Relationship between blood pressure repeatedly measured by a wrist-cuff oscillometric wearable blood pressure monitoring device and left ventricular mass index in working hypertensive patients

Short title: Wearable wrist BP and LVMI

Kazuomi Kario MD, PhD[1], Naoko Tomitani BSc[1], Tomoko Morimoto BEng[1], Hiroshi Kanegae BSc[1,2], Peter Lacy PhD[3], Bryan Williams MD, FMedSci[3]

[1] Division of Cardiovascular Medicine, Department of Medicine, Jichi Medical University School of Medicine, Tochigi, Japan
[2] Genki Plaza Medical Center for Health Care, Tokyo, Japan
[3] UCL Institute of Cardiovascular Sciences, University College London, London, United Kingdom.

Corresponding author: Dr. Kazuomi Kario
Division of Cardiovascular Medicine, Department of Medicine, Jichi Medical University School of Medicine, 3311-1, Yakushiji, Shimotsuke, Tochigi 329-0498, Japan. Tel: +81-285-58-7344; Fax: +81-285-44-2132; E-mail: kkario@jichi.ac.jp.

Abstract word count: 250 words

Text word count: 3787

No. of tables: 3

No. of figures: 3

No. of references: 32

No. of supplementary digital content files: 1

Abstract:

This study sought to evaluate the relationship between blood pressure (BP) taken by a new wrist-cuff oscillometric wearable BP monitoring device and left ventricular mass index measured by cardiac magnetic resonance imaging (cMRI-LVMI) in 50 hypertensive patients (mean age 60.5±8.9 years, 92.0% men, 96% treated for hypertension) with regular employment. Participants were asked to self-measure their wearable BPs twice in the morning and evening under a guideline-recommended standardized home BP measurement, and once each at 5 predetermined times and any additional time points under an ambulatory condition for a maximum of 7 days. In total, 2105 wearable BP measurements (home BP: 747 [morning: 409, evening: 338], ambulatory condition: 1358 [worksite: 942]) were collected over 5.5±1.2 days. The average of all wearable systolic BP (SBP) readings (129.8±11.0 mmHg) was weakly correlated with cMRI-LVMI (r=0.265, p=0.063). Morning home wearable SBP average (128.5±13.8 mmHg) was significantly correlated with cMRI-LVMI (r=0.378, p=0.013), but ambulatory wearable SBP average (132.5±12.7 mmHg) was not (r=0.215, p=0.135). The averages of the highest three values of all wearable SBPs (153.3±13.9 mmHg) and ambulatory wearable SBPs (152.9±13.9 mmHg) were 16 mmHg higher than that of the morning home wearable SBPs (137.0±15.9 mmHg). Those peak values were significantly correlated with cMRI-LVMI (r=0.320, p=0.023; r=0.310, p=0.029; r= 0.451, p=0.002, respectively). In conclusion, an increased number of wearable BP measurements, which could detect individual peak BP, might add to the clinical value of these measurements as a complement to the guideline-recommended home BP measurements, but further studies are needed to confirm these findings.

Key word: wristwatch-type wearable BP monitoring, left ventricular mass index, HeartGuide.

Introduction

Hypertension is the most important risk factor of cardiovascular disease. Recent international guidelines for the management of hypertension recommend the use of out- of-office blood pressure (BP) for the diagnosis of hypertension and monitoring of compliance with therapeutic targets.(1-3) Clinical evidence of home BP monitoring (HBPM) has accumulated, and self-measured HBPM is now recommended in clinical practice.(4-8) However, self-measured HBPM may underestimate the risk of masked hypertension, because the guideline-recommended self-measurements are only taken at specific times (usually in the morning and evening) under standardised conditions, i.e., while seated after 5 minutes rest. Ambulatory BP monitoring (ABPM) is the traditional standard for evaluating the risk of hypertension throughout a 24-h period, including the daytime and nighttime periods.(9) However, ABPM cannot be performed frequently, because of the discomfort of wearing the device and of repeated cuff inflations. Nighttime BP during sleep could be measured by some HBPM devices, including wristwatch-type devices,(10-17) but there has not been an adequate BP monitoring device that could measure daytime BP during activities of daily life.

Daytime BPs are extensively affected by the physical and psychological stressors encountered in daily life.(18-20) Frequent daytime BP measurements during daily activities over several days may be critical for detecting daytime BP risk. Especially in the era of digital management of hypertension (telemedicine), the development of less restrictive wearable BP monitoring devices could be a more convenient alternative to conventional BP monitors.(21, 22) However, only a few devices have been validated, and validation studies for those devices have only been performed under laboratory resting and sitting conditions.(21)

We previously validated the HeartGuideR, a wristwatch-type wearable BP monitoring device, by the protocol of the ANSI/AAMI/ISO81060-2:2013 guidelines under laboratory resting and sitting conditions(23) and verified its accuracy under the ambulatory condition in a comparison study of subjects simultaneously equipped with ABPM.(24) In the present study, we studied the association between wearable BPs as repeatedly measured by the validated wrist-cuff oscillometric wearable device and left ventricular mass index (LVMI) evaluated by cardiac magnetic resonance imaging

(cMRI) in working hypertensive patients, and also evaluated the wearable BP measurement timing and method.

Methods.

Study Population.

Patients receiving antihypertensive treatment or who had elevated office systolic BP (SBP) (>130 mmHg) and who had regular employment were recruited from Washiya Hospital, Tochigi, Japan. The study protocol was approved by the institutional review board of Jichi Medical University School of Medicine (rin-dai 20-043). The study protocol was registered on a clinical trials registration site (University Hospital Medical Information Network Clinical Trials Registry, UMIN000040939). All participants provided written informed consent.

