Ethnic Differences in the Degree of Morning Blood Pressure Surge and in Its Determinants Between Japanese and European Hypertensive Subjects

Data From the ARTEMIS Study

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Abstract**—**Morning blood pressure (BP) surge has been reported to be a prognostic factor for cardiovascular events. Its determinants are still poorly defined, however. In particular, it is not clear whether ethnic differences play a role in determining morning surge (MS) size. Aim of our study was to explore whether differences exist in the size of MS between Japanese and Western European hypertensive patients. We included 2887 untreated hypertensive patients (age 62.3±8.8 years) from a European ambulatory BP monitoring database and 811 hypertensive patients from a Japanese database (Jichi Medical School Ambulatory Blood Pressure Monitoring WAVE1, age 72.3±9.8 years) following the same inclusion criteria. Their 24-hour ambulatory BP monitoring recordings were analyzed focusing on MS. Sleep-trough MS was defined as the difference between mean systolic BP during the 2 hours after awakening and mean systolic BP during the 1-hour night period that included the lowest sleep BP level. The sleep-trough MS was higher in Japanese than in European hypertensive patients after adjusting for age and 24-hour mean BP levels (40.1 [95% confidence interval 39.0–41.2] versus 23.0 [22.4–23.5] mm Hg; *P*<0.001). This difference remained significant after accounting for differences in night-time BP dipping. Age was independently associated with MS in the Japanese database, but not in the European subjects. Our results for the first time show the occurrence of substantial ethnic differences in the degree of MS. These findings may help in understanding the role of ethnic factors in cardiovascular risk assessment and in identifying possible ethnicity-related differences in the most effective measures to be implemented for prevention of BP-related cardiovascular events. **(*Hypertension*. 2015;66:750-756. DOI: 10.1161/HYPERTENSIONAHA.115.05958.)**
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Key Words: ambulatory blood pressure monitoring ■ arterial hypertension ■ blood pressure variability ■ cardiovascular events ■ ethnicity ■ morning blood pressure surge ■ sympathetic nervous system

International databases, combining subjects with different ethnic origin,[1–3] have shown some ambulatory blood pressure (BP) parameters to be variably associated with a higher risk of cardiovascular events. However, the possibility that part of the between-studies variability in results might have depended on ethnic differences in ambulatory BP patterns was not carefully considered, possible regional differences being only managed through statistical analysis tools. In particular, little is known on whether Asian subjects differ from Western subjects in parameters describing 24-hour ambulatory BP profiles, and whether these differences remain significant when considering differences in lifestyles (and the resulting differences in body mass index) on the background of the reported differences in the rates of cardiovascular events.[4]

These considerations have become even more relevant in the light of recent hypertension guidelines recommending a larger use of ambulatory BP monitoring (ABPM) to improve prediction of cardiovascular risk in untreated and treated hypertensive patients.[5–7] In particular, these recommendations focus not only on average 24-hour BP levels,[6–9] but also on several

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patterns characterizing the diurnal BP profile, among which an exaggerated sleep-trough morning surge (MS) of BP has been reported to predict cardiovascular events.[10–13] However, when considering the association between the sleep-trough MS and stroke, different results have been reported from the analysis of different data sets. In Japanese elderly hypertensive patients, a significant association between stroke and the degree of MS was found,[10] whereas this was not the case when an international ABPM database or a European ABPM database was analyzed.[12,14,15] In the latter case, the inability to find a significant relationship between BP MS and cerebrovascular events was suggested to possibly depend on the occurrence of a different degree of sleep-trough MS among different ethnic groups contributing to this database,[3] but to date, no data are available on the occurrence of systematic differences in BP MS when comparing subjects of different ethnic origin.

Aim of this study was to investigate this issue by comparing the degree of sleep-trough MS of BP between a group of Japanese and a group of Western European untreated hypertensive patients.

