Original Paper

Factors Associated with Blood Pressure Variability Based on Ambulatory Blood Pressure Monitoring in Subjects with Hypertension in China

Wei Li^a YanXia Yu^a Dehong Liang^a En-Zhi Jia^b

^aDepartment of Hypertension, the Friendship Hospital of Ili Kazakh Autonomous Prefecture, Yining, Xinjiang; ^bDepartment of Cardiovascular Medicine, the First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu Province, China

Key Words

Hypertension • Blood pressure variability • Biochemical characteristics

Abstract

Background/Aims: We examined the factors associated with blood pressure variability in a multi-ethnicity prospective study in China to gain more evidence to guide the prevention and management of hypertension through risk factor intervention. **Methods:** A total of 318 consecutive adult subjects aged 29–94 years with suspected or known hypertension were enrolled in this study. Blood pressure variability measurements were based on ambulatory blood pressure monitoring. To measure short-term reading-to-reading blood pressure variability in this study, we used the standard deviation (SD) of the blood pressure to estimate the blood pressure variability. **Results:** The SDs of the blood pressure in this study ranged from 5.425 to 32.25, with a median of 10.81 (quartile range, 8.90–12.46). No significant difference regarding the level distribution of blood pressure variability was found across the various ethnicities. Spearman correlation analyses indicated that the SD of blood pressure was positively correlated with DSBP ($r=0.302$, $p<0.001$), NSBP ($r=0.383$, $p<0.001$), NDBP ($r=0.230$, $p<0.001$), and FBG ($r=0.129$, $p=0.023$) and was negatively correlated with triglyceride ($r=-0.289$, $p<0.001$), CR ($r=-0.242$, $p<0.001$), HDL-C ($r=-0.230$, $p<0.001$), LDL-C ($r=-0.186$, $p=0.001$), and apolipoprotein B levels ($r=-0.157$, $p=0.006$). Multiple linear regression analysis indicated that triglycerides ($\beta=-0.217$, $p<0.001$), NSBP ($\beta=0.174$, $p=0.003$), FBG ($\beta=0.128$, $p=0.024$), DDBP ($\beta=-0.128$, $p=0.022$), and apolipoprotein A ($\beta=-0.116$, $p=0.036$) were significantly and independently associated with the blood pressure variability. **Conclusions:** In this study, blood pressure variability was significantly associated with not only blood pressure levels but also patient demographic, clinical and biochemical characteristics.

© 2017 The Author(s)
Published by S. Karger AG, Basel

Dr. En-Zhi Jia

Department of Cardiovascular Medicine, the First Affiliated Hospital of Nanjing Medical University, Guangzhou Road 300, Nanjing 210029, Jiangsu Province (China)
Tel. +86-13951623205, Fax 0086-025-84352775, E-Mail enzhijia@njmu.edu.cn

Introduction

The most significant single contributor to the global burden of disease and to global mortality is hypertension. The number of people affected and the prevalence of high blood pressure worldwide are expected to increase over the next decade [1]. As the largest developing country, China urgently needs strategies to prevent hypertension. According to existing guidelines, the diagnosis of hypertension is based on a systolic blood pressure measured in the clinic of at least 140 mmHg, a diastolic blood pressure of at least 90 mmHg, or both [2-4]. However, a single blood pressure measurement is insufficient for an accurate diagnosis of hypertension. As ambulatory blood pressure monitoring (ABPM) can provide information about blood pressure levels, blood pressure load, and blood pressure variability, it has proven to be increasingly important in the diagnosis, management and prognosis of hypertension, as shown by various studies [5]. Although some studies have examined the relationship between ABPM parameters and the risk of cardiovascular disease and all-cause mortality, noting that abnormalities increase these risks [6, 7], these relationships still need to be elucidated in the Chinese population. Moreover, the factors associated with blood pressure variability based on ABPM in China have not been well studied. Therefore, we examined the factors associated with blood pressure variability in a multi-ethnicity prospective study in China to obtain more evidence to guide the prevention and management of hypertension through risk factor intervention.

Materials and Methods

This study was approved by the Ethics Committee of the Friendship Hospital of Ili Kazakh Autonomous Prefecture, Xinjiang Uygur Autonomous Regions, China, and by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University, Jiangsu Province, China. Written informed consent was obtained from each patient.

