Review

Management of Hypertension in the Digital Era
Small Wearable Monitoring Devices for Remote Blood Pressure Monitoring

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Abstract—Out-of-office blood pressure measurement is an essential part of diagnosing and managing hypertension. In the era of advanced digital health information technology, the approach to achieving this is shifting from traditional methods (ambulatory and home blood pressure monitoring) to wearable devices and technology. Wearable blood pressure monitors allow frequent blood pressure measurements (ideally continuous beat-by-beat monitoring of blood pressure) with minimal stress on the patient. It is expected that wearable devices will dramatically change the quality of detection and management of hypertension by increasing the number of measurements in different situations, allowing accurate detection of phenotypes that have a negative impact on cardiovascular prognosis, such as masked hypertension and abnormal blood pressure variability. Frequent blood pressure measurements and the addition of new features such as monitoring of environmental conditions allows interpretation of blood pressure data in the context of daily stressors and different situations. This new digital approach to hypertension contributes to anticipation medicine, which refers to strategies designed to identify increasing risk and predict the onset of cardiovascular events based on a series of data collected over time, allowing proactive interventions to reduce risk. To achieve this, further research and validation is required to develop wearable blood pressure monitoring devices that provide the same accuracy as current approaches and can effectively contribute to personalized medicine.

Key Words: blood pressure ■ hypertension ■ phenotype ■ prognosis ■ wearable electronic devices

Out-of-office blood pressure (BP) determined using ambulatory BP monitoring (ABPM) and/or home BP monitoring (HBPM) is recommended for the diagnosis of hypertension in major international guidelines.[1–11] Home and/or ambulatory BP readings have been shown to provide better prognostic information about target organ damage and cardiovascular risk than measurement of office BP.[12–23] However, current approaches to ABPM and HBPM also have a number of well-known limitations, including patient comfort, sleep disturbance, availability, and cost.[24–26]

Newer information and communication technology (ICT)-based strategies provide options and solutions for self-monitoring of BP.[27,28] These are designed to make it easier for patients to continuously monitor BP in a way that maximizes adherence. This approach has the potential to facilitate what has been defined as perfect 24-hour BP control: average 24-hour BP <130/80 mm Hg; normal circadian BP rhythm (including adequate dipping of nocturnal BP); and adequate BP variability (BPV).[29] However, the vast majority are unregulated and unvalidated.[30] There is therefore a need for more scientifically based and validated approaches to wearable BP technology to allow continuous monitoring of BP in an ambulatory setting. The optimal approach would be a wearable device that allows noninvasive cuff-less, beat-by-beat BP monitoring, with simultaneous determination of environmental conditions.[31]

The ultimate goal is that new information and communication technologies contribute to personalized solutions for hypertension management based on anticipation medicine with the goal of reducing cardiovascular risk (Figure 1).[32] In addition, the availability of big data collected by wearable BP monitoring could facilitate time-series analyses and be used to inform artificial intelligence strategies to predict hypertension.[33,34]

Wearable BP Monitoring Concept and Cardiovascular Risk

A wide variety of factors can influence BP at any time, highlighting the value of a wearable option that allows determination of associations between BP readings and potential triggers, such as environmental factors, physical activity, and psychological stress.[33]

