

# Bilateral Aldosterone Suppression in Patients With Right Unilateral Primary Aldosteronism and Review of the Literature

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**Introduction:** Adrenal vein sampling (AVS) identifies unilateral primary aldosteronism but may occasionally show paradoxically low aldosterone–cortisol ratios bilaterally. Postulated reasons include venous anomalies, fluctuating aldosterone secretion, or superselective cannulation. We report our findings in patients who underwent repeat AVS and reviewed the current literature.

**Methods:** We performed a retrospective observational study of patients undergoing AVS in an experienced high-volume tertiary center over a 5-year period.

**Results:** From 2015 to 2019, 61 patients underwent sequential cosyntropin-stimulated AVS and all had bilateral successful cannulation (100%). Four of 61 (6.6%) patients had bilaterally low aldosterone–cortisol ratios. Three patients underwent repeat AVS, with all 3 cases demonstrating right-sided lateralization and cure of disease postadrenalectomy. Right-sided disease was also more common in other reports. This may be due to inadvertent superselective cannulation of the short right adrenal vein, resulting in sampling of the adjacent normal gland. Cortisol results cannot detect this problem. In 1 patient, computed tomography venography excluded any accessory right adrenal veins. In another patient, repeat bilateral simultaneous unstimulated AVS was done, and measurements of metanephrines aided in accurately identifying right-sided lateralization.

**Conclusion:** In addition to technical difficulties in cannulating the right adrenal vein, we also have to avoid performing superselective cannulation inadvertently. In cases of inconclusive AVS, repeat sampling may identify patients with potentially curable unilateral primary aldosteronism. The role of corticotropin stimulation and metanephrines measurements during repeat AVS requires further study.

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**Key Words:** hyperaldosteronism, cortisol, ACTH stimulation, metanephrines, aldosterone suppression, endocrine hypertension

Abbreviations: AVS, adrenal vein sampling; BP, blood pressure; CT, computed tomography; IVC, inferior vena cava; PA, primary aldosteronism; PAC, plasma aldosterone concentration; PRA, plasma renin activity; RIA, radioimmunoassay

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Adrenal vein sampling (AVS) is widely regarded to be the reference test to identify unilateral disease in patients with primary aldosteronism (PA) [1,2]. However, AVS is invasive and technically challenging, particularly when cannulating the right adrenal vein with success rates of < 50% in many low-volume centers [3,4]. When AVS is successful, it has been described that 2.6% to 7.6% of patients may have paradoxically low aldosterone–cortisol ratios bilaterally [5–7]. These patients occasionally are found to have unilateral PA on repeat AVS, with cure of PA postadrenalectomy [5]. There have been several proposed explanations and approaches when repeat AVS is considered, such as use of cosyntropin stimulation (if unstimulated AVS was previously used) [5], assessing for an alternative drainage vein from an aldosterone-producing adenoma (APA) [8], and avoiding superselective cannulation of the adrenal vein. However, previous studies have found conflicting results with these approaches [5–7].

In our center, we followed these suggested recommendations and offered repeat AVS in patients with bilaterally low aldosterone–cortisol ratios on initial AVS. In addition, we conducted a review of the literature with similar cases. The aim of our study was to assess the possible etiology of these paradoxical results.

## 1. Patients and Methods

We conducted a retrospective review of all patients who underwent AVS in our tertiary center, Changi General Hospital, Singapore from January 2015 to December 2019. The inclusion criteria and diagnostic work-up of these patients have been previously described [9]. This study was approved by the local ethics committee and patient consent was obtained.

Baseline clinical characteristics and medical history were collected for all patients from medical records, and included age, gender, blood pressure, antihypertensive medication, serum potassium levels, plasma aldosterone concentration (PAC), and plasma renin activity (PRA). All patients fulfilled the diagnostic criteria recommended by the Endocrine Society guidelines [1]. Confirmatory tests were performed with intravenous saline infusion test, and all patients had a postinfusion PAC  $\geq$  140 pmol/L. Postoperative outcome was assessed using the Primary Aldosteronism Surgery Outcome criteria [10].

