1.15 (1.04,1.27) | 0.003 | 1.09 (0.98,1.21) | 0.09 | 1.10 (0.98,1.23) | 0.08 |

Minimal adjustment included covariates gender, age and BMI.

Full adjustment included covariates gender, age, BMI, race/ethnicity, education, income, smoking status, alcohol use, atrial fibrillation, diabetes, depression scale, exercise scale (log transform), AHI, and arousal index.

**Table 4**

Linear Regression of Imputed Systolic Blood Pressure By Periodic Limb Movements Indices

| | | Systolic Blood Pressure; Estimate (95% Confidence Interval) | | | | | |
|---|---|---|---|---|---|---|---|
| | **Group** | **Unadjusted** | **p-value** | **Minimally Adjusted** | **p-value** | **Fully Adjusted** | **p-value** |
| **PLMI (10 unit)** | | | | | | | |
| By Race | Overall | 0.65 (0.00,1.30) | 0.05 | 0.09 (−0.51,0.70) | 0.70 | 0.08 (−0.28,0.87) | 0.87 |
| | African-American | 1.53 (0.06,2.99) | 0.04 | 1.05 (−0.39,2.50) | 0.051 | 1.26 (−0.21,2.73) | 0.09 |
| | Caucasian | 0.54 (−0.39,1.47) | 0.25 | −0.07 (−0.98,0.84) | 0.72 | −0.08 (−0.98,0.82) | 0.86 |
| | Hispanic | 0.35 (−0.88,1.58) | 0.57 | −0.22 (−1.39,0.96) | 0.052 | −0.21 (−1.39,0.96) | 0.71 |
| | Chinese-American | 2.23 (0.41,4.05) | 0.02 | 1.04 (−0.65,2.73) | 0.07 | 1.01 (−0.69,2.71) | 0.24 |
| **PLMAI (1 unit)** | | | | | | | |
| By Race | Overall | 0.52 (0.06,0.97) | 0.03 | 0.19 (−0.23,0.62) | 0.37 | 0.35 (−0.09,0.79) | 0.12 |
| | African-American | 1.07 (0.09,2.04) | 0.03 | 0.84 (−0.11,1.79) | 0.08 | 1.01 (0.04,1.98) | 0.04 |
| | Caucasian | 0.32 (−0.28,0.93) | 0.29 | −0.02 (−0.60,0.56) | 0.94 | −0.01 (−0.59,0.58) | 0.98 |
| | Hispanic | 0.50 (−0.30,1.30) | 0.22 | 0.14 (−0.62,0.90) | 0.71 | 0.20 (−0.62,1.01) | 0.63 |
| | Chinese-American | 1.71 (0.33,3.08) | 0.02 | 0.88 (−0.40,2.16) | 0.17 | 0.82 (−0.50,2.14) | 0.22 |

Minimal adjustment included covariates gender, age and BMI.

Full adjustment included covariates gender, age, BMI, race/ethnicity, education, income, smoking status, alcohol use, atrial fibrillation, diabetes, depression scale, exercise scale (log transform), AHI, and arousal index.