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EDITORIAL

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

# Uncontrolled hypertension: the greatest challenge and perspectives in Asia

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A cross-sectional analysis of a community-based cohort study in Tarumizu demonstrated that patients with uncontrolled hypertension are associated with increased arterial stiffness compared with those without hypertension [1]. Uncontrolled hypertension is the greatest challenge worldwide [2]. In particular, uncontrolled hypertension is more common in Asian countries, except in South Korea and Taiwan [2, 3], although the benefit of strict BP control is greater for Asians than for westerners [3]. The HOPE Asia Network, a group of volunteer hypertension experts from Asian countries, has been working to improve hypertension control in Asian countries, collecting evidence on various issues related to hypertension treatment in Asia. In 2022, the HOPE Asia Network released seven effective approaches [4] and early morning hypertension practical treatment approaches for hypertension management in Asia and re-emphasized early morning home blood pressure as a quality index for hypertension management in Asia [5]. More recently, the hypertension societies of 14 Asian countries/regions agreed to provide future directions for overcoming hypertension in Asian populations [6].

In the Tarumizu population study, the uncontrolled hypertensive group exhibited a significantly higher prevalence of increased cardio-ankle vascular index (CAVI) scores, defined using the 9.0 pathological threshold, than the normal group (nonhypertensive individuals without medication), while there was no significant difference between the good BP control and normal BP groups [2]. The CAVI is the measure of arterial stiffness that reflects the stiffness from the ascending aorta to the ankle arteries, demonstrates less dependence on BP during evaluation, and is associated with risk factors, organ damage, and cardiovascular events [7–11]. A systematic review assessing the association between CAVI and cardiovascular disease (9 prospective studies ($n = 5214$) and 17 cross-sectional studies ($n = 7309$)), with most studies enrolling populations at high risk of cardiovascular disease in Asia, demonstrated a modest association between the CAVI and incident cardiovascular disease risk [8]. A recent prospective study, the CAVI-J study, demonstrated that a CAVI >9.5 is a predictor of stroke and heart failure in outpatients with cardiovascular risk [9]. Thus, the current analysis of the Tarumizu population study indicated that the detection of uncontrolled hypertension is an important first step of the population approach.

Increased arterial stiffness is one of the essential underlying conditions of uncontrolled hypertension, as the association between arterial stiffness and increased BP is observed in the early stages of hypertension [12, 13]. A prospective study of nonhypertensive subjects demonstrated that increased arterial stiffness assessed by the CAVI preceded the occurrence of hypertension [14]. BP increases artery wall tension and functional arterial stiffness, resulting in an increased pulse wave velocity. Increased arterial stiffness decreases baroreceptor sensitivity, resulting in BP dysregulation and increasing BP variability. The mutual vicious cycle between hemodynamic BP stress and arterial stiffness, proposed as a systemic hemodynamic atherothrombotic syndrome [13], would advance uncontrolled hypertension.

Is controlled office hypertension perfect?—This study provides another important insight into the quality of BP control for uncontrolled hypertension beyond office BP control. This study demonstrated that all hypertensive subjects exhibited a higher prevalence of increased CAVI scores above the threshold of 8.0, regardless of BP control status and/or medication use, than hypertensive patients without the use of medication, even after adjusting for age

