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COMMENT

The potential of a new nomogram for the diagnosis of primary aldosteronism

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Primary aldosteronism (PA) is one of the forms of endocrine hypertension caused by autonomous overproduction of aldosterone from the adrenal cortex. Its prevalence is said to account for 3–12% of hypertensive patients in primary care, making it one of the most common causes of secondary hypertension [1]. Aldosterone not only promotes Na^+ retention in the renal tubules but also directly acts on various organs such as the heart, kidney, fat tissues [2, 3], and blood vessels, inducing inflammation in these tissues [4]. Additionally, Morita et al. reported that higher aldosterone levels are significantly associated with a smaller dipping rate in nighttime blood pressure, resulting in a non-dipper pattern [5]. Therefore, patients with PA have a significantly higher risk of complications such as cardiovascular disease and chronic kidney disease, compared to patients with essential hypertension (EH) of the same level of blood pressures [6, 7]. To reduce the risk of these organ damage, it is important to initiate specific treatments (i.e., mineralocorticoid receptor antagonists or adrenalectomy) to correct hypertension and aldosterone activity [1, 8, 9]. It is important to initiate these treatments as early as possible, particularly before the progression of atherosclerosis [8]. Efficiently detecting PA in patients with hypertension and linking it to early initiation of treatments are very important.

On the other hand, diagnosing PA involves a multi-step procedure, which often poses an inconvenience for both patients and clinicians [1]. Generally, a diagnosis begins with screening tests to check a high plasma aldosterone concentration (PAC) and suppressed plasma renin activity (PRA). This is followed by several confirmation tests, including the captopril challenge test (CCT), the saline infusion test (SIT), the furosemide upright test (FUT), and the oral salt loading test (OST), for example. If any one of these tests returns a positive result, a diagnosis of PA can be made [1]. In other words, in order to strictly rule out PA according to current guidelines, it is necessary to conduct all confirmation tests and obtain negative results in each. This is because there is currently no consensus on limiting the confirmation process to just one functional test. Some of these tests typically require hospitalization, necessitating patients to stay in the hospital for several days. However, as PA often presents with few physical symptoms, patients frequently decline these procedures due to time constraints or financial concerns.

Given this context, scoring systems and nomograms have been developed with the aim of diagnosing PA more conveniently. Yamashita et al. proposed the PFK score, consisting of three factors: pH of urine, female sex, and low serum K^+ (AUC 0.73, 95% CI: 0.63–0.83) [10]. Lin et al. reported a model using age, sex, hypokalemia, serum sodium, serum sodium-to-potassium ratio, anion gap, and alkaline urine (AUC 0.84, 95% CI: 0.79–0.89) [11]. The present study by Liu et al. successfully distinguished between EH and PA with relatively high accuracy using only four factors: the history of hypokalemia, PRA, typical adrenal nodule findings on CT, and 24-h urine potassium (AUC 0.86, 95% CI: 0.79–0.93) [12]. While the accuracy of the scoring system or nomogram is important for its dissemination, its simplicity is also important. Even an excellent score is hard to use if it is more complicated than performing a confirmatory test. In this regard, the

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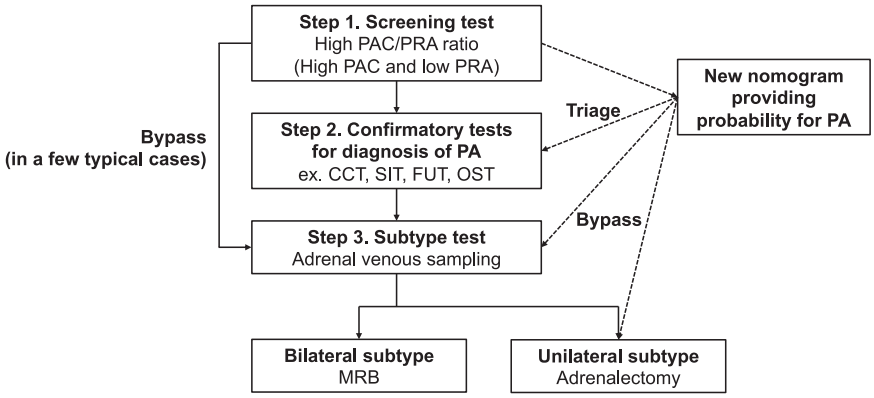