Resonance Hypothesis of BPV, 24-Hour BP Profiles, and BP Surge

The synergistic resonance theory proposes that each form of BPV (beat-by-beat, diurnal, day-by-day, seasonal and yearly) has the potential to create dynamic surges in BP, which could coincide with peak BP and different external triggers (eg, temperature, mental stress, sleep apnea, exercise) to precipitate cardiovascular events (Figure 2), especially in patients with arterial stiffness who are less able to absorb BP surges in the
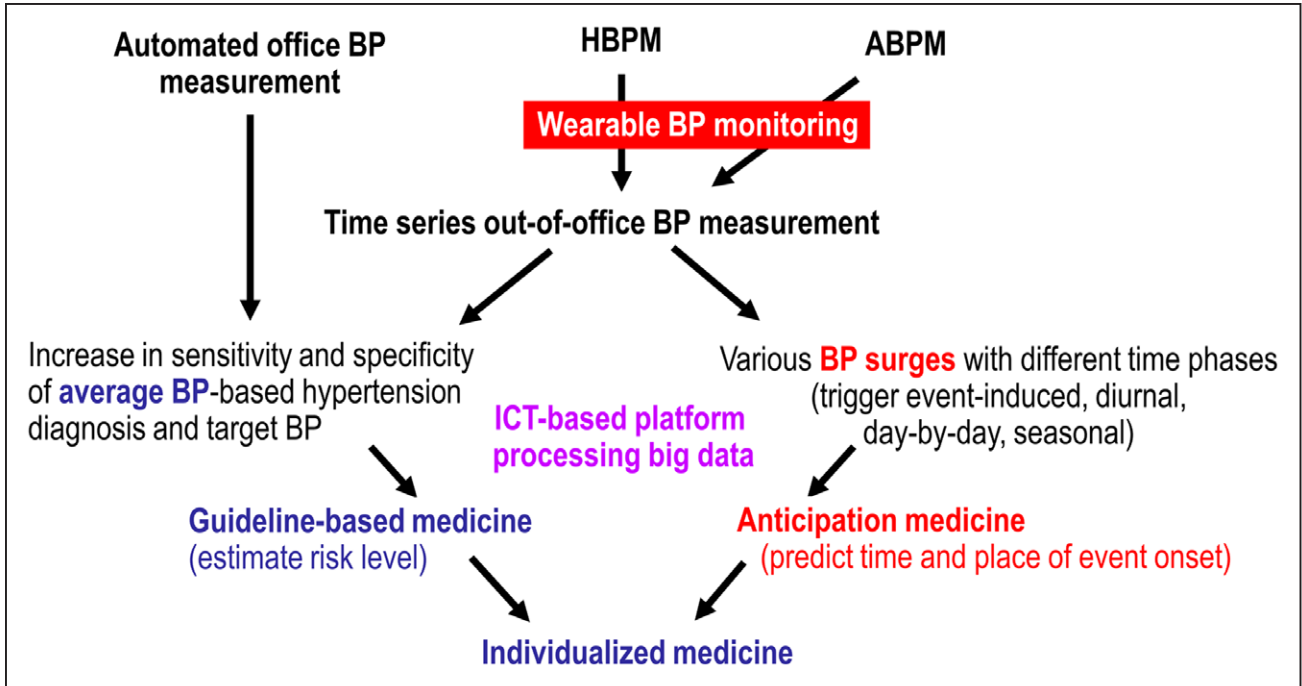
Figure 1. Time-series out-of-office blood-pressure (BP)-based anticipation management of hypertension.[32] ABPM indicates ambulatory blood pressure monitoring; HBPM, home blood pressure monitoring; and ICT, information and communication technology. Reprinted from Kario et al[32] with permission. Copyright© 2020, Wiley.

peripheral arteries.[29,35,36] Therefore, there are a variety of factors and triggers that contribute to the 24-hour BP profile and BP surges for each individual (Figure 3). There is also wide interindividual variation in daytime BP values, and in the response to stressful situations.[37] In addition, actisensitivity (the slope of the regression line of ambulatory BP against the log of physical activity) in patients with hypertension varies by

season, with higher trigger-specific surge in BP during exercise in winter compared with summer.[33]

In general, BP tends to be higher in the morning and lower at night. Variations from the normal physiological pattern include excessive morning BP surge, no decrease in BP at night (nondipper pattern), and increased nighttime BP (nocturnal hypertension, or riser pattern). Nocturnal hypertension is
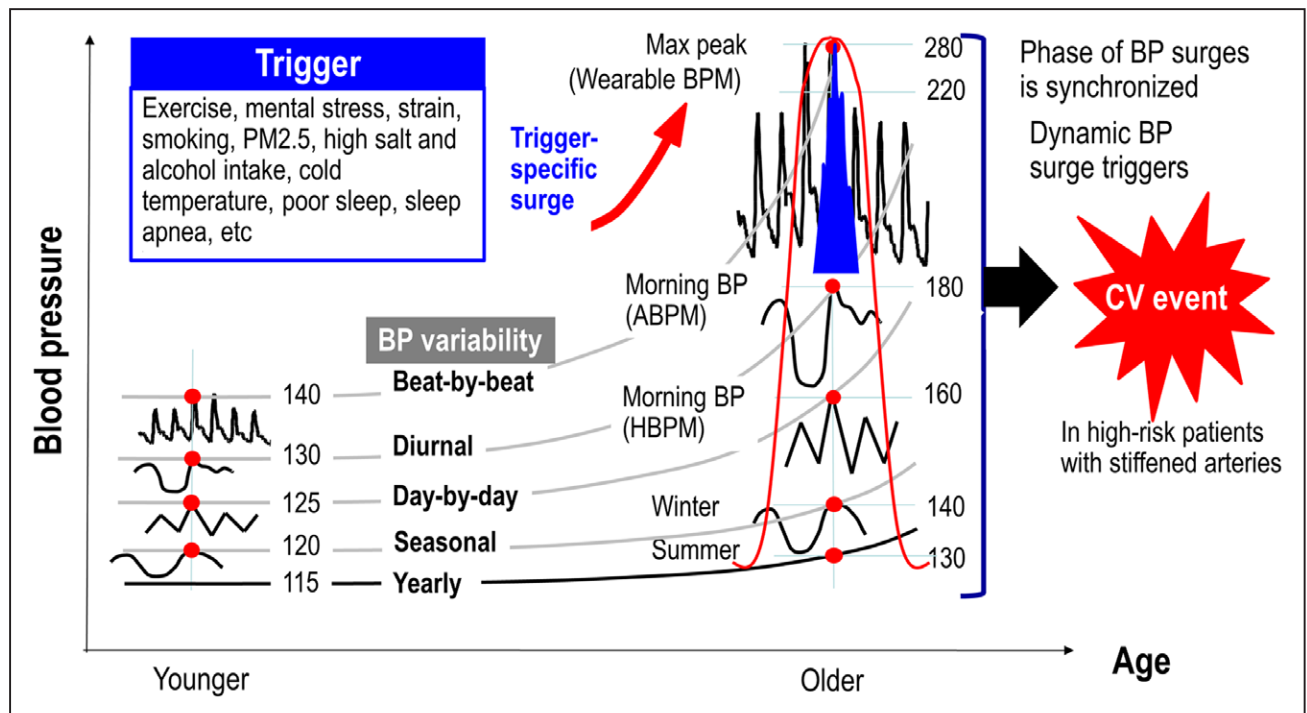

