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COMMENT

New wave of digital hypertension management for clinical applications

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Digital hypertension management is defined as a new information and communication technology-based research field in digital health care [1]. This includes not only the utilization of wearable devices, telemedicine, and personal health records (PHRs) but also contributions to develop blood pressure (BP) monitoring and guide the management of hypertension (Fig. 1). The popularization of digital platforms, such as smartphone applications, accelerates the accumulation of PHRs by self-measurements of body weight, physical activity, and pulse rate. In addition, during periods of infectious disease pandemics, PHRs can be increasingly utilized in medical care, and telemedicine can be recommended to reduce human contact worldwide. A new wave of exponential progression in digital health is coming to the health care field, including sensor technology (i.e., continuous blood sugar measurements) and therapeutic devices (i.e., portable electrocardiograms). In terms of the field of hypertension, several cuff-less BP monitoring devices are also available on the market; however, most of them are not recommended for clinical use due to their limited accuracy for BP measurements.

BP shows beat-by-beat variations, orthostatic variations, and diurnal variations in the short term and intervisit variations, seasonal variations, and secular variations in the long term. Ambulatory BP monitoring at predetermined intervals can detect variations, and early morning, midday, and nocturnal hypertension have been noted as masked hypertension, which can occur even when office BP is under control. However, when factors such as mental stress, physical activity, smoking, and sleep disturbances occur during these hours, BP rises further, leading to events such as plaque disruption and bleeding [2]. Recently, the wristwatch-type oscillometric device was developed with defined validation, which can allow us to monitor BP by self-measurement. Tomitani et al. utilized a wearable watch-type blood pressure monitor to measure BP under different conditions, such as different emotions, different locations, and stress-induced BP elevation [3]. There was a significant increase in systolic BP (SBP) when a participant's BP was measured at a time when they reported feeling angry, tense, anxious or sad (9.8, 4.6, 4.2, and 11.1 mmHg, respectively), and a significant decrease was observed when they reported feeling calm (−2.4 mmHg). Regarding the degree of stress as a variable, SBP measurements under moderate and high stress conditions were higher than those measured under nonstress conditions (6.8 and 13.1 mmHg, respectively). The increase in BP due to emotional factors and the intensity of stress was larger than that due to location (worksite measurement of 3.2 mmHg). In another study using the same wearable BP monitor, a 7.9 mmHg increase was also found while participants were experiencing negative emotions (anxiety, tension) compared to positive emotions (happiness, calm); a 4.6 mmHg increase was found while participants were at work compared to home; and a 4.5 mmHg increase was found while participants were performing moderate or intense exercise compared to being at rest [4]. Of importance, it has already been reported that the peak value of BP measurements recorded using a wearable daytime BP monitor was correlated with the left ventricular mass index [5], which suggests that increases in self-measured BP recorded using a wearable BP monitor are a risk factor for cardiovascular diseases. Thus, to prevent BP surges that can trigger cardiovascular disease, psychological stress or emotional stress should be considered, especially for patients at high risk of cardiovascular diseases.

BP might be affected by various stressors, including the thermal environment as well as mental stress or emotional

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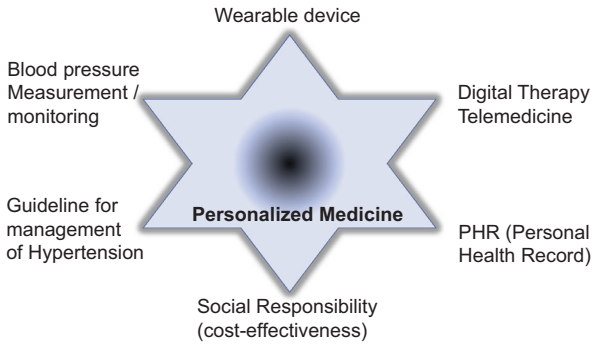

Fig. 1 The concept and contents of digital hypertension management: This not only includes the utilization of wearable devices, telemedicine, and PHRs (personal health records) but also contributions to develop blood pressure monitoring and guide the management of hypertension. The final goal is to achieve personalized medicine for hypertension management

status. BP quickly increases at cold temperatures because blood vessels constrict to suppress heat dissipation to maintain a constant core body temperature. Although rapid BP increases at cold temperatures cannot be detected in real time, self-measurements of BP will allow us to evaluate BP changes in thermal environments and know the suitable indoor temperature for BP management. The WHO Housing and Health Guidelines recommend a minimum indoor temperature of 18 °C to prevent cold-related diseases [6]. In a recent cross-sectional analysis in Japan, the average temperature in living rooms and bedrooms was 16.8 °C and 12.8 °C, respectively [7]. In contrast, in homes in the UK, the average living room and bedroom temperatures in winter were 19.3 °C and 18.9 °C, respectively [8]. We should pay more attention to the thermal environment at home, and self-measurements of BP will assist in determining individual comfortable environments. It may also contribute to preventing BP surges to prevent cardiovascular events in high-risk patients.

The last piece of the digital hypertension management concept is to evaluate its cost-effectiveness in the field of hypertension management. In clinical studies, the efficacy and safety of novel therapies are usually evaluated as endpoints. However, cost-effectiveness will also be important to effectively allocate medical resources in the real world. Nomura et al. analyzed the cost-effectiveness of prescription digital therapeutics (DTx) [9]. To assess the cost-effectiveness of essential hypertension, they developed an economic model using quality-adjusted life-years (QALYs) and compared the cost of DTx plus guideline-based lifestyle modification consultation treatment as usual (TAU) with TAU alone with a lifetime horizon based on their phase 3 clinical trial, the HERB-DH1 pivotal trial [10]. Of importance, in the incremental cost-effective ratio per QALY (the benchmark for cost-effectiveness), the monthly cost and attribution rate of DTx had a significant impact on hypertension. The DTx+TAU strategy was more cost-effective than the TAU-only strategy. Although the economic model to evaluate cost-effectiveness might be different for each disease, a few approaches have been reported for patients with hypertension [11, 12] and for patients with other diseases [13–15]. DTx for opioid use disorder and for low back pain were cost-effective in a relatively short time horizon (12 weeks to 3 years). In contrast, Nomura et al. showed that the benefit of the BP-lowering effect persisted for more than 3 years, resulting in the prevention of CVD, left ventricular hypertrophy, vascular events, heart failure, etc. Thus, in the evaluation of cost-effectiveness for lifestyle-related diseases, a long-term analysis would be valuable in considering the practical effect of DTx. In the future, a subanalysis of cost-effectiveness might need to be analyzed based on RCTs for hypertension or other diseases, which would help in identifying better therapy for patients and help society from the perspective of medical expenses.

The Japanese Society of Hypertension (JSH) proposed that digital hypertension management is a new science that includes the development of new technologies such as sensors, information processing and machine learning. The exponential progression of digital health will encourage significant developments in the approach to hypertension. Future medicine might integrate a multidimensional time series for each individual to prevent cardiovascular events by effective intervention, leading to personalized medicine (Fig. 1).

Compliance with ethical standards

Conflict of interest The Department of Health Development and Medicine is an endowed department supported by Anges, Daicel, and FunPep.

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