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COMMENT

Is diastolic blood pressure key to detecting risk and preventing heart failure with preserved ejection fraction?

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The rapid aging of society is a common phenomenon, and an increase in the incidence of heart failure (HF) is a cardiovascular health burden worldwide. Japan is one of the top aging countries around the world, and the aging population rate in Japan is still steeply rise [1]. HF has three phenotypes based on the ejection fraction (EF) percentage: HF with reduced EF (HFrEF), HF with mildly reduced EF (HFmrEF), and HF with preserved EF (HFpEF). Among these HF phenotypes, HFpEF especially has emerged as a critical public health problem that is increasing in prevalence with the aging population and the ongoing hypertension epidemics. The prognosis of patients with HFpEF is unfavorable, similar to the prognosis of those with HFrEF. The numerous HF-related symptoms and repeated hospitalizations for HF deteriorate a patient's quality of life (QOL) and increase their economic burden. For many years, the management of HFpEF has been limited to the reduction of symptoms and the care of the underlying conditions. Definitive pharmacological therapies for HFpEF remain elusive. Early detection and efficient prevention policies and programs may help improve patient outcomes and QOL and reduce costs for health systems and individuals. The Cerebrovascular and Cardiovascular Disease Control Act under Japanese national law was promulgated by a legislative act on December 14, 2018, and enacted on December 1, 2019 [2]. The Japanese National Plan for Promotion of Measures Against Cerebrovascular and Cardiovascular Disease was developed. It is emphasized that awareness of prevention measures and accurate information on HF should be spread.

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The present study by Kimura et al. [3] revealed that high-normal diastolic blood pressure (DBP) (≥85 mmHg) was the only independent factor associated with left ventricular diastolic dysfunction in postmenopausal women who did not have any history of hypertension, diabetes, or cardiovascular diseases. Women with high-normal DBP had a risk of left ventricular diastolic dysfunction that was 3.5 times higher than that of those without high-normal DBP. The other important result from their study is that the prevalence of left ventricular diastolic dysfunction, which is the main mechanism of HFpEF, was as high as 15% in healthy postmenopausal women.

In Western countries, obesity, diabetes mellitus, and ischemic heart disease play substantial roles in HFpEF, whereas in Japan, HFpEF patients are characterized by elderly women with hypertension [4]. This characteristic of Japanese HFpEF patients might have contributed to the results of the current study. Why was high-normal DBP (≥85 mmHg) rather than systolic blood pressure (SBP) important for left ventricular diastolic dysfunction? Arterial pressure directly corresponds to cardiac output, arterial elasticity, and peripheral vascular resistance. The lowest pressure, DBP, occurs just before the ventricle ejects blood into the aorta. The fundamental hemodynamic mechanism in elevated DBP is an elevated systemic vascular resistance accompanied by an inappropriately normal cardiac output. An increased neurohormonal drive and an autoregulatory reaction of vascular smooth muscle to an expanded plasma volume induce vasoconstriction at the level of the resistance arterioles. Elevated DBP is suggested to be more closely related to end-organ damage than elevated SBP. Essential hypertension typically begins with isolated elevation in the DBP or combined elevation in both the SBP and DBP (Fig. 1A) [5]. Isolated diastolic hypertension progresses to combined systolic-diastolic hypertension. Later, decreased arterial compliance (increased vessel stiffness) causes the systolic pressure to rise and the diastolic pressure to fall

