It is well-known that cardiovascular events occur more frequently in the morning (1). Ambulatory blood pressure (BP) varies along with various physical and psychological factors and this BP variability may be a risk for cardiovascular events (2, 3). In recent years, clinical research using ambulatory BP monitoring (ABPM) or self-measured home BP monitoring has clarified that morning BP and BP surge are more closely related to target organ damage and cardiovascular risk than clinic BP (4–14). Also, in hypertensive patients treated with antihypertensive medication, even patients whose clinic BP is well controlled, the morning BP level prior to taking medication is often high (15–17). Therefore, morning hypertension is currently the ‘blind spot’ in the clinical practice of hypertension.

As diabetes is one of the worst conventional cardiovascular risk factors. In our recent study on asymptomatic hypertensive patients with and without type 2 diabetes, silent cerebral damage including silent cerebral infarcts, decreased functional neuronal mass, and reduced cerebrovascular reserve were advanced in hypertensive patients with diabetes (18). Hypertensive patients were classified into four groups and the risk of multiple silent cerebral infarcts was comparable between diabetic patients with white-coat hypertension (WCHT) and nondiabetic patients with sustained hypertension (19). The patients with both diabetes and sustained hypertension had the highest risk for multiple silent cerebral infaracts. Cardiac remodelling is also advanced in diabetes; in hypertensive patients, the presence of diabetes increases the relative wall thickness (20). Concentric hypertrophy, which is the worst prognosis, was more frequently found in diabetic hypertensive patients.

Nighttime and morning BP levels should be monitored more closely in diabetic patients. In a cross-sectional study in newly-diagnosed type 2 diabetic normotensive patients, morning BP levels and morning BP surge were significantly increased in patients with microalbuminuria compared to those without microalbuminuria (21). In another study on type 2 diabetic patients, those with morning BP hypertension (morning BP level measured at home >130/85 mmHg) had marked frequencies of diabetic renal disease, retinopathy, microvascular disease and vascular complications, including coronary artery disease and cerebrovascular disease (22). In this study, hypertension defined by clinic BP level was not associated with these complications. Diabetic patients, particularly those with autonomic nervous dysfunction, are also likely to have a nondipping pattern of nocturnal falls in BP, which might precede microalbuminuria, leading to a poor prognosis (23). Nighttime BP is associated with a poor prognosis in diabetic patients (24).

In the international guidelines including the guideline of management of hypertension of the Japanese Society of Hypertension, target BP levels are lower for diabetic patients than nondiabetic patients. In addition, the persistent BP control for a 24-h period achieves more effective prevention for target organ damage and cardiovascular events particularly in these patients. However, in the practical sense, 24-h BP control is very difficult in diabetic patients particularly in those with nephropathy. In this issue, Kuriyama et al tried a unique antihypertensive medication for diabetic patients with nephropathy, whose BP was poorly controlled as morning hypertension (self-measured morning BPs >130/85 mmHg) (25).

Their special medication consists of calcium channel blockers and/or diuretics given in the morning, an angiotensin receptor blocker given in the evening, together with alphal-blockers given at bedtime. Actually, the “cocktail” medication successfully reduced morning BP levels with a significant reduction of urinary protein excretion. Considering that neurohumoral factors including sympathetic nervous activity and the renin-angiotensin-aldosterone system are activated in the morning, this sequential combined chronological medication could be physiologically considered as a specific medication for morning hypertension. In recent reports, a long-acting angiotensin receptor blocker (26), and the bedtime dosing of an alphal-blocker (27) or an angiotensin-converting enzyme inhibitor (28) were effective for controlling morning hypertension.

In addition to the standard clinical practice of hypertension, and following the guidelines issued on the subject, an important next step should be the specific combined chronobiological management targeting the higher blood pressure in the morning in order to achieve a more beneficial outcome particularly in high-risk hypertensive patients such
as in those with diabetes and/or chronic kidney disease.

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References