

## Is it Possible to Extirpate Cardiovascular Events in Primary Aldosteronism After Surgical Treatment

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**Abstract:** It is well known that primary aldosteronism (PA) due to aldosterone-producing adenoma (APA) is a surgically curable secondary hypertension. Thus, the differential diagnosis between unilateral hyperaldosteronemia due to APA and bilateral hyperaldosteronemia due to idiopathic hyperaldosteronism (IHA) is crucial to decide surgical indication for treatment in PA patients. Adrenal venous sampling (AVS) can diagnose the laterality of hypersecretion of aldosterone in those patients, while it is still impossible to differentiate bilateral hypersecretion of bilateral aldosterone-producing adenomas (Blt-APAs) from that of bilateral hyperplasia of IHA. To solve the problem, we try to develop a new method of super-selective ACTH-stimulated adrenal venous sampling (SS-ACTH-AVS). We performed SS-ACTH-AVS by using a strip-tip type 2.2 Fr micro-catheter (Koshin Medical Inc. Japan). Adrenal effluents were sampled super-selectively at the central veins and at one or two tributaries of adrenal veins in each gland. We would like to emphasize that SS-ACTH-AVS can precisely analyze the situation of hyperfunction of steroidogenesis in each side of adrenals as well as in some tiny lesions inside the adrenal cortex which are not visible in the CT images. Moreover, we can differentiate Blt-APAs from IHA, and postulate the decision of surgical treatment, such as partial adrenalectomy. Thus, we should perform SS-ACTH-AVS especially in the case demonstrating the existence of bilateral adrenal lesions such as unilateral and bilateral tumors, or even no tumor in both sides in the patients with PA.

**Keywords:** hypertension, adrenal adenoma, adrenal hyperplasia, adrenal vein sampling

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*Japanese Clinical Medicine* 2010:1 21–23

doi: [10.4137/JCM.S6316](https://doi.org/10.4137/JCM.S6316)

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The incidence rates for primary aldosteronism (PA) among hypertensives were recently reported to be widely ranged between 3.2% and 20%. Padfield had already reported that cardiovascular risk factors, which can affect as much as 50% of an older population, would be transformed if there were a specific cause or causes amenable to specific therapies.<sup>1</sup> There are now increasing numbers of critical reports suggesting that the prevalence of PA might be approximately 10% of all of those individuals with hypertension. This would make PA more common than diabetes or thyroid disease and would surely revolutionize our approach to the management of those thousands of patients with what has previously been called essential hypertension.<sup>1</sup> Moreover, the results of recent screening of hypertensive patients in Japan using the simultaneous measurements of the plasma aldosterone concentration (PAC) and plasma renin activity (PRA) or the aldosterone-renin ratio (ARR) have shown that PA is observed in 3.3%–10% of hypertensive patients and is the most frequent cause of secondary hypertension.<sup>2–6</sup> It is well known that PA is a disease caused by autonomic hypersecretion of aldosterone due to adrenocortical lesions, associated with increased urinary potassium excretion, and organ disorders (cerebral hemorrhage, cerebral infarction, myocardial infarction, cardiomegaly, arrhythmia, renal insufficiency, etc.) due to excessive aldosterone.<sup>7–9</sup> Therefore, we really notice the importance of this disease to accurately diagnose and treat for completely reducing aldosterone levels.

Here, we describe how to detect adrenal lesions, including CT-negative tiny adrenal adenoma in PA. There is a limitation for differentiating aldosterone-producing adenoma (APA) from bilateral adrenal hyperplasia (idiopathic hyperaldosteronism: IHA), because the size of APA is always so small that CT images cannot fully detect the lesions.<sup>10</sup> In evaluating whether the lesion involves the unilateral or bilateral adrenal glands, diagnostic imaging of the adrenal glands is less accurate, and microlesions may frequently be missed, resulting in a diagnosis of IHA. The Endocrine Society<sup>10</sup> and the Japan Endocrine Society<sup>11</sup> recommend that APA and IHA are differentiated by adrenal venous sampling (AVS), although AVS is technically difficult and adrenal effluents are often not obtained even when the catheter is properly inserted into the adrenal vein. Then we

tried to develop a new AVS method, such as super-selective ACTH-stimulated adrenal venous sampling (SS-ACTH-AVS), to obtain adrenal effluents both from central veins and tributary veins of each adrenal gland.<sup>13</sup> SS-ACTH-AVS can obtain blood samples from various parts of adrenal glands to easily detect the highest peak of aldosterone. Our results demonstrate that we can even treat the patients with bilateral APA by partial adrenalectomy after precise localization of the aldosterone producing lesions. We may remove the main lesion of hyperaldosteronemia by performing SS-ACTH-AVS, resulting in permanent reduction of aldosterone to avoid sodium+aldosterone-induced cardiovascular events. It is promising to achieve complete remission of PA after surgical treatment, according to the results of SS-ACTH-AVS.

## Acknowledgment

The present study was supported by a Grant-in-Aid for Scientific Research “Adrenal Disorders” provided from the Ministry of Public Health and Labor.

## Disclosure

This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers of this paper report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material.

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