Study procedures

Demographics and clinical data (including age, sex, body mass index, smoking status, habitual drinking, prevalence of hypertension, diabetes mellitus and hyperlipidemia, chronic kidney disease, hyperuricemia, sleep apnea syndrome, past history of atherosclerotic cardiovascular disease, and medication) were obtained from medical records. Diabetes mellitus was defined as a fasting glucose level of >126 mg/dl and/or a casual glucose level of >200 mg/dl or treated diabetes. Hyperlipidemia was defined as a total cholesterol level of >240 mg/dl or treated hyperlipidemia. Chronic kidney disease was defined as the presence of proteinuria or a value of <60ml/min/1.73m^2 for the estimated glomerular filtration rate. Sleep apnea syndrome was defined as an apnea-hypopnea index of >15 events/hour by overnight sleep polysomnography. Study patients were self-measured their wearable BPs by a provided wrist-cuff oscillometric wearable BP monitoring device for a maximum of 7 days. ABPM was conducted within one month before or after the wearable BP monitoring period, and on a different day from the day of wearable BP measurement. Cardiac MRI was performed within one month before or after the wearable BP monitoring period.

BP measurement devices

The device used was the HeartGuide (Omron Healthcare, Kyoto, Japan), a newly developed, wearable self (i.e., patient)-activated automatic oscillometric device for measuring BP at the wrist. The HeartGuide device was previously validated in a laboratory setting.(23) Further, the correspondence of BP values measured by the HeartGuide and ABPM in the out-of-office setting was shown to be acceptable.(24)
When using the HeartGuide device to measure BP, participants were asked to hold their wrist at heart level to reduce hydrostatic effects (Supplemental Figure).

Wearable BP monitoring (measurement schedule)

We asked the study patients to self-measure their BP using a HeartGuide device for up to 7 days. The BP measurement schedule was as follows: (i) twice in the morning and twice in the evening, replicating a guideline-recommended standardized home BP measurement protocol (seated after 5 minutes rest); (ii) once at each of the predetermined times (10:00, 12:00, 14:00, 16:00, 18:00) under ambulatory conditions; (iii) additional ambulatory BP measurements (up to 5 times per day) could be taken at the discretion of the participant at any other time points during the day. The HeartGuide was set to vibrate at the predetermined times to let the participants know when a measurement was scheduled. After the notification, the participants raised their wrist to heart level and initiated the BP measurement by the wrist device by pressing a button on the device.

Self-report wearable BP monitoring diary

Patients were provided a self-report diary in which they were asked to answer questions about body position, location, current activities, feelings, and degree of stress at the time of each wearable BP measurement. Worksite wearable BP measurements were confirmed by this self-reported diary.

Office and ambulatory BP measurement

Office BP was measured using a validated brachial oscillometric monitor (HEM-907; Omron Healthcare Co. Ltd., Kyoto, Japan) at the beginning of this study. Measurements were taken twice at a 1-minute interval, with participants seated in a comfortable position with their arm supported at the level of the heart, and their legs uncrossed with feet flat on the floor. The average of the two readings was recorded as the Office BP.

Twenty-four hour ambulatory BP measurement was performed within one month before or after the wearable BP monitoring period, and on a different day from the day of wearable BP measurement, using a validated oscillometric ABPM device (TM-2441; A&D Co. Ltd., Tokyo).(25) Individual measurements were taken at 30-minute intervals over 24 h. Participants were instructed to keep their arm stable and in a relaxed position during each BP measurement. A diary was provided to the participants to record the time of going to sleep and waking for the period of monitoring.(9) Daytime readings were defined as those taken from the self-reported waking time to the asleep time.

Definition of wearable BP

The definition of wearable BP indexes were shown in Figure 1. We defined "wearable BP" as BP self-measured by the wristwatch-type wrist-cuff oscillometric BP monitoring device (HeartGuide, Omron Healthcare, Kyoto). Wearable BP measured at home according to the JSH2019 guideline-recommended3 standardized home BP measurement protocol was defined as "guideline-recommended home wearable BP" and wearable BP measured under ambulatory conditions (excluding guideline-recommended home wearable measurements) was defined as "ambulatory wearable BP". "Worksite wearable BP" was defined as the ambulatory wearable BP measured only at a worksite as confirmed by the diary record in this study. Morning and evening home wearable BP were calculated as the average of 2 consecutive measurements of wearable BPs on one occasion in the morning and evening at home according to the JSH2019 guidelines.

The wearable peak BP indexes were calculated as a "maximum 1-day average," which is the highest 1-day average value during the measurement period, and as an "average of the highest three values," which is the average of the three highest readings from the whole measurement period (Figure 2). The three highest home wearable BP readings in the morning (or evening) were selected from all readings taken in the morning (or evening), not from the average values of 2 consecutive home wearable BP measurements.

