

Relationship between arterial stiffness and variability of home blood pressure monitoring

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Abstract

Variability of blood pressure (BP) is known as a prognostic value for the subsequent target organ damage in hypertensive patients. Arterial stiffness is a risk factor for cardiovascular morbidity and mortality. The relationship between the arterial stiffness and the BP variability has been controversial. The objective of the present study was to investigate the relationship between arterial stiffness and home BP variability in patients with high normal BP and new onset hypertension (HTN).

Four hundred sixty three patients (252 males, 49 ± 12 year-old) with high normal BP or HTN were enrolled. Using radial applanation tonometry, pulse wave analysis (PWA) was performed for evaluation of systemic arterial stiffness. All patients underwent both home BP monitoring (HBPM) and PWA. Home BP variability was calculated as the standard deviation (SD) of 7 measurements of HBPM. Multiple linear regression analysis was performed to estimate and test the independent effects of home BP variability on the arterial stiffness.

Multivariate analysis showed that both systolic and diastolic morning BP variabilities were correlated with arterial stiffness expressed as augmentation pressure (AP, β -coefficient = 1.622, $P = .01$ and β -coefficient = 1.07, $P = .035$). The SDs of systolic and diastolic BP of evening were also associated with AP (β -coefficient = 1.843, $P = .001$ and β -coefficient = 1.088, $P = .036$). The SDs of morning and evening systolic BP were associated with augmentation index (AI, β -coefficient = 1.583, $P = .02$ and β -coefficient = 1.792, $P = .001$) and heart rate (75 bpm) adjusted AI (β -coefficient = 1.592, $P = .001$ and β -coefficient = 1.792, $P = .001$).

In present study, the variability of systolic BP was closely related with arterial stiffness. The home BP variability might be important indicator of arterial stiffness.

Abbreviations: AI = augmentation index, AI@HR75 = heart rate (75 bpm) adjusted augmentation index, AP = augmentation pressure, BP = blood pressure, DBP = diastolic blood pressure, HBPM = home blood pressure monitoring, HTN = hypertension, PWA = pulse wave analysis, SBP = systolic blood pressure, SD = standard deviation.

Keywords: arterial stiffness, blood pressure variability, home blood pressure monitoring, hypertension, pulse wave analysis

1. Introduction

Independent of mean blood pressure (BP), BP variability has been known to be associated with clinical cardiovascular events.^[1,2] In

our previous study, we demonstrated the close relationship between visit-to-visit systolic BP (SBP) variability and long-term cardiovascular adverse events in patients with ST elevation myocardial infarction.^[3]

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Arterial stiffness is one of well-known risk factors for cardiovascular morbidity and mortality.^[4–6] Large elastic arteries stiffen progressively with age, whereas the stiffness of muscular arteries changes little with age. In the load-bearing media of elastic arteries, the orderly arrangement of elastic fibers and laminae is gradually lost over time, and thinning, splitting, fraying, and fragmentation are observed.^[7] Arterial stiffness relates to alterations of medial properties leading to reduced distensibility of the arterial wall, and decreasing the buffering capacity of arteries to pulsatile cardiac ejection.^[8] Arterial stiffness may reduce baroreceptor sensitivity, which is major determinant of BP variability.^[9,10] The relationship between the arterial stiffness and the BP variability has been incompletely understood.^[1,11]

The objective of the present study was to investigate the relationship between arterial stiffness by pulse wave analysis (PWA) and home BP variability in patients with high normal BP and hypertension (HTN).

2. Materials and methods

The study included 773 patients (442 males, 48 ± 12 year-old) with high normal BP or HTN, who were consecutively recruited in 11 university hospitals in Korea. We enrolled the patients with firstly diagnosed high normal BP or HTN. As drugs could affect central and peripheral pressure differently,^[12] we excluded the patients on any antihypertensive medication at enrollment. Among the study population, 463 patients (252 males, 49 ± 12 year-old), who underwent both home BP monitoring (HBPM) and pulse wave analysis (PWA), were finally enrolled in the present study. The study protocol and informed consent were reviewed and approved by the Institutional Review Board of each participating hospital.

