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NOCTURNAL HYPERTENSION: THE OTHER SIDE OF THE COIN

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INTRODUCTION

Office blood pressure (BP) measurement does not represent the only gold standard method for screening, diagnosis and treatment of hypertension. Ambulatory and home BP monitoring allow evaluation of BP in out-of-office settings and detection of white coat and masked hypertension. Ambulatory BP monitoring provides 24-h BP measurements and identification of circadian BP patterns, as well as isolated nocturnal hypertension. Increasing body of evidence has suggested that nocturnal hypertension is related with elevated risks of hypertension-mediated organ damage (HMOD) and adverse cardiovascular (CV) outcomes [1,2]. Recent study showed that nighttime BP and reverse BP pattern were independently associated with the total CV event rate and particularly with heart failure occurrence [3]. Fagard et al. revealed that nighttime BP is generally a better predictor of outcome than daytime BP in hypertensive patients [4]. Ogedegbe et al. reported that isolated nocturnal hypertension was related with increased left ventricular (LV) mass comparing with normotensive patients in African-American population [5]. Large Spanish study showed that nocturnal hypertension was associated with albuminuria and the worst CV risk profile was found in patients showing both nocturnal hypertension and nondipping BP pattern [6].

DEFINITION AND EPIDEMIOLOGY

According to the European Society Cardiology/European Society Hypertension (ESC/ESH) guidelines isolated nocturnal hypertension is defined as a nighttime BP of ≥120 mmHg systolic and/or 70 mmHg diastolic and a daytime BP <135/85 mmHg; isolated daytime hypertension as a daytime BP of ≥135 mmHg systolic or 85 mmHg diastolic and a nighttime BP <120/70 mmHg; day–night sustained hypertension as a nighttime BP of ≥120 mmHg or 70 mmHg diastolic and a daytime BP of ≥135 mm Hg systolic or 85 mmHg diastolic; and ambulatory normotension as a nighttime BP <120/70 mmHg and a daytime BP <135/85 mmHg [7]. Ambulatory BP monitoring is recommended method for diagnosis of nocturnal hypertension. Home BP measurement is important technique and recent study showed that it is more reliable and more strongly associated with LV mass index than office and ambulatory BP measurements [8]. However, home BP measurement does not provide information about nighttime BP and circadian BP patterns and therefore one should be careful in interpretation of the massage of this study that home BP monitoring might be the best approach for diagnosing hypertension.

In a multiethnic study the prevalence of isolated nocturnal hypertension was higher in Chinese (10.9%), Japanese (10.2%), and South Africans (10.5%) than in Western (6.0%) and Eastern Europeans (7.9%) [9]. The prevalence of nocturnal hypertension was reported to be higher (20.4%) in a population of patients with chronic kidney disease. In the Jackson Heart Study, nocturnal hypertension was found in 19% of the entire cohort [5]. In the Pressioni Monitorate E Loro Associazioni (PAMELA) study, which is representative for the population of Monza in Italy, elevated nighttime BP and normal awake BP was observed in 11.4% of the participants [10].

PATHOPHYSIOLOGY

The normal circadian BP rhythm is characterized by higher daytime and lower nighttime BP, which corresponds with increased sympathetic activity and secretion of cortisone during morning and day. Morning BP surge is often considered responsible for the rupture of atherosclerotic plaques or arteriosclerotic bleeding, which can be a trigger for stroke or myocardial infarction.

There are several mechanisms of nocturnal hypertension. Increased vascular resistance and elevated arterial stiffness, as well as increase in salt sensitivity and/or high-salt diet may be the main reasons of nocturnal hypertension. In patients with increased circulating volume, not only daytime but also nighttime BP are elevated over 24-h. The renal dysfunction, the activation of the renin–angiotensin–aldosterone system, and the sympathetic hyperactivity increase salt sensitivity. Aging, stress, obesity, diabetes, and sleeping disorders (obstructive sleep apnea and insomnia) emphasize all these potential mechanisms associated with nocturnal hypertension. Nevertheless, these conditions and comorbidities are also responsible for HMOD and CV morbidity and mortality. Therefore, it is not easy to differentiate the effect of nocturnal hypertension from those of conditions predisposing to nocturnal hypertension.

NOCTURNAL HYPERTENSION AND TARGET ORGAN DAMAGE

HMOD in hypertension includes LV structural and functional changes, primarily LV hypertrophy and LV diastolic dysfunction, as well as renal damage, which is mainly detected by microalbuminuria, and vascular impairment, that is measured by carotid intima-media thickness and parameters of arterial stiffness.