Cardiac MRI

Cardiac MRI was performed within one month before or after the wearable BP monitoring period. Cardiac MRI scans were conducted at Washiya Hospital. All scans were performed on a 1.5-Tesla scanner (OPTIMA MR450w Expert 1.5T; GE Healthcare, Chicago, IL) and

obtained by a single expert operator. Imaging of the heart was performed using an accelerated steady-state free precession protocol. Contrast was not used in any imaging for this study. Retrospectively gated, electrocardiographically triggered, balanced, steady-state free precession cine images were gained while patients were holding their breath in standard 4-chamber and 2-chamber long axis views, as well as short axis views of the entire left ventricle. The following scan parameters were used: slice thickness 10 mm, in-plane resolution 2.4×2.0 mm, echo time 1.5 ms, repetition time 3.4 ms, and flip angle 60°. Analysis of left ventricular (LV) mass was undertaken using dedicated software (CardiacVX: GE Healthcare). The stack of LV images was segmented to define the endocardial and epicardial borders. Individual slices were summed to determine LV mass and LV mass index (LVMI). For LV mass calculation, the myocardial volume was multiplied by the specific density of the myocardium (1.05 g/mL).(26) LV mass was determined including papillary muscles and trabeculae as myocardial tissue. LVMI was indexed to the body surface area.

Statistical analysis

All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). The association between LVMI and BP indices were analyzed using Pearson's correlation coefficient.. Pairwise differences between BP indices were tested using a paired t-test. Values of $p<0.05$ were considered significant. All data processing and analyses were independently conducted at the Global Analysis Center of BP (GAP) at the Jichi Medical University COE Cardiovascular Research and Development (JCARD) center.

Result

Participant characteristics

The characteristics of the study participants are shown in Table 1. All 50 participants were regularly employed hypertensive patients either receiving antihypertensive treatment (96%) or treatment naïve but with an elevated office SBP (>130 mmHg). The mean age was 60.5±8.9 years (42–77 years old), 92% were male, and the average body mass index (BMI) was 27.6±5.1 kg/m2. The prevalence of diabetes mellitus, hyperlipidemia, chronic kidney disease, hyperuricemia, sleep apnea syndrome, and past history of atherosclerotic cardiovascular disease were 22.0%, 50.0%, 2.0%, 24.0%, 34.0%, and 12.0%, respectively. The

mean seated office systolic/diastolic BP (pulse rate) was 133.1±15.2/81.3±11.2 mmHg (71.4±10.7 bpm). The median (interquartile range) of LVMI was 67.8 (59.3–76.0) g/m^2.

Average of wearable BP

All 50 study participants successfully self-measured their wearable BPs using the HeartGuide device according to the following study measurement schedule: twice in the morning and evening, and once at each predetermined time (10:00, 12:00, 14:00, 16:00, and 18:00) and at any additional time points for a maximum of 7 days. A total of 2105 wearable BP readings were obtained from 50 patients with a per patient average of 42.1±14.3 measurements over 5.5±1.2 days. A total of 747 readings were "guideline-recommended home wearable BP" measured at home, consisting 409 morning readings and 338 evening readings. A total of 1358 readings were "ambulatory wearable BP" measured under an ambulatory condition, and 942 of the "ambulatory wearable BP" readings were "worksite wearable BP" measured at the workplace of participants. (Table 2).

The average of all wearable SBPs was 129.8±11.0 mmHg. Regarding guideline-recommended home wearable BP, the averages of the morning home wearable SBPs and evening home wearable SBPs were 128.5±13.8 and 119.7±11.9 mmHg, respectively, and the combined morning-evening (M-E) average SBP was 124.6±12.1 mmHg. As for wearable BP measured under an ambulatory condition, the average of all ambulatory wearable SBPs was 132.5±12.7 mmHg and the average of worksite wearable SBPs was 133.4±12.7 mmHg (Table 2). The worksite wearable SBP was higher than any other wearable SBP index and 8.8 mmHg higher than the combined M- E average wearable SBP self-measured by HeartGuide (133.4±12.7 vs. 124.6±12.1 mmHg, $p<0.001$).

The averages of all wearable SBPs were almost the same as the averages of daytime ambulatory SBPs measured by ABPM (129.8±11.0 vs. 130.6±12.7 mmHg) (Table 2).

Correlation with cardiac MRI-measured LVMI (cMRI-LVMI)

The average of all wearable SBP measurements was weakly correlated with cMRI- LVMI ($r=0.265$, $p=0.063$). As for guideline-recommended home wearable SBP measured according to a standardized home BP measurement protocol, both morning home wearable SBP ($r=0.378$, $p=0.013$) and the combined M-E average wearable SBP ($r=0.349$, $p=0.019$) were

significantly correlated with cMRI-LVMI, but evening home wearable SBP was not (r=0.234, p=0.135). Ambulatory wearable SBP measured under ambulatory condition was not significantly correlated with cMRI-LVMI (r=0.215, p=0.135), whereas worksite wearable SBP (ambulatory wearable SBP measured at the workplace) trended to be correlated with cMRI-LVMI (r=0.237, p=0.098).

Regarding ABPM-measured BP indexes, 24-h SBP average and daytime SBP average were significantly correlated with cMRI-LVMI (24-h: r=0.279, p=0.049; daytime: r=0.301, p=0.034), while nighttime SBP average and morning SBP average (average of BP measured during 2h after waking) were not correlated with cMRI-LVMI (nighttime: r=0.192, p=0.181; morning: r=0.256, p=0.073) (Table 2).

Wearable peak BP

The wearable peak BP indexes are shown in Table 3. The averages of the highest three SBP readings of all measurements (153.3±13.9 mmHg) and ambulatory measurements (152.9±13.9 mmHg) were higher than that of guideline-recommended morning home measurements (137.0±15.9 mmHg) by approximately 16 mmHg. The averages of the three highest SBPs for all measurements, ambulatory measurements, and morning home wearable measurements were significantly correlated with cMRI-LVMI (r=0.320, p=0.023; r=0.310, p=0.029; and r= 0.451, p=0.002, respectively). All wearable peak BP indexes for both the maximum 1-day average value and the averages of the highest three values shown in Table 3 were significantly correlated with cMRI-LVMI. The average of the highest three ABPM-measured daytime SBP readings was 163.5±20.2 mmHg and higher than any other wearable peak BP indexes, whereas it was not correlated with cMRI-LVMI (r=0.233, p=0.103).