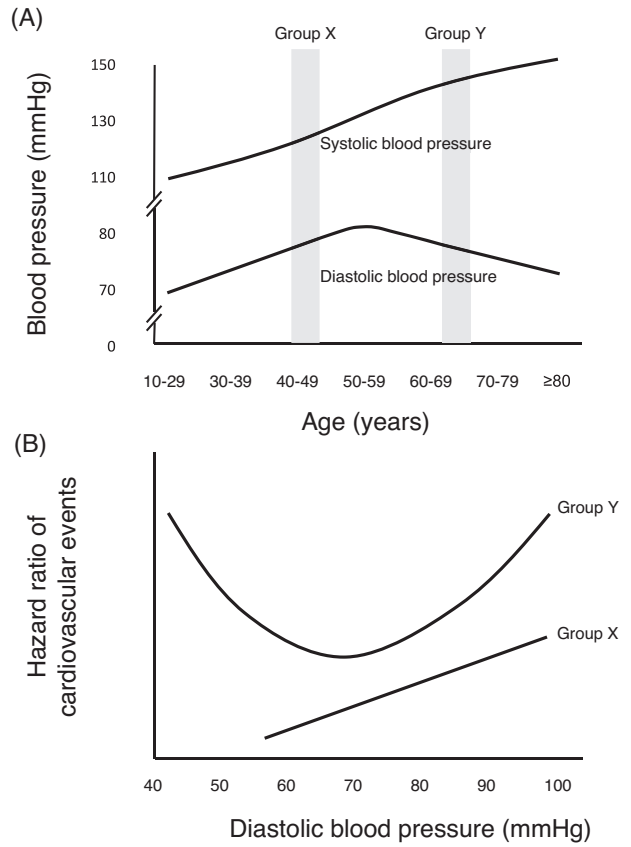

Fig. 1 The complex relationship between diastolic blood pressure and cardiovascular risk. **A** Systolic and diastolic blood pressure according to age. Diastolic blood pressure increases with age up to 60 years, and after the age of 60, stiffening of the arteries causes a decrease in diastolic blood pressure, whereas systolic blood pressure progressively increases with age. Group X indicates subjects with compliant arterial walls, and Group Y indicates those with noncompliant arteries (modified from Hypertension. 1995;25(3):305-13.). **B** Under the condition of compliant arteries (Group X), diastolic blood pressure has a positive linear relationship with cardiovascular risk. On the other hand, low diastolic blood pressure based on decreased arterial compliance (Group Y) is associated with a significant risk of cardiovascular events, resulting in a U-shaped relationship

(Fig. 1A) [5]. Therefore, DBP is elevated from the early phase of hypertension; however, the clinical meaning of an elevated or reduced DBP can be different depending on the stages of vascular and cardiac function. Although both systolic and diastolic blood pressure have been reported to be associated with future cardiovascular risk, the association of DBP with cardiovascular risk diminishes with age as vascular compliance is attenuated [6]. Although high DBP well reflects vascular and organ damage in subjects with preserved vascular compliance, the association of DBP with cardiovascular risk becomes complicated by a U-shaped relationship under the condition of noncompliant vasculature. In fact, several studies have been reported regarding DBP and prognosis in the advanced stages of vascular or cardiac dysfunction. It has been demonstrated that in adults treated for hypertension, low DBP, especially when coupled with high SBP, was associated with myocardial damage, coronary heart disease, heart failure hospitalization, stroke, and cardiovascular death [7–9]. Tsujimoto et al. investigated the relationship between low DBP and the risk of cardiovascular events in patients with HFpEF using data from the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial [10]. The risks of all-cause death, major cardiovascular events, and hospitalization for heart failure were significantly elevated in HFpEF patients with low DBP. A Japanese study of 206 HFpEF patients was recently reported by Fuchida et al. [11] The patients were divided into two groups by the median DBP value (77 mmHg), and those with low DBP had more than two times higher risk of HF admission than those with high DBP.

Along these lines, the cardiovascular risk associated with high or low DBP can differ based on the arterial wall and heart conditions. Fig. 1B shows the suggested relationship between DBP and the risk of cardiovascular events according to compliant or noncompliant arterial walls. There should be a positive linear relationship between DBP and cardiovascular risk if the arteries are compliant and heart function is normal. On the other hand, under noncompliant arterial wall conditions, low DBP can be associated with an elevated risk of cardiovascular events, and the relationship between DBP and cardiovascular risk would be U-shaped. Since the current study included healthy postmenopausal women and excluded subjects with cardiovascular diseases, hypertension, diabetes mellitus, and other systemic illnesses, vascular compliance and heart function were normal in most subjects included in this study. Two factors might play key roles in the results of the current study: (1) the high prevalence of hypertension as an etiology of HF in Japan [4], and (2) the characteristics of healthy postmenopausal nonhypertensive women in the current study.

