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COMMENTARY

Depression in hypertension and blood pressure variability over shorter time periods

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Depression and hypertension are common diseases, and the combination of depression and hypertension is not rare. The association between depression and blood pressure (BP) level has been controversial. In the Three-City Study, depression diagnosed using the Center for Epidemiological Study Depression Scale (CES-D) was shown to be significantly associated with lower BP.[1] The association remained significant after adjusting for the subjects' use of antihypertensive and antidepressant medication. Licht *et al.*[2] also reported that depression is associated with decreased BP. On the other hand, Shar *et al.* examined 2087 participants from the Baltimore Longitudinal Study of Aging,[3] and an age-stratified analysis showed that a greater CES-D score was significantly associated with higher average systolic BP (SBP) and diastolic BP for older adults (⩾58.8 years at first visit). In the same study's younger age cohort, gender moderated the relationship of CES-D to SBP; higher CES-D scores in women, but lower CES-D scores in men, were associated with higher SBP.

The association between depression and home BP has also afforded varying findings. Niu *et al.*[4] reported that higher home SBP values were independently and continuously related to a lower prevalence of depressive symptoms in participants not using antihypertensive medication, whereas in the Finn-Home study, masked hypertension patients had higher Beck Depression Inventory scores.[5]

Although the association between depression and BP has been controversial, it has been established that depression is associated with poor prognosis for hypertensive patients.[6–8] Among elderly persons (⩾60 years), significant and substantial excess risks of death (25%) and stroke (18%) or myocardial infarction (18%) were observed per 5-unit increase in the CES-D score.[6] Kuo *et al.*[7] reported that depression contributes to the all-cause mortality of hypertensive elderly persons (⩾70 years). Axon *et al.*[8] studied 10 025 participants in the National Health and Nutrition Epidemiologic Follow-up Study (NHANES I) who were alive and interviewed in 1982 and had complete data for CES-D: nondepressed hypertensive patients had significantly lower adjusted hazard ratios for all-cause mortality compared with depressed hypertensive patients (hazard ratio 0.85).

Why and how does depression affect poor prognosis in hypertensive patients? We should consider mechanisms other than those involving the BP level. In this issue of *Hypertension Research*, Kayano *et al.*[9] reports that masked hypertension and home BP variability are associated with depression. Their paper includes two important points addressing the above question; one is BP variability, and the other is insomnia.

BP variability has been a hot topic in recent years.[10–17] Rothwell *et al.*[10] showed that visit-to-visit variability in SBP was a strong predictor of stroke, independent of mean SBP. Compared with office BP measurements, home BP measurement has more diagnostic accuracy because it provides a larger number of measurements. Home BP variability also has been shown to contribute to the risks of total mortality, cardiovascular and stroke mortality.[18] Kayano *et al.*[9] reported that home BP variability was increased in depressive patients, but day-by-day office BP variability was similar in depressive and nondepressive patients.

Reaction to stress in depression was also studied. Hamer *et al.*[19] examined the effects of depressive symptoms on cardiovascular and catecholamine responses to the induction of depressive mood. In that study, participants were required to complete two separate speech tasks where they were asked to recall life events that made them feel angry or depressed. Their BP, heart rate and total peripheral resistance were significantly increased in response to both tasks, and higher diastolic BP and higher major metabolites of norephinephrine levels were observed in the participants with high depressive symptoms.[19] From this point of view, the measurement of BP variability over a shorter duration (for example, beat-by-beat BP variability) might better reflect hemodynamic changes in depressive patients.

Insomnia is also an important pathology that affects the prognosis of hypertensive patients. We reported short sleep duration as an independent predictor of cardiovascular events in Japanese patients with hypertension.[20] King *et al.*[21] showed that short sleep duration was associated with incident coronary artery calcification. Paciência *et al.*[22] showed an association between longer sleep duration and increased odds of high BP in adolescents, especially in females. In elderly patients at high risk for cardiovascular disease, long sleep duration and persistent insomnia each had synergetic interactions with carotid artery stiffness and with visit-to-visit BP variability.[23] Thus, optimal sleep duration and good sleep quality are favorable for good prognosis of hypertensive patients.