Control status of wearable BPs and ABPM-measured BPs

The correlation coefficient of the wearable SBP average (average of all wearable SBP measurements) and ABPM-measured daytime SBP average was 0.460 (p<0.001) (Figure 3). When we set the threshold of uncontrolled SBP at 135 mmHg, 52% and 24% of participants fit the categories of well-controlled and uncontrolled hypertension. In other words, 76% showed the same control status between wearable BP monitoring and ABPM.

Discussion

This is the first study on the association between wearable BPs measured by a validated wrist-cuff oscillometric wearable device, and organ damage in working hypertensive patients. We found that wearable BP measurement using the HeartGuide device was feasible both at home and in daily activities. When the average of wearable SBPs was limited to the readings measured at home according to the guideline-recommended standardized measurement protocol, it was more strongly correlated with cMRI-LVMI than when it included measurements at home and under an ambulatory condition. On the other hand, the peak wearable SBP values detected during ambulatory measurement were higher than those detected during home morning measurement.

Wearable BP levels and association with LVMI

As the measurement schedule of wearable BP monitoring has not reached consensus, in this study we evaluated a number of different measurement scenarios in which we asked the study patients to self-measure their BP twice each in the morning and evening according to a guideline-recommended standardized home BP measurement protocol and once at each predetermined time (10:00, 12:00, 14:00, 16:00, and 18:00) with additional time points under the ambulatory condition for a maximum of 7 days. As the vibration alerts at the preset times were effective at reminding participants to self- measure wearable BPs, significant numbers of wearable BPs were self-measured (number of measurements: 42.1±14.3/person). The averages of the ambulatory wearable SBP and worksite wearable SBP values were higher than the average of the guideline- recommended home wearable SBP by 7.9 mmHg and 8.8 mmHg, respectively. Especially in Asians, morning home BP is known as a strong risk factor for cardiovascular events,(27-29) but in our study the worksite wearable SBP was higher than the morning home wearable SBP by 4.9 mmHg.
However, the correlation of ambulatory wearable SBP with cMRI-LVMI was not significant, while that of home (morning average and morning-evening average) wearable SBP with cMRI-LVMI was significant. The ambulatory wearable SBP limited to measurements taken at the worksite of participants (worksite wearable SBP) tended to be correlated with cMRI-LVMI ($p=0.098$). In a previous study using an upper arm- type HBPM device, seated worksite SBP measured at four time points based on behaviour (before starting work, before the lunch break, after the lunch break, and before leaving the workplace) was significantly

correlated with LVMI evaluated by echocardiography.(18-20) One reason that a statistically significant correlation was not observed between worksite SBP and cMRI-LVMI may have been a lack of statistical power. Another possible reason is that the measurement time points at the worksite were based on clock time. The study participants engaged in a variety of working styles and hours. Worksite BP measured according to a standardized schedule based on work- related behaviour might be more likely to detect organ damage. These results indicate that wearable BP might be a more sensitive measure for evaluating organ damage, when the measurement methods are standardized. Further studies are needed to investigate the most sensitive and specific wearable BP measurement methods and schedule for detecting organ damage.

In agreement with the previous findings using an upper arm-type oscillometric device,(27-29) we found that morning BP measured according to the home BP measurement protocol was correlated with organ damage, even when measured by a wearable device. Morning might be a blind spot in hypertension treatment.(30) The home BP measurement protocol states that the morning BP measurement should be done before taking medication. Even well-controlled medicated patients such as those in the present study might have elevated BP levels in the morning before taking medication. In this study, ABPM-measured morning SBP was not significantly correlated with cMRI-LVMI. Morning BP measured by ABPM is measured under an ambulatory condition, the measurement location is not limited to the home, and the readings are only for a single day. The present results highlight the importance of repeated morning BP measurement according to a standardized protocol for hypertension management.

Wearable peak BP and association with LVMI

Both the wearable peak SBP index measured under a home condition and that measured under an ambulatory condition were significantly correlated with cMRI-LVMI. These results suggest that the detection of the peak BPs of patients both under a quiet home condition and during the performance of daily activities might be useful in predicting future cardiovascular risk. Interestingly, the peak index (the average of the highest three SBP readings) of ambulatory wearable SBP was 16 mmHg higher than that of the guideline-recommended home wearable SBP, and that of ABPM-measured daytime SBP was much higher, whereas the BP elevation detected by ABPM was not correlated with cMRI-LVMI.

Automatically measured ABPM captured BP under a wider range of conditions compared with ambulatory wearable BP, which can lead to greater BP variability and poor correlation. Therefore, wearable BP may be more sensitive than ABPM-measured BP for assessing cardiovascular risk during daily activity.

Potential clinical use of wearable BP

In clinical practice, HBPM using a validated brachial oscillometric device according to the guideline measurement schedule(1-3, 5) is widely recommended. However, home BP may underestimate the risk of hypertension and BP variability throughout 24 h, because home BP is measured under very standardized conditions, i.e., at rest, relaxed, and whilst seated, and only at specific times (morning and evening). In fact, in the IDH study (Improving the Detection of Hypertension), HBPM was reliable at detecting the risk of left ventricular hypertrophy,(31) but significant numbers of ABPM-determined masked hypertension cases, who are at risk of left ventricular hypertrophy, were not detected by HBPM alone.(32) Considering that 76% of the present study participants were classified into the same BP control status by both wearable BP monitoring and ABPM, wearable BPs might be useful for clinical detection of masked daytime hypertension. In addition, hypertension may be more detectable in multiple-day monitoring with variety of daily activities such as in the workplace (i.e., under a stressful condition). Wearable BP monitoring, which enables multiple BP measurements at several times per day (like ABPM) and for many days (like HBPM), would seem to be especially advantageous for detecting peak BP and personalized risk factor.