Methods

Study Patients

We considered 3 sets of ABPM data, most of which are included in the International Ambulatory Blood Pressure Registry: Telemonitoring of Hypertension and Cardiovascular Risk Project (ARTEMIS) study, an ABPM registry gathering 24-hour ABPM files, combined with basic clinical information, from hypertensive patients followed by hypertension centers or general practitioners in different regions of the world.[16] The first ABPM data set (n=811) comes from the Jichi Medical School Ambulatory Blood Pressure Monitoring (JMS-ABPM) study, which includes ABPM data from Japanese elderly hypertensive patients. Patients were enrolled in this study if they satisfied the following criteria: (1) average clinic BP ≥140/90 mm Hg, (2) age >50 years, (3) a high-quality 24-hour ABPM,[6] (4) no evidence of renal failure, liver disease, overt illness, or past history of cardiovascular disease, and (5) no intake of any antihypertensive medication for at least 14 days before the ambulatory BP recording. The remaining 2 data sets include European hypertensive subjects selected from the Spanish Society of Hypertension ABPM Registry (n=2732)[17–19] and from an Italian Society of Hypertension ABPM database (n=155), based on the criteria used for the Japanese population. All patients gave informed consent for their data to be used for research purposes. Spanish and Italian data were pooled because of (1) the ethnic and cultural similarities between these 2 Mediterranean populations, and (2) the 2 groups did not show systematic differences in ABPM parameters, as well as in demographic and clinical data.

Blood Pressure Measurements

In the JMS-ABPM study, clinic BP was defined as the average of 2 clinic BP measurements as obtained in the sitting position using the auscultatory technique on ≥2 occasions in different days. ABPM was performed by using validated devices (ABPM-630, Nippon Colin, Japan[20]; TM-2421 or TM-2425, A&D, Japan[21]), with the BP measurements programmed to be performed at 30-minute intervals over the 24 hours. In the Spanish Society of Hypertension and the Italian ABPM database, clinic BP values were defined as the average of 2 sitting clinic BP measurements obtained from 2 different visits by using the auscultatory method and according to the European Society of Hypertension recommendations.[22] Twenty-four-hour ABPM was performed by a validated device (Spacelabs 90207, Spacelabs[23]), with the automated measurements programmed at 20-minute intervals throughout the 24 hours.

Morning systolic BP (SBP) was defined as the average of the ambulatory BP values during the first 2 hours after the wake-up time (defined from patients' diary). The lowest nocturnal SBP was defined as the average of the 3 SBP readings (the lowest reading and the readings immediately before and after) centered at the time of the lowest night-time values. The sleep-trough MS in SBP was calculated as the morning SBP minus the lowest night-time SBP. The night-time period was defined from patients' diaries as the set of BP readings between the time patients went to bed and the time when they left the bed. The daytime period was defined as the set of BP readings obtained during the remaining portion of the 24 hours, after excluding that subjects went to bed for a nap. All ABPM recordings were performed during the working days. Subjects were asked to attend at their usual activities, avoiding either to remain resting at home or to perform unusually strenuous exercise during the recording time.

Unprocessed ABPM recording data were used for the analyses, and the same methodology was used for all the recordings to calculate the derived variables (mean values, MS, nocturnal fall).

Other Measurements

We used the questionnaires designed and administered in each database to obtain information on subject's medical history and habits. Body mass index was computed as body weight in kilograms divided by height in meters squared. We defined diabetes mellitus based on the data from each database as previously reported.[10,18]

Data Analysis

Data are expressed as means±SD or as percentages, as appropriate. A 2-sided unpaired *t* test and the χ^2 test were used to test differences in mean values and prevalence rates, respectively, between European and Japanese groups. Between-groups comparisons for MS were performed by analysis of covariance, with the data adjusted for age, sex, body mass index, smoking, diabetes mellitus, and 24-hour mean SBP. Given the previous demonstration that age and 24-hour mean BP are strong determinants of sleep-trough MS,[24] a matched case–control analysis of European and Japanese subjects identical for age and 24-hour BP was also performed. This also addressed the limitation associated with the imbalance in the number of subjects between the 2 groups. Multiple linear regression analysis was performed to estimate and test the determinants of the sleep-trough SBP MS, including age, sex, body mass index, smoking, diabetes mellitus, and 24-hour SBP as independent variables in the model. Analysis of covariance was performed to evaluate the between-group differences in the sleep-trough SBP MS among categories of age adjusted for sex, body mass index, smoking, diabetes mellitus, and 24-hour mean SBP. The possible confounding effect of night-time BP dipping on the degree of BP MS was assessed by categories of lowest SBP during night-time after adjusting for body mass index. All statistical analyses were performed with SPSS software, version 19.0 (SPSS, Chicago). Two-tailed $P<0.05$ was taken as the level of statistical significance.