Insomnia is risk factor of subsequent depression,[24] and screening for sleep-disordered breathing is important. Ambulatory

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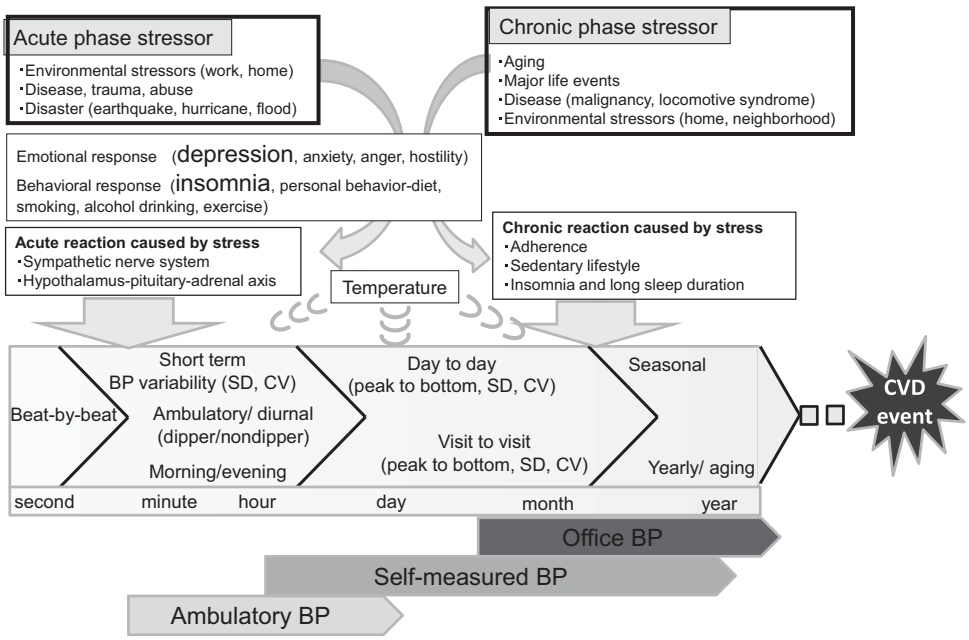

Figure 1 Psychological, physiological stress and various blood pressure variability pattern. BP, blood presure; CV coefficient of variation; CVD, cardiovascular disease; s.d. standard deviation.

BP monitoring has been widely used to noninvasively assess BP variation during sleeping periods, but regular ambulatory BP monitoring devices that measure BP values at fixed intervals, for example, every 30 min, do not seem useful for precisely detecting the sleep apnea-related short-term BP variation.

We developed a new BP-monitoring system based on an improved BP measurement-triggering algorithm, and we evaluated the system's ability to specifically detect sleep BP surges induced by severe O_2 desaturation.[25] BP variability and insomnia are associated with each other, and the measurement of shorter-duration BP variability might contribute to our understanding of this association.

The measurements of BP variability have included various time periods, and thus the meanings of the data obtained by these measurements also vary (Figure 1). According to the length of the time period, BP variability has been divided into yearly changes, seasonal variation, visit-to-visit variation, day-to-day variation, diurnal changes, ambulatory BP variation defined by the standard deviation of each measurement and beat-by-beat variation. Beat-by-beat variation may reflect acute physiological changes, and yearly changes may reflect slow responses to environmental factors and aging (Figure 1). BP variability over shorter periods has the potential to clarify the association between BP changes and various stressors (for example, psychological stress and sleep apnea). As shown in the Figure 1, all components of BP variability might be derived from beat-by-beat BP measurements.

As noted above, BP variability and insomnia are associated with depression. Further studies of BP variability over shorter time periods (for example, day-by-day, diurnal and beat-by-beat) will be useful to clarify the association between depression and poor prognosis in hypertensive patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