Office BP measurements were taken from both arms 3 times by the study nurse using a validated oscillometric device (Omron HEM 747 mCN BP, Omron Healthcare Co., Kyoto, Japan) after 5 minutes of seated rest and at 2-minute intervals. Using office BP, high normal BP and HTN were defined according to 2013 ESH/ESC practice guidelines (high normal BP as SBP 130 to 139 mm Hg and/or diastolic BP (DBP) 85 to 89 mmHg and HTN as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg).^[13]

Home BP was measured with the same device used in the measurement of office BP. Participants were instructed to measure their BP once every morning within 1 hour of waking and every evening 1 hour before going to bed for 7 consecutive days while seated at a quiet place after more than 2 minutes of rest, as specified by the Japanese guidelines for HBPM.^[14] Participants were also instructed to obtain the BP measurement in the morning after micturition and before breakfast. We defined BP variability as the intra-individual standard deviation (SD) of BP across the measurements. Each of home BP variability in morning and evening was calculated as the SD of 7 measurements of HBPM.

For evaluating the additional effects of circadian variability, 329 patients (171 males, 49 ± 12 year-old) among the enrolled patients underwent 24-hour ambulatory BP monitoring. The device was set to obtain BP readings at 30-minute intervals during the day (between 6:00 AM and 11:59 PM) and at 60-minute intervals during the night (between 12:00 AM and 5:59 AM). Participants were instructed to continue with their normal daily activities during the day. A valid measurement was defined as valid readings for more than 70% of the total measurement

attempts, and at least 14 measurements during the daytime and at least 7 measurements during the nighttime. Each of circadian BP variability in daytime and nighttime was calculated as the standard deviation (SD) of ambulatory BP measurements.

As carotid-femoral pulse wave velocity, considered the gold standard in arterial stiffness, is not convenient to measure,^[15] wave reflection analysis, which is more convenient to measure and widely accepted as a marker of arterial stiffness,^[16,17] was used. Using commercially available applanation tonometry (SphygmoCor, AtCor Medical, Sydney, Australia), central hemodynamics and parameters of arterial stiffness were assessed with PWA of the radial artery. After 20 sequential waveforms had been acquired, a validated generalized transfer function was used to generate the corresponding central aortic pressure waveform.^[18,19] Central systolic and diastolic BP, augmentation pressure (AP) and augmentation index (AI) were derived using the technique of PWA. Augmentation pressure is the difference between the second and the first systolic peaks, and the AI is the ratio of AP to aortic pulse pressure calculated as the difference between respective systolic and diastolic pressure. As AI is influenced by heart rate,^[20] an index adjusted for heart rate of 75 bpm (AI@HR75) was also calculated. As the calculated value of AI@HR75 has already been proven as a good measurement for risk prediction,^[16,17] AI@HR75 was also used as one of markers representing arterial stiffness in the present study.

SPSS 18.0 statistical software package (SPSS, Chicago, Illinois, USA) was used for all calculations. Data are shown as the mean \pm standard deviation for continuous variables and as numbers and percentages for categorical variables. Comparisons were conducted by unpaired Student's *t* test and ANOVA for continuous variables and Pearson chi-square test for categorical variables. To estimate and test the independent effects of home BP variability and circadian BP variability on the arterial stiffness, multivariate analyses were performed using linear regression. Null hypotheses of no difference were rejected if *P* values were $<.05$.

3. Results

Baseline clinical characteristics are summarized in Table 1. In the morning BP, home systolic BP (SBP) variability was 7 ± 20 and home diastolic BP (DBP) variability was 5 ± 14 . In the evening, home SBP variability was 8 ± 22 and home DBP variability was 6 ± 14 .

Multivariate logistic regression analysis demonstrated that both home SBP and DBP variabilities in the morning were correlated with arterial stiffness expressed as AP (Table 2, β -coefficient = 1.622, *P* = .01 and β -coefficient = 1.07, *P* = .035). Both home SBP and DBP variabilities in the evening were also related with AP (β -coefficient = 1.843, *P* = .01 and β -coefficient = 1.088, *P* = .036). The parameters of arterial stiffness, AI and AI@HR75 were correlated with home SBP variabilities, but not with home DBP variabilities. The variabilities of morning and evening SBP were associated with AI (β -coefficient = 1.583, *P* = .02 and β -coefficient = 1.792, *P* = .001) and AI@HR75 (β -coefficient = 1.592, *P* = .001 and β -coefficient = 1.792, *P* = .001).

For evaluating the additional effects of circadian variability, 329 patients (171 males, 49 ± 12 year-old) among the enrolled patients underwent 24-hour ambulatory BP monitoring. Baseline clinical characteristics of these are summarized in Table 3. Circadian BP variabilities included daytime ambulatory SBP and DBP variabilities and nighttime ambulatory SBP and DBP

Table 1
Baseline characteristics.