Study subjects

From 1 January 2014 to 16 December 2015, 318 consecutive adult subjects (169 males and 149 females) aged 29-94 years with suspected or known hypertension who were evaluated at the Friendship Hospital of Ili Kazakh Autonomous Prefecture in China were enrolled in this study. Among the 318 subjects, 189 subjects were of Han nationality, 62 were of Uygur nationality, 35 were of Kazakh nationality, 26 were of Hui nationality, and 6 were of other nationalities (1 subject was of Mongol nationality, and 5 subjects were of Sibe nationality). The exclusion criteria for the subjects were as follows: 1) heart failure, 2) infections within 2 weeks of enrolment, 3) adrenal or thyroid dysfunction, and 4) cancer. The history of prior stroke and coronary artery disease for subjects was obtained using a standardized questionnaire.

Cigarette smoking and alcohol intake

A standardized questionnaire was employed to assess the cigarette smoking and alcohol intake status of the subjects. The subjects' smoking status was classified as either "never smoking" or "smoking". The former referred to individuals who never smoked, and the latter group included both former and current smokers [8-9]. In addition, alcohol intake status was classified as either "never drinkers" or "drinkers" (including both former and current drinkers), and subjects who reported consuming at least 50 g/week of alcohol were considered current drinkers. [10].

Blood pressure variability measurements based on ambulatory blood pressure monitoring

The blood pressure variability measurements performed in this study were based on ambulatory blood pressure monitoring, which was conducted using a Mobil-O-Graph ABPM device (Stolberg, Germany). The Mobil-O-Graph ABPM device provided fully automated and programmable oscillometric BP readings, which were obtained from the upper arm. The data analysis was performed according to the European Society of Hypertension (ESH) protocol [11]. Portable monitors were programmed to obtain ambulatory

blood pressure readings at 15-minute intervals throughout the day. Accounting for the daily activity patterns of the subjects, daytime was defined as the interval from 8:00 AM to 10:59 PM, and the corresponding nighttime interval ranged from 11:00 PM to 7:59 AM. To measure short-term reading-to-reading blood pressure variability in this study, we used the SDs of daytime (SDd) and nighttime (SDn) blood pressure variability. The blood pressure variability was defined as follows: blood pressure variability=(the SD of daytime systolic blood pressure + the SD of daytime diastolic blood pressure + the SD of nighttime systolic blood pressure + the SD of nighttime diastolic blood pressure)/4.

Laboratory measurements

Total cholesterol (TCH, mmol/L), triglyceride (TG, mmol/L), fasting blood glucose (FBG, mmol/L), creatinine (CR, μ mol/L), fasting high-density lipoprotein cholesterol (HDL-C, mmol/L), fasting low-density lipoprotein cholesterol (LDL-C, mmol/L), apolipoprotein A (apoA, g/L) and apolipoprotein B (apoB, g/L) levels were measured via enzymatic procedures using a Hitachi 7600 automated autoanalyzer (Hitachi Co., Tokyo, Japan).

Statistical analyses

Data were analyzed using the Statistics Package for Social Sciences (ver. 16.0; SPSS Incorporated, Chicago, IL, USA). The patients were classified into four groups according to blood pressure variability, using the quartile values as cutoff points; therefore, each group had a similar number of patients to minimize any biases that might have affected the statistical analyses. Data pertaining to average nighttime systolic blood pressure (NSBP, mmHg) and apolipoprotein A were normally distributed and were presented as the mean $\pm$ standard deviation (SD), and the comparisons were analyzed via one-way analysis of variance (ANOVA). Skewed data, including the data pertaining to age, average daytime diastolic blood pressure (DDBP, mmHg), average daytime systolic blood pressure (DSBP, mmHg), average daytime diastolic blood pressure (DDBP, mmHg), average nighttime diastolic blood pressure (NDBP, mmHg), the SD of daytime systolic blood pressure (SD_{DSBP} , mmHg), the SD of daytime diastolic blood pressure (SD_{DDBP} , mmHg), the SD of nighttime systolic blood pressure (SD_{NSBP} , mmHg), the SD of nighttime diastolic blood pressure (SD_{NDBP} , mmHg), the SD of blood pressure (SD_{BP} , mmHg), total cholesterol (TCH, mmol/L), low-density lipoprotein cholesterol (LDL-C, mmol/L), high-density lipoprotein cholesterol (HDL-C, mmol/L), triglycerides (TGs, mmol/L), fasting blood glucose (FBG, mmol/L), and creatinine, were expressed as the median $\pm$ standard deviation (SD), and the comparisons were analyzed using the Kruskal-Wallis H test. Categorical variables, including sex, cigarette smoking status, alcohol intake status, history of prior stroke and coronary artery disease, were compared among the groups using chi-squared analyses. Spearman's two-way test assessed the relationship between two quantitative variables, and we evaluated the independent predictors of blood pressure variability via multiple linear regression analyses. Significance was noted if the null hypothesis could be rejected with >95% confidence. All p-values given are two-tailed.

