



# Predicting the laterality of the autonomous aldosterone production from adrenal vein sampling

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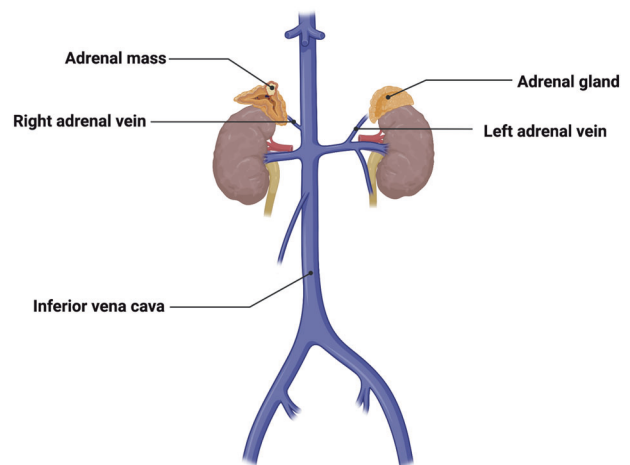
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One of the difficult aspects of primary aldosteronism (PA) is to detect which side of the adrenal glands engages in aldosterone excess [1, 2]. The presence of an adrenal mass in clinically diagnosed PA patients does not always imply that such adrenal nodules are functional culprits of PA, since autonomous production of aldosterone may occur in visually indiscernible lesions [3]. At present, adrenal vein sampling (AVS) is the modality of choice to identify the lateralization of PA (Fig. 1). Yet, the procedure, including cannulation into the adrenal veins, requires skills and experience of the operators; thus, AVS occasionally ends up with a sampling of the adrenal vein on one side alone, and fails to yield the lateralization index.

Given the possible incomplete AVS, O'Malley et al. compared the diagnostic performance of the ipsilateral versus contralateral AV/IVC index, which is defined by the aldosterone to cortisol ratio in the adrenal vein divided by that in the inferior vena cava [4]. Analyzing the area under the receiver operating characteristic (AUROC) of the AV/IVC index, they revealed that the contralateral AV/IVC index outperforms the ipsilateral counterpart in both left and right unilateral PA cases. This finding suggests that assessing the suppression of contralateral aldosterone production possesses a higher diagnostic value than evaluating the degree of excess of ipsilateral aldosterone secretion. The contralateral suppression of the adrenocortical hormones such as aldosterone and cortisol in unilateral PA and Cushing syndrome, respectively, is a common hallmark of the functional adrenal mass; hence, low levels (<1) of the

contralateral AV/IVC is considered reflective of the contralateral suppression of aldosterone and indicative of the presence of excessive aldosterone synthesis on the ipsilateral side. In contrast, the ipsilateral AV/IVC represents the overproduction of aldosterone in the adrenal vein as compared to the systemic circulation, which per se does neither verify the excess or autonomy of aldosterone secretion from the ipsilateral side nor imply the suppression of aldosterone from the contralateral side. Notably, the difference in AUROC between the ipsilateral and contralateral sides seems attributed to the relatively low sensitivity of the ipsilateral AV/IVC. This suggests that a meaningful degree of unilateral PA patients fall under the ipsilateral AV/IVC less than 5.5. In our institution, laterality is determined by the lateralization index of more than 4 and the contralateral AV/IVC less than 1. There do exist unilateral PA patients diagnosed by such criteria, whose ipsilateral AV/IVC is less than 5.5 (personal observation). This



**Fig. 1** Adrenal vein sampling. Anatomical illustration of the adrenal veins and inferior vena cava. Adapted from “Effects of Opioids on the Human Body” by BioRender.com (2023). Retrieved from <https://app.biorender.com/biorender-templates>

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could be explained by the notion that the ipsilateral AV/IVC does not theoretically corroborate the autonomous aldosterone production on that side. On the other hand, lowering the threshold of ipsilateral AV/IVC presumably compromises the specificity. Overall, this study sheds light on the differential performance of the ipsilateral versus contralateral AV/IVC index, and supports the concept that the autonomous aldosterone production suppresses its secretion from spared adrenal glands.

### Compliance with ethical standards

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

**Ethics approval** Reporting observation of patients with primary aldosteronism, who underwent adrenal vein sampling in Keio University Hospital, Tokyo, Japan, was approved by the Research Ethics Committee of Keio University School of Medicine (approval number: 20180135).

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### References

1. Vaidya A, Carey RM. Evolution of the primary aldosteronism syndrome: updating the approach. *J Clin Endocrinol Metab.* 2020;105:3771–83.
2. Vaidya A, Mulatero P, Baudrand R, Adler GK. The expanding spectrum of primary aldosteronism: implications for diagnosis, pathogenesis, and treatment. *Endocr Rev.* 2018;39:1057–88.
3. Parksook WW, Yozamp N, Hundemer GL, Moussa M, Underhill J, Fudim T. et al. Morphologically normal-appearing adrenal glands as a prevalent source of aldosterone production in primary aldosteronism. *Am J Hypertens.* 2022;35:561–71.
4. O'Malley KJ, Alnablsi MW, Xi Y, Pathak M, Khan F, Pillai AK, et al. Diagnostic performance of the adrenal vein to inferior vena cava aldosterone ratio in classifying the subtype of primary aldosteronism. *Hypertens Res.* 2023. <https://doi.org/10.1038/s41440-023-01421-9>.