Figure 2. The resonance hypothesis of blood pressure (BP) variability. ABPM indicates ambulatory blood pressure monitoring; BPM, blood pressure monitoring; CV, cardiovascular; HBPM, home blood pressure monitoring; and PM2.5, particulate matter 2.5 micrometres or less in diameter. Reprinted from Kario[31] with permission. Copyright ©2020, WKH.
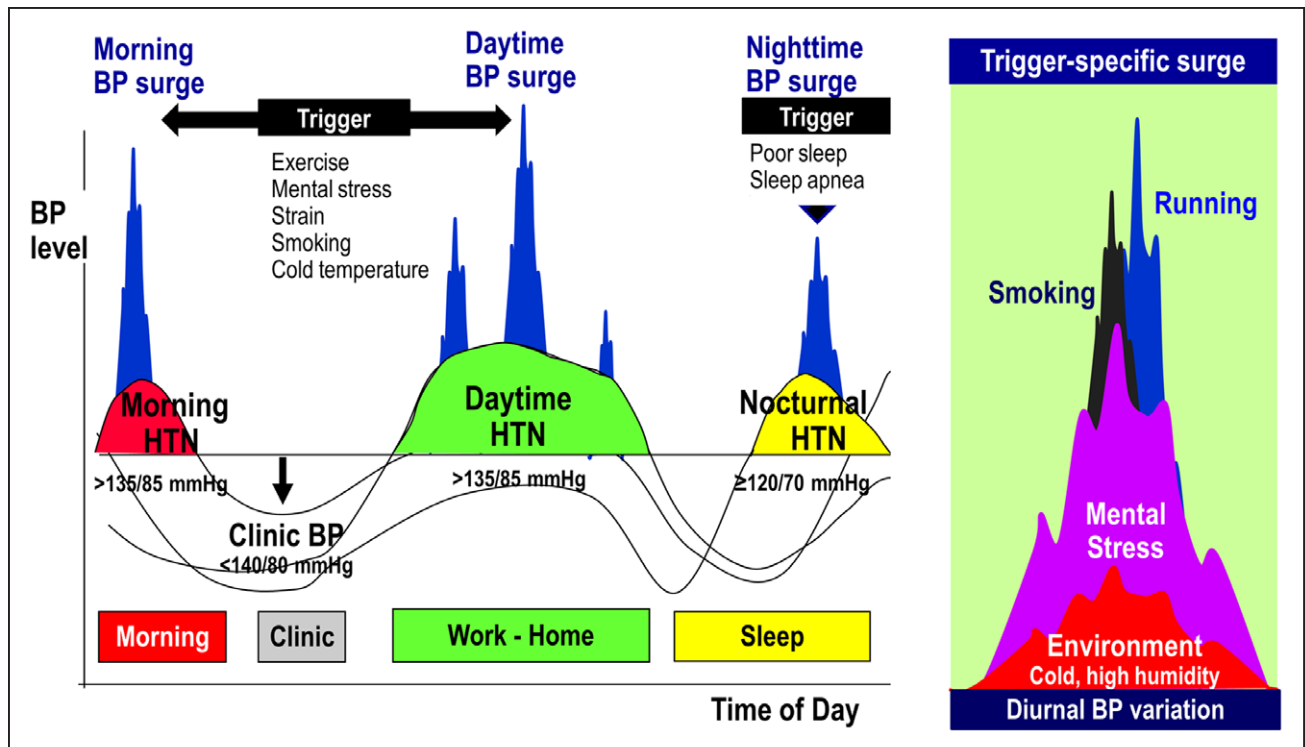
Figure 3. Synergistically accumulated trigger-specific blood pressure (BP) surges and diurnal variation. HTN indicates hypertension.