Results

Baseline characteristics of the subjects grouped according to ethnicity

The baseline characteristics of the subjects grouped according to ethnicity are presented in Table 1. Significant differences in age ($p=0.010$), average nighttime diastolic blood pressure ($p=0.006$), total cholesterol ($p=0.016$) and LDL-C ($p=0.001$) were observed across the various ethnicities. Furthermore, no significant difference was found across the various ethnicities with regard to the frequency distribution of gender, cigarette smoking status, alcohol intake status, history of prior stroke and coronary artery disease.

Patient demographic, clinical and biochemical characteristics according to blood pressure variability

The SD_{BP} (mmHg) of the subjects in this study ranged from 5.425 to 32.25, with a median of 10.81 (quartile range, 8.90–12.46). Table 2 shows the patient demographic, clinical and biochemical characteristics according to blood pressure variability. Quartile

Table 1. Baseline characteristics of the subjects grouped according to ethnicity

Variable	Ethnicity (n=318)					<i>F</i> from chi- square test	<i>P</i>
	Han (n=189)	Uygur (n=62)	Kazakh (n=35)	Hui (n=26)	Other (n=6)		
Age (years)	53.00±13.51	63.00±11.25	53.00±13.47	57.00±12.10	51.50±12.95	13.382	0.010
Sex (M/F)	104/85	31/31	17/18	13/13	4/2	1.353	0.852
Smoking (yes/no)	68/121	19/43	13/22	9/17	2/4	0.676	0.954
Drinking (yes/no)	57/132	12/50	10/25	2/24	1/5	8.079	0.089
History of stroke (yes/no)	3/186	3/59	1/34	1/25	1/5	6.246	0.182
History of CHD (yes/no)	32/157	14/48	6/29	6/20	0/6	2.775	0.596
DSBP (mmHg)	122.00±17.40	123.50±19.01	126.00±14.29	129.00±21.79	133.50±5.79	9.386	0.052
DDBP (mmHg)	81.00±13.26	80.00±13.17	84.00±10.44	83.50±12.65	84.50±32.76	7.494	0.112
NSBP (mmHg)	116.14±17.39	112.23±21.94	119.71±18.63	120.23±21.48	123.17±11.92	1.508	0.200
NDBP (mmHg)	73.00±14.31	70.00±15.46	76.00±21.17	79.00±12.31	82.50±11.99	14.549	0.006
SD _{BP} (mmHg)	10.60±3.07	10.06±2.82	11.75±3.02	11.41±2.26	11.59±4.04	5.796	0.215
Total cholesterol (mmol/L)	4.96±1.35	5.06±0.94	4.29±1.05	4.82±0.81	3.82±1.45	3.720	0.006
Triglycerides (mmol/L)	2.15±1.67	2.32±1.42	1.52±1.43	2.01±1.49	1.10±2.46	5.435	0.245
Glucose (mmol/L)	4.60±1.51	4.37±1.64	4.35±1.00	4.90±1.21	4.70±0.31	8.175	0.085
CR (μmol/L)	69.00±23.67	70.65±23.34	69.00±24.69	64.55±23.45	57.50±12.35	6.410	0.171
HDL-C (mmol/L)	1.27±0.50	1.45±0.42	1.38±0.63	1.28±0.38	1.53±0.37	6.770	0.149
LDL-C (mmol/L)	2.88±0.79	3.09±0.51	2.71±0.69	2.70±0.65	1.91±0.40	4.979	0.001
apolipoprotein A (g/L)	1.35±0.23	1.36±0.25	1.25±0.21	1.29±0.19	1.41±0.20	1.919	0.107
apolipoprotein B (g/L)	0.97±0.79	0.95±0.17	0.91±0.25	0.98±0.15	0.76±0.30	3.860	0.425