PAC was measured using a solid-phase <sup>125</sup>I radioimmunoassay (RIA) (Siemens Medical Solutions Diagnostics, LA, USA). PRA was measured by standard RIA (DiaSorin, Stillwater, MN, USA) [11]. The lower analytical limit for PRA was 0.2 ng/mL/hour. From 2017, PRA and PAC were sent to Mayo Clinic Laboratories, Rochester, MN, USA, for determination using liquid chromatography tandem mass spectroscopy, and the reference ranges were 0.6 to 3.0 ng/mL/hour and  $\leq$  21 pmol/L respectively. Our laboratory reference range for serum potassium level was 3.5 to 5.3 mmol/L.

All patients underwent thin-slice computed tomography (CT) scan. Unilateral adenoma was defined as a unilateral nodule with diameter at least 8 mm, with the contralateral gland appearing smooth and not enlarged. In our routine AVS protocol, patients undergo sequential AVS under continuous cosyntropin stimulation infusion (50  $\mu$ g/hour), with majority performed by the same interventional radiologist (N.K.S.) with > 90% success rate. Two right adrenal vein samples are taken to improve successful cannulation. AVS was deemed successful if plasma cortisol concentrations were  $\geq$  5 times higher in both adrenal veins than in the peripheral vein (cortisol gradient). The lateralization ratio was calculated by dividing the higher adrenal aldosterone/cortisol ratio by the lower one, with a lateralization ratio of  $\geq$  4 taken to be consistent with unilateral PA.

Repeat AVS procedures were done either using the same protocol, or bilateral simultaneous. Bilateral simultaneous AVS was performed via a single 10F right femoral vein sheath, and adrenal vein samples were taken both before and after cosyntropin stimulation. For unstimulated AVS, placement was considered successful if cortisol gradient was  $\geq$  2. After successful sampling was confirmed, AVS was repeated at least 15 minutes after cosyntropin stimulation (250- $\mu$ g bolus followed by 50  $\mu$ g/hour infusion). In patients with

suspected cortisol cosecreting APA, plasma metanephrines were also measured from each sampling site.

## 2. Results

Sixty-one patients underwent AVS from 2015 to 2019, with all 61 patients having successful bilateral cannulation of both adrenal veins (100.0%). Four of 61 cases (6.6%) had bilaterally low aldosterone–cortisol ratios in both adrenal veins compared with the peripheral vein. Three of these patients underwent a repeat AVS, while the fourth patient declined. In all 3 patients, repeat AVS clearly demonstrated right-sided aldosterone lateralization, and all 3 patients underwent surgery. All 3 patients had biochemical cure of PA, with two patients completely cured of hypertension.

### A. Case 1

A 34-year-old woman presented with cramps, polyuria, and polydipsia and serum potassium was 2.7 mmol/L. She had hypertension for 3 years, and blood pressure (BP) was 146/96 mmHg on amlodipine 5 mg daily. Baseline PAC 4848 pmol/L and PRA < 0.6 ng/mL/hour confirmed diagnosis of PA. An adrenal CT scan revealed a 1.1-cm lipid-rich right adrenal adenoma. Initial AVS done under cosyntropin stimulation showed bilateral low aldosterone–cortisol ratios (Table 1). An adrenal artery angiography carried out prior to the second AVS showed only 1 adrenal vein and excluded any accessory veins draining the adenoma, both on angiogram and Dyna-CT. This was performed via a left common femoral artery puncture and cannulation of the right adrenal artery with a microcatheter (Fig. 1C-F). After angiography, the second AVS was performed similarly under cosyntropin stimulation. The catheter was intentionally positioned closer toward the inferior vena cava (IVC) using a reversed Simmons 1 catheter (Fig. 1B). This second AVS showed lateralization to the right, with lateralization ratios 21.0 and 119.5. Six months after right adrenalectomy, the patient is normotensive (BP 129/73 mmHg) and normokalemic (potassium 4.1 mmol/L) without medications. The aldosterone–renin ratio has normalized (PAC 110.8 pmol/L, PRA 1.2 ng/mL/hour).