Results

The general characteristics of the European and the Japanese populations are shown in Table 1. Compared with the European group, the Japanese group was older, had a lower prevalence of male subjects, a lower body mass index, a lower rate of dyslipidemia, and a slightly higher rate of smoking. Average clinic, 24-hour, daytime, and night-time BP values and standard deviation of BP were almost always higher in the Japanese group than in the European group. Morning SBP surge in the Japanese group was significantly higher than that in the European group (40.3±18.6 mm Hg versus 22.9±13.5 mm Hg, $P<0.001$). After adjustment for all confounding factors by analysis of covariance test, this difference remained similar. When we further divided the population of our study into 3 ethnic groups (Japanese, Italian, and Spanish groups), Italian group was younger and had higher clinic, 24-hour, and daytime diastolic BP and standard deviation of daytime

Table 1. Patient Characteristics

Variable	Japanese Group, n=811	European Group, n=2887	*P* Value
Age, y	72.3±9.8	62.3±8.8	<0.001
Male, %	38.3	53.3	<0.001
Body mass index, kg/m^2	23.9±3.5	28.1±4.1	<0.001
Smoking, %	20.5	17.1	0.033
Diabetes mellitus, %	12.2	12.4	0.904
Clinic SBP	164.2±17.7	156.9±14.1	<0.001
Clinic DBP	90.5±14.2	90.9±10.1	0.451
Clinic PR, bpm	76.8±12.0	76.4±13.5	0.419
24-h SBP	138.1±16.3	132.6±13.3	<0.001
24-h DBP	78.2±9.7	78.0±9.4	0.597
24-h PR, bpm	70.8±7.5	71.3±9.2	0.104
Daytime SBP	144.9±17.7	137.3±13.8	<0.001
Daytime DBP	81.6±10.6	82.3±10.2	0.126
Daytime PR, bpm	76.6±8.5	75.5±10.3	0.006
SD of daytime SBP	18.2±5.6	12.2±3.5	<0.001
SD of daytime DBP	12.8±5.0	8.6±2.4	<0.001
Night-time SBP	126.8±18.2	122.1±15.5	0.004
Night-time DBP	72.1±10.6	69.4±10.1	<0.001
Night-time PR, bpm	61.0±8.1	64.2±9.1	<0.001
SD of night-time SBP	13.4±4.9	10.1±3.9	<0.001
SD of night-time DBP	8.5±3.1	7.9±2.9	<0.001
Morning surge	40.3±18.6	22.9±13.5	<0.001
Dipping pattern, %			<0.001
Extreme dipper	20.3	11.3	
Dipper	42.4	45.1	
Nondipper	27.7	35.3	
Riser	9.6	8.3	

All blood pressure variables are in mm Hg. DBP indicates diastolic blood pressure; PR, pulse rate; SBP, systolic blood pressure; and SD, standard deviation.

and night-time diastolic BP. However, morning BP surge remained the highest in the Japanese group as compared with either the Spanish group or the Italian group considered separately (Table S1 in the online-only Data Supplement). When we divided the lowest SBP during night-time into quintiles in the whole group, morning SBP surge remained significantly higher in the Japanese group than in the European group within each quintile of lowest night-time SBP (Figure 1), and this result did not change after adjusting for body mass index (*P*<0.001 in each quintile). In addition, there was no significant difference in lowest SBP during night-time between the corresponding quintiles of Japanese and European groups, with the exception of the lowest quintiles, where lowest night-time SBP was lower in the Japanese than in the European group, even if of a few mm Hg only (87.3±8.5 mm Hg versus 92.2±4.9 mm Hg, *P*<0.001) (Figure 1).