CHD, coronary heart disease; DSBP, average daytime systolic blood pressure; DDBP, average daytime diastolic blood pressure; NSBP, average nighttime systolic blood pressure; NDBP, average nighttime diastolic blood pressure; SD_{BP}, SD of blood pressure; CR, creatinine; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CHD, coronary heart disease

Table 2. Ages and clinical and biochemical characteristics of patients grouped according to quartiles of the SD of blood pressure

Variable	SD of blood pressure (SD _{BP}) (mmHg)				<i>F</i> or <i>chi- square test</i>	<i>P</i>
	0~8.90 (n=80)	8.91~10.81 (n=79)	10.82~12.46 (n=80)	12.47~ (n=79)		
Age (years)	53.00±12.24	58.00±13.19	60.50±13.08	54.00±13.90	3.92	0.27
Sex (M/F)	37/43	45/34	42/38	45/34	2.465	0.482
Smoking (yes/no)	33/47	26/53	26/54	26/53	1.897	0.594
Drinking (yes/no)	30/50	17/62	17/63	18/61	7.720	0.052
History of stroke (yes/no)	1/79	3/76	2/78	3/76	1.296	0.730
History of CHD (yes/no)	15/65	13/66	16/64	14/65	0.363	0.948
DSBP (mmHg)	118.00±14.64	123.00±12.42	127.00±19.75	129.00±20.43	33.329	<0.001
DDBP (mmHg)	83.00±13.27	80.00±12.82	80.50±13.00	84.00±15.17	5.825	0.120
NSBP (mmHg)	105.86±15.20	113.84±19.20	122.19±15.73	123.13±19.68	16.93	<0.001
NDBP (mmHg)	65.00±16.47	75.00±14.38	75.00±13.02	77.00±15.44	25.833	<0.001
Total cholesterol (mmol/L)	5.12±1.35	4.85±1.14	4.53±1.23	4.96±1.15	3.256	0.022
Triglycerides (mmol/L)	3.22±1.81	2.07±1.57	1.64±1.29	2.01±1.30	43.342	<0.001
Glucose (mmol/L)	4.37±0.83	4.60±1.41	4.63±1.62	4.80±1.79	5.893	0.117
CR (μmol/L)	93.50±26.23	66.00±22.23	65.00±17.99	67.00±21.05	39.774	<0.001
HDL-C (mmol/L)	1.57±0.53	1.35±0.37	1.22±0.57	1.23±0.42	30.290	<0.001
LDL-C (mmol/L)	3.14±0.72	2.77±0.56	2.76±0.75	2.79±0.82	5.22	0.002
apolipoprotein A (g/L)	1.37±0.21	1.35±0.24	1.31±0.22	1.32±0.25	1.219	0.303
apolipoprotein B (g/L)	0.99±0.16	0.94±0.17	0.89±1.15	0.91±0.43	11.433	0.010

CHD, coronary heart disease; DSBP, average daytime systolic blood pressure; DDBP, average daytime diastolic blood pressure; NSBP, average nighttime systolic blood pressure; NDBP, average nighttime diastolic blood pressure; CR, creatinine; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

values were used as cutoff points. The results indicate that significant differences in DSBP ($p<0.001$), NSBP ($p<0.001$), NDBP ($p<0.001$), TCH ($p=0.022$), TG ($p<0.001$), CR ($p<0.001$), HDL-C ($p<0.001$), LDL-C ($p=0.002$), and apolipoprotein B ($p=0.010$) were observed among the groups and that age ($p=0.270$), DDBP ($p=0.120$), FBG ($p=0.117$), and apolipoprotein A ($p=0.303$) levels did not significantly differ among the groups. In addition, no significant difference regarding the frequency distribution of gender, cigarette smoking status, alcohol intake status, history of prior stroke and coronary artery disease for the subjects was found across the different levels of blood pressure variability.

