Left-right differences in adrenal vein sampling for primary aldosteronism

Arina Miyoshi¹, Norio Wada¹, Shuhei Baba¹, Shinji Obara¹, Bunya Takahashi², Hiroaki Usubuchi² and Satoshi Terae²

¹ Department of Diabetes and Endocrinology, Sapporo City General Hospital, Sapporo 060-8604, Japan
² Department of Radiology, Sapporo City General Hospital, Sapporo 060-8604, Japan

Abstract. In adrenal venous sampling (AVS) for patients with primary aldosteronism (PA), adrenocorticotropic hormone (ACTH) stimulation generally increased the success rate. The effect of ACTH stimulation on the left-right differences of laterality diagnosis in AVS remains unclear. A total of 167 patients with PA underwent successful AVS were examined. Patients with autonomous cortisol secretion were excluded. The proportion of dominant side in AVS was compared before and after ACTH stimulation.Unilateral disease on AVS was defined as a lateralization index of more than 4, both before and after ACTH stimulation. Before ACTH stimulation, unilateral disease was more frequently observed on the right side than the left side (right 33.5% vs. left 13.8%, p < 0.01). After ACTH stimulation, unilateral disease was more frequently observed on the left side than the right side, without statistical significance (left 15.6% vs. right 10.8%, p = 0.20). Among the 56 patients who had right unilateral disease before ACTH stimulation, 17 patients (30.0%) also had right unilateral disease after ACTH stimulation. The affected side of AVS was changed from right unilateral to bilateral after ACTH stimulation in 34 (60.7%) out of 56 patients. These patients had milder PA and CT scans showed no nodular lesions on the right side. In AVS, ACTH stimulation not only decreased unilateral results but also shifted to the dominant side. Overestimation should be carefully considered when the surgical indication for the right adrenal gland was decided based on AVS results without ACTH stimulation.

Key words: Primary aldosteronism, Adrenal venous sampling, Left-right difference

PRIMARY ALDOSTERONISM (PA) is the most common form of secondary endocrine hypertension, accounting for 5–10% of all hypertensive patients [1, 2]. The two common subtypes of PA, aldosterone-producing adenoma (APA) and idiopathic hyperaldosteronism (IHA) should be differentiated, because the former requires adrenalectomy and the latter is treated by medication [1, 3]. Adrenal venous sampling (AVS) is recognized as the most reliable method for subtype diagnosis; therefore, patients should undergo this procedure to determine the need for adrenalectomy. To decide whether the disease is either unilateral or bilateral, the lateralization index (LI) is commonly used [4-6], i.e., the ratio of aldosterone/cortisol (A/C) in the dominant adrenal vein relative to that in the non-dominant adrenal vein.

One of the most important issues related to AVS is the significance of ACTH stimulation during AVS procedure. ACTH stimulation has been known to increase the success rate and decrease the rate of cases determined as unilateral disease [7]. In contrast, left-right differences in AVS have not been investigated yet.

Therefore, this study aimed to evaluate left-right differences in AVS parameters and determine the laterality before and after ACTH stimulation during the AVS procedure.

Patients and Methods

Patients

Patients with PA who successfully underwent AVS in Sapporo City General Hospital from July 2009 to August 2018 were examined. The diagnostic procedure for confirmation of PA was performed with reference to the guidelines of both the Japan Endocrine Society [8] and the Japan Society of Hypertension [9]. PA screening was performed based on the ratio of plasma aldosterone concentration (PAC; pg/mL) to plasma renin activity (PRA; ng/mL/h) (aldosterone renin ratio [ARR]), >200, after
changing from potentially interfering antihypertensive drugs to calcium channel blockers and/or to α-blockers where applicable. The PA diagnosis was established by at least one positive result of confirmatory testing, captopril challenge test, furosemide-upright test, saline infusion test, and oral salt loading test. In our hospital, AVS was suggested to all patients with PA, except for those who preferred not to be admitted or undergo surgery.

We excluded patients with unsuccessful AVS either before or after ACTH stimulation. Patients with autonomous secretion of cortisol defined as serum cortisol levels of >1.8 μg/dL in overnight 1-mg dexamethasone suppression test (1-mg DST) were also excluded [10].

This study was approved by the ethics committee of Sapporo City General Hospital (H30-059-520).