Study limitations

There are several possible limitations to our study. First, this is a cross-sectional study with a limited number of study subjects and limited power. To reduce this weakness, we used cMRI, the most sensitive objective method to evaluate LVMI.29 The ambulatory wearable BP and worksite wearable BP were higher than the home wearable BP measured according to the standardized home BP measurement protocol, but the relationship with cMRI-LVMI was not shown to be significant. This may have been due to a lack of statistical power. However, wearable BP detected BP elevation during daytime activities that could not be detected by seated home BP measurements. Second, most of our study patients were older

male workers. Therefore, the results of this study cannot be generalized to all working hypertensive patients. Further studies with a larger number of participants are needed to confirm these results and establish the utility of the wearable BP measurement method.

Conclusion and perspectives

Monitoring wearable BP by a wristwatch-type device over the course of multiple days was feasible and acceptable for working adults, and this newly developed, wrist-cuff oscillometric, wearable BP monitoring device was able to detect the BP elevation during daily activity. The correlation of cMRI-LVMI with the average of all wearable SBP measurements was weak, but that with guideline-recommended morning home wearable SBP measurements was strong. On the other hand, higher peak values of wearable BP were obtained in the ambulatory wearable BP monitoring during daily activities. Measuring wearable BP repeatedly during daily activities might add clinical value, based on guideline-recommended home morning measurement. This is the first exploratory study to use a wrist-cuff oscillometric device to evaluate the link with hypertension-mediated organ damage. Therefore, the scale and power of this study are limited and further studies is needed.

Acknowledgements

The HeartGuide device was supplied by Omron Healthcare Co., Ltd., who also provided funding for the study. However, the collection and analysis of BP data in this study were entirely independent of Omron Healthcare Co., Ltd..

Disclosures

K. Kario has received a research grant from Omron Healthcare, A&D and Fukuda Denshi. N. Tomitani was the recipient of a JSPS KAKENHI grant (no. 20K17127). B. Williams has received a research grant from Omron Healthcare.

Sources of funding

This study was financially supported by Omron Healthcare.

Figure legends

Figure 1. Definition of wearable BP

BP, blood pressure.

Figure 2. Wearable BP average and peak indexes

BP, blood pressure.

Figure 3. Control status of wearable SBP and ABPM-measured daytime SBP in 50 working hypertensives

SBP, systolic blood pressure; ABPM, ambulatory blood pressure monitoring; HG, HeartGuide. Wearable SBP shown on the X-axis was the average of all wearable SBP self-measured using a validated wrist-type oscillometric wearable BP monitor (HeartGuideR), and daytime ambulatory SBP shown on the Y-axis was the average of daytime SBP measured by a standard validated ABPM (TM-2441).

References

1. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39(33):3021-104.
2. Whelton PK, Carey RM, Aronow WS, Casey DE, Jr., Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Taskforce on Clinical Practice Guidelines. J Am Coll Cardiol 2018; 71:9199 2199-269.
3. Umemura S, Arima H, Arima S, Asayama K, Dohi Y, Hirooka Y, et al. The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2019). Hypertens Res. 2019;42(9):1235-481.
4. Stergiou GS, Palatini P, Parati G, O'Brien E, Januszewicz A, Lurbe E, et al. 2021 European Society of Hypertension practice guidelines for office and out-of-office blood pressure measurement. J Hypertens 2021.
5. Kario K, Park S, Chia YC, Sukonthasarn A, Turana Y, Shin J, et al. 2020 Consensus summary on the management of hypertension in Asia from the HOPE Asia Network. J Clin Hypertens (Greenwich). 2020;22(3):351-62.
6. Park S, Buranakitjaroen P, Chen CH, Chia YC, Divinagracia R, Hoshide S, et al. Expert panel consensus recommendations for home blood pressure monitoring in Asia: the Hope Asia Network. J Hum Hypertens. 2018;32(4):249-58.
7. Kario K, Shimbo D, Hoshide S, Wang JG, Asayama K, Ohkubo T, et al. Emergence of Home Blood Pressure-Guided Management of Hypertension Based on Global Evidence. Hypertension. 2019:HYPERTENSIONAHA11912630.
8. Shimbo D, Artinian NT, Basile JN, Krakoff LR, Margolis KL, Rakotz MK, et al. Self-Measured Blood Pressure Monitoring at Home: A Joint Policy Statement From the American Heart Association and American Medical Association. Circulation. 2020;142(4):e42-e63.
9. Kario K, Shin J, Chen CH, Buranakitjaroen P, Chia YC, Divinagracia R, et al. Expert panel consensus recommendations for ambulatory blood pressure monitoring in Asia: The HOPE Asia Network. J Clin Hypertens (Greenwich). 2019;21(9):1250-83.