Spearman correlations between blood pressure variability and age and clinical and biochemical characteristics

Table 3 shows the Spearman correlations between blood pressure variability and age and various clinical and biochemical characteristics. The Spearman correlation analyses indicated that the SD of blood pressure was positively correlated with DSBP ($r=0.302$, $p<0.001$), NSBP ($r=0.383$, $p<0.001$), NDBP ($r=0.230$, $p<0.001$), FBG ($r=0.129$, $p=0.023$) and was

negatively correlated with triglyceride ($r=-0.289$, $p<0.001$), CR ($r=-0.242$, $p<0.001$), HDL-C ($r=-0.230$, $p<0.001$), LDL-C ($r=-0.186$, $p=0.001$), and apolipoprotein B ($r=-0.157$, $p=0.006$).

Multiple linear regression analysis with blood pressure variability as the dependent variable

To determine the factors that are independently associated with blood pressure variability, multiple linear regression analysis was performed. In this model, the SD of blood pressure was employed as dependent variables, and age, sex, cigarette smoking status, alcohol intake status, history of prior stroke and coronary artery disease, DSBP, DDBP, NSBP, NDBP, total cholesterol, triglycerides, fasting blood glucose, creatinine, HDL-C, LDL-C, apolipoprotein A, and apolipoprotein B were employed as independent variables. In the final model (Table 4 and Fig. 1-5), triglycerides ($\beta=-0.217$, $p<0.001$), NSBP ($\beta=0.174$, $p=0.003$), FBG ($\beta=0.128$,

Table 3. Spearman correlations between blood pressure variability and age and clinical and biochemical characteristics

Variable	SD of blood pressure (mmHg)	
	Correlation coefficient	P value
Age (years)	0.012	0.834
DSBP (mmHg)	0.302	0.000
DDBP (mmHg)	0.032	0.571
NSBP (mmHg)	0.383	0.000
NDBP (mmHg)	0.230	0.000
Total cholesterol (mmol/L)	-0.072	0.204
Triglycerides (mmol/L)	-0.289	0.000
Glucose (mmol/L)	0.129	0.023
CR ($\mu\text{mol/L}$)	-0.242	0.000
HDL-C (mmol/L)	-0.230	0.000
LDL-C (mmol/L)	-0.186	0.001
apolipoprotein A (g/L)	-0.102	0.072
apolipoprotein B (g/L)	-0.157	0.006

DSBP, average daytime systolic blood pressure; DDBP, average daytime diastolic blood pressure; NSBP, average nighttime systolic blood pressure; NDBP, average nighttime diastolic blood pressure; CR, creatinine; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

Table 4. Predictors of SD_{BP} via multiple linear regression among the subjects

Variable	Unstandardized Coefficient		Standardized Coefficients (Beta)	T	P
	B	Std. Error			
Constant	11.888	1.794	----	6.627	0.000
Triglycerides (mmol/L)	-0.405	0.103	-0.217	-3.930	0.000
NSBP(mmHg)	0.028	0.009	0.174	3.041	0.003
Glucose (mmol/L)	0.260	0.114	0.128	2.274	0.024
DDBP(mmHg)	-0.028	0.012	-0.128	-2.295	0.022
apolipoprotein A (g/L)	-1.502	0.711	-0.116	-2.112	0.036

SD_{BP}, SD of blood pressure; NSBP, average nighttime systolic blood pressure; DDBP, average daytime diastolic blood pressure

$p=0.024$), DDBP ($\beta=-0.128$, $p=0.022$), and apolipoprotein A ($\beta=-0.116$, $p=0.036$) were significantly and independently associated with the blood pressure variability, based on multiple linear regression analysis.

Discussion

In this hospital-based multi-ethnicity study of adult Chinese subjects with hypertension, the main findings were as follows: the blood pressure variability did not differ across the various ethnicities, and blood pressure variability was significantly associated with not only blood pressure levels but also patients' demographic, clinical and biochemical characteristics.

Blood pressure variability, which is defined as the continuous fluctuation in blood pressure, includes both short-term and long-term variability and has drawn substantial amount of attention recently because cross-sectional and cohort studies have indicated that blood pressure variability is closely associated with target-organ damage independent of mean blood pressure values [11–16]. Therefore, attenuating blood pressure variability and reducing mean blood pressure values may be

equally important goals in the management of cardiovascular disease. The most widely used measurements for estimating blood pressure variability during a 24-h period are the standard deviations of the mean daytime and nighttime blood pressure; therefore, the standard devi-

Fig. 1. Partial regression plot for average daytime diastolic blood pressure.

