## Potential beneficial impact of angiotensin receptor blockers on arterial stiffness in hypertension

Kouichi Tamura, Nozomu Kishio, Kotaro Haruhara, Kazushi Uneda, Kengo Azushima, Hiromichi Wakui

Department of Medical Science and Cardiorenal Medicine, Yokohama City University Graduate School of Medicine, Yokohama 236-0004, Japan *Correspondence to*: Kouichi Tamura, MD, PhD, FACP, FAHA. Department of Medical Science and Cardiorenal Medicine, Yokohama City University Graduate School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan. Email: tamukou@med.yokohama-cu.ac.jp.

Submitted Apr 07, 2016. Accepted for publication Apr 18, 2016. doi: 10.21037/jtd.2016.05.10

View this article at: http://dx.doi.org/10.21037/jtd.2016.05.10

Hypertension is highly prevalent worldwide and is one of the major risk factors for cardiovascular and renal diseases. Accumulated results of clinical trials showed that strict control of blood pressure (BP) is essential to prevent target organ damage and to reduce cardiovascular mortality in hypertensive patients. In many countries, major antihypertensive drugs are calcium channel blockers (CCBs), angiotensin II receptor blockers (ARBs), angiotensin-converting enzyme (ACE) inhibitors, diuretics, and betablockers (including alpha/beta-blockers), according to the international hypertension guidelines (1-5).

The vascular function parameters (arterial stiffness and central hemodynamics), including ankle-brachial pressure index (ABI), pulse wave velocity (PWV), cardio-ankle vascular index (CAVI), augmentation index (AI) and central systolic blood pressure (cSBP), do not always correlate with the peripheral brachial BP value, but do reflect the pressure load in the major organs. Several previous studies demonstrated that these variables (cSBP, AI, and PWV) are more closely related to organ damage than brachial BP (6-9). Previous meta-analyses also showed that the cSBP, AI, and PWV are independent risk factors for cardiovascular disease, and that these variables may reflect the different characteristics of the pathophysiologic abnormalities related to arterial stiffness (10,11). Therefore, it would be important to improve the vascular parameters of both arterial stiffness and central hemodynamics, in addition to reduction in the peripheral brachial BP value (clinic BP), for the efficient cardiovascular protection.

Experimental and clinical evidence has reported that activation of the renin-angiotensin system (RAS) is involved in the pathogenesis of hypertension and the related target

organ damage, and multiple studies have shown the usefulness of RAS blockade induced by ACE inhibitors and ARBs for the management of hypertension. In addition, several previous studies showed beneficial effects of the RAS inhibitors on the vascular function parameters (12-14). Furthermore, several preceding meta-analyses for effects of the RAS inhibitors on arterial stiffness and/or wave reflections also demonstrated the RAS inhibitors improved PWV and/or AI in certain pathological conditions (15,16).

Interestingly, the system review and meta-analysis by Chen et al. in the recent issue of the Journal of Thoracic Disease (7TD) was conducted to analyze the clinical benefits of different antihypertensive agents in improving arterial stiffness in hypertensive patients (17). The effect of ARB on the improvement of the PWV was not superior to other types of antihypertensive agents, but ARB was superior to other types of antihypertensive agents for improving the AI in this system review and meta-analysis, thereby suggesting that ARB maybe superior to other antihypertensive agents to improve of arterial stiffness (17). The results of this systematic review and meta-analysis by Chen et al. would strengthen the clinical evidence in favor of ARB as one of the first-line antihypertensive drugs for most patients with hypertension with its ability to exert efficient BP lowering effects and to inhibit cardiovascular and renal events (5).

However, monotherapy with either an ARB or a CCB, another first-line antihypertensive drug, achieves the target BP recommended by the hypertension guidelines in only a limited number of patients and, thus, combination therapy is required in a majority of patients (5). The results of a recent meta-analysis of the efficacy and safety of adding an ARB to a CCB following ineffective CCB

monotherapy demonstrated that adding an ARB to CCB significantly improved BP control and the percentage of on-target hypertension treatment with significantly reduced incidence of adverse events (18). Therefore, further research to investigate the therapeutic effects of different types of antihypertensive agents, as a monotherapy or in combination, is necessary for efficient suppression of cardiovascular and renal events in hypertension (19,20).

## **Acknowledgements**

This work was supported by a Health and Labor Sciences Research grant, by Grants-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (JSPS), and by grants from SENSHIN Medical Research, Banyu Life Science Foundation International and Salt Science Research Foundation. Kouichi Tamura received research grants from AstraZeneca, Ono Pharmaceutical and Tsumura.