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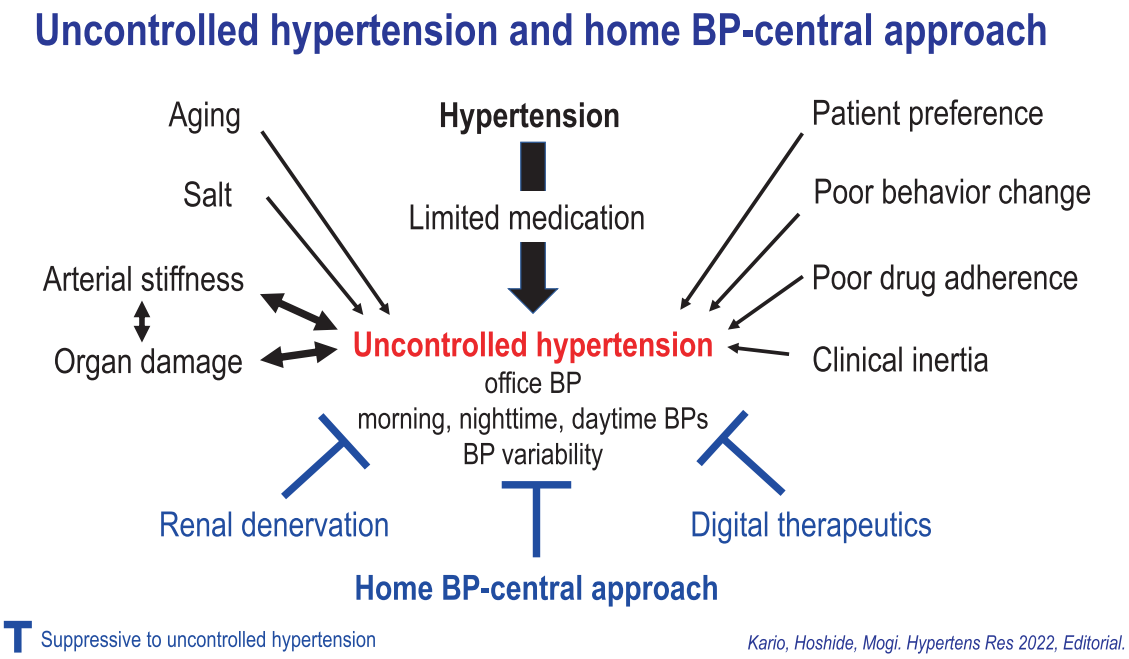
**Graphical Opinion**




and other covariates. Recent guidance from the management of vascular failure proposed the two CAVI thresholds of 8.0 and 9.0 (<8 for normal, ≥8 and <9 for borderline, ≥9 for abnormal) [15]. The Tarumizu study indicated that even a good BP control group who received antihypertensive medication exhibited a significantly higher prevalence of a CAVI score >8.0 [2]. This may suggest the limitation of current medications based on office BP control to suppress CAVI increases. Insufficient 24-h BP control, especially during the nighttime and morning based on the current medication strategy, increases BP variability and masked uncontrolled hypertension in medicated hypertensive patients [4, 5, 12, 16, 17]. A longer sustained 24-h BP lowering effect over 24 h is reported for digital therapeutics [18, 19] and renal denervation [20–22]. Thus, the detection of hypertension and controlling office BP are important first steps for the population approach. For the next step, the personalized home BP-central approach in consideration of a patient's preferences, poor behavioral change, poor drug adherence, and clinical inertia, ultimately targeting uncontrolled morning and nocturnal hypertension, seems to be the direction for the population and high-risk strategies for the number of cardiovascular events to be "zero" [23].

Other interesting studies have different directions of clinical implications of diastolic BP in the elderly population [24, 25]. One study demonstrated that high-normal diastolic BP was the only independent risk factor for LV diastolic dysfunction, indicating an increased risk of heart failure with preserved ejection fraction in postmenopausal women [24]. Another study demonstrated a J-curve association between diastolic BP and cardiovascular prognosis in elderly patients aged >80 years with a history of acute myocardial infarction [25]. Another retrospective study using the electronic medical records of a single university hospital indicated that the possible metastatic risk of skin and renal cancers is increased with the use of renin-angiotensin system inhibitors [26]. All four papers provide clinically meaningful evidence in Asia. The results found in the correctional studies should be confirmed in prospective studies in different Asian populations in comparison with western and other ethnic populations in the future.

## Compliance with ethical standards

**Conflict of interest** The authors declare no competing interests.

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