The official journal of the Japan Atherosclerosis Society and
the Asian Pacific Society of Atherosclerosis and Vascular Diseases

Editorial

J Atheroscler Thromb, 2022; 29: 143-145. http://doi.org/10.5551/jat.ED167

Changes in the Association between Blood Pressure Indices and Subclinical Cerebrovascular Diseases

Michihiro Satoh[1, 2]

[1]Division of Public Health, Hygiene and Epidemiology, Faculty of Medicine, Tohoku Medical and Pharmaceutical University, Sendai, Japan
[2]Department of Preventive Medicine and Epidemiology, Tohoku Medical Megabank Organization, Tohoku University, Sendai, Japan

Key words: **Blood pressure, Blood pressure monitoring, Ambulatory, Cerebrovascular disorders, Subclinical cerebrovascular diseases, Epidemiology**

See article vol. 29: 174-187

Subclinical cerebrovascular diseases (SCVDs) refer to all pathologic processes that affect the small and large vessels of the brain. Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) enable us to easily detect SCVDs, including small vessel diseases in the brain. SCVDs have been associated with all-cause mortality, future cardiovascular diseases, cognitive impairment, dementia, or decline in high-level functional capacity[1-3]. To extend not only patients' but also healthy individuals' healthy life expectancy, small vessel disease in the brain should be a target for preventive and treatment strategies[4].

The Shiga Epidemiological Study of Subclinical Atherosclerosis (SESSA), which is a cohort study of Japanese men, assessed the associations of blood pressure (BP) levels from two separate examinations with lacunar infarcts, periventricular hyperintensity (PVH), microbleeds, deep and subcortical white matter hyperintensity (DSWMH), and intracranial artery stenosis (ICAS)[5]. The years of examination varied according to the measurements: BP measurement at Visit 1 (2006–2008), BP measurement at Visit 2 (2010–2014), and MRI during 2012–2015. Salman *et al.*[5] observed differences in the associations between BP indices and later SCVDs, as summarized in **Table 1**. These results can be clues to explore the pathogenesis of the effect of BP on SCVDs. Elevated BP levels are known to affect the small artery of the brain and cause lacunar infarction. Here, the association between pulse pressure (PP) and lacunar infarction seems to strengthen with time. An elevation of systolic BP with widening PP can be a risk factor for lacunar infarction. Compared with the result regarding lacunar infarction, the associations of BP with PVH or DSWMH were weaker, especially at Visit 2. White matter hyperintensity may be linked to high BP levels observed several years ago. Microbleeds could be associated with recent BP elevation since the stronger association was observed in the data from Visit 2 than that from Visit 1. High systolic BP with a wide PP was a strong factor associated with ICAS regardless of the measurement timing. This evidence suggests that we may be able to predict present or future brain vascular conditions by considering the change in BP indices. It should be noted that they did not confirm the presence of SCVDs at each examination. Since cerebral vascular diseases are generally irreversible, their study might have not indicated the precise longitudinal association between BP and SCVDs. As they well discussed, for instance, there is the possibility that SCVDs had occurred immediately after Visit 1, which could have affected the results at Visit 2.

Overall, the associations between BP and SCVDs based on home BP were weaker than those based on office BP **(Table 1)**. In general, home BP must be more strongly associated with target organ damage than office BP[6, 7]. A report by Salman et al implies that white-coat effect is involved in their results. However, this possibility is partly denied because the

Address for correspondence: Michihiro Satoh, Department of Public Health and Hygiene, Faculty of Medicine, Tohoku Medical and Pharmaceutical University, 1-15-1 Fukumuro, Miyagino-ku, Sendai, Miyagi 983-8536, Japan E-mail: satoh.mchr@gmail.com

Received: February 26, 2021 Accepted for publication: March 2, 2021

Table 1. Summary of the association between BP indices and Subclinical cerebrovascular diseases in the SESSA study

	Lacunar	PVH	DSWMH	Microbleeds	ICAS
Office BP					
SBP at Visit 1	◎	×	○	○	◎
SBP at Visit 2	◎	×	×	◎	◎
DBP at Visit 1	○	○	○	○	×
DBP at Visit 2	○	○	○	◎	×
PP at Visit 1	○	×	×	×	◎
PP at Visit 2	◎	×	×	○	◎
MAP at Visit 1	◎	○	○	○	○
MAP at Visit 2	○	△	△	◎	○
Home BP					
SBP at Visit 1	○	○	○	○	○
SBP at Visit 2	○	×	×	○	○
DBP at Visit 1	○	○	○	○	△
DBP at Visit 2	△	×	×	○	×
PP at Visit 1	○	×	×	×	○
PP at Visit 2	◎	×	×	×	○
MAP at Visit 1	○	○	○	○	○
MAP at Visit 2	○	×	×	○	×

Summary of Fig. 1 and Supplemental Fig. 2 in the report by Salman E *et al.*[5] The " ◎ " and " ○ " indicates significantly high odds ratios per 1 standard deviation increase in each BP index are ≥ 1.50 and 1.20–1.49, respectively. The " △ " indicates odds ratio ≥ 1.20 but not statistically significant (around $P=0.05$). The "×" indicates odds ratio < 1.20 with no statistical significant ($P>0.05$).
SESSA, The Shiga Epidemiological Study of Subclinical Atherosclerosis; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure, PVH, periventricular hyperintensity; DSWMH, deep and subcortical white matter hyperintensity; and ICAS, intracranial artery stenosis.

office BP was measured with a strict 5-minute rest period at the silent office in the SESSA study. Previous reports from the SESSA study indicated the strictly measured office BP and home BP measured over 7 days were similarly associated with coronary artery calcification[8]. The correlation between office BP and home BP levels was 0.74[8]. If the reproducibility of office BP in the SESSA study is well and there is no involvement of white coat effect, the time period of BP measurement would be another reason for the weak association between home BP and SCVDs. The Ohasama study previously reported that ambulatory daytime BP was more strongly associated with SCVDs than home morning BP[9]. The office BP in the SESSA study can be regarded to reflect daytime BP and not BP in the early morning.