In either group, we identified 631 subjects who could be matched for age (range 2 years) and 24-hour SBP level (range 2 mm Hg). For clinic BP, daytime BP, BP variability, and BP MS, comparison between these 2 selected groups yielded essentially the same results as in the whole sample (Table S2).

In Japanese subjects, linear regression analysis showed that age and 24-hour SBP were independent determinants of sleep-trough MS, whereas this association was not found in the European subjects (Table 2). Likewise, although in Japanese subjects, sleep-trough MS was associated with daytime SBP (*r*=0.19, *P*<0.001), night-time SBP (inverse correlation, *r*=−0.08, *P*=0.018), and nocturnal SBP fall (*r*=0.33, *P*<0.001), this association was not found in the European subjects. Furthermore, when we assessed the degree of sleep-trough MS by quintiles of age, we found an age-related difference only in Japanese and not in European subjects (Figure 2).

Discussion

Our study, based on the large international ARTEMIS database, offers for the first time information on the presence of significant differences in the degree of morning SBP surge between Asian and European untreated hypertensive subjects, with the sleep-trough MS of Japanese hypertensive patients being significantly higher than that of Western European hypertensive patients living in Mediterranean countries. In addition, age was an important determinant of the sleep-trough MS in the Japanese subjects, but not in the European subjects.

On the background of our previous report that excessive sleep-trough MS was an independent predictor of stroke in elderly Japanese hypertensive patients,[10] the present data are relevant to the interpretation of recent studies, which assessed the association between MS and target organ damage or cardiovascular events through the analysis of international databases, including subjects with different ethnic background,[11,25–27] sometimes reaching discrepant conclusions. For example, recently, in The Progetto Ipertensione Umbria Monitoraggio Ambulatoriale (PIUMA) study, sleep-trough MS was not found to be a significant risk factor for cardiovascular events. Although ethnicity was suggested to contribute explaining the different results concerning the clinical impact of sleep-trough MS of BP on cardiovascular complications obtained in different studies, to our knowledge, our study is

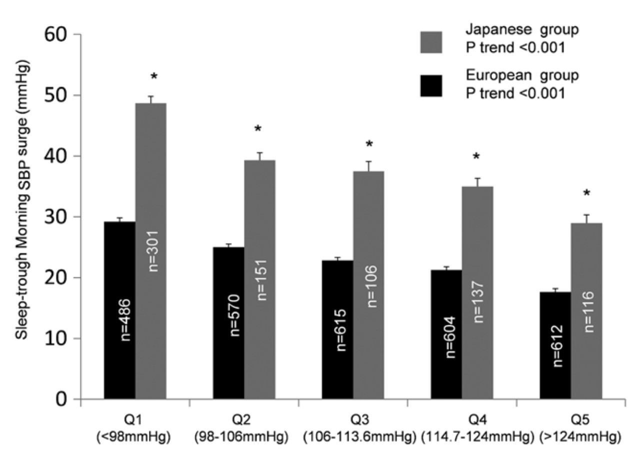

Figure 1. Sleep-trough morning systolic blood pressure (SBP) surge in 2 groups of Japanese (gray) and European (black) subjects, respectively. Data are separately shown for different quintiles of lowest SBP during night-time. Values are expressed as means±SEM. **P*<0.001 Japanese vs European group in the same category.

Table 2. Multiple Linear Regression Analysis for Morning Surge in Japanese and European Hypertensive Patients

	Japanese Group, n=811		European Group, n=2887	
Variable	Standardized β	*P* Value	Standardized β	*P* Value
Age	0.104	0.004	−0.023	0.227
Male	−0.003	0.944	−0.001	0.956
Body mass index	0.078	0.030	0.042	0.024
Smoking	−0.010	0.796	0.011	0.584
Diabetes mellitus	0.014	0.698	−0.015	0.430
24-h systolic blood pressure	0.110	0.002	−0.010	0.608

the first to provide a direct demonstration of the occurrence of ethnicity-related differences in MS.