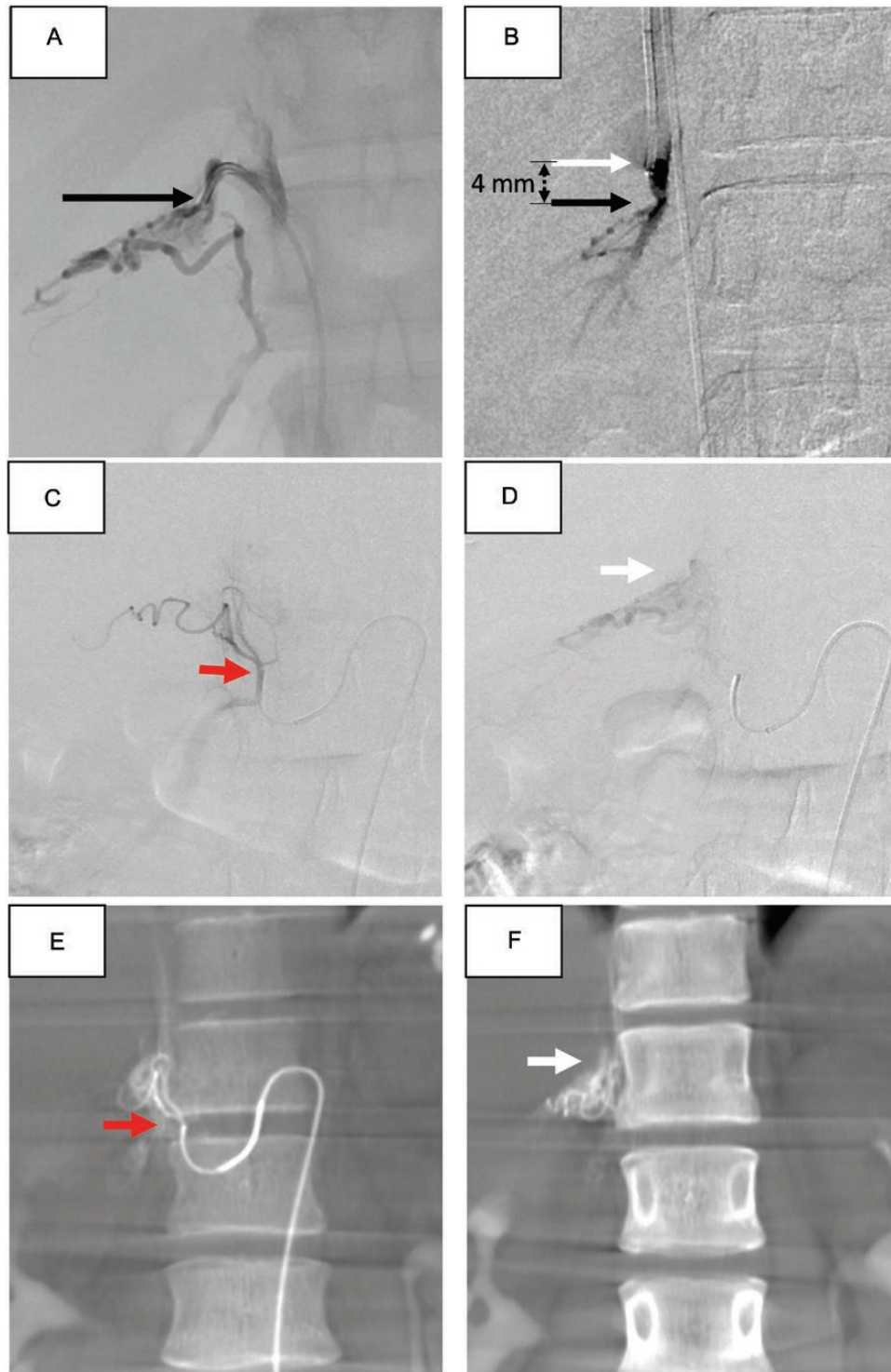
### B. Case 2

A 42-year-old man with hypertension for 20 years, diabetes mellitus, and hyperlipidemia was noted with serum potassium ranging from 3.3 to 3.5 mmol/L. Baseline PRA was < 0.6 ng/mL/hour and postsaline infusion PAC was 388 pmol/L. His baseline BP was 153/96 mmHg

**Table 1. Both AVS for Case 1 done sequentially under continuous cosyntropin stimulation and conducted several weeks apart.**

	First AVS—sequential under cosyntropin stimulation			
	Right AV #1	Right AV #2	IVC	Left AV
Aldosterone, pmol/L	4848	4681	3546	4238
Cortisol, nmol/L	17 547	22 272	707	20 865
A/C ratio	0.28	0.21	5.01	0.20
	Second AVS—sequential under cosyntropin stimulation			
	Right AV #1	Right AV #2	IVC	Left AV
Aldosterone, pmol/L	105 260	554 000	3324	4155
Cortisol, nmol/L	19 596	18 156	808	16 267
A/C ratio	5.37	30.51	4.11	0.26

Abbreviations: AV, adrenal vein; AVS, adrenal vein sampling; A/C, aldosterone–cortisol.