particularly associated with a salt-sensitive hypertension phenotype, as often seen in individuals of Asian ethnicity,[38] and may be associated with sleep apnea.[31]

Excessive morning BP surge has been associated with increased stroke risk, cerebral hemorrhage, and a variety of forms of target organ damage.[39–45] In addition, both nocturnal hypertension and a nondipper/riser pattern identified on ABPM have been shown to increase the risk of target organ damage and cardiovascular events.[46–55] This means that accurate detection of perturbations in the BP profile and any associated triggers is important to reduce cardiovascular risk and the occurrence of adverse cardiovascular events. Wearable devices with beat-by-beat monitoring and sensors to determine environmental conditions are ideally suited to fulfill this role as part of the overall management of patients with hypertension.

Small Wearable Devices

App-based measurements are limited by reliability,[56] and a large proportion of devices marketed for home BP monitoring are unvalidated.[57] Nevertheless, there is a growing body of evidence to support wearable medical devices from experienced manufacturers. These use a variety of different approaches to determine BP, and some have recently been validated using currently accepted clinical standards.

Oscillometric Measurement at the Wrist

The oscillometric technique is widely used in current office, home, and ambulatory BP measurement devices. New wrist-cuff devices use the same technique but are expected to cause less discomfort and muscle compression than traditional upper arm cuffs. Two recent studies[58,59] have validated watch-type wrist devices for BP measurement against the American National Standards Institute,

Inc/Association for the Advancement of Medical Instrumentation/International Organization for Standardization (ANSI/American Association for the Advancement of Medical Instrumentation/ISO) 81060-2:2013 guidelines.[60] The data showed that the HEM-6410T-ZM and HEM-6410T-ZL devices (Omron Healthcare, Kyoto, Japan) fulfilled the validation criteria when used in the sitting position with the wrist at heart level.[59] Mean differences between reference BP values and HEM-6410T-ZM readings were −0.9±7.6/−1.1±6.1 mm Hg for SBP/DBP for criterion 1, and −0.9±6.8/−1.1±5.5 mm Hg for criterion 2; corresponding differences for HEM-6410T-ZL readings were 2.4±7.3/0.7±7.0 and 2.4±6.5/0.7±6.5 mm Hg.[59] These seem to be the first wrist-type wearable devices validated against standardized criteria. Another Omron device (HEM9600T) also fulfilled the ANSI/American Association for the Advancement of Medical Instrumentation/ISO81060-2:2013 criteria when patients were in the sitting position, whereas accuracy in the supine position was only achieved when the palm was in the downward position.[58]

