



Special Issue: Current evidence and perspectives for hypertension management in Asia

Topics 2023 in Hypertension Research leading to guidelines in Asia

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To overcome uncontrolled hypertension is one of the biggest challenges in Asia and the globe due to the heterogeneity among different countries [1]. International Society of Hypertension Guidelines have been released to improve blood pressure (BP) control status in globe [2]. Research on hypertension has advanced in the last 5 years, and several important evidence have been released since the previous guidelines. The guidelines, including those of the Japanese Society of Hypertension, are expected to be revised within a few years. There are several hot topics that will contribute to next guidelines for the management of hypertension (Fig. 1). Hypertension Research is now collecting various types of articles (original papers, brief reports, review/mini-review papers, commentaries, and correspondence) on four main topics for a special issue* (digital hypertension [3], renal denervation [4], home blood pressure-centered approach [5], and Asia [6], as shown in Fig. 1). In addition, new medication drugs, environmental factors, coronavirus disease 2019 (COVID-19) pandemic, and specific populations are also hot topics with recently released evidence (Fig. 1). In this Editorial, we summarized the evidence recently released on these topics.

Digital hypertension and digital therapeutics

“Digital hypertension” is a novel entity of research field that integrates digital technology into hypertension management

and promotes research activities proactively proposed by the Japanese Society of Hypertension (JSH) [3, 7–10]. Digital hypertension includes developing new technologies for better management of BP, such as wearable BP monitoring, sensors for detecting environmental factors (e.g., temperature, humidity, physical activity affecting BP), information processing and machine learning/AI, among others. It also involves analyzing big data in healthcare and clarifying the characteristics of region-specific medical needs, including patients’ behavior, and linking and organizing those data to generate novel values for providing better hypertension treatment and healthcare [3]. Hypertension Research is eagerly collecting and releasing related papers [3].

The development of small wearable BP monitoring devices is important for digital hypertension management [11]. A small watch-type oscillometric BP monitoring device was validated, and the wearable BPs measured by this device were comparable to those measured by ambulatory BP monitoring in the simultaneous ambulatory comparison study of wearable BP monitoring and ABPM [12], and wearable BP surges were significantly associated with negative emotions and psychological stress in the workplace [13, 14]. The wearable BP measured by this device was correlated with the left ventricular mass index (LVMI) measured by cardiac MRI [15]. Wrist continuous BP monitoring (tonometry) has successfully detected sleep BP surges, and a data processing algorithm has successfully been developed to detect nighttime BP surges in seconds during sleep [11, 16, 17]. Nighttime BP surges in seconds are associated with left ventricular hypertrophy (LVH) [18] and the upsloping time to the peak of BP surges in seconds was collated with arterial stiffness in sleep apnea patients [19]. Various cuffless BP monitoring using different technologies are developed and released on the market [20–22].

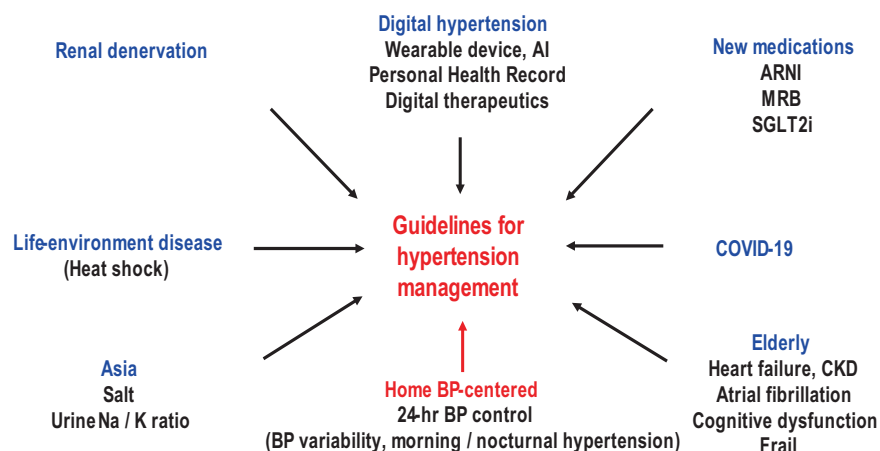
A recent randomized controlled trial (HERB Digital Hypertension) successfully demonstrated that the digital therapeutics (treatment app) reduced all office, home, and

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Fig. 1 Hot topics 2023 in Hypertension Research to Guidelines



ambulatory BPs in hypertensive patients. The positive results of this pivotal study led to the first global approval of this app for the treatment of hypertension in Japan in 2022, including medical insurance reimbursement [23–28]. Future research will focus on finding behavioral index (B-index) to detect responders [5]. A retrospective responder analysis of the HERB DH1 found that home BP reduction by digital therapeutics was associated with a higher baseline body mass index (BMI) and salt intake, and greater reductions in BMI and salt intake [29].

Renal denervation

The recent Sham-controlled clinical trials using the devices of two different denervation techniques have finished [30–34]. All the off-medication studies clearly demonstrated that renal denervation significantly reduces 24-h BP, including nighttime and morning BPs. On-Med studies also demonstrated the comparable BP-lowering effect of RDN. However, some studies could not demonstrate a significant difference in BP reduction due to comparable BP reduction in the Sham group [33]. Recent long-term 3-year results demonstrated significant 24-h BP reduction, including nighttime and morning BPs in the RDN group compared with the Sham group [31], especially in those medicated with multiple antihypertensive drugs [32]. Based on these results, two RDN systems are now under consideration for regulatory approval.