Variables	Mean ± standard deviation (n=463)
Age (yr-old)	48 ± 12
Men, n (%)	252 (54%)
BMI (kg/m ²)	25 ± 3
Office SBP (mmHg)	146 ± 15
Office DBP (mmHg)	90 ± 13
Morning home SBP (mmHg)	138 ± 16
Morning home DBP (mmHg)	88 ± 12
Morning home SBP variability	7 ± 20
Morning home DBP variability	5 ± 14
Evening home SBP (mmHg)	139 ± 17
Evening home DBP (mmHg)	87 ± 13
Evening home SBP variability	8 ± 22
Evening home DBP variability	6 ± 14
Central SBP (mmHg)	133 ± 18
Central DBP (mmHg)	91 ± 14
AP (mmHg)	14 ± 19
AI (%)	33 ± 29
AI@HR75 (%)	27 ± 26

AI=augmentation index, AI@HR75=AI adjusted for heart rate of 75 bpm, AP=augmentation pressure, BMI=body mass index, DBP=diastolic BP, SBP=systolic blood pressure.

variabilities. Daytime ambulatory SBP variability was 13 ± 4 and daytime ambulatory DBP variability was 11 ± 4. Nighttime ambulatory SBP variability was 10 ± 7 and nighttime ambulatory variability was 8 ± 3.

Multivariate logistic regression analyses of circadian BP variabilities for the arterial stiffness are listed in Table 4. There was no statistical significance between circadian BP variabilities and parameters of arterial stiffness.

4. Discussion and conclusions

The present study demonstrated the significant relationship between home BP variability and arterial stiffness in patients with high normal BP or HTN. Especially, the variability of SBP measured by HBPM was closely related with arterial stiffness.

Table 2
Multivariate logistic regression analysis of home blood pressure variability for the arterial stiffness.

Variables	β-Coefficient	P
Augmentation pressure		
Morning home SBP variability	1.622	.001
Morning home DBP variability	1.07	.035
Evening home SBP variability	1.843	.001
Evening home DBP variability	1.088	.036
Augmentation index		
Morning home SBP variability	1.583	.002
Morning home DBP variability	0.656	.202
Evening home SBP variability	1.792	.001
Evening home DBP variability	0.675	.198
Augmentation index @ HR75		
Morning home SBP variability	1.592	.001
Morning home DBP variability	1.385	.167
Evening home SBP variability	1.792	.001
Evening home DBP variability	0.716	.17

Augmentation index @ HR75 = augmentation index adjusted for heart rate of 75 bpm, DBP = diastolic BP, SBP = systolic blood pressure.

Table 3
Baseline characteristics of 329 patients who underwent additional ambulatory blood pressure monitoring.

Variables	Mean ± standard deviation (n=329)
Age (yr-old)	49 ± 12
Men, n (%)	171 (52%)
BMI (kg/m ²)	25 ± 3
Office SBP (mmHg)	145 ± 16
Office DBP (mmHg)	91 ± 13
Daytime ambulatory SBP (mmHg)	140 ± 13
Daytime ambulatory DBP (mmHg)	91 ± 11
Daytime ambulatory SBP variability	13 ± 4
Daytime ambulatory DBP variability	11 ± 4
Nighttime ambulatory SBP (mmHg)	127 ± 15
Nighttime ambulatory DBP (mmHg)	80 ± 13
Nighttime ambulatory SBP variability	10 ± 7
Nighttime ambulatory DBP variability	8 ± 3
Central SBP (mmHg)	135 ± 17
Central DBP (mmHg)	93 ± 13
AP (mmHg)	15 ± 22
AI (%)	36 ± 32
AI@HR75 (%)	30 ± 30

AI=augmentation index, AI@HR75=AI adjusted for heart rate of 75 bpm, AP=augmentation pressure, BMI=body mass index, DBP=diastolic BP, SBP=systolic blood pressure.

However, there was no relationship between circadian BP variability measured by ambulatory BP monitoring and arterial stiffness.

