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COMMENTARY

Impact of nocturnal blood pressure variability on renal arterioles

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To date, blood pressure (BP) variability has been observed in clinical settings. As a result of the recent development of BP measurement tools, it has become more convenient to evaluate BPs frequently at any time out of the office. BP variability includes several types, such as beat-to-beat, day-to-day, day-to-night, visit-to-visit, month-to-month and so on. Increasing evidence has suggested the importance of BP variablity on cardiovascular events and target organ damage. For example, visit-to-visit BP variability has been associated with cardiovascular disease and all-cause mortality.[1] Day-to-day variability has been associated with cognitive impairment.[2]

Intrarenal arteriosclerosis is a key pathological characteristic of nephrosclerosis. Arteriole hyalinosis is often observed in arteriosclerosis-related kidney diseases, such as nephrosclerosis and diabetic nephropathy. The precise mechanism that develops arteriole hyalinosis in the kidney still remains unclear. However, it appears that hypertension is closely associated with it; in addition, uric acid levels are reported to be associated with renal arteriopathy in patients with chronic kidney disease.[3] The presence of arteriole hyalinosis, as shown by renal biopsy, indicates the existence of kidney damage, irrespective of renal dysfunction severity.

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Immunoglobulin A (IgA) nephropathy displays various types of kidney injury, as summarized in the Oxford classification, from mild to severe in both histological and clinical grades.[4] It still remains unclear what causes a variable prognosis in patients with IgA nephropathy. Some cases with IgA nephropathy develop rapidly progressive glomeluronephritis with a crescent formation; others present only a mild increase of mesangial matrix and cells. Some cases have a poor prognosis; others do not. We often observe that histological findings in some patients with IgA nephropathy demonstrate severe arteriosclerosis in medium-sized arteries, such as the arcuate artery, to small or capillary arteries, such as afferent/efferent arterioles, without any classical risk factors for atherosclerosis such as hypertension, dyslipidemia, diabetes mellitus, smoking habit, metabolic syndrome or obesity. It is likely that arteriosclerosis with an unknown cause might be associated with pregnancy, especially in young females.

Isobe *et al.*[5] proposed one possible underlying mechanism for arteriolosclerosis in the kidney. They highlighted a significant effect of nighttime BP variability on arteriole hyalinosis in the kidney in relatively young patients with IgA nephropathy, although their average BPs present within normal range ($<$140 mm Hg). This result emphasizes the importance of subclinical BP management, even in normotensive subjects with kidney disease, especially during the night.

Known as the strain vessel hypothesis,[6,7] juxtamedullary afferent arterioles in the kidney are exposed to a high pressure and therefore have to maintain a strong vascular tone in order to provide a large pressure gradient over a short distance. In this structural aspect, afferent arterioles are susceptible to blood pressure changes. Given the result of the report,[5] it is assumed that high BP variability, even within a normal range of BPs, could influence these arterioles.

Several issues should be resolved in the future. First, how is BP variability assessed? The ideal method to examine BP variability should be devised. Because frequent BP measurements are required, a non-invasive and reproducible tool will be acceptable. Second, what increases BP variability? As BP is affected by many factors, such as hemodynamic changes, sympathetic nerve activity, salt intake and so on, the etiology should be identified. Indeed, nocturnal variability of the heart rate has been reported to progress cerebral small-vessel disease.[8] Third, it should be noted that nighttime BP variability may affect arterialsclerosis and arteriole hyalinosis in specific types of kidney disease.[9] A further disease-specific analysis in patients with chronic kidney disease could clarify new confounding factors. Finally, a proper strategy to reduce BP variability should be established.

CONFLICT OF INTEREST

The author declares no conflict of interest.

1 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.
2 Matsumoto A, Satoh M, Kikuya M, Ohkubo T, Hirano M, Inoue R, Hashimoto T, Hara A, Hirose T, Obara T, Metoki H, Asayama K, Hosokawa A, Totsune K, Hoshi H, Hosokawa T, Sato H, Imai Y. Day-to-day variability in home blood pressure is associated with cognitive decline: the Ohasama study. *Hypertension* 2014; **63**: 1333–1338.
3 Kohagura K, Kochi M, Miyagi T, Kinjyo T, Maehara Y, Nagahama K, Sakima A, Iseki K, Ohya Y. An association between uric acid levels and renal arteriolopathy in chronic kidney disease: a biopsy-based study. *Hypertens Res* 2013; **36**: 43–49.

4 Working Group of the International IgA Nephropathy Network and the Renal Pathology Society, Roberts IS, Cool HT, Troyanov S, Alpers CE, Amore A, Barratt J, Berthoux F, Bonsib S, Bruijn JA, Cattran DC, Coppo R, D'Agati V, D'Amico G, Emancipator S, Emma F, Feehally J, Ferrario F, Fervenza FC, Florquin S, Fogo A, Geddes CC, Groene HJ, Haas M, Herzenberg AM, Hill PA, Hogg RJ, Hsu SI, Jennette JC, Joh K, Julian BA, Kawamura T, Lai FM, Li LS, Li PK, Liu ZH, Mackinnon B, Mezzano S, Schena FP, Tomino Y, Walker PD, Wang H, Weening JJ, Yoshikawa N, Zhang H. The Oxford classification of IgA nephropathy: pathology definitions, correlations, and reproducibility. *Kidney Int* 2009; **76**: 546–556.
5 Isobe S, Ohashi N, Ishigaki S, Tsuji N, Tsuji T, Kato A, Yasuda H. Increased nocturnal blood pressure variability is associated with renal arteriolar hyalinosis in normotensive patients with IgA nephropathy. *Hypertens Res* 2017; **40**: 921–926.
6 Ito S, Nagasawa T, Abe M, Mori T. Strain vessel hypothesis: a viewpoint for linkage of albuminuria and cerebrocardiovascular risk. *Hypertens Res* 2009; **32**: 115–121.
7 Ito S. Cardiorenal connection in chronic kidney disease. *Clin Exp Nephrol* 2012; **16**: 8–16.
8 Yamaguchi Y, Wada M, Sato H, Nagasawa H, Koyama S, Takahashi Y, Kawanami T, Kato T. Impact of nocturnal heart rate variability on cerebral small-vessel disease progression: a longitudinal study in community-dwelling elderly Japanese. *Hypertens Res* 2015; **38**: 564–569.
9 Haruhara K, Tsuboi N, Koike K, Fukui A, Miyazaki Y, Kawamura T, Ogura M, Yokoo T. Renal histopathological findings in relation to ambulatory blood pressure in chronic kidney disease patients. *Hypertens Res* 2015; **38**: 116–122.