Due to the rapidly aging population in Japan, it is expected that the prevalence of HF among elderly women and its associated costs will continue to grow. From these perspectives, this study presents valuable data on the early risk stratification of left ventricular diastolic dysfunction in postmenopausal women and provides an important contribution. Several drugs, such as sodium-glucose cotransporter 2 (SGLT2) inhibitors, mineralocorticoid receptor antagonists (MRAs), and angiotensin receptor-neprilysin inhibitors (ARNis), have been developed; however, unlike in HFrEF patients, there are no medical therapies that reduce mortality in HFpEF patients. The most important solution for the HF epidemic should be primary prevention. The increasing prevalence of HF among the older population has a multifactorial etiology. The complex pathophysiology of HFpEF makes it a diagnostic and therapeutic

challenge. Rather than single interventions, broad, multi-organ, multidisciplinary interventions might be required to prevent HFpEF and improve overall survival. As our understanding of HFpEF continues to evolve, so does our approach to treatment. The present study showed that a high-normal DBP (≥85 mmHg) among postmenopausal healthy women was a significant risk factor for left ventricular diastolic dysfunction in the multivariate model. One possible measure may be to intervene in high-normal DBP to prevent HFpEF. Because the prevalence of hypertension increases with age and because hypertensive heart disease tends to represent an accumulation of years of pressure overload, early detection and early intervention for high-normal DBP may diminish the incidence of hypertensive heart disease and may be effective in stopping the HF epidemic. Further trials are needed to investigate this hypothesis.

Compliance with ethical standards

Conflict of interest The author declares no competing interests.

References

1. The Ministry of Health, Labour and Welfare. Abridged life table [Internet]. 2017 [cited 2018 Oct 22]. Available from: https://www.mhlw.go.jp/toukei/saikin/hw/life/life17/dl/life17-04.pdf (in Japanese).
2. Kuwabara M, Mori M, Komoto S. Japanese national plan for promotion of measures against cerebrovascular and cardiovascular disease. Circulation. 2021;143:1929–31.
3. Kimura M, Sekiguchi H, Shimamoto K, Kawana M, Takemura Y, Hagiwara N. High-normal diastolic blood pressure as a risk factor for left ventricular diastolic dysfunction in healthy postmenopausal women. Hypertension Res. 2022; https://doi.org/10.1038/s41440-022-01024-w (in press).
4. Nagai T, Yoshikawa T, Saito Y, Takeishi Y, Yamamoto K, Ogawa H, et al. Clinical characteristics, management, and outcomes of Japanese patients hospitalized for heart failure with preserved ejection fraction- A report from the Japanese Heart Failure Syndrome With Preserved Ejection Fraction (JASPER) registry. Circ J. 2018;82:1534–45.
5. Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, et al. Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey, 1988–91. Hypertension. 1995;25:305–13.
6. Lee H, Yano Y, Cho SMJ, Park S, Lloyd-Jones DM, Kim HC. Cardiovascular risk of isolated diastolic hypertension defined by the 2017 American College of Cardiology/American Heart Association blood pressure guideline: a nationwide age-stratified cohort study. Hypertension. 2020;76:e44–e46.
7. McEvoy JW, Chen Y, Rawlings A, Hoogeveen RC, Ballantyne CM, Blumenthal RS, et al. Diastolic blood pressure, subclinical myocardial damage, and cardiac events: implications for blood pressure control. J Am Coll Cardiol. 2016;68:1713–22.
8. Suzuki K, Claggett B, Minamisawa M, Nochioka K, Mitchell GF, Anand IS, et al. Pulse pressure, prognosis, and influence of sacubitril/valsartan in heart failure with preserved ejection fraction. Hypertension. 2021;77:546–56.
9. Sandesara PB, O'Neal WT, Kelli HM, Topel M, Samman-Tahhan A, Sperling LS. Diastolic blood pressure and adverse outcomes in the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist) Trial. J Am Heart Assoc. 2018;7:e007475.
10. Tsujimoto T, Kajio H. Low diastolic blood pressure and adverse outcomes in heart failure with preserved ejection fraction. Int J Cardiol. 2018;263:69–74.
11. Fuchida A, Suzuki S, Motoki H, Kanzaki Y, Maruyama T, Hashizume N, et al. Prognostic significance of diastolic blood pressure in patients with heart failure with preserved ejection fraction. Heart Vessels. 2021;36:1159–65.