



Special Issue: Current evidence and perspectives for hypertension management in Asia

# Long-term blood pressure lowering effect of renal denervation and its patient preference, salt intake, and stroke in Asia

Kazuomi Kario<sup>1</sup> · Satoshi Hoshide<sup>1</sup> · Masaki Mogi<sup>2</sup>

**Keywords** Renal denervation · Patient preference · Salt intake · Stroke · Asia

Received: 29 March 2022 / Accepted: 29 March 2022 / Published online: 6 June 2022  
© The Author(s), under exclusive licence to The Japanese Society of Hypertension 2022

In this editorial for Asian session of June issue of Hypertension Research, we introduce two original papers, one review and one brief report.

Recently, literatures on blood pressure (BP) lowering effect of renal denervation (RDN) have been increasingly accumulated [1, 2]. Recent metaanalysis of 9 randomized sham-controlled trials demonstrated the significantly BP lowering effect on office and 24-hr ambulatory BP in both unmedicated and/or medicated hypertensive patients [1]. However, BP lowering effect is evaluated 2–3 months after the RDN procedure in these clinical trials, and long-term follow-up data has been limited especially in Asia. In this issue, Panchavinnin P et al. reported much longer-term outcome of RDN up to nearly 9 years in Thailand [3], and confirmed that the BP lowering effect of RDN greater than 10 mmHg for systolic office BP was sustained up to nearly nine years in the medicated patients with resistant hypertension. This result is consistent with the previous papers of Kario K, et al. [4], and of Kim BK [5], et al. which demonstrated the marked BP lowering effect on office BP at 36 months after RDN. The longer-follow up data of 24-hr BPs in the SPYRAL-HTN On-Med trial has been just released in the Lancet [6]. This study demonstrated the all the 24-hr, morning, and nighttime systolic BPs were more significantly reduced by 10 mmHg or more in the RDN group than in the Sham-controlled group in medicated hypertensive patients. In our recent results of the JAMP study using ambulatory BP monitoring [7], and of the J-HOP study

using home BP monitoring [8], both demonstrated that drug-resistant hypertensive patients with uncontrolled 24-hr systolic BP  $\geq$  130 mmHg or home systolic BPs  $\geq$  135 mmHg exhibited the poor cardiovascular prognosis in the patients with resistant hypertension. Asians are more likely to exhibit masked hypertension such as morning and nocturnal hypertension than Westerners [9]. In Asia, long-term BP lowering effect of RDN on BPs during 24-hrs including morning and nighttime indicate that RDN will effectively reduce the cardiovascular events.

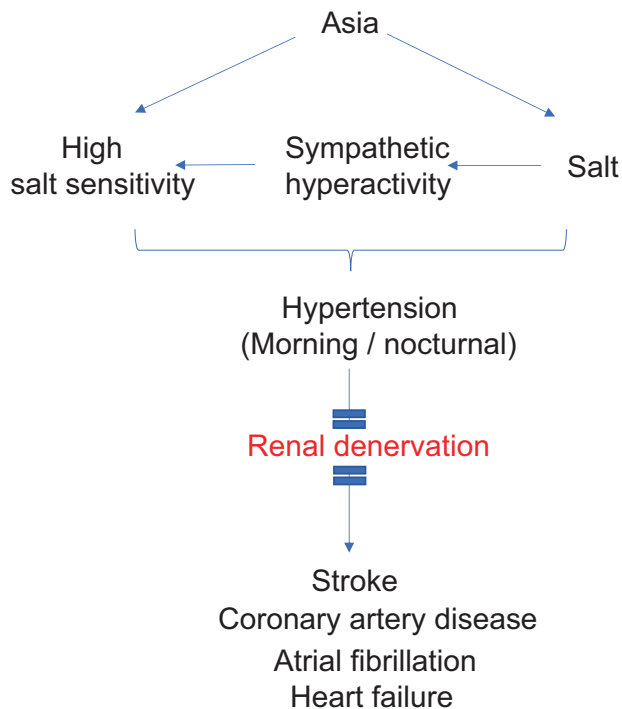
Another interested paper on RDN was written by Zhang Z et al. from China [10]. The paper presents the results of survey using questionnaire on patient preferences for renal denervation (RDN) therapy as a therapeutic option of hypertension. The result is consistent with the reports of Kario et al. from Japan [11], and of Schmieder from Germany [12]. It seems that Chinese, Japanese, European hypertensive patients has similar preference of the RDN therapy. Patient-centered hypertension management considering patient preference will extensively increase the BP control rate, resulting in reduction of cardiovascular events. Recently, European and US experts released the position papers of RDN [13, 14]. The Asia Renal Denervation Consortium (ARDeC), and each Asian country released the position papers in Asia [15, 16]. The RDN will have significant positioning in Asian management of hypertension in near future.