Large meta analysis that included 2,083 patients with nocturnal hypertension and 1,574 patients with nocturnal normotension showed significantly higher LV mass index and carotid intima-media thickness in participants with nocturnal hypertension, which showed an association between nocturnal hypertension pattern and increased likelihood of cardiac and carotid structural alterations [1]. The same group of authors reported no significant difference in LV, carotid intima-media thickness and urinary albumin excretion between dipping and non-dipping BP pattern among patients with nocturnal hypertension [11].

Our study group demonstrated that nocturnal hypertension was associated with deteriorated LV strain, right ventricular strain and left atrial strain [12-14], which corresponds to overall cardiac mechanics. Deterioration in cardiac strain in patients with nocturnal hypertension

was comparable to patients with daytime hypertensio [12-14]. Patients with day-nighttime hypertension had worse cardiac mechanics than those with isolated daytime or nighttime hypertension. However, it is difficult to differentiate the influence of LV hypertrophy from the impact of nighttime hypertension on cardiac mechanics.

NOCTURNAL HYPERTENSION AND OUTCOME

Nocturnal BP is very important predictor of adverse outcome in hypertensive population. Recently published the Japan Morning Surge-Home Blood Pressure study that included 2,745 high CV risk participants showed that nocturnal and sustained hypertension were independent predictors of CV events (angina pectoris, myocardial infarction, and stroke) [15]. Daytime hypertension was not associated with risk of CV events after adjustment for demographic variables (age and sex) and clinical and behavioral characteristics [15]. On the other hand, nocturnal and sustained hypertension were independently associated with CV events even after adjustment.

Large investigation that involved 8,711 participants randomly recruited from 10 populations demonstrated that isolated nocturnal hypertension defined by ambulatory BP monitoring was related with a higher risk of total mortality and CV events (stroke, myocardial infarction, myocardial revascularization, heart failure) [16]. Patients with isolated daytime and nocturnal hypertension had similar total mortality and risk of CV events, which was significantly higher than in normotensive subjects, but still significantly lower than in patients with sustained hypertension. However, after adjustment for sex, age, body mass index, smoking and drinking, serum cholesterol, history of CV disease and diabetes mellitus isolated nocturnal hypertension was associated only with all-cause mortality and all CV events, but not with non-CV mortality, cardiac events or stroke. Isolated daytime hypertension was independently associated with all CV and cardiac events [16].

MANAGEMENT OF NOCTURNAL HYPERTENSION

Medical therapy represents the first line therapy in treatment of patients with nocturnal hypertension. The cornerstone is chronotherapy and a bedtime dosing of antihypertensive medications. Recently published the Hygia Chronotherapy Trial demonstrated that routine taking of ≥1 prescribed BP-lowering medications at bedtime resulted in improved BP control and significantly reduced occurrence of major CV events (CV death, myocardial infarction, coronary revascularization, heart failure, or stroke) in comparison with an awaking dosing even after adjusting for age, sex, type 2 diabetes, chronic kidney disease, smoking, HDL cholesterol, asleep systolic BP mean, sleep-time relative systolic BP decline, and previous CV event [17]. A bedtime dosing decreased the risk of each component of composite CV outcome – CV mortality, myocardial infarction, coronary revascularization, heart failure, and stroke. The authors included all major classes of antihypertensive medications.

Non-pharmacological therapy considers treatment of obstructive sleep apnea – continuous positive airway pressure (CPAP) and/or weight reduction. Picard et al. reported that CPAP therapy reduces nocturnal BP fluctuations, nocturnal BP, and arterial stiffness [18]. CPAP therapy decreased the maximum systolic BP by 9 mmHg even after the first night. After 6-month CPAP therapy, there was an additional decrease in average nocturnal systolic BP by 10 mmHg [18].

CONCLUSION

Available data demonstrate a strong relationship between nocturnal BP and HMOD, as well as outcome in hypertensive patients. The nocturnal BP management is therefore particularly important in prevention of cardiovascular events, especially heart failure, as well as HMOD, such as LV hypertrophy and dysfunction, and kidney dysfunction. Recent findings support the use of home BP monitoring as a good substitution to ambulatory BP monitoring for diagnosing of hypertension in clinical practice. However, this method is not practical for detection of isolated nocturnal hypertension or assessment of circadian BP pattern, which is important predictor of CV morbidity and mortality. Thus, ambulatory BP monitoring should remain the cornerstone of diagnosing and monitoring of hypertensive patients whenever is available and feasible. Chronotherapeutic approach in drug treatment and supportive in such as CPAP should be strongly considered in patients with nocturnal hypertension.

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