The report by Salman *et al.*[5] suggests the importance of consecutive BP measurements for the management and prevention of target organ damage. Meanwhile, the previous Ohasama study and a recent prospective study demonstrated that an elevated ambulatory nighttime BP was also a strong factor for SCVDs[9, 10]. The latter prospective study also indicated that there was no association between the ambulatory BP change and SCVDs although the number of participants and the follow-up duration were limited ($n=233$ with a median follow-up of 4 years)[10]. Further longitudinal evidence regarding the association between change in BP or BP variability and SCVDs is needed.

Disclosures

None.

References

1) Rensma SP, van Sloten TT, Launer LJ, Stehouwer CDA. Cerebral small vessel disease and risk of incident stroke, dementia and depression, and all-cause mortality: A systematic review and meta-analysis. Neurosci Biobehav Rev, 2018; 90: 164-173
2) Tsubota-Utsugi M, Satoh M, Tomita N, Hara A, Kondo T, Hosaka M, Saito S, Asayama K, Inoue R, Hirano M, Hosokawa A, Murakami K, Murakami T, Metoki H, Kikuya M, Izumi SI, Imai Y, Ohkubo T. Lacunar Infarcts Rather than White Matter Hyperintensity as a Predictor of Future Higher Level Functional Decline: The Ohasama Study. J Stroke Cerebrovasc Dis, 2017; 26: 376-384

3) Elnimr EM, Kondo T, Suzukamo Y, Satoh M, Oouchida Y, Hara A, Ohkubo T, Kikuya M, Hirano M, Hosokawa A, Hosokawa T, Imai Y, Izumi S. Association between white matter hyperintensity and lacunar infarction on MRI and subitem scores of the Japanese version of mini-mental state examination for testing cognitive decline: the Ohasama study. Clin Exp Hypertens, 2012; 34: 541-547
4) Pantoni L. Cerebral small vessel disease: from pathogenesis and clinical characteristics to therapeutic challenges. Lancet Neurol, 2010; 9: 689-701
5) Salman E, Kadota A, Hisamatsu T, Segawa H, Torii S, Fujiyoshi A, Kondo K, Watanabe Y, Arima H, Shiino A, Nozaki K, Ueshima H, Miura K, The SESSA Research Group. Relationship of Four Blood Pressure Indexes to Subclinical Cerebrovascular Diseases Assessed by Brain MRI in General Japanese Men. J Atheroscler Thromb, 2022; 29: 174-187
6) Umemura S, Arima H, Arima S, Asayama K, Dohi Y, Hirooka Y, Horio T, Hoshide S, Ikeda S, Ishimitsu T, Ito M, Ito S, Iwashima Y, Kai H, Kamide K, Kanno Y, Kashihara N, Kawano Y, Kikuchi T, Kitamura K, Kitazono T, Kohara K, Kudo M, Kumagai H, Matsumura K, Matsuura H, Miura K, Mukoyama M, Nakamura S, Ohkubo T, Ohya Y, Okura T, Rakugi H, Saitoh S, Shibata H, Shimosawa T, Suzuki H, Takahashi S, Tamura K, Tomiyama H, Tsuchihashi T, Ueda S, Uehara Y, Urata H, Hirawa N. The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2019). Hypertens Res, 2019; 42: 1235-1481
7) Satoh M, Asayama K, Kikuya M, Inoue R, Metoki H, Hosaka M, Tsubota-Utsugi M, Obara T, Ishiguro A, Murakami K, Matsuda A, Yasui D, Murakami T, Mano N, Imai Y, Ohkubo T. Long-Term Stroke Risk Due to Partial White-Coat or Masked Hypertension Based on Home and Ambulatory Blood Pressure Measurements: The Ohasama Study. Hypertension, 2016; 67: 48-55
8) Satoh A, Arima H, Hozawa A, Ohkubo T, Hisamatsu T, Kadowaki S, Kadota A, Fujiyoshi A, Miyagawa N, Zaid M, Torii S, Okamura T, Sekikawa A, Miura K, Ueshima H, The SESSA Research Group. The association of home and accurately measured office blood pressure with coronary artery calcification among general Japanese men. J Hypertens, 2019; 37: 1676-1681
9) Hara A, Tanaka K, Ohkubo T, Kondo T, Kikuya M, Metoki H, Hashimoto T, Satoh M, Inoue R, Asayama K, Obara T, Hirose T, Izumi S, Satoh H, Imai Y. Ambulatory versus home versus clinic blood pressure: the association with subclinical cerebrovascular diseases: the Ohasama Study. Hypertension, 2012; 59: 22-28
10) Jimenez-Balado J, Riba-Llena I, Maisterra O, Pizarro J, Palasi A, Pujadas F, Mundet X, Vinyoles E, Delgado P. Ambulatory Blood Pressure Levels in the Prediction of Progression of Cerebral Small Vessel Disease. J Am Geriatr Soc, 2020; 68: 2232-2239