1 Lenoir H, Lacombe JM, Dufouil C, Ducimetière P, Hanon O, Ritchie K, Dartigues JF, Alpérovitch A, Tzourio C. Relationship between blood pressure and depression in the elderly. The Three-City Study. *J Hypertens* 2008; **26**: 1765–1772.
2 Licht CM, de Geus EJ, Seldenrijk A, van Hout HP, Zitman FG, van Dyck R, Penninx BW. Depression is associated with decreased blood pressure, but antidepressant use increases the risk for hypertension. *Hypertension* 2009; **53**: 631–638.
3 Shah MT, Zonderman AB, Waldstein SR. Sex and age differences in the relation of depressive symptoms with blood pressure. *Am J Hypertens* 2013; **26**: 1413–1420.
4 Niu K, Hozawa A, Awata S, Guo H, Kuriyama S, Seki T, Ohmori-Matsuda K, Nakaya N, Ebihara S, Wang Y, Tsuji I, Nagatomi R. Home blood pressure is associated with depressive symptoms in an elderly population aged 70 years and over: a population-based, cross-sectional analysis. *Hypertens Res* 2008; **31**: 409–416.
5 Hänninen MR, Niiranen TJ, Puukka PJ, Mattila AK, Jula AM. Determinants of masked hypertension in the general population: the Finn-Home study. *J Hypertens* 2011; **29**: 1880–1888.
6 Wassertheil-Smoller S, Applegate WB, Berge K, Chang CJ, Davis BR, Grimm R Jr, Kostis J, Pressel S, Schron E. Change in depression as a precursor of cardiovascular events. SHEP Cooperative Research Group (Systolic Hypertension in the elderly). *Arch Intern Med* 1996; **156**: 553–561.
7 Kuo PL, Pu C. The contribution of depression to mortality among elderly with self-reported hypertension: analysis using a national representative longitudinal survey. *J Hypertens* 2011; **29**: 2084–2090.
8 Axon RN, Zhao Y, Egede LE. Association of depressive symptoms with all-cause and ischemic heart disease mortality in adults with self-reported hypertension. *Am J Hypertens* 2010; **23**: 30–37.
9 Kayano H, Koba S, Matsui T, Fukuoka H, Kaneko K, Shoji M, Toshida T, Watanabe N, Geshi E, Kobayashi Y. Impact of depression on masked hypertension and variability in home blood pressure in treated hypertensive patients. *Hypertens Res* 2015; **38**: 751–757.
10 Rothwell PM, Howard SC, Dolan E, O'Brien E, Dobson JE, Dahlof B, Sever PS, Poulter NR. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. *Lancet* 2010; **375**: 895–905.
11 Kario K. Prognosis in relation to blood pressure variability: pro side of the argument. *Hypertension* 2015; **65**: 1163–1169.
12 Kario K, Pickering TG, Umeda Y, Hoshide S, Hoshide Y, Morinari M, Murata M, Kuroda T, Schwartz JE, Shimada K. Morning surge in blood pressure as a predictor of silent and clinical cerebrovascular disease in elderly hypertensives: a prospective study. *Circulation* 2003; **107**: 1401–1406.
13 Diaz KM, Tanner RM, Falzon L, Levitan EB, Reynolds K, Shimbo D, Muntner P. Visit-to-visit variability of blood pressure and cardiovascular disease and all-cause mortality: a systematic review and meta-analysis. *Hypertension* 2014; **64**: 965–982.
14 Stergiou GS, Ntineri A, Kollias A, Ohkubo T, Imai Y, Parati G. Blood pressure variability assessed by home measurements: a systematic review. *Hypertens Res* 2014; **37**: 565–572.
15 Okada H, Fukui M, Tanaka M, Matsumoto S, Mineoka Y, Nakanishi N, Tomiyasu K, Nakano K, Hasegawa G, Nakamura N. Visit-to-visit variability in systolic blood pressure is a novel risk factor for the progression of coronary artery calcification. *Hypertens Res* 2013; **36**: 996–999.
16 Yokota K, Fukuda M, Matsui Y, Hoshide S, Shimada K, Kario K. Impact of visit-to-visit variability of blood pressure on deterioration of renal function in patients

with non-diabetic chronic kidney disease. *Hypertens Res* 2013; **36**: 151–157.
17 Kamezaki F, Sonoda S, Nakata S, Muraoka Y, Okazaki M, Tamura M, Abe H, Tekeuchi M, Otsuji Y. Association of seasonal variation in the prevalence of metabolic syndrome with insulin resistance. *Hypertens Res* 2013; **36**: 398–402.
18 Kikuya M, Ohkubo T, Metoki H, Asayama K, Hara A, Obara T, Inoue R, Hoshi H, Hashimoto J, Totsune K, Satoh H, Imai Y. Day-by-day variability of blood pressure and heart rate at home as a novel predictor of prognosis: the Ohasama study. *Hypertension* 2008; **52**: 1045–1050.
19 Hamer M, Tanaka G, Okamura H, Tsuda A, Steptoe A. The effects of depressive symptoms on cardiovascular and catecholamine responses to the induction of depressive mood. *Biol Psychol* 2007; **74**: 20–25.
20 Eguchi K, Pickering TG, Schwartz JE, Hoshide S, Ishikawa J, Ishikawa S, Shimada K, Kario K. Short sleep duration as an independent predictor of cardiovascular events in Japanese patients with hypertension. *Arch Intern Med* 2008; **168**: 2225–2231.
21 King CR, Knutson KL, Rathouz PJ, Sidney S, Liu K, Lauderdale DS. Short sleep duration and incident coronary artery calcification. *JAMA* 2008; **300**: 2859–2866.
22 Paciência I, Barros H, Araújo J, Ramos E. Association between sleep duration and blood pressure in adolescents. *Hypertens Res* 2013; **36**: 747–752.
23 Nagai M, Hoshide S, Nishikawa M, Shimada K, Kario K. Sleep duration and insomnia in the elderly: associations with blood pressure variability and carotid artery remodeling. *Atherosclerosis* 2014; **233**: 19–26.
24 Katz DA, McHorney CA. Clinical correlates of insomnia in patients with chronic illness. *Arch Intern Med* 1998; **158**: 1099–1107.
25 Kario K. Proposal of a new strategy for ambulatory blood pressure profile-based management of resistant hypertension in the era of renal denervation. *Hypertens Res* 2013; **36**: 478–484.