10. Kario K. Nocturnal Hypertension: New Technology and Evidence. Hypertension. 2018;71(6):997-1009.
11. Asayama K, Fujiwara T, Hoshide S, Ohkubo T, Kario K, Stergiou GS, et al. Nocturnal blood pressure measured by home devices: evidence and perspective for clinical application. J Hypertens. 2019;37(5):905-16.
12. Kario K, Kanegae H, Tomitani N, Okawara Y, Fujiwara T, Yano Y, et al. Nighttime Blood Pressure Measured by Home Blood Pressure Monitoring as an Independent Predictor of Cardiovascular Events in General Practice. Hypertension. 2019;73(6):1240-8.
13. Hoshide S KH, Kario K. Nighttime home blood pressure as a mediator of N- terminal pro-brain natriuretic peptide in cardiovascular events. Hypertension Research. 2021:in press.
14. Kuwabara M, Harada K, Hishiki Y, Kario K. Validation of wrist-type home nocturnal blood pressure monitor in the sitting and supine position acording to ANSI/AAMI/ISO81060-2: 2013 guidelines: Omron HEM-9600T. J Clin Hypertens (Greenwich). 2019;21(4): 463-9.
15. Kuwabara M, Harada K, Hishiki Y, Ohkubo T, Kario K, Imai Y. Validation of wrist-type home nocturnal blood pressure monitor in the sitting and supine position acording to ANSI/AAMI/ISO81060-2: 2013 guidelines: Omron HEM-9600T. J Clin Hypertens (Greenwich). 2020;22(6): 970-8.
16. Kario K, Tomitani N, Iwashita C, Shiga T, Kanegae H. Simultaneous self- monitoring comparison of a supine algorithm-equipped wrist nocturnal home blood pressure monitoring device with an upper arm device. J Clin Hypertens (Greenwich). 2021;23(4):793-801.
17. Tomitani N, Kanegae H, Kario K. Comparison of nighttime measurement schedules using a wrist-type nocturnal home blood pressure monitoring device. J Clin Hypertens (Greenwich). 2021.
18. Kario K, Tomitani N, Kanegae H, Yasui N, Nishizawa M, Fujiwara T, et al. Development of a New ICT-Based Multisensor Blood Pressure Monitoring System for Use in Hemodynamic Biomarker-Initiated Anticipation Medicine for Cardiovascular Disease: The National IMPACT Program Project. Prog Cardiovasc Dis. 2017;60(3):435-49.
19. Tomitani N, Kanegae H, Suzuki Y, Kuwabara M, Kario K. Stress-Induced Blood Pressure Elevation Self-Measured by a Wearable Watch-Type Device. Am J Hypertens. 2021;34(4):377-82.

20. Tomitani N, Hoshide S, Kario K. Self-measured worksite blood pressure and its association with organ damage in working adults: Japan Morning Surge Home Blood Pressure (J-HOP) worksite study. J Clin Hypertens (Greenwich). 2021;23(1):53-60.
21. Kario K. Management of Hypertension in the Digital Era: Small Wearable Monitoring Devices for Remote Blood Pressure Monitoring. Hypertension. 2020;76(3):640-50.
22. Omboni S, McManus RJ, Bosworth HB, Chappell LC, Green BB, Kario K, et al. Evidence and Recommendations on the Use of Telemedicine for the Management of Arterial Hypertension: An International Expert Position Paper. Hypertension. 2020;76(5):1368-83.
23. Kuwabara M, Harada K, Hishiki Y, Kario K. Validation of two watch-type wearable blood pressure monitors according to the ANSI/AAMI/ISO81060-2:2013 guidelines: Omron HEM-6410T-ZM and HEM-6410T-ZL. J Clin Hypertens (Greenwich). 2019;21(6):853-8.
24. Kario K, Shimbo D, Tomitani N, Kanegae H, Schwartz JE, Williams B. The first study comparing a wearable watch-type blood pressure monitor with a conventional ambulatory blood pressure monitor on in-office and out-of-office settings. J Clin Hypertens (Greenwich). 2020;22(2):135-41.
25. Kario K, Hoshide S, Saito K, Sato K, Hamasaki H, Suwa H, et al. Validation of the TM-2441 ambulatory blood pressure measurement device according to the ISO 81060-2: 2013 standard. Blood Press Monit. 2019;24(1):38-41.
26. Schulz-Menger J, Bluemke DA, Bremerich J, Flamm SD, Fogel MA, Friedrich MG, et al. Standardized image interpretation and post-processing in cardiovascular magnetic resonance - 2020 update : Society for Cardiovascular Magnetic Resonance (SCMR): Board of Trustees Task Force on Standardized Post-Processing. J Cardiovasc Magn Reson. 2020;22(1):19.
27. Kario K, Saito I, Kushiro T, Teramukai S, Ishikawa Y, Mori Y, et al. Home blood pressure and cardiovascular outcomes in patients during antihypertensive therapy: primary results of HONEST, a large-scale prospective, real-world observational study. Hypertension. 2014;64(5):989-96.
28. Hoshide S, Yano Y, Haimoto H, Yamagiwa K, Uchiba K, Nagasaka S, et al. Morning and Evening Home Blood Pressure and Risks of Incident Stroke and Coronary Artery Disease in the Japanese General Practice Population: The Japan Morning Surge-Home Blood Pressure Study. Hypertension. 2016;68(1):54-61.

29. Kario K, Saito I, Kushiro T, Teramukai S, Tomono Y, Okuda Y, et al. Morning Home Blood Pressure Is a Strong Predictor of Coronary Artery Disease: The HONEST Study. J Am Coll Cardiol. 2016;67(13):1519-27.
30. Kario K. Time for focus on morning hypertension: pitfall of current antihypertensive medication. Am J Hypertens. 2005;18(2 Pt 1):149-51.
31. Schwartz JE, Muntner P, Kronish IM, Burg MM, Pickering TG, Bigger JT, et al. Reliability of Office, Home, and Ambulatory Blood Pressure Measurements and Correlation With Left Ventricular Mass. J Am Coll Cardiol. 2020;76(25):2911-22.
32. Anstey DE, Muntner P, Bello NA, Pugliese DN, Yano Y, Kronish IM, et al. Diagnosing Masked Hypertension Using Ambulatory Blood Pressure Monitoring, Home Blood Pressure Monitoring, or Both? Hypertension. 2018;72(5):1200-7.