Fig. 2. Partial regression plot for average nighttime systolic blood pressure.

Fig. 3. Partial regression plot for triglycerides.

ations of the mean daytime and nighttime blood pressure were used as indicators of blood pressure variability in this study. The results of this study are consistent with previous studies showing that blood pressure variability is greatest during the daytime and lowest during the night [17].

Blood pressure variability has been documented since the 18th century, but the factors associated with the occurrence of continuous blood pressure fluctuations over time have not been explored thus far. Based on the results of this study, biochemical characteristics significantly influence blood pressure variability independently of the mean blood pressure levels. Reducing the 24-h mean blood pressure has been the central focus with respect to attenuating blood pressure variability, but it is clear that attention should also be given to biochemical characteristics, especially blood lipid profiles.

This study had several limitations. Its sample size was small; thus, large-scale studies are necessary to substantiate our findings. Furthermore, given that the study involved subjects hospitalized for hypertension, its results may not be applicable to an unselected community population. Additionally, the mechanism underlying the apparent relationship between blood pressure variability and biochemical characteristics was not examined. Moreover, blood pressure is associated with sympathetic activity [18], which we did not consider. Therefore, although a significant relationship between these parameters appears to exist, the biological plausibility of this relationship remains unproven and warrants clarification in future studies.

Conclusion

The most relevant findings of this study are that biochemical characteristics significantly influence the blood pressure variability independently of mean blood pressure levels.

Fig. 4. Partial regression plot for glucose.

Fig. 5. Partial regression plot for apolipoprotein A.

Abbreviations

SD: standard deviation; DDBP: daytime average diastolic blood pressure; DSBP: daytime average systolic blood pressure; NDBP: nighttime average diastolic blood pressure; NSBP: nighttime average systolic blood pressure; FBG: fasting blood glucose; CR: creatinine; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; ABPM: ambulatory blood pressure monitoring; ESH: European Society of Hypertension; TCH: total cholesterol; TG: triglyceride; ApoA: apolipoprotein A; ApoB: apolipoprotein B; SPSS: Statistics Package for Social Sciences; ANOVA: one-way analysis of variance

Disclosure Statement

The authors declare no conflicts of interest.

Acknowledgments

The study was supported by the National Natural Science Foundation of China (grants 30400173, 30971257, and 81170180) and by a project funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions.

References

- 1 Poulter NR, Prabhakaran D, Caulfield M: Hypertension. *Lancet* 2015;386:801-812.
- 2 NICE. 2011 Guidelines for Hypertension: Clinical Management of Primary Hypertension in Adults. <http://publications.nice.org.uk/hypertension-cg127> (accessed Jan 8, 2015).
- 3 Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F, Redon J, Dominiczak A, Narkiewicz K, Nilsson PM, Burnier M, Viigimaa M, Ambrosioni E, Caulfield M, Coca A, Olsen MH, Schmieder RE, Tsioufis C, van de Borne P, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Clement DL, Coca A, Gillebert TC, Tendera M, Rosei EA, Ambrosioni E, Anker SD, Bauersachs J, Hitij JB, Caulfield M, De Buyzere M, De Geest S, Derumeaux GA, Erdine S, Farsang C, Funck-Brentano C, Gerc V, Germano G, Gielen S, Haller H, Hoes AW, Jordan J, Kahan T, Komajda M, Lovic D, Mahrholdt H, Olsen MH, Ostergren J, Parati G, Perk J, Polonia J, Popescu BA, Reiner Z, Rydén L, Sirenko Y, Stanton A, Struijker-Boudier H, Tsioufis C, van de Borne P, Vlachopoulos C, Volpe M, Wood DA: 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013;34: 2159-2219.
- 4 James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Ogedegbe O, Smith SC Jr, Svetkey LP, Taler SJ, Townsend RR, Wright JT Jr, Narva AS, Ortiz E: 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 2014;311: 507-520.
- 5 Hodgkinson J, Mant J, Martin U, Guo B, Hobbs FD, Deeks JJ, Heneghan C, Roberts N, McManus RJ: Relative effectiveness of clinic and home blood pressure monitoring compared with ambulatory blood pressure monitoring in diagnosis of hypertension: systematic review. *BMJ* 2011;342:d3621.