Salt restriction has always been an important factor for lowering BP and prevent cardiovascular events and organ damages. Especially, high salt intake is the big problem in Asia [17]. Ohashi et al. showed annual changes in plasma brain natriuretic peptide (BNP) levels were associated with salt intake in the general population [18]. BNP is the important biomarker of cardiac stress, which indicate the risk of heart failure, atrial fibrillation, stroke, and coronary artery disease [9]. The cardiovascular risk of BNP is partly mediated by nocturnal hypertension [19], which is residual risk for stroke and heart failure [20, 21].

✉ Kazuomi Kario  
kkario@jichi.ac.jp

<sup>1</sup> Division of Cardiovascular Medicine, Jichi Medical University School of Medicine, Tochigi 329-0498, Japan

<sup>2</sup> Department of Pharmacology, Ehime University Graduate School of Medicine, Tohon, Ehime, Japan



**Fig. 1** Importance of salt restriction, strict 24-hr blood pressure control, and renal denervation in Asia

Kitagawa writes a state-of-art review and stress the importance of more strict BP control for the secondary prevention of stroke [22], based on the results of RESPECT study and metaanalysis [23, 24]. Asians are more likely to develop stroke, especially hemorrhagic stroke, which is more closely associated with hypertension than Westerners [9]. Taken together with the recent results of STEP study which demonstrate the benefit of BP control <130 mmHg in older Chinese hypertensive patients [25], strict BP control seems extremely important for both primary and secondary prevention of cardiovascular events in Asia.

In conclusion, the papers in this special issue indicate the importance of salt restriction, strict 24-hr BP control, and RDN in Asia (Fig. 1) and they are on the same global direction of the latest hypertension researches [26].

## Compliance with ethical standards

**Conflict of interest** The authors declare no competing interests.

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

## References

- Ogoyama Y, Tada K, Abe M, Nanto S, Shibata H, Mukoyama M, et al. Effects of renal denervation on blood pressures in patients with hypertension: a systematic review and meta-analysis of randomized sham-controlled trials. *Hypertens Res.* 2022;45:210–20.
- Katsurada K, Ogoyama Y, Imai Y, Patel KP, Kario K. Renal denervation based on experimental rationale. *Hypertens Res.* 2021;44:1385–94.
- Panchavinnin P, Wanthong S, Tresukosol D, Buranakitjaroen P, Chotruangnapa C, Watanapa W, et al. Long-term Outcome of Renal Nerve Denervation (RDN) for Resistant Hypertension. *Hypertens Res.* 2022, <https://doi.org/10.1038/s41440-022-00910-7>.
- Kario K, Yamamoto E, Tomita H, Okura T, Saito S, Ueno T, et al. SYMPLICITY HTN-Japan investigators. sufficient and persistent blood pressure reduction in the final long-term results from SYMPLICITY HTN-Japan - safety and efficacy of renal denervation at 3 years. *Circ J.* 2019;83:622–9.
- Kim BK, Kim HS, Park SJ, Park CG, Seung KB, Gwon HC, et al. Long-term outcomes after renal denervation in an Asian population: results from the Global SYMPLICITY Registry in South Korea (GSR Korea). *Hypertens Res.* 2021;44:1099–104.
- Mahfoud F, Kandzari DE, Kario K, Townsend RR, Weber MA, Schmieder RE, et al. Long-term efficacy and safety of renal denervation in the presence of antihypertensive drugs: results from the randomised, sham-controlled SPYRAL HTN-ON MED trial. *Lancet* 2022, in press.
- Kario K, Hoshida S, Narita K, Okawara Y, Kanegae H, Investigators' network. Cardiovascular prognosis in drug-resistant hypertension stratified by 24-hour ambulatory blood pressure: the JAMP study. *Hypertension* 2021;78:1781–90.
- Narita K, Hoshida S, Kario K. Association of treatment-resistant hypertension defined by home blood pressure monitoring with cardiovascular outcome. *Hypertens Res.* 2022;45:75–86.
- Kario K. Essential manual of perfect 24-hour blood pressure management from morning to nocturnal hypertension. London, Wiley, 2022. pp. 1–374.
- Zhang Z, Zhang X, Ye R, Li Y, Chen X. Patient preference for renal denervation therapy in hypertension: a cross-sectional survey in Chengdu, China. *Hypertens Res.* 2022, <https://doi.org/10.1038/s41440-022-00912-5>.
- Kario K, Kagitani H, Hayashi S, Hanamura S, Ozawa K, Kanegae H. A Japan nationwide web-based survey of patient preference for renal denervation for hypertension treatment. *Hypertens Res.* 2022;45:232–40.
- Schmieder RE, Kandzari DE, Wang TD, Lee YH, Lazarus G, Pathak A. Differences in patient and physician perspectives on pharmaceutical therapy and renal denervation for the management of hypertension. *J Hypertens.* 2021;39:162–8.
- Schmieder RE, Mahfoud F, Mancia G, Azizi M, Böhm M, Dimitriadis K, et al. European Society of Hypertension position paper on renal denervation 2021. *J Hypertens.* 2021;39:1733–41.
- Kandzari DE, Mahfoud F, Weber MA, Townsend R, Parati G, Fisher NDL, et al. Clinical trial design principles and outcomes definitions for device-based therapies for hypertension: a consensus document from the hypertension academic research consortium. *Circulation.* 2022;145:847–63.
- Kario K, Kim BK, Aoki J, Wong AY, Lee YH, Wongpraparut N, et al. Renal denervation in Asia: consensus statement of the Asia Renal Denervation Consortium. *Hypertension* 2020;75:590–602.
- Wang TD, Lee YH, Chang SS, Tung YC, Yeh CF, Lin YH, et al. 2019 consensus statement of the taiwan hypertension society and the Taiwan society of cardiology on renal denervation for the management of arterial hypertension. *Acta Cardiol Sin.* 2019;35:199–230.
- Kario K, Chia YC, Siddique S, Turana Y, Li Y, Chen CH, et al. Seven-action approaches for the management of hypertension in Asia - The HOPE Asia network. *J Clin Hypertens (Greenwich).* 2022;24:213–23.