Many studies demonstrated that higher BP variability was one of predictors of cardiovascular outcome over and beyond BP level.^[1-3,21] Higher BP variability could attenuate hemodynamic homeostasis, cause end-organ damage, and have negative impacts on the vascular system, leading to cardiovascular mortality.^[22,23] Especially SBP variability has been known to be linked to macro-, such as myocardial infarction, stroke, and peripheral artery disease, and microvascular complications, such as nephropathy and retinopathy.^[2,24,25] Excessive SBP variability might create stress on vascular system that in turn accelerate cholesterol plaque deposition. In high risk patients, shear stress from the exaggerated variability of blood pressure could trigger rupture of advanced vulnerable plaque and diminish attenuation of the pulse transmitted to the peripheral arteries, resulting in the onset of cardiovascular events.^[26,27]

In the present study, the variability of SBP measured by HBPM was closely related with arterial stiffness. Circadian BP variabilities calculated as the SD of ambulatory BP measurements were not significantly related with arterial stiffness. Our previous study demonstrated that arterial stiffness was closely related with the pattern of non-dipping in young patients with HTN and high normal BP.^[28] The underlying mechanisms, clinical significance, and prognostic implications might differ between types of BP variability.^[29] When interpreting BP variability, the method and time interval of its measurement should be taken into account. Although HBPM does not assess BP during sleep or at work, it provides measurements over a longer period than 24-hour ambulatory BP monitoring. The BP variability of relatively longer period, compared with 24-hour ambulatory BP monitoring, might be more closely related with arterial stiffness.

Compared to 24-hour ambulatory BP monitoring, HBPM is cheaper, more widely available, and more convenient for patients. The higher practicality of HBPM over ambulatory BP

Table 4
Multivariate logistic regression analysis of circadian blood pressure variability for the arterial stiffness.

Variables	β -Coefficient	P
Augmentation pressure		
Daytime ambulatory SBP variability	0.043	.798
Daytime ambulatory DBP variability	0.029	.874
Nighttime ambulatory SBP variability	-0.036	.611
Nighttime ambulatory DBP variability	0.001	.991
Augmentation index		
Daytime ambulatory SBP variability	0.042	.799
Daytime ambulatory DBP variability	0.029	.875
Nighttime ambulatory SBP variability	-0.038	.586
Nighttime ambulatory DBP variability	0.004	.954
Augmentation index @ HR75		
Daytime ambulatory SBP variability	-0.037	.857
Daytime ambulatory DBP variability	-0.006	.979
Nighttime ambulatory SBP variability	0.013	.166
Nighttime ambulatory DBP variability	-0.028	.747

Augmentation index @ HR75 = augmentation index adjusted for heart rate of 75 bpm, DBP = diastolic BP, SBP = systolic blood pressure.

measurement is widely recognized.^[30] Additionally, HBPM might have the advantage of better prediction of prognosis than 24-hour ambulatory BP monitoring. Several studies already demonstrated the significant association between home SBP variability and cardiovascular or stroke death.^[31,32] Especially in patients with end stage renal disease, that is, in high risk hypertensive patients, relative long term SBP variability was strongly related with adverse cardiovascular outcomes.^[33] Close relationship between home SBP variability and arterial stiffness might be potential underlying mechanism of these phenomena. Despite the present study did not evaluate the cardiovascular events, close relationship between home SBP variability and arterial stiffness might suggest potential future risk. The results of the present study suggest that home SBP variability could be useful predictor not only for high risk hypertensive patients.

This study has several limitations. First, home BP variability could be influenced by methodological problems. There is possibility of artifacts and errors at the time of self-BP measurements by the patients, given that the quality of HBPM was not checked any longer after an initial training. To lessen this methodological errors, all the participants were strictly instructed to measure their BP in accordance with the Japanese guidelines for HBPM. Nevertheless, a possible interference of artifactual measurements with the quantification of home BP variability cannot be completely excluded. Second, we examined the relationship between home SBP variability and arterial stiffness, suggesting prognostic significance of home SBP variability, and did not evaluate whether the home SBP variability could be therapeutic target for reducing adverse cardiovascular outcomes. Reducing home SBP variability might affect the clinical outcomes. Further studies would be needed to demonstrate the beneficial effect of reducing home SBP variability on cardiovascular outcomes. Third, the present study could not demonstrate the effect of comorbidities, such as diabetes or dyslipidemia, on BP variability, due to the relatively small number of patients with comorbidities. Owing to increased oxidative stress and decreased endothelial function, hypertensives with diabetes had higher BP variability.^[34,35] Further studies would be needed to demonstrate the effect of comorbidities on BP variability.

In conclusion, the variability of SBP measured by HBPM was closely related with arterial stiffness in patients with high normal BP or HTN. The HBPM might have additive value in predicting future cardiovascular events.

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