Recently, guidelines/guidance, and consensus statements have included RDN as an option in the anti-hypertensive treatment strategy [35, 36]. The positioning of renal denervation in the total management of hypertension, in combination with non-pharmacological interventions and medication, should be discussed [37, 38]. In addition, patient preference studies have consistently demonstrated that a significant number of hypertensive patients prefer

renal denervation [39, 40]. Cost-effectiveness should be addressed soon before clinical use.

New medication drugs

We already have good drugs and single pill combination available in clinical practice. However, the current BP control status is still insufficient [1]. Even with an increased number of antihypertensive drugs, around 45% of nighttime BP, and 55% of morning BP are still not well controlled, with levels remaining above 120/70 mmHg, and 135/85 mmHg, respectively [41]. Recently, several new antihypertensive drugs have been developed, such as the angiotensin receptor-neprilysin inhibitor, sacubitril/valsartan [42, 43], new mineralocorticoid receptor blockades with a nonsteroidal structure such as esaxerenone [44] and finerenone [45], and SGLT2 inhibitor [46], which have been introduced in clinical practice to reduce the risk for cardiovascular outcomes including heart failure and effectively reduces 24-h BPs including nighttime and morning BPs [47]. In addition, an aminopeptidase A inhibitor that has central effects on vasopressin, a combined endothelin A and B receptor blocker, and an aldosterone synthase inhibitor devoid of glucocorticoid activity, are involved in the ongoing recruitment of Phase III trials [48, 49].

Environment, COVID-19 pandemic

Seasonal changes in BP and cardiovascular risk (higher in winter and lower in summer) and seasonal hypertension management are hot topics [50–53]. BP is closely affected by environmental conditions such as temperature, humidity, light, PM2.5, etc. as well as individual behavioral factors such as physical activity and psychological stress [54]. Thus, hypertension is considered a disease

both life-environment and lifestyle [55]. A major environmental factor affecting BP is cold temperature in the morning during winter, while nighttime BP increases in hot summers [51, 56, 57]. Indoor temperature instability has affected the diurnal and day-by-day variability of home BP in winter [58]. Adequate adjustment of room temperature decreases BP in winter [59]. Antihypertensive treatment considering seasonal variation with up-titration in winter and down-titration in summer will improve the quality of BP control, resulting in a reduction of cardiovascular events.

The ongoing COVID-19 pandemic has a significant impact on hypertension management [60–63] and has facilitated the digital healthcare system and telemedicine [64–68]. The longer sedentary lifestyle by COVID-19 pandemic worsen BP control and metabolic profiles, resulting in an increased risk of cardiovascular disease [69]. In Japan, after the initial reduction in cardiovascular death during the first several months (spring to autumn, 2020) just after the first year of the COVID-19 pandemic, the long-lasting sedentary lifestyle caused overshooting of cardiovascular death occurred in the winter of 2020 when compared to the previous year before the COVID-19 pandemic occurred [70].

Home blood pressure centered

Home BP is the lifetime central index of BP metrics in the digital era of hypertension [5]. There are significant clinical evidence on the association of home BP and its variability with organ damage and cardiovascular prognosis [71–74]. The Japanese hypertension guidelines stressed the home BP-guided approach for the management of hypertension [75]. The Taiwan Hypertension Society released the new guideline 2022 that defines hypertension based on home BPs [76]. In future guidelines and clinical practice, home BP should be centered on the individual optimized treatment of hypertension.

Asia and guidelines

There is significant heterogeneity in the management of hypertension in globe [77, 78]. It would be effective to consider cultural and ethnic differences for the management of hypertension. There are several academic activities such as the HOPE Asia Network [79–91], Pulse of Asia [92, 93], and Asia Hypertension Society Network [94, 95], aim to improve the management of hypertension in Asia. Two journals, *Journal of Clinical Hypertension* and *Hypertension Research*, eagerly released articles on Asian evidence, reviews, opinions, and consensus. In this issue, Kang et al.

proposed a new classification of focal renal artery fibromuscular dysplasia based on intravascular ultrasound, which is related to prognosis [96]. Heizhati et al. reported that primary aldosteronism is prevalent in co-existent hypertension and obstructive sleep apnea in a large Chinese database, indicating the need for primary aldosteronism screening [97].

These hot-topic articles closely related to clinical issues will contribute to the next guidelines for the management of hypertension in Asia.

Compliance with ethical standards

Conflict of interest KK reports lecture fees from Viatris, Otsuka pharmaceuticals, Otsuka Medical Device, Daiichi Sankyo, Terumo, Novartis Pharma, Omron Healthcare, JIMRO, A&D, CureApp, Sanwa Kagaku Kenkyusho, Terumo, Mylan EPD, Takeda Pharmaceuticals, Bayer, Boehringer Ingelheim Japan; funded research or joint research expenses from Fukuda Denshi, Omron Healthcare, Teijin Pharma, Otsuka Holdings, A&D, Sanwa Kagaku Kenkyusho, Fukuda lifetec, Taisho Pharmaceuticals; scholarship donations from Otsuka Pharmaceuticals, Daiichi Sankyo, Sumitomo Dainippon pharma, Boehringer Ingelheim Japan, Takeda pharmaceuticals, Taisho Pharmaceuticals, Astellas pharma, Eisai, Mochida Pharmaceuticals, outside the submitted work.

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