An additional contribution of our study is the demonstration that these differences in the sleep-trough BP MS persist after accounting for age and 24-hour BP levels. This demonstration is important on the background of previous findings by Kario et al, which clearly showed that BP MS is related to 24-hour BP levels and to age, at least in Japanese subjects.[24,28] In fact, when we compared the sleep-trough MS between our 2 ethnic groups, by considering only subjects carefully matched for age and 24-hour BP levels, the difference in sleep-trough MS of BP between these 2 groups remained significant.

Our results should be interpreted in the light of previous observations on this issue (Table 3). Although several studies reported on MS values in different populations, their direct comparison is difficult because of heterogeneity in the type of population under study (general population, hypertensive subjects, or normotensive subjects), in the method used to describe MS distribution, and sometimes in the methodology of MS calculation itself. For instance, our data in Japanese patients are similar to those obtained in the study by Kario et al[27] in elderly hypertensive patients. Also the MS size we observed in the European population was comparable to that reported in the Italian population of PIUMA study[14] and to that observed in the meta-analysis by Li et al.[3] Conversely, in the latter meta-analysis, MS size reported in Asian subjects was markedly smaller than that in our study, possibly because of the inclusion of Chinese subjects. In fact, it seems that sleep-trough MS values may be higher in the Japanese compared with other Asian ethnic groups. In a study in untreated Korean hypertensive patients, the reported sleep-trough MS values were considerably lower than those in our study and comparable with those obtained in Europeans.[28]

Further data supporting the presence of higher MS in the Japanese population come from the Ohasama study. In this study, sleep-trough BP MS was higher than that in the European hypertensive patients in our study (33 mm Hg), even though Ohasama study included subjects from a general population with lower age (mean 61 years) and lower 24-hour BP levels (mean 123/72 mm Hg).[11] On the contrary, in the study by Ohira et al,[29] the top decile of the MS distribution was almost superimposable to that of our European hypertensive patients. It has to be emphasized, however, that this Japanese population was much younger and had much lower 24-hour BP levels and that MS was computed by considering as night-time value the average night-time SBP instead of the 3 consecutive readings centered on the lowest reading during sleep, possibly leading to MS underestimation.

The possible mechanisms responsible for the higher sleep-trough MS levels found in Japanese hypertensive patients as compared with other hypertensive populations have not been elucidated yet. Japanese subjects, as compared with Western subjects, are known to be characterized by lower levels of renin activity and to be more susceptible to salt and volume-dependent type of hypertension.[30] Concomitantly, they might be characterized by higher levels of sympathetic nerve activity in the morning period, which represents one of the acknowledged causes of morning BP surge, and might thus be one of the factors leading to pronounced sleep-trough MS found in Japanese hypertensive patients. Indeed, we found that the difference in sleep-trough MS between Japanese and European group was mainly driven by differences in morning BP level reached, with no major differences in lowest night-time BP. Also the finding in Japanese subjects of higher values of clinic and daytime BP and the finding of higher values of all BP standard deviations support the hypothesis of BP over-reactivity to behavioral challenges (such as morning awakening).[31–35] This hypothesis could be further supported by investigating the relationship between

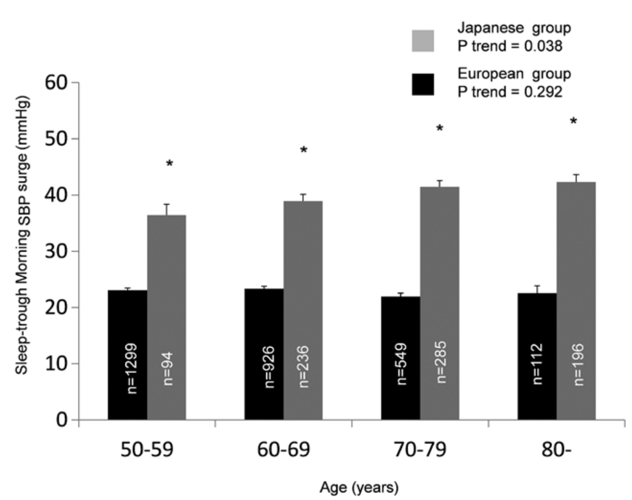

Figure 2. Sleep-trough morning systolic blood pressure (SBP) surge in 2 groups of Japanese (gray) and European (black) subjects, respectively, in 2 groups of European and Japanese hypertensive patients after adjusted for sex, body mass index, smoking, diabetes mellitus, and 24-h mean systolic blood pressure. Data are separately shown for 4 different age groups. Values are expressed as means±SEM. **P*<0.001 Japanese vs European group in the same category.