In addition to recognized standards, it is also of interest how wearable watch-type BP monitors compare with conventional out-of-office techniques (ABPM and HBPM). In outpatients, wearable watch-type BP monitor (HEM6410T) and ABPM device were simultaneously worn on the same arm. Mean difference in SBP values (average of 2 readings) between the wearable HEM6410T devices and ABPM were 0.8±12.8 mm Hg in the office ($P=0.564$) and 3.2±17.0 mm Hg outside the office ($P<0.001$).[61] The proportion of differences that were within ±10 mm Hg was 58.7% in the office and 47.2% outside the office. In a mixed-effects model analysis, the temporal trend in the difference between the out-of-office BP values measured by the 2 devices was not statistically significant, indicating that there was an acceptable difference between the devices with respect
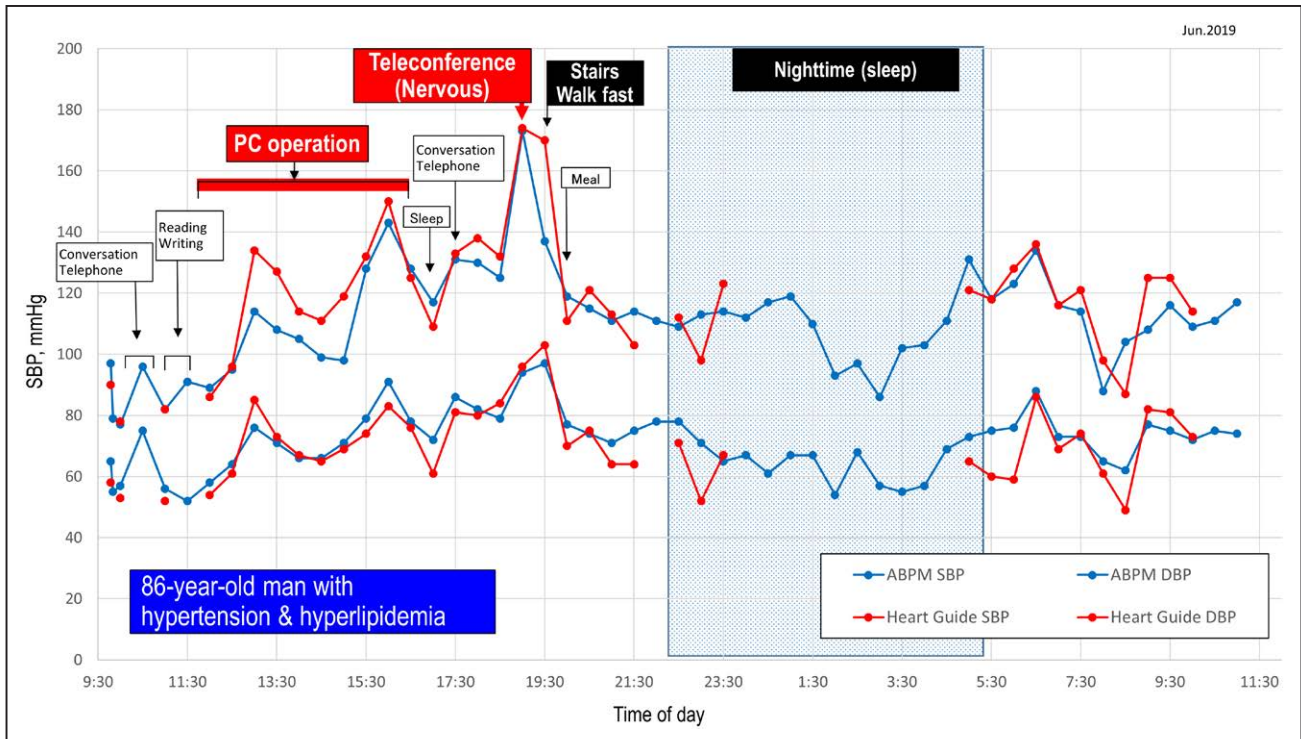
Figure 4. Comparison showing simultaneous monitoring with a wearable device (HeartGuide; Omron Healthcare Co, Ltd) and ambulatory blood pressure monitoring (ABPM). DBP indicates diastolic blood pressure; PC, personal computer; and SBP, systolic blood pressure.

to BP measurements.[61] An example of BP readings taken using the wearable device from the above study and ABPM is shown in Figure 4. In another study, 24-hour BP measurements with the Model T2 wearable cuff-less device (TMART Technologies Ltd) in volunteers were within acceptable limits compared with ABPM, but BP measures showed systematic differences from HBPM determined over 7 days.[62] Study participants did find the wearable device easy to wear and use.[62]

The devices above were validated against current standards developed for traditional BP monitoring devices and were shown to perform adequately. However, there is not yet any standardized, specific approach to validating small wearable devices. It may be that the standards need to be modified and refined to provide the best data on wearable device performance, and this is an important area for future research in this developing field.

Applanation Tonometry Method

This approach uses arterial wall applanation to measure the waveform of arterial BP. The radial artery at the wrist is ideally suited for applanation because it is shallow beneath the skin and fixed on a radial bone.[31] However, the sensor needs to be well secured so that it is in a stable position over the artery and does not move during measurements. Devices using this technology have been validated against ESH and American Association for the Advancement of Medical Instrumentation criteria under static conditions,[63] but accuracy is lower under ambulatory conditions.[64] Another limitation is that the positional relationship between the heart and the measurement site varies, which introduces an influence of hydrostatic pressure alternations on BP.[31]

Devices using the applanation tonometry method have been used to monitor nighttime BP and detect BP surges that are common in patients with sleep apnea.[31] An algorithm to

detect pathological surge BP (BP surge in seconds) was developed based on beat-by-beat BP readings obtained over one night.[65] Figure 5 highlights successful use of this approach in a patient with diabetes mellitus, resistant hypertension, and sleep apnea, and suppression during treatment with a SGLT2 (sodium-glucose co-transporter 2) inhibitor. This case highlights a BPV profile detected using a new BP monitoring and BP surge detection algorithm.

