

Is Primary Aldosteronism a Hidden Cause of Resistant Hypertension in Mongolia?

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Drug-resistant hypertension (RH) is defined as uncontrolled blood pressure (BP) despite treatment with at least three drugs or controlled BP using four or more antihypertensive medications, including diuretics, at maximum or maximally tolerated doses [1]. Primary aldosteronism (PA) is the most common underdiagnosed and undertreated cause of RH, prevailing in about 20% of hypertensive patients [2–4]. Therefore, the prevalence of hypertension-mediated organ damage (HMOD) is higher in patients with PA in comparison to essential hypertensive patients of the same age and same BP level [5]. Owing to the poor clinical awareness of PA, with ensuing “under suspicion,” unduly complex diagnostic workup, [4,6] limited availability of invasive investigations for localizing unilateral PA (uPA), constrained surgical capacity, and uncertainties about clinical outcomes [4]. Timely diagnosed and treated uPA can provide not only a cure for HT but also prevention of HMOD.

The case detection for HT patients with a high probability of PA relies on measuring the aldosterone-to-renin ratio (ARR) [6,7]. Confirmatory tests purposed for these ARR-positive patients comprised the captopril challenge test, the fludrocortisone suppression test, the saline infusion test, the oral sodium loading test, and the furosemide upright test [4,8]. Confirmatory tests might be skipped for the diagnostic procedure simplification since neither test furnished a diagnostic gain over carefully performed baseline ARR [9,10].

Bilateral aldosteronism should prompt appropriate medical treatment, including mineralocorticoid receptor antagonists; in contrast, uPA potentially can be cured by adrenalectomy, and to distinguish excess aldosterone secretion side, adrenal vein sampling (AVS) plays a crucial role [11]. However, the AVS is technically challenging and performed only in a few tertiary referral centers of developed countries, even though tertiary centers perform AVS under different protocols. Moreover, carefully performed AVS also did not provide a final diagnosis of PA. The gold diagnostic standard relies on the biochemical cure of PA patients after adrenalectomy retrospectively, including normalized plasma aldosterone concentration and renin concentration with a further normalized aldosterone-to-renin ratio [12].

Recognizing the critical association with uncontrolled blood pressure levels, Mongolia, facing the highest stroke rate globally, emphasizes the alarming prevalence of hypertension (HT) at 46.5% in the latest randomized cross-sectional study. Uncontrolled hypertension, identified as the most common risk factor for ischemic heart disease and stroke – the leading causes of death in Mongolia's adult population – underscores the need to diagnose secondary causes

of hypertension. Given the potential underdiagnosis of PA in Mongolia, adopting the latest diagnostic procedures for PA is crucial to prevent HMOD. Furthermore, Enkhtungalag et al.'s [13] research reveals a concerning trend in Mongolian salt consumption, exceeding WHO recommendations by more than two times. This excessive salt intake, coupled with under diagnosed PA, poses severe consequences on the heart and arterial walls, including volume expansion, renin suppression, increased cardiac

preload, left ventricular hypertrophy, atrial fibrillation [14], and an elevated risk of stroke.

In conclusion, recognizing the need for a more in-depth study, it is essential to investigate whether Primary Aldosteronism is a hidden cause of resistant hypertension in Mongolia. This additional inquiry would contribute to a comprehensive understanding of the factors contributing to the high prevalence of hypertension and associated cardiovascular risks in the Mongolian population.

References

1. Williams B, Mancia G, Spiering W, et al. 2018 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC). *Blood Press*. 2018;36(12):2284-309. <https://doi.org/10.1097/HJH.0000000000001961>
2. Xu Z, Yang J, Hu J, et al. Primary Aldosteronism in Patients in China With Recently Detected Hypertension. *J Am Coll Cardiol*. 2020;75(16):1913-22. <https://doi.org/10.1016/j.jacc.2020.02.052>
3. Rossi GP, Bernini G, Caliumi C, et al. A Prospective Study of the Prevalence of Primary Aldosteronism in 1,125 Hypertensive Patients. *J Am Coll Cardiol*. 2006;48(11):2293-300. <https://doi.org/10.1016/j.jacc.2006.07.059>
4. Funder JW, Carey RM, Mantero F, et al. The management of primary aldosteronism: Case detection, diagnosis, and treatment: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2016;101(5):1889-916. <https://doi.org/10.1210/nc.2015-4061>
5. Seccia TM, Letizia C, Muiesan ML, et al. Atrial fibrillation as presenting sign of primary aldosteronism: Results of the Prospective Appraisal on the Prevalence of Primary Aldosteronism in Hypertensive (PAPPHY) Study. *J Hypertens*. 2020;38(2):332-9. <https://doi.org/10.1097/HJH.0000000000002250>
6. Rossi GP, Bisogni V, Bacca AV, et al. The 2020 Italian Society of Arterial Hypertension (SIIA) practical guidelines for the management of primary aldosteronism. *Int J Cardiol Hypertens*. 2020 Apr 15;5:100029. <https://doi.org/10.1097/01.hjh.0000745016.79540.85>
7. Rossi GP, Seccia TM, Palumbo G, et al. Within-patient reproducibility of the aldosterone:renin ratio in primary aldosteronism. *Hypertension*. 2010;55(1):83-9. <https://doi.org/10.1161/HYPERTENSIONAHA.109.139832>
8. Nishikawa T, Omura M, Satoh F, et al. Guidelines for the diagnosis and treatment of primary aldosteronism -The Japan Endocrine Society 2009. *Endocr J*. 2011;58(9):711-21. <https://doi.org/10.1507/endocrj.EJ11-0133>
9. Leung AA, Symonds CJ, Hundemer GL, et al. Performance of Confirmatory Tests for Diagnosing Primary Aldosteronism: A Systematic Review and Meta-Analysis. *Hypertension*. 2022;79(8):1835-44. <https://doi.org/10.1161/HYPERTENSIONAHA.122.19377>
10. Zhu R, Shagjaa T, Rossitto G, et al. Exclusion Tests in Unilateral Primary Aldosteronism (ExcluPA) Study. *J Clin Endocrinol Metab*. 2023 Feb 1;108(2):496-506. <https://doi.org/10.1210/clinem/dgac654>
11. Rossi GP, Rossitto G, Amar L, et al. Clinical Outcomes of 1625 Patients With Primary Aldosteronism Subtyped With Adrenal Vein Sampling. *Hypertension*. 2019;74(4):800-8. <https://doi.org/10.1161/HYPERTENSIONAHA.119.13463>
12. Rossi GP, Bisogni V, Rossitto G, et al. Practice Recommendations for Diagnosis and Treatment of the Most Common Forms of Secondary Hypertension. *High Blood Press Cardiovasc Prev*. 2020;27(6):547-60. <https://doi.org/10.1007/s40292-020-00415-9>
13. Enkhtungalag B, Batjargal J, Chimedsuren O. Developing a national salt reduction strategy for Mongolia. *Cardiovasc Diagn Ther*. 2015;5(3):229-37. <https://doi.org/10.3978/j.issn.2223-3652.2015.04.11>
14. Rossi GP. Primary Aldosteronism: JACC State-of-the-Art Review. *J Am Coll Cardiol*. 2019;74(22):2799-811. <https://doi.org/10.1016/j.jacc.2019.09.057>