Table 1. Characteristics of the study participants (n=50)

Variables	**n=50**
Age, yrs	60.5 ± 8.9
Male, %	92.0
Body mass index, kg/m^2	27.6 ± 5.1
Current smoker, %	16.0
Regular drinker, %	30.0
Treated hypertension, %	96.0
- Number of antihypertensive medications	1.8 ± 1.0
- Alpha blocker	4.0
- Beta blocker	20.0
- Angiotensin II receptor blocker	68.0
- Calcium channel blocker	66.0
- Diuretics	26.0
Diabetes mellitus, %	22.0
Treated diabetes mellitus, %	20.0
Hyperlipidemia, %	50.0
Treated hyperlipidemia, %	38.0
Chronic kidney disease, %	2.0
Hyperuricemia, %	24.0
Sleep apnea syndrome, %	34.0
Past history of atherosclerotic cardiovascular disease, %	12.0
- Myocardial infarction, %	4.0
- Angina pectoris, %	2.0
- Stroke, %	6.0
Seated office systolic blood pressure, mmHg	133.1 ± 15.2
Seated office diastolic blood pressure, mmHg	81.3 ± 11.2
Seated office pulse rate, bpm	71.4 ± 10.7
left ventricular mass index , median (Q1-Q3), g/m^2	67.8 (59.3 - 76.0)

Values are means ± standard deviations or % patients.

None of the patients had atrial fibrillation or heart failure.

Q1: the first quartile; Q3: the third quartile.

Table 2. Systolic blood pressure and left ventricular mass index measured by cardiac MRI in 50 hypertensive patients

	Number of measurements	Systolic blood pressure, mmHg	Correlation coefficient of cardiac LVMI (p-value)
Seated office SBP measured by the upper-arm type device at one visit			
Average of measurements at one visit	1.9±0.2	133.1±15.2	0.152 (0.291)
Wearable SBP measured by HeartGuide^{R} for multiple days (measured for 5.5±1.2 days)			
All wearable SBP measurements (n=2105)			
Average of all SBP measurements	42.1±14.3	129.8±11.0	0.265 (0.063)
Guideline-recommended home wearable SBP (measured according to a standardized home BP measurement protocol, n=747)			
- Morning home wearable SBP (measured at home in the morning, n=409 from the 43 patients)			
Average of morning measurements	9.5±2.8	128.5±13.8	0.378 (0.013)
- Evening home wearable SBP (measured at home in the evening, n=338 from the 42 patients)			
Average of evening measurements	8.0±3.4	119.7±11.9	0.234 (0.135)
Morning-Evening (M-E) average wearable SBP (n=237 average values from the 45 patients)			
Average of M-E average values	5.3±1.4	124.6±12.1	0.349 (0.019)
Wearable SBP measured under an ambulatory condition			
Ambulatory wearable SBP (excluding morning and evening home measurements from all wearable measurements, n=1358)			
Average of all measurements	27.2±8.3	132.5±12.7	0.215 (0.135)
- Worksite wearable SBP (measured only at the worksite, n=942)			
Average of worksite measurements	18.8±7.4	133.4±12.7	0.237 (0.098)
Ambulatory SBP measured by ABPM on a single day			
24-h average	44.6±3.3	123.9±11.4	0.279 (0.049)
Daytime average	30.7±4.3	130.6±12.7	0.301 (0.034)
Nighttime average	13.9±2.8	109.3±11.2	0.192 (0.181)
Morning (2h after waking) average	3.7±0.7	133.7±18.1	0.256 (0.073)

Values are means ± standard deviations or % patients. SBP, systolic blood pressure; MRI, magnetic resonance imaging; LVMI, left ventricular mass index; ABPM, ambulatory BP monitoring. Guideline-recommended home wearable SBP: wearable SBP measured at home according to a guideline- recommended standardized home BP measurement protocol; Ambulatory wearable SBP: wearable SBP measured under ambulatory conditions excluding home wearable measurements

Table 3. Peak systolic blood pressure index and left ventricular mass index measured by cardiac MRI in 50 hypertensive patients

	Number of measurements	Systolic blood pressure, mmHg	Correlation coefficient of cardiac LVMI (p-value)
Wearable SBP measured by HeartGuide^{R} for multiple days (measured for 5.5±1.2 days)			
All wearable SBP measurements (n=2105)			
Maximum 1-day average value	7.4±2.2	137.7±11.5	0.340 (0.016)
Average of the highest three values	3.0	153.3±13.9	0.320 (0.023)
Guideline-recommended home wearable SBP (measured according to a standardized home BP measurement protocol, n=747)			
Morning home wearable SBP (measured at home in the morning, n=409 from the 43 patients)			
Maximum 1-day average value	1.7±0.4	137.7±15.5	0.476 (0.001)
Average of the highest three values	3.0±0.3	137.0±15.9	0.451 (0.002)
Evening home wearable SBP (measured at home in the evening, n=338 from the 42 patients)			
Maximum 1-day average value	1.9±0.3	129.1±12.8	0.376 (0.014)
Average of the highest three values	2.8±0.5	128.0±13.0	0.349 (0.023)
Wearable SBP measured under an ambulatory condition			
- Ambulatory wearable SBP (excluding morning and evening home measurements from all wearable measurements, n=1358)			
Maximum 1-day average value	5.2±1.3	141.0±12.3	0.288 (0.043)
Average of the highest three values	3.0±0.1	152.9±13.9	0.310 (0.029)
- Worksite wearable SBP (measured only at the worksite, n=942)			
Maximum 1-day average value	4.0±1.5	141.6±13.3	0.304 (0.032)
Average of the highest three values	3.0±0.1	150.2±15.0	0.299 (0.035)
Ambulatory SBP measured by ABPM on a single day			
Average of the highest three daytime values	3.0	163.5±20.2	0.233 (0.103)