Photoplethysmography

In this approach, a photoplethysmography sensor is worn over the finger and secured with a pressure cuff.[66] Oscillations of pressure in the cuff are representative of the arterial pressure wave, allowing determination of SBP and DBP.[67] Use of photoplethysmography has been shown to be suitable for use in wearable BP monitoring devices.[68,69] Disadvantages of this approach include cuff pressure on the finger and sensitivity to movement.[66]

A device using a single photoplethysmography sensor has been validated against the Institute of Electrical and Electronics Engineers standard 1708-2014 under static and dynamic conditions and was able to document rapid changes in BP.[70] In addition, sleep quality was better when the wearable device was used compared with cuff-based BP monitoring.[70] Another device worn on the wrist that includes 2 photoplethysmography sensors was shown to have good accuracy compared with oscillometric-based devices but did not quite meet the American Association for the Advancement of Medical Instrumentation standard for nonautomated sphygmomanometers.[71] A systematic review and meta-analysis concluded that although many studies have investigated the use of multisite photoplethysmography-based technologies for BP
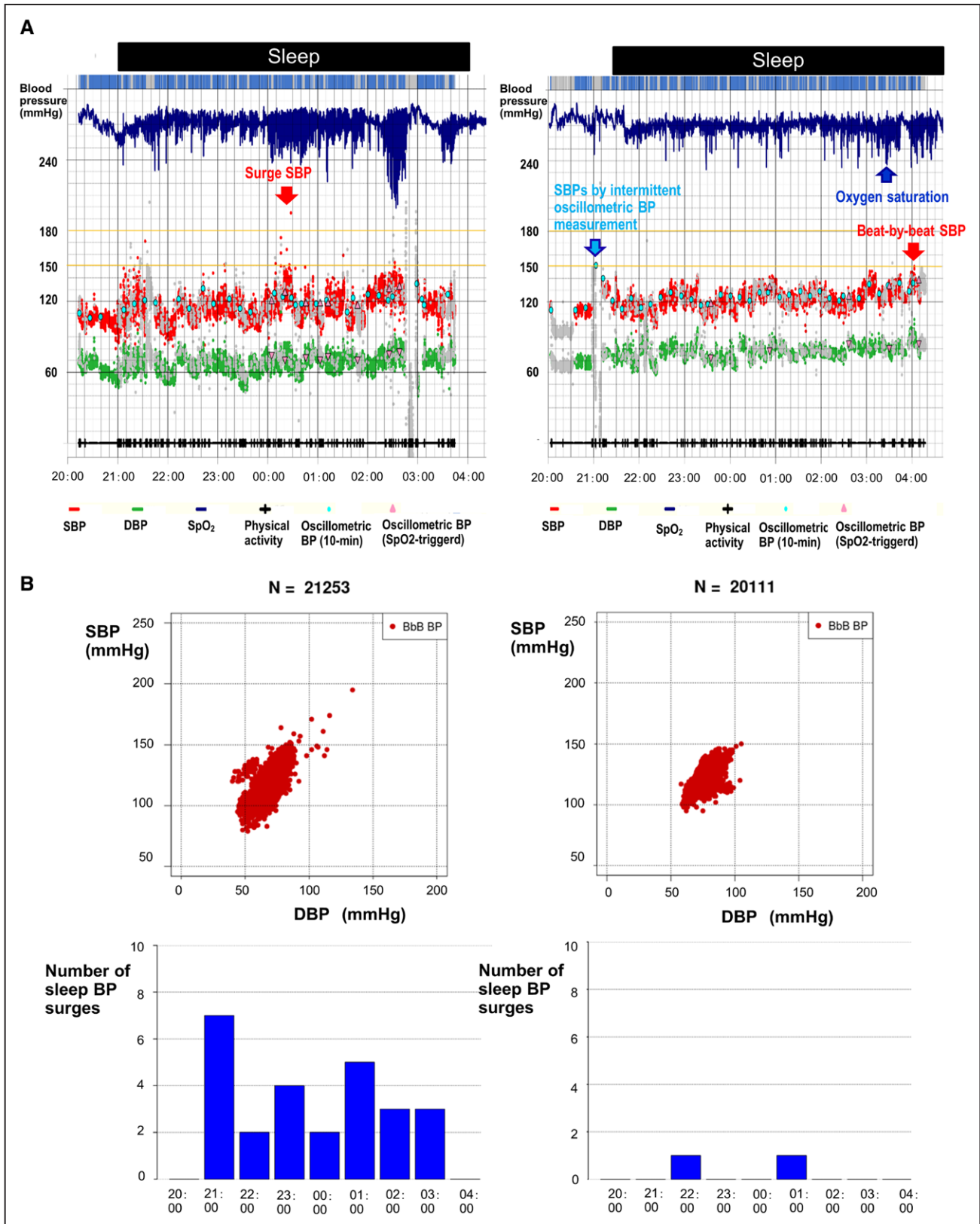
Figure 5. Pathological surge blood pressure (BP) detected by a new beat-by beat 'surge' BP monitoring and BP surge detection algorithm. **A**, Data showing suppression of BP surges trigged by apneic episodes during sleep in a 77-y-old woman with hypertension, diabetes mellitus, and obstructive sleep apnea. Sleep surge systolic (red dots) and diastolic (green dots) BP values were detected by the newly developed nocturnal beat-by-beat continuous BP monitoring (tonometry method) at baseline (treatment regimen: amlodipine 5 mg/d, aspirin 100 mg/d, and sitagliptin 25 mg/d) (left) and after 4 wk of add-on therapy with dapagliflozin 10 mg/d (right). **B**, The upper panels show the distribution of systolic BP (SBP) and diastolic BP (DBP) before (left) and after (right) 4 wk of dapagliflozin. The lower panels show nighttime BP surges detected by a newly developed surge autodetection algorithm.