**AVS**

Blood samples obtained via AVS were generally collected before and 30-min after administering 0.25 mg of cosyntropin (ACTH 1-24) from both adrenal veins and the inferior vena cava (IVC) at a point distal to the renal vein. They were sequentially collected from the left to right before ACTH stimulation with various intervals, whereas after ACTH stimulation, they were drawn from right to left with short intervals. The tip of the catheter was placed into the left adrenal vein at a point distal to the division of the left inferior phrenic vein, known as the central vein, and at the junction between the inferior phrenic vein and the left adrenal vein as a common trunk [11]. Although 5-French catheters were simultaneously placed in the left and right adrenal veins through independent routes, blood samples were sequentially collected using a microcatheter if necessary. Successful cannulation in the right adrenal vein was determined with the support of imaging using a C-arm computed tomography (CT). Successful AVS was defined as selectivity index (SI) >2 before and >5 after ACTH stimulation. Catheterization was also considered successful if the serum cortisol concentration was >200 μg/dL in the adrenal vein after ACTH administration [12]. Unilateral disease on AVS was defined as LI of >4, during both before and after ACTH stimulation [13-15]. The contralateral ratio (CR), the ratio of aldosterone/cortisol in the non-dominant adrenal vein relative to that in the central vein, was also validated to evaluate accuracy of laterality diagnosis by LI [8]. If aldosterone/cortisol in adrenal veins were bilaterally lower than that in IVC (apparent bilateral aldosterone suppression; ABAS), the AVS was determined to be inconclusive [16]. The indication of adrenalectomy was decided for each patient according to AVS results mainly after ACTH stimulation.

**Analysis**

Data were studied retrospectively. We compared AVS parameters between the left and right adrenal veins. In addition, the dominant side in AVS was compared between before and after ACTH stimulation. The nodular lesion observed on CT scans was defined as a distinct nodule diagnosed by radiologists in our hospital, and equivocal findings were determined as normal adrenal gland on CT scans. Postoperative clinical and biochemical outcomes were estimated according to the method of PASO study [17].

**Assay Methods**

PAC and PRA were measured using commercially available kits: radioimmunoassay for the former (SPAC-S Aldosterone Kit; Fuji Rebio, Co., Ltd, Tokyo, Japan), with the reference range in supine position of 30–159 pg/mL, and radioimmunoassay for the latter, with the reference range in supine position of 0.2–2.7 ng/mL/h (PRA radioimmunoassay kits; Yamasa, Co., Ltd).

**Statistics**

Data were analyzed and compared using BellCurve for Excel (Social Survey Research Information Co., Ltd., Tokyo, Japan). Continuous variables were analyzed using t-test or Mann–Whitney u test, as appropriate. Comparison of frequency between the two groups was estimated by either the χ² test or Fisher’s exact test, as appropriate. Statistical significance was achieved when p-value was <0.05.

**Results**

A flowchart of this study is summarized in Fig. 1. A total of 408 patients were diagnosed with PA. The consecutive 252 patients with PA, who occupied 61.7% of all patients confirmed as PA, underwent AVS over the same period. Among them, 183 patients had successful AVS both before and after ACTH stimulation. Sixteen patients with cortisol levels of ≥1.8 μg/dL after an overnight administration of 1-mg DST were excluded. Fifteen patients of them had adrenal tumors. Characteristics of the 167 patients examined in this study are presented in Table 1. The mean age of study participants was 50.0 years, and 61.1% of them were women. At baseline, patients used a median of 1.3 antihypertensive drugs. The median ARR was 1,128.

Table 2 demonstrates comparisons of parameters related to AVS between the left and right adrenal vein. Before ACTH stimulation, the cortisol concentration and selectivity index in the left adrenal vein were significantly higher than that in the right adrenal vein (all p < 0.01). The aldosterone concentration was not different between
### Fig. 1 Flowchart of the study.

SI; selectivity index, DST; dexamethasone suppression test.

