Definition of Nocturnal Hypertension
Hypertension is a major cardiovascular risk factor, and treatment by controlling blood pressure (BP) is important to prevent cardiovascular disease. The variation of BP during the day and night depends on circadian rhythm, and is associated with interaction of the sympathetic nervous system and renin-angiotensin system. This BP variation consists of dipping, extreme dipping, non-dipping and reverse-dipping. Nocturnal hypertension is defined as systolic BP >120 mmHg and/or diastolic BP >70 mmHg at night.

The pathophysiology of nocturnal hypertension is considered to be multifactorial and includes an increase in circulating blood volume (heart failure, renal failure), autonomic neuropathy (orthostatic hypertension, diabetes mellitus), sleep apnea syndrome, depressive state, cognitive hypofunction, and cerebrovascular disorders.

Clinical Significance of Nocturnal Hypertension
The International Database on Ambulatory blood pressure monitoring in relation to Cardiovascular Outcomes (IDACO) investigators analyzed 24-h BP monitoring in 7,458 people enrolled in prospective population studies for a median follow-up of 9.6 years. Adjusted for daytime BP, nighttime BP predicted total, cardiovascular, and non-cardiovascular mortality. Conversely, adjusted for night-time BP, daytime BP predicted only non-cardiovascular mortality, with lower BP levels being associated with increased risk. Both daytime and night-time BP consistently predicted all cardiovascular events and stroke. Adjusted for night-time BP, daytime BP lost prognostic significance only for cardiac events. Antihypertensive drug treatment removed the significant association between cardiovascular events and the daytime BP, suggesting that antihypertensive drugs might reduce BP during the day, but not at night.

Furthermore, Hansen et al performed a meta-analysis of 23,856 hypertensive patients separately from 9,641 individuals randomly recruited from populations. In both patients and the populations, in analyses in which night-time BP was additionally adjusted for daytime BP and vice versa, night-time BP was a stronger predictor than daytime BP.

Therefore, the nocturnal hypertension is the next target to prevent cardiovascular events in patients with hypertension.

How to Diagnose Nocturnal Hypertension
Usually, ambulatory BP monitoring (ABPM) is used to diagnose nocturnal hypertension and it has provided us evidence of the clinical importance of nocturnal hypertension in treated and untreated hypertensive patients and the general population. Although ABPM is the gold standard to analyze 24-h BP variations, it is not easy to measure and difficult to measure for a long time.

In this issue of the Journal, Kario et al describe the development and use of information and communication technology (ICT)-based nocturnal home BP monitoring (HBPM) using a cuff oscillometric device equipped with a mobile network communication function. All data obtained by this device were transmitted automatically to a cloud-based remote monitoring system, which eliminated measurer bias. The nocturnal home BP measured with this device has been reported as comparable to nocturnal ambulatory BP, and to be significantly correlated with various measures of organ damage, such as the urinary albumin/creatinine ratio, N-terminal pro-brain natriuretic peptide levels, carotid intima-media thickness, and left ventricular hypertrophy diagnosed by echocardiography. This ICT-based nocturnal HBPM is...
easy to use and able to measure for a long time at home. Therefore, we believe this device is a novel and useful tool for diagnosing and managing nocturnal hypertension.

**How to Treat Nocturnal Hypertension**

BP control may be important for organ protection in the management of nocturnal hypertension. Using their ICT-based nocturnal HBPM, Kario et al. conducted the NOCTURNE study, which is a prospective, multicenter, randomized, open-label, parallel-group design clinical trial investigating the efficacies and safety of 2 fixed-dose drug combinations, an angiotensin II receptor blockers (ARB) plus calcium-channel blocker (CCB) or an ARB plus a diuretic, on nocturnal home BP and target organ damage in patients with uncontrolled nocturnal hypertension. They report that the ARB/CCB combination therapy achieved a significantly greater reduction in nocturnal home systolic BP than the ARB/diuretic combination, independent of urinary sodium excretion and/or nocturnal BP dipping status. However, the change in nocturnal home systolic BP was comparable among the post-hoc subgroups with higher salt-sensitivity (diabetes, chronic kidney disease, and elderly patients).

Nocturnal hypertension is associated with increased circulation volume in patients with heart failure, renal failure and high salt-sensitivity. Therefore, the combination of ARB and diuretic initiates a natriuresis and is expected to lower nocturnal BP. However, Kario et al. report that the ARB/CCB combination was superior to ARB/diuretic in patients with uncontrolled nocturnal hypertension. We think that 2 months of study may be too short to achieve the stable maximum effect of ARB/diuretic combination on nocturnal hypertension, because ABPM-measured nocturnal BP tended to be greater in the ARB/diuretic group than in the ARB/CCB group at 6 months in the follow-up period in J-CORE. Further prospective studies are needed to address the clinical outcomes of treatment for nocturnal hypertension in a large-scale population with a long time period.

In addition, the SYMPLICITY HTN-3 trial demonstrated that renal denervation reduced the night-time systolic BP in patients with obstructive sleep apnea and resistant hypertension. Therefore, renal denervation is expected to be a useful treatment for nocturnal hypertension.

**Conflicts of Interests**

The authors declare no conflicts of interest.

**References**

1. Morgan TO, Anderson A. Different drug classes have variable effects on blood pressure depending on the time of day. *Am J Hypertens* 2003; **16**: 46 – 50.