Table 3. Comparison of Morning Blood Pressure Surge Values in Available Studies With Those Observed in the Japanese and in the European Populations of Our Study

			SBP MS Value, mm Hg		
Reference Study	Population	Variable	Reference Study	Japanese Population of Our Study	European Population of Our Study
Yano et al[27]	Japanese (hypertensive)	Median of top quartile	60	61.9	38
Li et al[3]	European/South American (general)	Threshold of top decile	35	64.3	40
Li et al[3]	Japanese/Chinese (general)	Threshold of top decile	43	64.3	40
Verdecchia et al[14]	European (hypertensive)	Threshold of top decile	44	64.3	40
Metoki et al[11]	Japanese (general)	Threshold of top quintile	40	54.8	33
Ohira et al[29]*	Japanese (normotensive)	Threshold of top decile	37	64.3	40
Lee et al[28]	Korean (hypertensive)	Threshold of top quartile	28	51.5	31

MS indicates morning surge; and SBP, systolic blood pressure.
*Average night-time SBP was used for MS calculation.

morning BP surge and the BP surge caused by siesta, in the light of previous study showing that in ≈70% of the patients, excessive morning BP surge coexists with the siesta BP surge.[36] Unfortunately, information on siesta was not available in our study, and the issue of possible racial difference in siesta BP surge should be addressed by future studies.

An important factor that may influence the 24-hour BP profile is a poor sleep quality, previously shown to be associated with a diminished nocturnal BP fall.[37,38] Because sleep quality is worse in the elderly, the higher mean age of the Japanese group may have contributed to between-group differences in ambulatory BP, not easily accounted for in statistical analyses. A possible contribution of sleep-disordered breathing to the observed differences in MS could also be hypothesized. Data on sleep quality were not available for our subjects; therefore, we cannot exclude an impact of this factor on MS, although it is unlikely that it might have led to the assessment of a greater MS in the Japanese group. If anything, a reduced nocturnal BP dipping because of sleep alterations might have led to the estimate of a smaller MS. Thus, we believe that a possible influence of a reduced sleep quality on our findings is unlikely, also, considering a previous report showing that poor sleep quality assessed by actigraphy was associated with diminished, rather than increased nocturnal BP fall.[39]

Additional explanations for our findings could be provided by investigating the relationship between morning BP surge and the BP surge associated with siesta, in the light of a previous study showing that in ≈70% of the patients, excessive morning BP surge coexists with the siesta-related BP surge.[36] Unfortunately, information on siesta was not available in our study, and the issue of possible ethnic differences in siesta BP surge would deserve to be addressed in future investigations.

Finally, our study has also shown that age was a determinant of the degree of morning BP surge in Japanese hypertensive subjects, whereas this association was not found in the European hypertensive subjects. No apparent explanation could be found in our data set for such a difference between populations, which would need to be specifically addressed by future studies. We can only speculate, based on the International Cooperative Study on Salt, Other Factors, and Blood Pressure (INTERSALT) study findings, that age was more positively related with BP levels and variability in those regions characterized by a high salt intake.[40] Indeed, the facilitating effect of age on the degree of morning BP surge found in our Japanese hypertensive patients might be related to their increased susceptibility to BP increases as a result of the higher salt intake reported in the Japanese population, compared with European and, in particular, the Mediterranean subjects.[41] A previous report suggested that in African subjects, nondipping could be a compensatory pressure diuresis mechanism favoring nocturnal excretion of sodium excess.[42] Considering that, despite a likely higher salt intake, nondipping pattern was not more prevalent in our Japanese subjects than in their European counterparts, one could hypothesize that the above mechanism was less efficient in the Japanese group. Of course, an ad hoc study would be needed to confirm this hypothesis.