**Figure 1.** Case 1. Right adrenal vein catheter placement during AVS (A,B), right adrenal arterial angiogram (C-F). Initial AVS (A) performed using a 4F Cobra 2 catheter; repeat AVS performed using a 4F Simmons 1 catheter (B). Black arrows indicate right adrenal vein catheter position during initial sampling which was more advanced. White arrow indicates right adrenal vein catheter during repeat sampling which was placed 4 mm less advanced and correctly identified aldosterone excess from the right. (C) Catheter arteriogram with microcatheter in right adrenal artery (red arrow). (D) Catheter arteriogram (venous phase) demonstrating a single right adrenal vein (white arrow). (E) Coronal image from catheter arteriogram with Dyna-CT, showing right adrenal artery (red arrow). (F) Coronal image on Dyna-CT showing single right adrenal vein (white arrow).

on amlodipine 10 mg and terazosin 2 mg daily. CT scan did not show any discrete adrenal nodule. The first AVS was performed via right forearm vein approach under cosyntropin stimulation (Table 2). Upon review of the angiography films, there was suggestion that there was superselective cannulation of the right adrenal vein. Hence, the decision was made for a repeat AVS, via the conventional right femoral vein approach, with avoidance of selective cannulation. Repeat AVS was performed simultaneously, with both pre- and postcosyntropin sampling done (Fig. 2B). The second AVS revealed high aldosterone–cortisol ratio on the right, with lateralization ratios to the right of 63.7 (precosyntropin) and 10.7 (postcosyntropin), and left contralateral suppression. This patient recently underwent right adrenalectomy. One week postsurgery, the aldosterone–renin ratio has normalized (PAC < 110.8 pmol/L, PRA 6.8 ng/mL/hour), and BP has improved to 132/92 mmHg on amlodipine 10 mg daily.