- 6 Hansen TW, Thijs L, Li Y, Boggia J, Kikuya M, Björklund-Bodegård K, Richart T, Ohkubo T, Jeppesen J, Torp-Pedersen C, Dolan E, Kuznetsova T, Stolarz-Skrzypek K, Tikhonoff V, Malyutina S, Casiglia E, Nikitin Y, Lind L, Sandoya E, Kawecka-Jaszcz K, Imai Y, Wang J, Ibsen H, O'Brien E, Staessen JA; International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcomes Investigators: Prognostic value of reading-to-reading blood pressure variability over 24 hours in 8938 subjects from 11 populations. *Hypertension* 2010;55:1049-1057.
- 7 Stolarz-Skrzypek K, Thijs L, Li Y, Hansen TW, Boggia J, Kuznetsova T, Kikuya M, Maestre G, Mena L, Kawecka-Jaszcz K, Staessen JA: Short-term blood pressure variability in relation to outcome in the International Database of Ambulatory blood pressure in relation to Cardiovascular Outcome (IDACO). *Acta Cardiol* 2011;66:701-706.
- 8 Lahti-Koski M, Pietinen P, Heliövaara M, Vartiainen E: Associations of body mass index and obesity with physical activity, food choices, alcohol intake, and smoking in the 1982–1997 FINRISK Studies. *Am J Clin Nutr* 2002;75:809-817.
- 9 Jia EZ, Liang J, Yang ZJ, Zhu TB, Wang LS, Chen B, Cao KJ, Huang J, Ma WZ: Smoking and coronary atherosclerosis: follow-up study in China. *Clin Exp Pharmacol Physiol* 2009;36:690-695.
- 10 Jia EZ, An FH, Liu P, Li F, Mao HW, Cui WJ, Xu HY: Relationship between brachial-ankle pulse wave velocity and cardiovascular risk factors: a multi-ethnic study. *Intern Med* 2012;51:537-543.
- 11 O'Brien E, Atkins N, Stergiou G, Karpettas N, Parati G, Asmar R, Imai Y, Wang J, Mengden T, Shennan A; Working Group on Blood Pressure Monitoring of the European Society of Hypertension: European Society of Hypertension International Protocol revision 2010 for the validation of blood pressure measuring devices in adults. *Blood Press Monit* 2010;15:23-38.
- 12 Frattola A, Parati G, Cuspidi C, Albini F, Mancia G: Prognostic value of 24-hour blood pressure variability. *J Hypertens* 1993;11:1133-1137.
- 13 Parati G, Pomidossi G, Albini F, Malaspina D, Mancia G: Relationship of 24-hour blood pressure mean and variability to severity of target-organ damage in hypertension. *J Hypertens* 1987;5:93-98.
- 14 Parati G, Lantelme P: Blood pressure variability, target organ damage and cardiovascular events. *J Hypertens* 2002;20:1725-1729.
- 15 Pessina AC, Palatini P, Sperti G, Cordone L, Libardoni M, Mos L, Mormino P, Di Marco A, Dal Palù C: Evaluation of hypertension and related target organ damage by average day-time blood pressure. *Clin Exp Hypertens A* 1985;7:267-278.
- 16 Rowlands DB, Ireland MA, Glover DR, McLeay RA, Stallard TJ, Littler WA: The relationship between ambulatory blood pressure and echocardiographically assessed left ventricular hypertrophy. *Clin Sci* 1981;61:101S-103S.
- 17 Mancia G, Parati G, di Rienzo M, Zanchetti A: Blood pressure variability. In: Mancia G, Zanchetti A (editors): *Handbook of Hypertension: Pathophysiology of Hypertension*. Amsterdam, Elsevier Science, pp. 117-169, 1997.
- 18 Jimenez ZN, Silva BC, Reis LD, Castro MC, Ramos CD, Costa-Hong V, Bortolotto LA, Consolim-Colombo F, Dominguez WV, Oliveira IB, Moysés RM, Elias RM: High Dialysate Calcium Concentration May Cause More Sympathetic Stimulus During Hemodialysis. *Kidney Blood Press Res* 2016;41:978-985.