### Table 1 Baseline characteristics of 167 patients with successful AVS both before and after ACTH stimulation, whose cortisol levels were below 1.8 μg/mL after overnight administration of 1-mg DST

| Characteristic                                      | Value                                      |
|-----------------------------------------------------|--------------------------------------------|
| Age (y)                                             | 50.0 ± 10.9                                |
| Female gender                                       | 102 (61.1%)                                |
| Duration of hypertension (y)                        | 5.7 ± 6.5                                  |
| Number of antihypertensive drugs                    | 1.3 ± 1.2                                  |
| Systolic blood pressure at diagnosis of hypertension (mmHg) | 171.6 ± 24.2                                |
| Diastolic blood pressure at diagnosis of hypertension (mmHg) | 103.1 ± 13.7                                |
| Systolic blood pressure at diagnosis of PA (mmHg)   | 139.5 ± 16.8                                |
| Diastolic blood pressure at diagnosis of PA (mmHg)  | 83.4 ± 13.5                                 |
| Serum potassium (mEq/L)                             | 3.7 ± 0.5                                  |
| Estimated glomerular filtration (mL/min/1.73 m²)    | 80.6 ± 16.6                                 |
| Plasma renin activity (ng/mL/h)                     | 0.3 [0.3, 0.4]                             |
| Plasma aldosterone concentration (pg/mL)           | 231 [198, 264]                             |
| Aldosterone renin ratio                             | 1,128 [904, 1,351]                         |
| Adrenal tumor on CT scans                           | Left 43 (25.8%), Right 24 (14.4%), Bilateral 6 (3.6%) |
| Size of adrenal tumor on CT scans (mm)              | 13.9 [12.6, 15.2]                          |
| Adrenalectomy                                       | 49 (29.3%)                                 |

Data are expressed as mean ± SD, median [interquartile range], and number (percentage).
the left and right adrenal vein (p = 0.81). Aldosterone/cortisol (A/C) ratio was significantly higher in the right adrenal vein than that in the left adrenal vein (p = 0.02). After ACTH stimulation, cortisol concentration and SI in the right adrenal vein were higher than those in the left adrenal vein (p < 0.01). Aldosterone concentration was not different between the left and right adrenal veins (p = 0.27). A/C ratio was not different between the left and right adrenal veins (p = 0.67).

Fig. 2 presents the distribution of dominant side in AVS both before and after ACTH stimulation. Before ACTH stimulation, 56 patients (33.5%) had unilateral results on the right side and 23 (13.8%) had unilateral results on the left side. Unilateral results of AVS were more frequently observed on the right side than on the left side before ACTH stimulation (p = 0.03). In contrast, after ACTH stimulation, 18 patients (10.8%) had unilateral results on the right and 26 (15.6%) had unilateral results on the left. The frequency tended to be higher on the left side than on the right side in AVS lateralization after ACTH stimulation without statistical significance (p = 0.32).

Among the patients with unilateral results on AVS, the proportion of patients with CR <1 was greater after ACTH than before ACTH (56/79, 70.9% before ACTH stimulation, 41/44, 93.2% after ACTH stimulation, p < 0.01).

Among the 56 patients who had unilateral results on the right side in AVS before ACTH stimulation, 17 also had unilateral results on the right side and 34 had bilateral results after ACTH stimulation. In addition, one patient was switched to left side unilateral result and four

---

**Table 2** Comparison of AVS parameters before and after ACTH stimulation between the left and right adrenal veins (n = 167)

|                      | Before ACTH stimulation | Right adrenal vein | p-value |
|----------------------|-------------------------|--------------------|---------|
| **Cortisol (μg/dL)** | 454 [269.3, 638.9]      | 193 [157.1, 228.6] | <0.01   |
| **Selectivity index**| 41.9 [30.2, 53.6]       | 20.1 [15.3, 24.9]  | <0.01   |
| **Aldosterone (pg/mL)** | 12,034 [8039, 16,030]   | 11,407 [8,741, 14,073] | 0.81 |
| **A/C ratio**        | 69.9 [46.0, 93.7]       | 168.5 [88.2, 248.7] | 0.02    |

**After ACTH stimulation**

|                      | Cortisol (μg/dL) | Selectivity index | Aldosterone (pg/mL) | A/C ratio |
|----------------------|-----------------|-------------------|--------------------|-----------|
| **Before ACTH stimulation** | 909 [844, 974]     | 47.6 [44.1, 47.6]   | 37,709 [30,544, 44,874] | 49.4 [38.4, 60.3] |
| **Right adrenal vein** | 1,065 [992, 1,139]   | 55.1 [50.8, 59.3]   | 49,250 [30,453, 68,047] | 56.5 [26.2, 86.9] |
| **p-value**           | <0.01           | <0.01             | 0.27               | 0.67      |

Data are expressed as median [interquartile range]. A/C ratio; aldosterone/cortisol ratio.