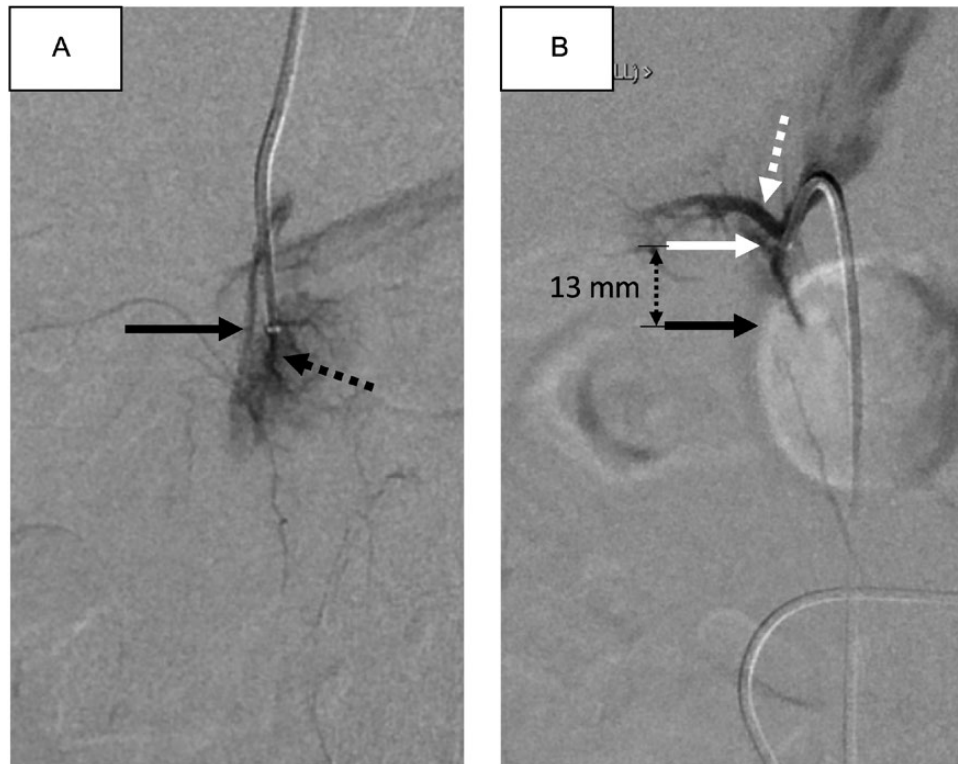
### C. Case 3

A 54-year-old woman had a history of hypertension and hypokalemia for 8 years, with a potassium nadir of 2.2 mmol/L. BP was 131/74 mmHg on amlodipine 5 mg and valsartan 80 mg daily. Baseline PRA was < 0.6 ng/mL/hour with post saline infusion PAC 1075 pmol/L. Cortisol was unsuppressed at 63 nmol/L (after overnight 1-mg dexamethasone suppression) and 137 nmol/L (after low-dose dexamethasone suppression, 0.5 mg 6 hourly for 3 days). CT of the adrenals identified a 2.4-cm right lipid-rich adrenal adenoma. Initial AVS done under cosyntropin stimulation showed bilateral low aldosterone–cortisol ratios, with conflicting results in right adrenal vein samples #1 and #2, with neither demonstrating lateralization of > 4 (Table 3). In view of the markedly discordant right adrenal vein levels, repeat bilateral simultaneous AVS was performed, with pre- and postcosyntropin stimulation sampling (Fig. 3B). Given the possibility of a cortisol cosecreting APA, plasma metanephrines were measured. In the second AVS, precosyntropin showed right-sided lateralization

**Table 2. First AVS for Case 2 done sequentially under continuous cosyntropin stimulation. Several months later, AVS was done with bilateral simultaneous cannulation, and unstimulated and postcosyntropin stimulation samplings were taken on the same day (second AVS).**

	First AVS—sequential under cosyntropin stimulation			
	Right AV #1	Right AV #2	IVC	Left AV
Aldosterone, pmol/L	15 207	NA	970	10 332
Cortisol, nmol/L	22 273	706	760	17 442
A/C ratio	0.68	NA	1.28	0.59
	Second AVS—bilateral simultaneous unstimulated			
	Right AV		IVC	Left AV
Aldosterone, pmol/L	58 170		271	942
Cortisol, nmol/L	546		76	564
Metanephrine, nmol/L	15.89		0.12	19.51
A/C ratio	106.54		3.57	1.67
Aldosterone/metanephrine ratio	3660.79		2258.33	48.28
	Second AVS—bilateral simultaneous after cosyntropin stimulation			
	Right AV		IVC	Left AV
Aldosterone, pmol/L	141 270		1025	17 174
Cortisol, nmol/L	19 878		515	26 130
Metanephrine, nmol/L	23.01		0.17	26.35
A/C ratio	7.11		1.99	0.66
Aldosterone/metanephrine ratio	6139.50		6029.41	651.76

Abbreviations: AV, adrenal vein; AVS, adrenal vein sampling; A/C, aldosterone–cortisol; NA, not available.



**Figure 2.** Case 2. Right adrenal vein catheter placement during AVS. Initial sampling performed via forearm approach (left, A); repeat sampling done simultaneously (right, B) via single right femoral vein access with right and left samples taken. Black arrows indicate right adrenal vein catheter position during initial sampling which was 13 mm more advanced, and black dashed arrow shows branch of right adrenal vein with only the medial portion of the gland opacified, consistent with superselective sampling. White arrow indicates catheter tip position during repeat sampling with catheter positioned less advanced and white dashed line shows the main right adrenal vein being cannulated.

(lateralization ratio 11.8). The cortisol level in the right adrenal vein was more than twice that of the left adrenal vein (1544 versus 614 nmol/L), whereas metanephrine levels were more similar (21.0 versus 15.7 nmol/L), suggesting that there was concomitant cortisol hypersecretion on the right. Postcosyntropin sampling showed bilateral low aldosterone–cortisol ratios again. Catheter placement likely contributed discordant right aldosterone–cortisol ratios and this patient was offered right adrenalectomy. Six months after right adrenalectomy, our patient has been cured of hypokalemia and hypertension, with normalization of the aldosterone–renin ratio, PAC < 110.8 pmol/L, PRA 0.6 ng/mL/hour.