Values are means ± standard deviations or % patients. SBP, systolic blood pressure; MRI, magnetic resonance imaging; LVMI, left ventricular mass index; ABPM, ambulatory BP monitoring. Guideline-recommended home wearable SBP: wearable SBP measured at home according to a guideline-recommended standardized home BP measurement protocol; Ambulatory wearable SBP: wearable SBP measured under ambulatory conditions excluding home wearable measurements.

Figure 1. Definition of wearable BP

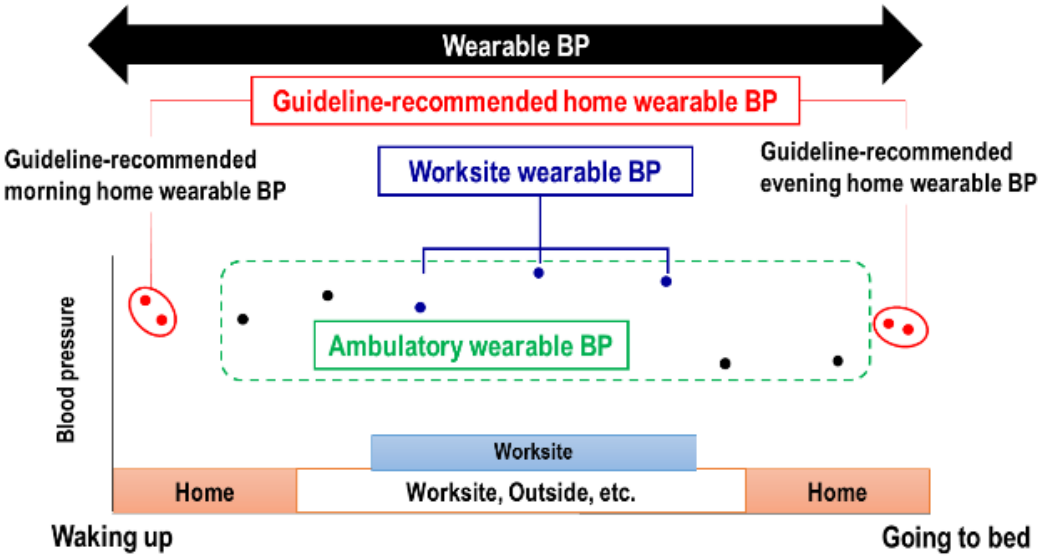
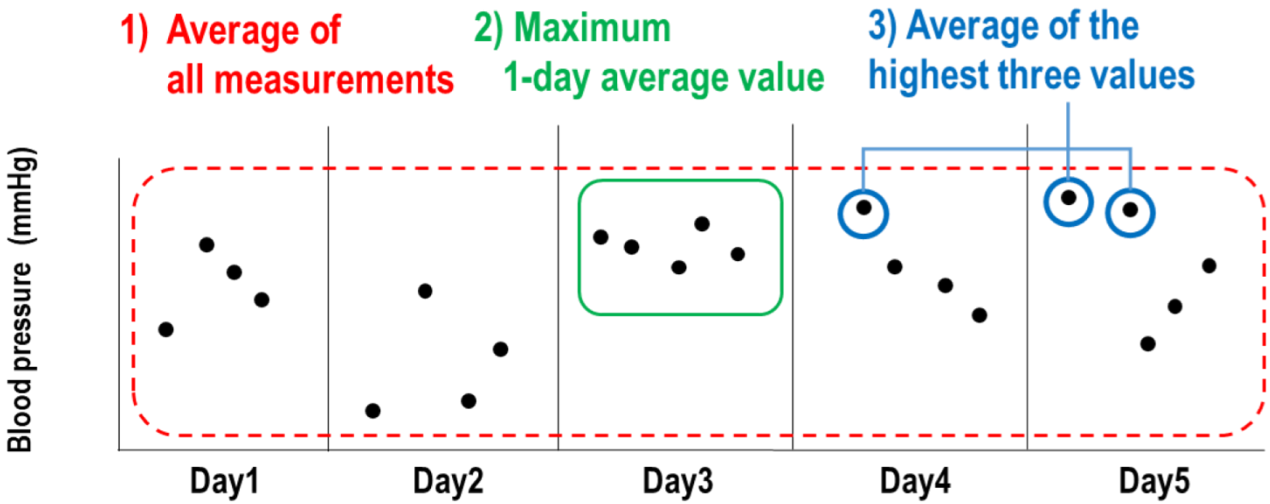


Figure 2. Wearable BP average and peak indexes



1) Average of all measurements:
the average value of all measurements (surrounded by dotted lines)

2) Maximum 1-day average value:
the highest 1-day average value (shown in green) throughout the measurement period

3) Average of the highest three values:
the average of the highest three values (blue circled dots) throughout the measurement period

Figure 3. Control status of wearable SBP and ABPM-measured daytime SBP in 50 working hypertensives