Intermediate mechanisms are likely complex and may involve the impairment of vascular endothelial function caused by reduced nitric oxidase activity possibly related to a higher sodium intake. In fact, endothelial function was reported to be impaired by high salt intake[43] and to decrease in the early morning compared with late morning and evening in healthy patients.[44] Both these mechanisms could synergistically contribute to a higher morning BP surge in the Japanese group.

We should acknowledge possible limitations of our study. These include first of all the enrollment of subjects from 2 European countries, which could have contributed to some heterogeneity of the European population. This is unlikely to be the case, however, because subjects recruited from Spain and Italy had similar characteristics, and the degree of BP MS was also superimposable between these 2 subpopulations. Second, in theory, use of different types of ABPM devices and protocols in the populations considered might have contributed to the occurrence of some difference in ABPM-derived parameters, including MS. This is also unlikely, however, because all the devices used in this study had been previously validated according to international protocols and found to be equally accurate. Moreover, the lower frequency of BP measurements in the Japanese group of the study may have led to some MS underestimation because of BP undersampling. Therefore, if anything, the difference between the 2 ethnic groups might be even larger than that reported in our article. Third, age was significantly higher in Japanese group than in European group in unadjusted baseline characteristics. Although statistical methods were used to control for the differences between the 2 groups, they cannot be considered as fully comparable in terms of general characteristics.

Finally, in our study, we are unable to translate the observed between populations differences in MS into differences in cardiovascular risk because we did not include measures of organ damage or prognostic data derived from a longitudinal follow-up. The main aim of our study, however, was to provide the first direct demonstration of the presence of ethnic differences in ABPM-derived parameters, such as the sleep-trough MS. The clinical relevance of these differences now needs to be addressed by ad hoc designed outcome studies.

Perspectives

Several aspects of the diurnal BP profile assessed by ABPM have been shown to provide additional prognostic information beyond that associated with 24-hour average BP. Based on evidence gathered in previous studies, morning BP surge seems to be a potential risk factor for cardiovascular disease independent of the average 24-hour BP. However, possible ethnic differences in its clinical relevance need to be taken into account. The discrepancies we observed in the degree of morning BP surge across different ethnicities might contribute to the higher incidence of stroke found in Japanese subjects as compared with a Western population. The above considerations support the notion that among various cardiovascular risk factors, for which ethnical differences were reported, also 24-hour ABPM patterns should be interpreted taking into account these differences. In particular, this aspect should be considered when strategies of cardiovascular prevention aimed at reducing BP-related risk are being defined.

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Disclosures

None.

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Novelty and Significance

What Is New?

- A direct demonstration of differences in size and determinants of morning systolic blood pressure surge between different ethnic groups.

What Is Relevant?

- Differences in size of morning surge may explain differences in its prognostic relevance reported between Asian and European subjects. Different therapeutic approaches might thus be needed to reduce risk associated with morning surge in different ethnic groups.

Summary

Sleep-trough morning blood pressure surge was higher in Japanese than in European hypertensive patients matched for age and 24-h mean blood pressure levels, also after accounting for differences in night-time blood pressure. Age was independently associated with morning blood pressure surge in Japanese but not in European subjects.

Online supplement

Ethnic differences in the degree of morning blood pressure surge and in its determinants between Japanese and European hypertensive subjects. Data from the ARTEMIS study.

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Short Title: Ethnic differences in morning BP surge

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Contents:

Table S1. Patient's characteristics. Data are separately shown for Japanese, Spanish and Italian subrgroups.