---

**Fig. 2** Change of the dominant side in AVS before and after ACTH stimulation (n = 167)

Data are expressed as number. ABAS; apparent bilateral aldosterone suppression.
remaining had ABAS results after ACTH stimulation. Among the 23 patients who had unilateral results on the left side in AVS before ACTH stimulation, 18 also had unilateral results on the left side and five remaining had bilateral results after ACTH stimulation.

In the 34 patients who had unilateral results on the right side in AVS before ACTH stimulation and had bilateral results after ACTH stimulation, right-sided adrenal nodular lesions were not observed on CT scans, PAC and ARR were significantly lower than those of 17 patients who had unilateral results on the right side both before and after ACTH stimulation. The rate of CR >1 before ACTH stimulation in AVS was greater in the former 34 patients than in the latter 17 patients (44.1% vs. 5.9%, p < 0.01) (Table 3).

In addition, 67 patients who showed no adrenal tumors in both sides on CT scans and whose serum potassium was normal were examined, and their data were similarly analyzed. Before ACTH stimulation, the cortisol concentration and selectivity index in the left adrenal vein were significantly higher than that in the right adrenal vein (all p < 0.01). The aldosterone concentration was not different between the left and right adrenal veins (p = 0.53). A/C ratio was significantly higher in the right adrenal vein than that in the left adrenal vein (p = 0.01). After ACTH stimulation, the cortisol concentration and SI in the right adrenal vein were higher than that in the left adrenal vein (p = 0.03, p = 0.03, respectively). Aldosterone concentration and A/C ratio were not different between the left and right adrenal veins (p = 0.19, p = 0.27, respectively).

Before ACTH stimulation, unilateral disease of AVS was more frequently observed on the right side than on the left side (19, 28.4% vs. 3, 4.4%, p < 0.01). After ACTH stimulation, unilateral disease of AVS was observed only on the left side in 3 patients (4.4%).

Of 49 patients who underwent adrenalectomy, 39 had data at 6–12 months postoperatively. Clinical and bio-

Table 3  Comparisons of clinical characteristics between the group with right dominance both before and after ACTH stimulation and the group with right dominance only before ACTH stimulation (n = 51)

|                                      | Right dominant both before and after ACTH stimulation (n = 17) | Right dominant before, bilateral after ACTH stimulation (n = 34) | p-value |
|--------------------------------------|---------------------------------------------------------------|-------------------------------------------------------------|---------|
| Age (y)                              | 51.1 ± 11.3                                                   | 51.5 ± 10.3                                                 | 0.88    |
| Female gender                        | 8 (47.1%)                                                    | 23 (67.6%)                                                  | 0.16    |
| Duration of hypertension (y)         | 7.1 ± 6.4                                                    | 5.4 ± 6.8                                                   | 0.40    |
| Number of antihypertensive drugs     | 1.9 ± 1.4                                                    | 1.0 ± 0.7                                                   | 0.02    |
| Systolic blood pressure (mmHg)       | 143.8 ± 14.5                                                 | 135.8 ± 14.5                                                | 0.07    |
| Diastolic blood pressure (mmHg)      | 85.4 ± 10.5                                                  | 82.0 ± 10.3                                                  | 0.29    |
| Body mass index (kg/m²)              | 25.6 ± 4.1                                                   | 25.9 ± 3.9                                                  | 0.74    |
| Serum potassium (mEq/L)              | 3.3 ± 0.5                                                    | 3.9 ± 0.3                                                   | <0.01   |
| Estimated glomerular filtration (mL/min/1.73 m²) | 80.7 ± 25.9                                                  | 79.2 ± 14.5                                                 | 0.80    |
| Plasma renin activity (ng/mL/h)      | 0.2 [0.1, 0.3]                                               | 0.4 [0.3, 0.5]                                              | 0.01    |
| Plasma aldosterone concentration (pg/mL) | 408 [216.5, 600.5]                                      | 167 [143.3, 190.8]                                         | <0.01   |
| Aldosterone renin ratio (pg/mL/ng/mL/h) | 2.345[1,243, 3,347]                                      | 658 [495, 821]                                             | <0.01   |
| Laterality of adrenal tumor on CT scans | Left 1 (5.9%), Right 14 (82.4%), Bilateral 2 (11.8%),         | Left 7 (20.6%)                                              | <0.01*  |
| Contralateral ratio >1 before ACTH stimulation | 0 (0%)                                                      | 15 (44.1%)                                                 | <0.01   |
| Adrenalectomy                        | 15 (88.2%)                                                   | 0 (0%)                                                      | <0.01   |
| Complications of PA                  |                                                              |                                                            |         |
| hypokalemia                          | 12 (70.6%)                                                   | 7 (20.6%)                                                   | 0.02    |
| Chronic kidney disease               | 1 (5.8%)                                                     | 3 (8.8%)                                                   | 0.46    |
| Occurrence of cardiovascular or cerebrovascular events | 1 (5.8%)                                                   | 1 (2.9%)                                                   | 0.46    |

