EnM
ENDOCRINOLOGY AND METABOLISM

Editorial

Endocrinol Metab 2018;33:352-354
https://doi.org/10.3803/EnM.2018.33.3.352
pISSN 2093-596X · eISSN 2093-5978

Update on the Aldosterone Resolution Score and Lateralization in Patients with Primary Aldosteronism

Eun-Hee Cho

Department of Internal Medicine, Kangwon National University School of Medicine, Chuncheon, Korea

Primary aldosteronism (PA), first described by Jerome W. Conn in 1955 [1], is characterized by excessive, autonomous aldosterone production relative to suppressed plasma renin. PA is currently an important curable cause of secondary hypertension, and has been increasingly diagnosed in patients with hypertension because of emerging interest in PA and advances in knowledge of this condition. Patients with PA have been found to be at a higher risk of cardiovascular events and target organ damage in the heart and kidney than patients with essential hypertension [2-4], suggesting that early diagnosis and appropriate clinical management are important. PA is usually caused by a unilateral aldosterone-producing adenoma (APA) or unilateral or bilateral adrenal hyperplasia, although in rare cases, it may be caused by adrenal carcinoma or inherited familial hyperaldosteronism. PA is specifically treated by surgery (unilateral adrenalectomy) or medical treatment with a mineralocorticoid receptor antagonist.

After unilateral adrenalectomy for APA, hypertension outcomes and the factors associated with complete resolution of hypertension are variable. Zarnegar et al. [5] first developed the simple aldosterone resolution score (ARS) to predict the complete resolution of hypertension after adrenalectomy with unilateral APA, based on four routinely available initial clinical variables (≤2 antihypertensive medications, body mass index [BMI] ≤25 kg/m^2, duration of hypertension ≤6 years, and female sex) that predicted hypertension resolution. In the same study, taking ≤2 antihypertensive medications was found to be the strongest independent predictor of resolution of hypertension, with an odds ratio of roughly twice that of other variables. In another study of 91 Japanese patients who underwent unilateral adrenalectomy for APA, taking fewer than three antihypertensive medications, a duration of hypertension ≤6 years, and female sex were demonstrated to be predictors of complete resolution of hypertension, confirming the factors included in the ARS, except for BMI [6]. However, in a recent study of 310 French patients with APA, of the variables included in the ARS, only a BMI ≤25 kg/m^2 and taking ≤2 antihypertensive medications were significant predictors [7].

A study by Loh et al. [8] demonstrated that only a short duration of hypertension (≤6 years) and an ARS of 3 to 5 were associated with resolution of hypertension after adrenalectomy in 40 patients with PA in Singapore, in contrast to the results of previous studies of ARS [5,6]. In 376 Chinese patients with APA, only a duration of hypertension of ≥6 years and a level of plasma aldosterone ≥35 ng/dL were significant independent negative predictors for complete hypertension cure [9]. In an international cohort study of patients with PA [10], unilateral adrenalectomy achieved complete clinical success in 37% of 705 patients, and complete biochemical success (correction of hypokalemia and normalization of the aldosterone-to-renin ratio) was found in 94% (range, 83% to 100%) of 699 patients. In that study, patients with younger age and female sex received greater surgical clinical benefits from adrenalectomy [10]. Hypertension with PA is dependent not only on excessive aldosterone se-

Received: 20 August 2018, **Accepted:** 27 August 2018
Corresponding author: Eun-Hee Cho
Department of Internal Medicine, Kangwon National University School of Medicine, 1 Gangwondaehak-gil, Chuncheon 24341, Korea
Tel: +82-33-258-9167, **Fax:** +82-33-258-2455, **E-mail:** ehcho@kangwon.ac.kr

cretion, but also on existing essential hypertension and vascular or renal damage induced by a long duration of antecedent aldosterone-induced hypertension.

Since the updated recommendation of the Endocrine Society practice guideline on PA was released in 2016 [4], accumulating evidence has advanced our knowledge of the genetics, case detection, screening, diagnosis, subtype differentiation, and treatment of PA. Lateralization of the source of excessive aldosterone secretion between unilateral and bilateral disease is critical in the management of PA. Adrenal venous sampling (AVS) is regarded as the gold-standard method for differentiating between unilateral and bilateral disease in patients with PA [4]. However, AVS is considered to be a difficult procedure because of the technical difficulty of cannulating the right adrenal vein. Recently, there have been advances in AVS cannulation with the introduction of rapid on-site measurements of adrenal vein cortisol concentrations [11] and C-arm computed tomography-guided cannulation [12]. New immunoassay measurements of hybrid steroids, such as 18-hydroxycorticosterone, 18-hydroxycortisol, and 18-oxocortisol, have recently shown improved sensitivity and specificity, suggesting their potential use as surrogate markers for the diagnosis and lateralization of unilateral PA in combination with adrenal imaging [13,14].

^{11}C-metomidate positron emission tomography tracers were developed as an alternative to AVS because metomidate binds to steroidogenic enzymes, including CYP11B, and enzymes involved in the biosynthesis of aldosterone and cortisol, suggesting its suitability in adrenocortical functional imaging for the lateralization of APA [15]. The study by Loh et al. [8] suggested that the contralateral ratio (CR) might be a useful alternative to AVS for considering surgery in the setting of unilateral cannulation of the adrenal vein, but their study acknowledged that many unanswered questions remained to be resolved and that prospective clinical trials must be conducted to determine appropriate cut-offs of the CR and the efficacy of the CR relative to AVS.

For future research, a prospective multi-center large-scale design with standardized blood pressure assessments in the general population is required to develop and verify a novel and effective prediction model of the outcomes of adrenalectomy, including the resolution of hypertension and the incidence of cardiovascular events.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Eun-Hee Cho *https://orcid.org/0000-0002-1349-8894*

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