monitoring, there was not yet enough information to make a powerful and statistically significant contribution toward the reliable noninvasive measurement of arterial blood pressure.[72]

Pulse Transit Time

Pulse transit time is the interval of the pulse wave propagation between 2 arterial sites, is inversely proportional to BP, and has been shown to provide a good estimate of BP.[73–77] Limitations of this approach include the ability to accurately estimate both SBP and DBP, and the influence of changes in arterial elasticity with age.[78] Pulse transit time-based approaches to continuous BP monitoring often use an ECG provide and a finger photoplethysmography sensor, and can also provide information on heart rate.[77,79,80]

A device consisting of a finger photoplethysmography and 3 ECG leads connected to a watch-like device has been validated against the European Society of Hypertension International Protocol revision 2010 for the validation of BP measuring devices in adults.[81,82] This is promising, but the device still needs to be tested outside laboratory conditions to provide its ability to continuously and reliably record 24-hour BP under real-life conditions. A device where the ECG and photoplethysmography signal detection systems are incorporated into a single wearable patch seems to have potential for real-time BP monitoring and would be convenient for patients.[83]

Another approach to measuring pulse transit time used an array of 2×2 bioimpedance sensors placed on the wrist and eliminates the need for ECG.[84] This allowed continuous and accurate measurement of BP in a way that was comfortable for patients.[84] Use of a bioimpedance system for BP monitoring was also investigated in another study. A wrist device with 4 bioimpedance sensors on the wrist in a horizontal structure showed good detection ratios for pulse wave velocity, and the estimated BP showed low root-mean-squared-errors of 7.47 ± 2.15 mm Hg (SBP) and 5.17 ± 1.81 mm Hg (DBP) compared with standard measurements.[85] This suggests that such an approach is feasible for wearable BP devices, with refinement to reduce the estimated BP errors with the latter device.

Other Approaches

Several other techniques for measuring BP with a wearable device have been evaluated. One is a finger-wearable monitor consisting of a 2-dimensional, 30-element, capacitive tactile sensor array to measure contact pressure with the finger, a pump-driven pneumatic bladder to press the tactile array and the finger steadily toward each other; and a cuff that houses the sensor array and bladder.[86] Mean±SD difference compared with brachial dual-observer auscultation was 0.9 ± 6.9 mm Hg for SBP and -3.2 ± 7.0 mm Hg for DBP, which is consistent with international standard validation requirements.[86] Another device that was shown to perform well compared with standard criteria was a low-cost piezoelectric-based system worn on the wrist (mean absolute error of 1.52 ± 0.30 and 1.83 ± 0.50 for SBP and DBP, respectively).[87] Soft pressure sensors using wrinkled thin films worn on the wrist have the benefit of being able to deform without breaking during normal force and movement.[88] These have been shown to determine BP with similar accuracy to validated devices and therefore have potential for beat-to-beat BP monitoring.[88]

Machine Learning

The fact that BP is influenced by a variety of factors has driven research into use of machine learning technology based on big data to extract the optimal features required to monitor BP and develop algorithms that produce values that meet system validation requirements.[89] The central concept is to examine time and frequency domains from physiological signals to extract BP-related features and then use machine learning to eliminate unwanted features and calculate BP from optimal data. The most common machine learning algorithms evaluated in the development of BP models to date include neural networks, linear regression, support vector machine, random forest, and deep learning. However, although these are showing promise, techniques need to be refined to improve and optimize accuracy before machine learning approaches are sufficiently precise to allow widespread clinical usage.[89]

Potential for Digital Platforms and Artificial Intelligence in Anticipation Medicine

The latest guidelines from the American College of Cardiology/American Heart Association highlight the important future role for health information technology solutions in hypertension diagnosis and management.[7] In addition to wearable technologies, telemedicine solutions are also increasingly being used to manage hypertension. These have been shown to significantly reduce both SBP and DBP compared with usual care,[90,91] but further research is needed to better define and standardize the optimal components and determine how interactive digital interventions might be widely incorporated into clinical practice across a range of healthcare settings.