Data are expressed as mean ± SD, median [interquartile range], and number (percentage). *For laterality of adrenal tumor on CT scans, the proportions of unilateral adrenal tumor on the right side are compared.
chemical outcomes after adrenalectomy were compared between 29 patients with concordant AVS results between before and after ACTH stimulation and 10 patients with discordant results. In 29 patients with concordant results, left unilateral results were observed in 12 patients and right unilateral results in 17. In addition, bilateral results were observed in two patients and ABAS results in two remaining. In 10 patients with discordant results, 4 had unilateral result only before ACTH stimulation: 3 on the right side and one on the left side. Five patients had unilateral result only after ACTH stimulation on the left side. In the concordant group, complete, partial, and absent clinical successes were observed in 9 (31.0%), 15 (51.7%), and 5 (17.2%) patients, respectively. Complete, partial, and absent biochemical successes were observed in 22 (75.9%), 5 (17.2%), and 2 (6.9%) patients, respectively. In the discordant group, complete, partial, and absent clinical successes were observed in 4 (40.0%), 2 (20.0%), and 4 (40.0%) patients, respectively. Complete, partial, and absent biochemical success were observed in 9 (90.0%), 0 (0%), and 1 (10.0%) patients, respectively. The complete clinical and biochemical success rate was not different between patients with concordant results of both CT and AVS and those with discordant results (p = 0.60, p = 0.34, respectively) (Table 4).

**Discussion**

This study demonstrated the decreased proportion of unilateral disease after ACTH stimulation and the higher frequency of right dominant laterality before ACTH stimulation became higher frequency of left dominant laterality after ACTH stimulation.

These findings could result from lower cortisol levels in the right adrenal vein before ACTH stimulation and lower cortisol levels in the left adrenal vein after ACTH stimulation. The mechanism of this phenomenon remains unclear. In our hospital, blood samples were collected from left to right adrenal veins before ACTH stimulation with various intervals, whereas after ACTH stimulation, blood samples were drawn from right to left veins with short intervals. There is a report demonstrated that the cortisol concentration in adrenal vein decreased by 63% on the APA side and by 45% on the contralateral side in 15 minutes using simultaneous procedure without ACTH stimulation [18]. In the patients of our study, it is thought that cortisol concentration in the adrenal vein collected later was reduced during the interval of sampling the left and right adrenal veins regardless of the presence of ACTH stimulation. Another explanation is the effect of blood flowing into the adrenal veins from surrounding veins. The degree of dilution due to the inflow of venous blood from surrounding veins may be various between the left and right adrenal veins and before and after ACTH stimulation, which may affect the difference in cortisol concentrations in the adrenal veins. However, discrepancies of cortisol and aldosterone levels cannot be explained. This phenomenon may occur due to the difference of the timing of fluctuation induced by stress or ACTH administration between cortisol and aldosterone.

Based on the results from this study, it is unclear which determination of laterality before or after ACTH stimulation is correct. Schnellar et al. reported that the mean adrenal volume was significantly larger on the left side than on the right side in normal patients [19]. Therefore, APA is theoretically likely to occur in the left adrenal gland. In this study, nodular lesions observed on CT scans were more frequently observed on the left side than that on the right side. Furthermore, in this study, the
patients who had unilateral results on the right side in AVS before ACTH stimulation and had bilateral results after ACTH stimulation had higher proportion of CR >1 before ACTH stimulation in AVS. These findings suggest that laterality diagnosis on AVS in our study is more reliable after ACTH stimulation than before ACTH stimulation.