### 3. Discussion

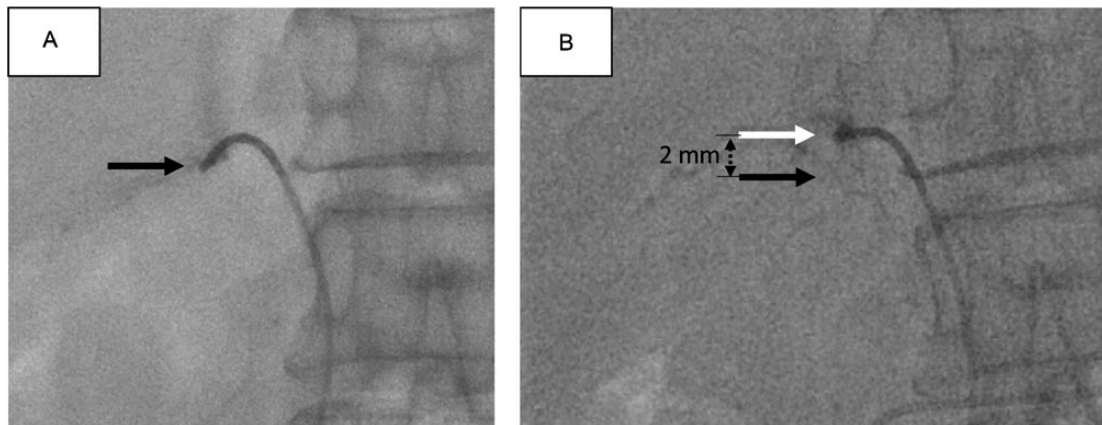
We demonstrated through repeat AVS, that 3 patients with initially inconclusive results, had right-sided unilateral PA. In our center, although all AVS procedures were deemed successful by current criteria [1,2], 4 of 61 (6.6%) patients had paradoxically low aldosterone–cortisol ratios bilaterally. This was similar to that observed in other studies (2.6–7.6%) [5–7]. Three patients underwent repeat AVS with careful avoidance of superselective right sampling. All patients had right-sided lateralization on repeat AVS and cure of PA after adrenalectomy. In addition, we found that cosyntropin stimulation and use of cortisol correction may affect AVS interpretation in cortisol cosecreting APA. Using metanephrines for correction may help to circumvent this problem [12].

A literature search demonstrated several case reports and articles with patients having bilaterally low aldosterone on AVS, summarized in Table 4 [5-7,13-16]. Several theories

**Table 3.** First AVS for Case 3 done sequentially under continuous cosyntropin stimulation. Several months later, AVS was done with bilateral simultaneous cannulation, and unstimulated and postcosyntropin stimulation samplings were taken on the same day (second AVS).

	First AVS—sequential under cosyntropin stimulation			
	Right AV #1	Right AV #2	IVC	Left AV
Aldosterone, pmol/L	25 833	2139	1778	3889
Cortisol, nmol/L	11 636	9823	752	5896
A/C ratio	2.22	0.22	2.36	0.66
	Second AVS—bilateral simultaneous unstimulated			
	Right AV		IVC	Left AV
Aldosterone, pmol/L	30 470		609	1025
Cortisol, nmol/L	1544		217	614
Metanephrine, nmol/L	21.00		0.08	15.67
A/C ratio	19.73		2.81	1.67
Aldosterone/metanephrine ratio	1450.95		7612.5	65.41
	Second AVS—bilateral simultaneous after cosyntropin stimulation			
	Right AV		IVC	Left AV
Aldosterone, pmol/L	3601		1163	4986
Cortisol, nmol/L	8265		491	7981
Metanephrine, nmol/L	15.33		0.10	21.09
A/C ratio	0.44		2.37	0.62
Aldosterone/metanephrine ratio	234.89		11 630	236.41

Abbreviations: AV, adrenal vein; AVS, adrenal vein sampling; A/C, aldosterone–cortisol.



**Figure 3.** Case 3. Right adrenal vein catheter placement during AVS. Initial sampling (left, A), repeat simultaneous sampling (right, B). Black arrows indicate right adrenal vein catheter during initial sampling which was more advanced. White arrow indicates catheter tip position during repeat sampling, where catheter was positioned 2 mm less advanced (white arrow, B).

have been proposed for this: sampling during the quiescent period of an APA with episodic secretion, other accessory veins draining an APA [16], ectopic aldosterone–producing tumor, cosecreting adrenal nodules [17], and superselective sampling of the normal adjacent adrenal gland [5,6,8]. Two case reports and 1 case series all found unilateral PA with right-sided disease, similar to our 3 cases. While this may be coincidental, we hypothesize that inadvertent superselective cannulation of the right adrenal vein may have contributed.