18. Ohashi N, Takasa H, Aoki T, Ishigaki S, Iwakura T, Isobe S, et al. Positive relationships between annual changes in salt intake and plasma B-type natriuretic peptide levels in the general population without hypertension and heart diseases. *Hypertens Res.* 2022, <https://doi.org/10.1038/s41440-022-00914-3>.
19. Hoshide S, Kanegae H, Kario K. Nighttime home blood pressure as a mediator of N-terminal pro-brain natriuretic peptide in cardiovascular events. *Hypertens Res.* 2021;44:1138–46.
20. Kario K, Hoshide S, Nagai M, Okawara Y, Kanegae H. Sleep and cardiovascular outcome in relation to nocturnal hypertension: the J-HOP nocturnal blood pressure study. *Hypertens Res.* 2021;44:1589–96.
21. Fujiwara T, Hoshide S, Kanegae H, Kario K. Cardiovascular event risks associated with masked nocturnal hypertension defined by home blood pressure monitoring in the J-HOP nocturnal blood pressure study. *Hypertension* 2020;76:259–66.
22. Kitagawa K. Blood pressure management for secondary stroke prevention. *Hypertens Res.* 2022, <https://doi.org/10.1038/s41440-022-00908-1>.
23. Kitagawa K, Yamamoto Y, Arima H, Maeda T, Sunami N, Kanzawa T, et al. Effect of standard vs intensive blood pressure control on the risk of recurrent stroke: a randomized clinical trial and meta-analysis. *JAMA Neurol.* 2019;76:1309–18.
24. Kitagawa K, Arima H, Yamamoto Y, Ueda S, Rakugi H, Kohro T, et al. Intensive or standard blood pressure control in patients with a history of ischemic stroke: RESPECT post hoc analysis. *Hypertens Res.* 2022;45:591–601.
25. Zhang W, Zhang S, Deng Y, Wu S, Ren J, Sun G, et al. Trial of intensive blood-pressure control in older patients with hypertension. *N Engl J Med.* 2021;385:1268–79.
26. Kario K, Mogi M, Hoshide S. Latest hypertension research to inform clinical practice in Asia. *Hypertens Res* 2022, <https://doi.org/10.1038/s41440-022-00874-8>.