The success rate of AVS increases using ACTH stimulation because Selectivity Index (SI) moves significantly upward [20-23]. However, the correctness of AVS using ACTH stimulation as regards the final decision of the dominant side remains controversial [20-22, 24-27]. There is not enough evidence that ACTH stimulation increases the sensitivity or specificity of laterality diagnosis.

This study has some limitations. First, results of AVS parameters were not investigated as it is an opposite procedure to our protocol, in which blood samples were sequentially collected from the right to left side before ACTH stimulation and drawn from the left to right side after ACTH stimulation. Second, in majority of patients whose laterality was right dominant before ACTH stimulation and changed to bilateral after ACTH stimulation, the segmental adrenal venous sampling (S-AVS) [28] or confirmation of histopathological tissue of adrenal glands was not performed. If these procedures were performed, it might have clarified which determination of laterality before or after ACTH stimulation is correct. Finally, the sample size in this study was small, and all participants were Japanese.

In conclusion, ACTH stimulation not only decreased unilateral results but also shifted the dominant side from the right to left. Patients determined to have unilateral disease with right dominance only before ACTH stimulation showed biochemically milder PA, and none of them showed right adrenal tumor on CT scans in this study. Therefore, many false-positive cases may be included in patients with right dominance alone before ACTH stimulation. The determination of surgical indication should be made by considering the results after ACTH stimulation and other clinical findings.

**Disclosure Summary**

The authors have nothing to disclose.

**References**

1. Young WF (2007) Primary aldosteronism: renaissance of a syndrome. *Clin Endocrinol (Oxf)* 66: 607–618.
2. Hannemann A, Wallaschofski H (2012) Prevalence of primary aldosteronism in patient’s cohorts and in population-based studies: a review of the current literature. *Horm Metab Res* 44: 157–162.
3. Monticone S, Viola A, Rossato D, Veglio F, Reincke M, et al. (2015) Adrenal vein sampling in primary aldosteronism: towards a standardized protocol. *Lancet Diabetes Endocrinol* 3: 296–303.
4. Rossi GP, Auchus RJ, Brown M, Lenders JW, Naruse M, et al. (2014) An expert consensus statement on use of adrenal vein sampling for the subtyping of primary aldosteronism. *Hypertension* 63: 151–160.
5. Doppman JL, Gill JR Jr (1996) Hyperaldosteronism: sampling the adrenal veins. *Radiology* 198: 309–312.
6. Espiner EA, Ross DG, Yandle TG, Richards AM, Hunt PJ (2003) Predicting surgically remedial primary aldosteronism: role of adrenal scanning, posture testing, and adrenal vein sampling. *J Clin Endocrinol Metab* 88: 3637–3644.
7. Monticone S, Sato H, Giacchetti G, Viola A, Morimoto R, et al. (2012) Effect of adrenocorticotropic hormone stimulation during adrenal vein sampling in primary aldosteronism. *Hypertension* 59: 840–846.
8. Nishikawa T, Omura M, Satoh F, Shibata H, Takahashi K, et al. (2011) Task Force Committee on Primary Aldosteronism, The Japan Endocrine Society. Guidelines for the diagnosis and treatment of primary aldosteronism: the Japan Endocrine Society 2009. *Endocr J* 58: 711–721.
9. Shimamoto K, Ando K, Fujita T, Hasebe N, Higaki J, et al. (2014) Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2014). *Hypertens Res* 37: 253–390.
10. Nieman LK, Biller BM, Findling JW, Newell-Price J, Savage MO, et al. (2008) The diagnosis of Cushing’s syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 93: 1526–1540.
11. Umakoshi H, Wada N, Ichijo T, Kammura K, Matsuda Y, et al. (2015) Optimum position of left adrenal vein sampling for subtype diagnosis in primary aldosteronism. *Clin Endocrinol (Oxf)* 83: 768–773.
12. Omura M, Sasano H, Saito J, Yamaguchi K, Kakuta Y, et al. (2006) Clinical characteristics of aldosterone-producing microadenoma, macroadenoma, and idiopathic hyperaldosteronism in 93 patients with primary aldosteronism. *Hypertens Res* 29: 883–889.
13. Young WF, Stanson AW, Thompson GB, Grant CS, Farley DR, et al. (2004) Role for adrenal venous sampling in primary aldosteronism. *Surgery* 136: 1227–1235.
14. Monticone S, Viola A, Rossato D, Veglio F, Reincke M, et al. (2015) Adrenal vein sampling in primary aldosteronism: towards a standardized protocol. *Lancet Diabetes Endocrinol* 3: 296–303.
15. Webb R, Mathur A, Chang R, Baid S, Nilubol N, et al. (2012) What is the best criterion for the interpretation of adrenal vein sample results in patients with primary hyper-
aldosteronism? Ann Surg Oncol 19: 1881–1886.