## **Footnote**

Conflicts of Interest: The authors have no conflicts of interest to declare.

Comment on: Chen X, Huang B, Liu M, et al. Effects of different types of antihypertensive agents on arterial stiffness: a systematic review and meta-analysis of randomized controlled trials. J Thorac Dis 2015;7:2339-47.

## **References**

- Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens 2013;31:1281-357.
- James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014;311:507-20.
- Go AS, Bauman MA, Coleman King SM, et al. An effective approach to high blood pressure control: a science advisory from the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention. Hypertension 2014;63:878-85.

- Weber MA, Schiffrin EL, White WB, et al. Clinical practice guidelines for the management of hypertension in the community: a statement by the American Society of Hypertension and the International Society of Hypertension. J Clin Hypertens (Greenwich) 2014;16:14-26.
- Shimamoto K, Ando K, Fujita T, et al. The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2014). Hypertens Res 2014;37:253-390.
- Williams B, Lacy PS, Thom SM, et al. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. Circulation 2006;113:1213-25.
- Wang KL, Cheng HM, Chuang SY, et al. Central or peripheral systolic or pulse pressure: which best relates to target organs and future mortality? J Hypertens 2009;27:461-7.
- 8. Wang KL, Cheng HM, Sung SH, et al. Wave reflection and arterial stiffness in the prediction of 15-year all-cause and cardiovascular mortalities: a community-based study. Hypertension 2010;55:799-805.
- Gómez-Marcos MA, Recio-Rodríguez JI, Rodríguez-Sánchez E, et al. Central blood pressure and pulse wave velocity: relationship to target organ damage and cardiovascular morbidity-mortality in diabetic patients or metabolic syndrome. An observational prospective study. LOD-DIABETES study protocol. BMC Public Health 2010;10:143.
- Vlachopoulos C, Aznaouridis K, O'Rourke MF, et al.
  Prediction of cardiovascular events and all-cause mortality
  with central haemodynamics: a systematic review and
  meta-analysis. Eur Heart J 2010;31:1865-71.
- Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol 2010;55:1318-27.
- 12. Klingbeil AU, John S, Schneider MP, et al. AT1-receptor blockade improves augmentation index: a double-blind, randomized, controlled study. J Hypertens 2002;20:2423-8.
- 13. Mahmud A, Feely J. Effect of angiotensin ii receptor blockade on arterial stiffness: beyond blood pressure reduction. Am J Hypertens 2002;15:1092-5.
- 14. Takami T, Shigemasa M. Efficacy of various antihypertensive agents as evaluated by indices of vascular stiffness in elderly hypertensive patients. Hypertens Res 2003;26:609-14.
- 15. Shahin Y, Khan JA, Chetter I. Angiotensin converting

- enzyme inhibitors effect on arterial stiffness and wave reflections: a meta-analysis and meta-regression of randomised controlled trials. Atherosclerosis 2012;221:18-33.
- Peng F, Pan H, Wang B, et al. The impact of angiotensin receptor blockers on arterial stiffness: a meta-analysis. Hypertens Res 2015;38:613-20.
- Chen X, Huang B, Liu M, et al. Effects of different types of antihypertensive agents on arterial stiffness: a systematic review and meta-analysis of randomized controlled trials. J Thorac Dis 2015;7:2339-47.
- 18. Ma J, Wang XY, Hu ZD, et al. Meta-analysis of the efficacy and safety of adding an angiotensin receptor blocker (ARB)

Cite this article as: Tamura K, Kishio N, Haruhara K, Uneda K, Azushima K, Wakui H. Potential beneficial impact of angiotensin receptor blockers on arterial stiffness in hypertension. J Thorac Dis 2016;8(7):E564-E566. doi: 10.21037/jtd.2016.05.10

- to a calcium channel blocker (CCB) following ineffective CCB monotherapy. J Thorac Dis 2015;7:2243-52.
- 19. Azushima K, Uneda K, Tamura K, et al. Effects of single pill-based combination therapy of amlodipine and atorvastatin on within-visit blood pressure variability and parameters of renal and vascular function in hypertensive patients with chronic kidney disease. Biomed Res Int 2014;2014;437087.
- 20. Kobayashi R, Tamura K, Wakui H, et al. Effect of single-pill irbesartan/amlodipine combination-based therapy on clinic and home blood pressure profiles in hypertension with chronic kidney disease. Clin Exp Hypertens 2016. [Epub ahead of print].