Fig. 1 The typical diagnostic process for primary aldosteronism. CCT captopril challenging test, FUT furosemide upright test, MRB mineralocorticoid receptor blockers, OST oral salt loading test, PA primary aldosteronism, PAC plasma aldosterone concentration, PRA plasma renin activity, SIT saline infusion test

nomogram in the present study is composed of only four factors, all of which can be obtained in daily practice. Although it may sometimes be difficult to accurately evaluate 24-h urine potassium in an outpatient setting, it can be managed by handing a urine bag to the patient. In addition, the authors have developed a free web application, which has freed us from the need to carry around this nomogram. Unfortunately, the diagnostic accuracy of the nomogram in this study may still be slightly inferior to that of the confirmation tests themselves (AUC for CCT = 0.92, AUC for SIT = 0.92) [13]. However, it is very interesting that this diagnostic performance can be achieved without administering any drugs, and it may be worth considering in cases where it is difficult to perform a confirmation test. Alternatively, by using this simple scoring system, we may be able to objectively triage the patients who should undergo the confirmatory tests, or whether it might be acceptable to skip them. In other words, we may be able to consider using this nomogram in addition to traditional screening test (Fig. 1). The traditional screening test using the PAC/PRA ratio (ARR) has been reported to have unstable performance in a meta-analysis [14]. This implies that we may need to reconsider using ARR as a standalone screening test. By combining the present nomogram with ARR, it may be possible to screen for PA more efficiently and narrow down the target population for confirmation tests. On this point, further discussion is expected in the future, taking into account its cost-effectiveness.

This study has several limitations. Firstly, external validation has not yet been completed for this nomogram. The population studied was ~400 people in a single institution, and further verification will be needed in the future to confirm its generalizability. In addition, the authors have suggested that this nomogram may be useful in differentiating subtypes of PA, however, the sample size for this analysis was limited. Despite the need for these additional verifications, this new nomogram has shown us the potential to discover PA more simply and more efficiently.

Compliance with ethical standards

Conflict of interest The author declares no competing interests.

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References

1. Naruse M, Katabami T, Shibata H, Sone M, Takahashi K, Tanabe A, et al. Japan Endocrine Society clinical practice guideline for the diagnosis and management of primary aldosteronism 2021. Endocr J. 2022;69:327–59.
2. Haze T, Ozawa M, Kawano R, Haruna A, Ohki Y, Suzuki S, et al. Effect of the interaction between the visceral-to-subcutaneous fat ratio and aldosterone on cardiac function in patients with primary aldosteronism. Hypertens Res. 2023;46:1132–44.
3. Haze T, Hatakeyama M, Komiya S, Kawano R, Ohki Y, Suzuki S, et al. Association of the ratio of visceral-to-subcutaneous fat volume with renal function among patients with primary aldosteronism. Hypertens Res. 2021;44:1341–51.
4. Neves MF, Cunha AR, Cunha MR, Gismondi RA, Oigman W. The role of renin-angiotensin-aldosterone system and its new components in arterial stiffness and vascular aging. High Blood Press Cardiovasc Prev. 2018;25:137–45.
5. Morita R, Azushima K, Sunohara S, Haze T, Kobayashi R, Kinguchi S, et al. High plasma aldosterone concentration is associated with worse 24-h ambulatory blood pressure profile in patients with primary aldosteronism. Hypertens Res. 2023;46:1995–2004. https://doi.org/10.1038/s41440-023-01325-8.
6. Ohno Y, Sone M, Inagaki N, Yamasaki T, Ogawa O, Takeda Y, et al. Prevalence of cardiovascular disease and its risk factors in primary aldosteronism: a multicenter study in Japan. Hypertension. 2018;71:530–7.
7. Fernández-Argüeso M, Pascual-Corrales E, Bengoa Rojano N, García Cano A, Jiménez Mendiguchía L, Araujo-Castro M. Higher risk of chronic kidney disease and progressive kidney function impairment in primary aldosteronism than in essential hypertension. Case-control study. Endocrine. 2021;73:439–46.
8. Haze T, Hirawa N, Yano Y, Tamura K, Kurihara I, Kobayashi H, et al. Association of aldosterone and blood pressure with the risk for cardiovascular events after treatments in primary aldosteronism. Atherosclerosis. 2021;324:84–90.
9. Haze T, Yano Y, Hatano Y, Tamura K, Kurihara I, Kobayashi H, et al. Association of achieved blood pressure after treatment for

primary aldosteronism with long-term kidney function. J Hum Hypertens. 2022;36:904–10.
10. Yamashita T, Shimizu S, Koyama M, Ohno K, Mita T, Tobisawa T, et al. Screening of primary aldosteronism by clinical features and daily laboratory tests: combination of urine pH, sex, and serum K. J Hypertens. 2018;36:326–34.
11. Lin W, Gan W, Feng P, Zhong L, Yao Z, Chen P, et al. Online prediction model for primary aldosteronism in patients with hypertension in Chinese population: a two-center retrospective study. Front Endocrinol. 2022;13:882148.
12. Liu Y, Wang M, Qiu X, Ma G, Ji M, Yang Y, et al. A novel clinical-imaging nomogram for predicting primary aldosteronism in patients with hypertension. Hypertens Res. 2023. https://doi.org/10.1038/s41440-023-01374-z.
13. Wu S, Yang J, Hu J, Song Y, He W, Yang S, et al. Confirmatory tests for the diagnosis of primary aldosteronism: a systematic review and meta-analysis. Clin Endocrinol. 2019;90:641–8.
14. Hung A, Ahmed S, Gupta A, Davis A, Kline GA, Leung AA, et al. Performance of the aldosterone to renin ratio as a screening test for primary aldosteronism. J Clin Endocrinol Metab. 2021;106:2423–35.