Table 4. Summary of current and previous studies.

	Current	Velega et al. [16]	Viola et al. [14]	Zelinka et al. [13]	Wolley et al. [5]	Shibayama et al. [6]	Shibayama [7]
Type No. of cases (% of total)	Article 4 of 61 (6.6%)	Case report 1	Case report 1	Case Series 7	Article 37 of 1397 (2.6%)	Article 29 of 304 (9.5%)	Article 45 of 591 (7.6%) with Cosyntropin
Initial AVS method	Sequential cosyntropin stimulations	Sequential cosyntropin stimulation	With and without cosyntropin stimulation	Sequential without cosyntropin stimulation	Sequential without cosyntropin stimulation	Sequential (8 centers)/simultaneous (1 center) with and without cosyntropin	Sequential (23 centers)/simultaneous (4 center) with and without cosyntropin sampling at 2 left adrenal vein sites <sup>a</sup>
Repeat AVS done?	Yes	Yes	No	No	Yes (for 22 of 37)	Poststimulation AVS data in 24 patients	As above, and in addition 2 patients had repeat AVS
Repeat AVS method	Sequential/simultaneous with/without cosyntropin	Sequential with cosyntropin	NA	NA	Sequential without cosyntropin	As above	As above
Repeat AVS result (unilateral/bilateral; right/left)	All unilateral Right	Unilateral Right	NA	NA	10 of 22 with unilateral PA 7 right 3 left	BAS resolved after ACTH stimulation in 22 of 24 patients. BAS was newly observed after ACTH stimulation in 5 patients	18 of 45 had lateralized AVS using different left adrenal vein sampling site
Final diagnosis with unilateral PA	All 3 right	Right	Right	All 7 right	7 right 3 left	2 right 2 left 20 bilateral	2 right 16 left
Outcome	All cured after right adrenalectomy	Cured after right adrenalectomy	Cured after right adrenalectomy	All underwent surgery with normalization of ARR and hypokalemia	8 underwent surgery (4 of 5 normal fluocortisone suppression)	9 underwent surgery (based on AVS and CT), with 5 of 9 cured of PA	20 underwent surgery 13 evaluated postop and 12 had biochemical cure of PA

Abbreviations: ACTH, adrenocorticotropin; AVS, adrenal vein sampling; PA, primary aldosteronism; ARR, aldosterone–renin ratio.

<sup>a</sup>Study assessed if bilateral aldosterone suppression was affected by use of cosyntropin, and position of left adrenal vein catheter (sampling was done at 2 sites on the left: junction of inferior phrenic vein and left adrenal vein; and distal to this junction).



In support of this, Zelinka et al. [13] described 7 patients with PA who all responded to right adrenalectomy despite failure of AVS to lateralize. When they used less selective right-sided samples, there was suggestion of right-sided lateralization. However, repeat AVS was not done to confirm this hypothesis. Similarly, Wolley et al. found that 10 of 22 patients with initially low aldosterone–cortisol ratios bilaterally had unilateral disease on repeat AVS, with majority (7 of 10) having right-sided disease [5]. In 1 case report, superselective sampling of the right adrenal vein illustrated this phenomenon. The right adrenal vein has a short main trunk and drains directly into the IVC, making its cannulation notoriously difficult [1]. Advancing the catheter further to improve its stability may result in going beyond the common right adrenal vein, and sampling only the normal adjacent adrenal gland and not the APA, which can explain these findings. Because superselective AVS is not widely practiced [14,18], accidental superselective sampling may not be recognized. Furthermore, cortisol levels in the adrenal vein tributaries can be similar to the main adrenal vein and do not detect this problem [18]. In our 3 patients, repeat AVS sampling, with the catheter deliberately placed more superficially in the right adrenal vein, demonstrated right-sided lateralization. This was most evident in the radiological images from Case 2, which show a branch of the adrenal vein cannulated on initial AVS, while the main adrenal vein cannulated on repeat AVS when the catheter was placed more superficially.