Variable	Japanese group n=811	Italian group n=155	Spanish group n=2732	P
Age, y	72.3±9.8	57.9±6.7 †	62.5±8.8 †‖	<0.001
Male, %	38.3	51.2	53.4	<0.001
Body mass index, kg/m^2	23.9±3.5	27.5±4.6 †	28.1±4.1 †	<0.001
Smoking, %	20.5	45	15.8	<0.001
Diabetes, %	12.2	3.7	13.1	<0.001
Clinic SBP	164.2±17.7	158.0±17.9 †	156.8±13.8 †	<0.001
Clinic DBP	90.5±14.2	94.7±9.2 †	90.7±10.1 ‖	<0.001
Clinic PR, bpm	76.8±12.0	74.2±11.3	76.5±13.6	0.101
24hr SBP	138.1±16.3	131.6±13.9 †	132.6±13.3 †	<0.001
24hr DBP	78.2±9.7	80.9±9.6 †	77.9±9.4 ‖	<0.001
24hr PR, bpm	70.8±7.5	72.0±7.2	71.3±9.3	0.211
Daytime SBP	144.9±17.7	137.4±14.7 †	137.3±13.8 †	<0.001
Daytime DBP	81.6±10.6	85.7±10.2 †	82.1±10.1 ‖	<0.001

Daytime PR, bpm	76.6±8.5	76.1±8.1		75.5±10.4	†	0.017
SD of daytime SBP	18.2±5.6	12.5±2.6	†	12.2±3.5	†	<0.001
SD of daytime DBP	12.8±5.0	9.8±1.9	†	8.6±2.4	†‖	<0.001
Nighttime SBP	126.8±18.2	120.4±17.1	†	122.2±15.4	†	0.004
Nighttime DBP	72.1±10.6	71.6±11.2	*	69.3±10.0	†	<0.001
Nighttime PR, bpm	61.0±8.1	64.2±8.3	†	64.2±9.2	†	<0.001
SD of nighttime SBP	13.4±4.9	10.3±3.5	†	10.1±3.9	†	<0.001
SD of nighttime DBP	8.5±3.1	8.6±2.6		7.8±2.9	†‡	<0.001
Morning surge	40.3±18.6	27.0±13.9	†	22.7±13.4	†‡	<0.001
Dipping pattern, %						<0.001
Extreme-dipper	20.3	12.2		11.3		
Dipper	42.4	48.2		44.9		
Non-dipper	27.7	34.1		35.3		
Riser	9.6	5.5		8.5		

SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse rate; SD, standard deviation,

*P<0.05, †P<0.001 vs. Japanese group, ‡P<0.01, ‖P<0.001 vs. Italian group.

Table S2.Patient's characteristics for the group of 631 Japanese and 631 European subjects matched for age and 24-hour systolic blood pressure (all blood pressure variables in mmHg)

Variable	Japanese group n=631	European group n=631	P
Age, y	69.7±8.6	69.7±8.7	0.990
Male, %	36.6	48.8	<0.001
Body mass index, kg/m^2	24.1±3.5	28.3±4.0	<0.001
Smoking, %	19.2	12	0.001
Diabetes, %	12.2	15.1	0.163
Clinic SBP	162.9±16.6	159.9±15.7	0.001
Clinic DBP	90.4±13.5	88.7±10.5	0.013
Clinic PR, bpm	76.7±11.5	76.4±17.3	0.678
24hr SBP	136.1±14.0	136.1±13.9	0.991
24hr DBP	77.7±8.7	75.9±9.5	0.005
24hr PR, bpm	71.0±7.2	70.4±8.8	0.207
Daytime SBP	143.2±15.8	139.9±14.6	<0.001
Daytime DBP	81.3±9.8	79.7±10.3	0.005

Daytime PR, bpm	76.9±8.4	74.3±9.9	<0.001
SD of daytime SBP	17.9±5.5	13.3±3.9	<0.001
SD of daytime DBP	12.5±4.8	9.0±2.5	<0.001
Nighttime SBP	124.3±15.7	126.8±16.4	0.004
Nighttime DBP	71.4±9.5	68.0±10.2	<0.001
Nighttime PR, bpm	61.0±8.1	63.9±8.9	<0.001
SD of nighttime SBP	13.0±4.6	10.6±3.9	<0.001
SD of nighttime DBP	8.3±3.0	8.0±2.8	0.046
Morning surge	40.0±18.3	22.8±13.4	<0.001

SBP, systolic blood pressure; DBP, diastolic blood pressure,; PR, pulse rate; SD, standard deviation

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