16. Shibayama Y, Wada N, Umakoshi H, Ichijo T, Fujii Y, et al. (2016) Bilateral aldosterone suppression and its resolution in adrenal vein sampling of patients with primary aldosteronism: analysis of data from the WAVES-J study. Clin Endocrinol (Oxf) 85: 696–702.

17. Williams TA, Lenders JWM, Mulatero P, Burrello J, Rottenkolber M, et al. (2017) Outcomes after adrenalectomy for unilateral primary aldosteronism: an international consensus on outcome measures and analysis of remission rates in an international cohort. Lancet Diabetes Endocrinol 5: 689–699.

18. Seccia TM, Miotto D, Battistel M, Motta R, Barisa M, et al. (2012) A stress reaction affects assessment of selectivity of adrenal venous sampling and of lateralization of aldosterone excess in primary aldosteronism. Eur J Endocrinol 166: 869–875.

19. Schneller J, Reiser M, Beuschlein F, Osswald A, Pallauf A, et al. (2014) Linear and volumetric evaluation of the adrenal gland—MDCT-based measurements of the adrenals. Acad Radiol 21: 1465–1474.

20. Rossi GP, Pitter G, Bernante P, Motta R, Feltrin G, et al. (2008) Adrenal vein sampling for primary aldosteronism: the assessment of selectivity and lateralization of aldosterone excess baseline and after adrenocorticotropic hormone (ACTH) stimulation. J Hypertens 26: 989–997.

21. Elliott P, Holmes DT (2013) Adrenal vein sampling: substantial need for technical improvement at regional referral centres. Clin Biochem 46: 1399–1404.

22. Seccia TM, Miotto D, De Toni R, Pitter G, Mantero F, et al. (2009) Adrenocorticotropic hormone stimulation during adrenal vein sampling for identifying surgically curable subtypes of primary aldosteronism: comparison of 3 different protocols. Hypertension 53: 761–766.

23. Tanemoto M, Suzuki T, Abe M, Abe T, Ito S (2009) Physiologic variance of corticotropin affects diagnosis in adrenal vein sampling. Eur J Endocrinol 160: 459–463.

24. Satoh F, Abe T, Tanemoto M, Nakamura M, Abe M, et al. (2007) Localization of aldosterone-producing adrenocortical adenomas: significance of adrenal venous sampling. Hypertens Res 30: 1083–1095.

25. Mathur A, Kemp CD, Dutta U, Baid S, Ayala A, et al. (2010) Consequences of adrenal venous sampling in primary hyperaldosteronism and predictors of unilateral adrenal disease. J Am Coll Surg 211: 384–390.

26. Phillips JL, Walther MM, Pezzullo JC, Rayford W, Choyke PL, et al. (2000) Predictive value of preoperative tests in discriminating bilateral adrenal hyperplasia from an aldosterone-producing adrenal adenoma. J Clin Endocrinol Metab 85: 4526–4533.

27. Rossi GP, Ganzaroli C, Miotto D, De Toni R, Palumbo G, et al. (2006) Dynamic testing with high-dose adrenocorticotropic hormone does not improve lateralization of aldosterone oversecretion in primary aldosteronism patients. J Hypertens 24: 371–379.

28. Makita K, Nishimoto K, Kiriyama-Kitamoto K, Karashima S, Seki T, et al. (2017) A novel Method: Super-selective Adrenal Venous Sampling. J Vis Exp 127, e55716: 1–11.