We recognize that there are other possible reasons to explain our findings. Firstly, cosyntropin stimulation can affect aldosterone secretion and has been suggested to improve diagnosis in patients with initially low aldosterone–cortisol ratios [5]. Shibayama et al. described that bilateral aldosterone suppression resolved in 22 of 24 patients on repeat AVS postcosyntropin stimulation. However, new-onset bilateral aldosterone suppression was also observed in 5 patients postcosyntropin stimulation [6], suggesting that other factors may play a role. This strategy was less useful for our patients since the initial AVS was done under cosyntropin stimulation. While cosyntropin stimulation helps to improve success rates of cannulation by increasing cortisol gradients, most studies show that it also lowers lateralization ratios [2,19–21]. In addition, in 2 of our cases, repeat AVS was done simultaneously instead of sequentially, and this may have been a factor. Secondly, accessory veins [22,23] draining APA have been described and was responsible in 1 case report [16]. We excluded accessory veins in our Case 1 using angiography and DynaCT. Thirdly, physiological fluctuation of aldosterone secretion can lead to discrepant results, as shown by Murashima et al. [24] when AVS was repeated in 6 patients after several months or years, with different lateralization ratios. In our Case 3 (first AVS), 2 right adrenal vein samples had markedly different aldosterone–cortisol ratios (2.22 versus 0.22). The samples were taken minutes apart under continuous cosyntropin stimulation, making it is less likely that fluctuations in aldosterone were responsible here. Another less common cause is ectopic aldosterone production [25]. Ultimately, in cases where AVS results are inconclusive, repeat AVS should be advised especially if suspicion of unilateral PA is high.

Measurement of metanephrines may be useful, particularly if cortisol-secreting APA is suspected, such as our Case 3. Her second unstimulated AVS showed greater lateralization to the right (ratio 11.8) compared with initial cosyntropin-stimulated AVS (ratio 3.4). While metanephrine levels in the right and left adrenal veins were relatively similar (21.00 nmol/L and 15.67 nmol/L respectively), cortisol levels in the right adrenal vein was twice as high as the left (1544 nmol/L versus 614 nmol/L respectively). This was consistent with the impression of a right cortisol cosecreting APA. In this context, metanephrine may be a preferable correction factor. Using the aldosterone–metanephrine ratio, lateralization to the right will be more evident (ratio 22.2). Although plasma metanephrine has been shown to be useful to indicate correct catheter placement [12], it has not been studied for use as a correction factor in lieu of cortisol. One similar case has been reported where plasma metanephrine was useful in a patient with a cortisol cosecreting APA [15], and this requires further study.

There were several strengths of our study. All AVS were done in a center led by a single experienced radiologist, N.K.S, and 61 consecutive patients have undergone successful procedures over the last 5 years. While bilateral simultaneous AVS is conventionally

done using access from both the right and left femoral veins, our experienced radiologist performed this via a single right femoral vein puncture using a 10F sheath, which has less morbidity for the patient (Fig. 2A). Limitations include the retrospective nature of our study. In our center, initial AVS was done sequentially under continuous cosyntropin simulation. Hence, we cannot explain the occurrence of bilateral suppression in AVS procedures without cosyntropin stimulation. While we suggest that superselective cannulation may occur on the right, we did not study this possibility on the left, which was previously addressed by Shibayama et al. [7]. They similarly found that discrepant results can occur whether the left adrenal vein catheter was placed at the junction of the inferior phrenic vein and left adrenal vein, versus distal to this junction. They suggested that superselective cannulation may occur on the left, and that sampling from the junction may be preferable.

To conclude, we found a small proportion of patients with bilateral aldosterone suppression on AVS that is consistent with previous studies. As there was a preponderance of right-sided disease, we propose that it may be explained by inadvertent superselective cannulation of the right adrenal vein, leading to sampling of normal adjacent adrenal gland. This may be subtle on radiological images and cannot be detected by measurement of cortisol levels. In patients with suspected cortisol cosecreting adenomas, plasma metanephrines may help confirm catheter placement and potentially be used as a correction factor. Further prospective studies are needed to assess this alternative. Ultimately, in cases of inconclusive results, repeat AVS should be considered if unilateral disease is still suspected.

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## Additional Information

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**Disclosure Summary:** No conflicts of interest to disclose.

**Data Availability:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

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