Utilizing individual time-series data combined with data on environmental factors is increasingly being seen as important for taking a holistic approach to BP measurement (Figure 6).[32] Cold temperatures may increase BP via sympathetic nervous system activation, vasoconstriction, and decreased endothelial function,[92–94] and cold temperatures have consistently been shown to be associated with higher BP and greater BPV,[95–101] and increased risk of cardiovascular disease events.[96,102] A new semiautomatic HBPM device that automatically measures BP at fixed intervals during sleep has successfully been used to monitor nighttime BP in clinical trials[103–108] and an updated version of this device that includes a temperature sensor has also been used in clinical trials of patients with uncontrolled nocturnal hypertension.[109,110] However, this approach is resource intensive, meaning that initial usage may be limited and there would be challenges to overcome before widespread usage became possible.

One example of putting remote management of hypertension into practice occurred during the aftermath of the Great East Japan Earthquake, which occurred on March 11, 2011. The Disaster Cardiovascular Prevention Network used a web-based HBPM system in a town devastated by the earthquake and subsequent tsunami.[111] This enabled strict control of home BP to be achieved and seasonal variations in BP to be minimized over the months and years after the disaster and suggests that such an approach could be successfully applied for routine monitoring of BP in the wider community.

Anticipation medicine refers to approaches designed to identify increasing risk and predict the onset of cardiovascular events based on a series of data collected over time, allowing

Figure 6. Information/communication technology (ICT) multisensor environment blood pressure monitoring system. **A**, A novel approach to individual management for hypertension. Biologic and environmental signals corresponding to an individual's living conditions at home were simultaneously collected from multiple devices and sensors by an IoT (Internet of Things) gateway, and bridges based on the hybrid Wi-SUN/Wi-Fi transmission system. **B**, Time-trend reporting system of ambulatory blood pressure and environmental conditions along with an individual's high-risk places and times. ABPM indicates ambulatory blood pressure monitoring; AF, atrial fibrillation; BLE, Bluetooth; BP, blood pressure; IMS, ICT-based multi-sensor; and PR, pulse rate. Reprinted from Kario et al[32] with permission. Copyright ©2020. Wiley. http://www.jichi.ac.jp/usr/card/research/index_en.html

proactive interventions to reduce risk and eliminate events. Combining this with precision medicine, defined as customization of healthcare, with medical decisions, treatments and management tailored for each individual patient, offers the possibility of effectively managing hypertension to reduce cardiovascular risk.[31] Effective utilization of digital platforms

and solutions utilizing real-time data, such as that provided by wearable technologies, combined with artificial intelligence is another area with potential.[31] Using data from 18 258 individuals, machine learning methods were able to develop a highly precise model to predict the development of hypertension in a general population.[34] This could be used to identify individuals at risk of developing hypertension and allow early intervention with tools such as lifestyle modification to prevent future hypertension development. Another artificial intelligence-based prediction model using multi-input multi-output deep neural networks based on time-series BP data and related contextual information showed that this approach has the potential to predict both mean BP and BPV.[112] Given that abnormal BPV is a known risk factor for CVD, the ability to predict BP over periods of 4 weeks using this model could have important clinical implications, although this remains to be determined.

While it is clear that wearable BP technologies have the potential to provide the types of data likely to be useful in developing cardiovascular risk reduction strategies, additional research is needed to determine whether more frequent and continuous monitoring using small wearable devices provides prognostic information that can be used to reduce cardiovascular event rates in clinical practice.

In conclusion, currently available data indicate that digital management of hypertension and wearable BP monitoring technology are the way of the future. These approaches make the aim of reducing, or even eliminating, the occurrence of cardiovascular events in patients with hypertension a realistic possibility. Using these approaches, it is possible to assess all types of BPV simultaneously, enabling a paradigm shift from BP management based on dots to seamless individualized anticipation medication for zero cardiovascular events. Smartphone apps are not yet useful in this setting, and none have currently been approved by the US FDA or European Commission.[113] However, recent research shows that wearable devices produced by companies specializing in BP monitoring technology are validated and reliable,[58,59,61,70,71,81,82] opening the way for their use in clinical practice. Wrist-worn wearable devices have also been shown to perform well against current out-of-office BP measurement approaches.[61,62] Initial data suggest that wearable technology could also be useful for detecting arrhythmias, such as atrial fibrillation.[114]

The next important question is how best to incorporate the new technologies into clinical practice for both physicians and patients. Lower levels of technology literacy in some older patients may limit the usefulness of these approaches in an important subset of the population with hypertension, and this is something that needs to be considered as part of device development and implementation. Nevertheless, wearable BP monitoring technology is a promising and exciting field. Both current and future developments will ensure that wearable technologies become user-friendly, reliable, accurate, and flexible to provide real-time data to facilitate risk factor modification for the prevention of cardiovascular events.

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